



JIMSA

July-September 2012

Vol.25 No.3

JOURNAL OF INTERNATIONAL MEDICAL SCIENCES ACADEMY

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APPEAL FOR IMSA BUILDING FUND

Dear Colleagues,

International Medical Sciences Academy (IMSA) is a global organization established as a registered society on 28th March 1981 with world headquarters at New Delhi. It is the only international body which encompasses all disciplines of medicine. It has regions in America, Australia, Europe, Africa, rest of Asia and India. There are 28 chapters world over. IMSA is run by Board of Trustees apart from other executive committees. IMSA is an associate member of Council for International Organizations of Medical Sciences (CIOMS). It has about 2160 members world over and the membership is expanding. Many Nobel Laureates are its fellows.

The main objectives of IMSA is to bring together national and international medical scientists, medical educationists, medical and public health administrators and research workers in medical and health sciences on a world wide basis for advancement of health of all the people in the world. The academy also arranges courses, training programs, CME programs and Rural CME programs. IMSA publishes quarterly journal, JIMSA in which original articles, updates, symposia, special issues on topics of current interest are published.

An annual conference - IMSACON is a regular feature; being an International organization every alternate year, the annual conference is held outside India. This year's **IMSACON** was held at Hotel Park, Hyderabad, Andhra Pradesh, India between 4th and 5th November 2011 and was an extremely successful event.

Though IMSA has been in service of medical profession and has been encouraging development of medical sciences by bringing information technology into the profession thus improving the health of nations, yet we do not have our own building to work more effectively. Our organization is committed to the medical profession for promoting Continuing Medical Education and also hold educational programmes on topics of National and public health importance. We need to conduct seminars, organise lectures by National and International experts and hold regular workshops and group discussions. For arranging such activities we are badly in need of our own building with adequate infrastructure and facilities like an Auditorium, projection room, library, committee rooms for interactive sessions etc. So far we have been operating from small rented space which can hardly accommodate our office.

Friends, we have been fortunate to get a piece of land about one acre allotted to us by the Lt. Governor of Delhi for developing the IMSA World Head Quarters at Delhi. I am approaching all Fellows and Members to donate at least Rs. 5000/- each to meet the cost of the land as well as construction of our own building. The donations are exempted from tax under 80G; the cheque may please be made in the name of "IMSA – Building Fund" payable at New Delhi, and sent to the Headquarters.

Thanking you in anticipation and warm regards,

Yours Sincerely,

Dr. K.Jagadeesan, President, IMSA,WHQ

IMSA Chapter Activities/ CME Programmes

IMSA Karnataka Chapter CME's conducted

3-4.08.12 Dr. R.R.Thukral Southern Chapters Midterm IMSA Conference.

IMSA Tamil Nadu Chapter CME's conducted

08.07.12 Dr Avijith Basu, Dr T M Srinivasan: Topic: Recent Trends in Adult Cardiac Surgery.

12.08.12 Dr G Jayaraj: Topic: Era of Changing and Challenging Role of Doctors in Health Practice.

09.09.12

Dr T Vidyasakaran: Topic: Occlusive Arterial Disease.

IMSA Bihar Chapter CME's conducted

29.07.12 Dr G P Sinha, Dr Chandra Shekhar, Dr Satish Kumar, Dr P Dayal, Dr Lakhan Lal: Interactive session on Neuro Otological emergency – Coordinated approach at Patna

Election of Fellows and Members 03.08.2012

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Dr Rajgopal P Menon

Dr Praveen Kumar

Dr M J Ravindranath

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Dr N S Neki, Prof. of Medicine, Govt. Medical College, Amritsar (India) has been elected **Fellow of the Royal College of Physicians** (Glasgow).

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The President Dr. K Jagadeesan and the members of board of Trustees of IMSA, WHQ, request all the fellows and members of IMSA to contribute at least Rs. 5000/- towards Building Fund for IMSA, WHQ, New Delhi. Cheque may please be drawn in favour of "IMSA Building Fund".

Secretary General, IMSA, WHQ, New Delhi

IMSA Conference News

IMSACON 2012

Date: Saturday 6th & Sunday 7th, October, 2012, Venue: Gulf Medical University, Ajman, United Arab Emirates

Contact for Registration: Prof. Gita Ashok Raj, Provost, GMU, P.O. Box 4184, Ajman, UAE Tel.: 00971 6 7431333 ; Fax: 00971 6 7430313; E-mail: provost@gmu.ac.ae;

Website: www.gmu.ac.ae Or Secretary General, IMSA: imsawhq06@gmail.com

International Conference on "Healthcare Associated Infection & Control"

Date: February 1st and 2nd, 2013, Venue: S M V Medical College and Hospital, Puducherry - 605 107. This conference is jointly organized with Healthcare Infection Society of United Kingdom, Prof.J.Shanmugam, Organizing Chairman, (Mobile: 09486623094, E mails: drjshanmugam@gmail.com & haiconsmv@gmail.com



IMSA

INTERNATIONAL MEDICAL SCIENCES ACADEMY

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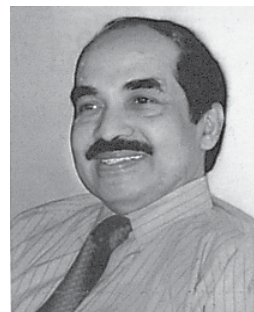
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PRESIDENT WRITES

Dear Fellows & Members,

Recently we had a good mid term IMSA meeting at Rajarajeswari Medical college and hospital at Bangalore- "**Dr.R.R.Thukral IMSA Southern Chapters Conference**". Dr. Rani Devadoss had put up a good show with excellent scientific programme which was quite informative. This will be an incentive for other zones to promote CME activities.



Health care industry needs a total change in respect of the service aspect, primarily health care is looked up by everyone as a service. The second is the business aspect, here ethical consideration is the foremost and necessity for an audit of healthcare delivery is the need of the hour, where our organization; IMSA fellows and members; could volunteer to remove this anomaly; this will go a long way in remodeling the healthcare industry.

Looking forward to meet all the fellows and members during the Imsacon 2012 at Gulf Medical University, Ajman, UAE on 6th & 7th October.

K. Jagadeesan

Dr. K. Jagadeesan
President, IMSA

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All fellows and members of IMSA can have **access** to the site and get information about its objectives, benefits to the fellows/members, chapters and their activities including seminars, refresher courses, rural CMEs etc. and also IMSACON - a regular annual event of international standard; *application form for enrollment as fellow/member can also be downloaded.* Fellows - members and even non fellows-members can have access to full text in the quarterly journal - jimsa from July - Sept. 2003 onwards by putting their E-mail address under '**user name**' and using the **password 'UserJimsa'**.

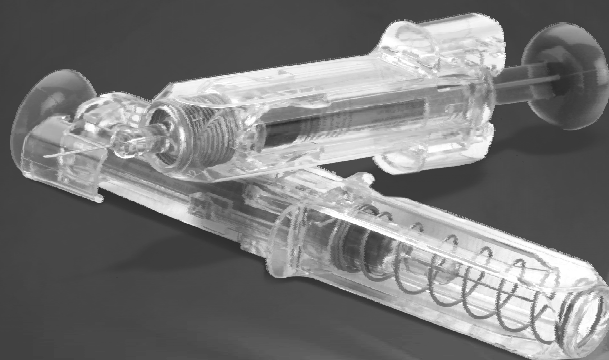


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FROM EDITOR'S DESK

Dear Colleagues,

Health care systems, worldwide, are striving hard to improve healthcare in terms of quality, accessibility and cost effectiveness so as to meet the needs and expectations of patients at large. In spite of the increasing cost of providing health care, India still has one of the most privatized health providing system; unfortunately, the expenses incurred are borne by a fairly large proportion of the individuals, themselves. There are three major challenges facing healthcare in India today; these are (i) access to healthcare in rural regions and for the poor in urban India; (ii) availability of qualified medical professionals; (iii) low capacity for purchasing medical care and medicines for the poor. There is an urgent need to collectively focus on these areas.

The present issue on **Recent Advances & Future trends in Health care** is the outcome of hard work done by **Prof. Syed Amin Tabish**, from Srinagar, India, who has over 25 years of illustrious experience in healthcare administration, medical education and biomedical research. Dr Tabish is an internationally known expert in matters concerning health planning and policy making and has been invited by several universities abroad. He is responsible for introducing continuous quality improvement in health delivery systems and clinical audit, in hospitals. He has quite brilliantly planned this voluminous special number of JIMSA, focusing on some of the topics of national importance. I am confident it will serve as useful guideline for health planners and providers, both.

I, on behalf of the editorial board of JIMSA extend felicitations as well as thanks to Prof. Syed Amin Tabish, for bringing out this very informative monogram on health Sciences.

P. D. Gulati

JIMSA BEST PUBLISHED ARTICLE AWARDS 2012

Journal of International Medical Sciences Academy has instituted award for **three (3)** best original articles published during the previous 3 years; **guidelines** are as below:

- (1) **Original articles** belonging to any discipline of medicine published in JIMSA during the previous one years.
- (2) Number of awards: Three (3) annually, carrying a gold plated medal, citation and cash prize (1st-Rs. 5000/-, 2nd-Rs. 3000/- , 3rd-Rs. 2000/-)
- (3) Awardee should preferably be a fellow/member of IMSA; non-fellows/ non members can also be considered for the award if the original work is outstanding; and if selected for the award will be required to apply for fellowship/membership of IMSA.
- (4) Awardees should preferably plan to receive the award at the forthcoming annual **IMSACON 2013**.

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OUR GUEST EDITOR



Professor Tabish is a medical scientist with several distinctions to his credit – an ace academician, a brilliant medical administrator and a dedicated researcher with 25 year's illustrious professional experience in Healthcare, Medical Education and Biomedical Research.

After obtaining postgraduate degrees in Hospital Administration/Health care Management/Emergency Medicine/Epidemiology from apex medical universities in India and the United Kingdom, Dr Tabish has been providing academic and administrative leadership to premier medical universities and hospitals (with HR strength of 4000-8000). Dr Tabish has an innovative vision, excellent analytical, conceptual & strategic planning skills besides quest for excellence through creativity.

Prof. Tabish recently worked as Professor of Medical Education cum Project Director for four Medical Colleges & two University Hospitals in Saudi Arabia. He has been Technical Advisor to another premier Medical University in Saudi Arabia. He played a key role in establishing Colleges of Allied Medical Sciences, Nursing Colleges and Regional Research Resource Centre at Saudi Arabia.

He also worked as Chairman of Curriculum Development Committee and Patron Continuing Medical Education Programmes at this premier University.

He has authored more than a dozen books (including Handbook of Emergency Medicine (Valley Publishers: 1998), Textbook of Hospital & Health Services Administration (Oxford University Press New York 2000/2005), Planning, Organization & Management of Hospitals (JayPee Brothers Medical Publishers: 2003), The Future of Health (Paras Medical Publishers: 2004), Hospital Infection Control: Conceptual Framework. Academia Publishers. 2005 and Evidence Based Nursing Practice: 2010), has **400 Research publications** in international medical journals and about 500 literary publications. He is on the Editorial Board of several medical journals besides being **Editor-in-Chief of International Journal of Health Sciences**. He represented India in "The World Health Assembly" held at Dallas Texas (the USA) during 1998 (first medical scientist from India).

He has been supervising research at postgraduate and post-doctoral level for two decades. Dr. Tabish has been contributing to planning and policy-making (Health and Medical Education) at international, national and local levels for the last 20 years.

Prof. Tabish organized a number of International, National, Regional and Local Conferences, Symposia, Workshops, Seminars within India and abroad. He is also Visiting Professor, Qassim, Al Rajhi Universities (Saudi Arabia). Prof. Tabish is External Examiner, AIIMS, and National Board of Examinations for the award of Diplomate National Board, New Delhi.

He has been trying to develop confidence in the ability of academic medical institutions to produce doctors and nurses of high quality. He has been on the panel of experts for the selection of medical teachers (professors etc), consultants, registrars and other healthcare professionals. He has made a significant contribution towards prevention & control of emerging infectious diseases. He introduced the concept of Continuous Quality Improvement and Clinical Audit in hospitals. Dr. Tabish has played a key role in introducing Quality Assurance Programmes in Health Services. Equally important is the role he played in developing ideas for strengthening District Health System. He advocated the strategy for developing a sound referral system between primary, secondary and tertiary health care.

Professor Tabish established a Disaster Management programme besides establishing Departments of Accident & Emergency (with unique concept of Level System – first of its kind in the world) at SKIMS, which helped save lives and limbs, and disability prevention of thousands in Kashmir. He created awareness among people in general and health professionals in particular regarding disaster reduction, preparedness and mitigation. He conceived up-gradation plan for SKIMS and prepared the Preliminary Project Report which was approved in principle for funding under PMRP (rupees 300 crore).

Professor Tabish has been working towards achieving a knowledge-based, equitable, just and civil society. He has been pleading the cause of Education for All, Health for All, Eradication of child labour, Environmental protection, Women's empowerment and extends help to those who need it most.

Dr. Tabish has been advocating new or changing roles of doctors and other health professionals in response to emerging or refractory social problems, under-served populations, inequalities, rising costs of care, continuous quality improvement, lack of community involvement and imbalance between the preventive, promotive & curative services. Dr. Tabish believes that intelligentsia has a responsibility of social service during peacetime and social response in wartime.

Dr. Tabish has been acknowledged by many international organizations for his professional accomplishments, scholarship, personal integrity, superior competence and outstanding contribution to medical profession and social service.

Professor Tabish is presently working as Medical Superintendent cum Head, Department of Hospital Administration and Chairman Accident & Emergency Department at Sher-e-Kashmir Institute of Medical Sciences, Srinagar.



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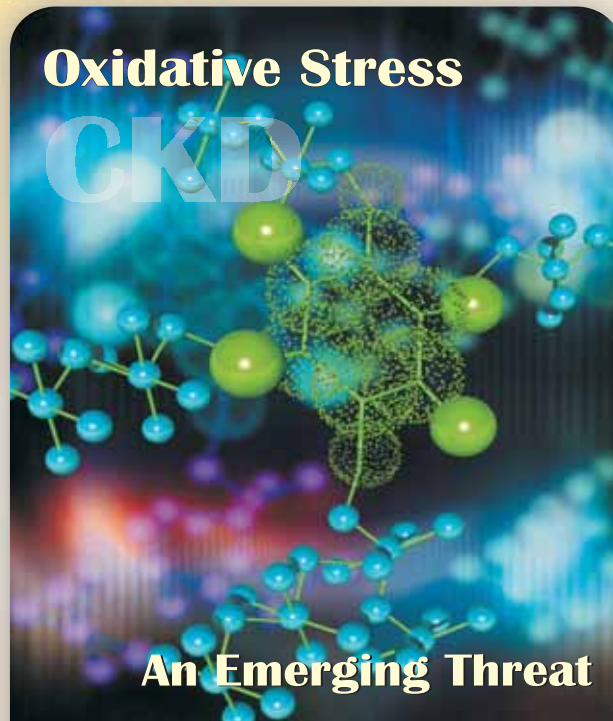
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1. Nephrol Dial Transplant (2011) 0: 17
2. Clin J Am Soc Nephrol 5: 905-911, 2010



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1. Nephrol Dial Transplant (2003) 18: 1272-1280, 2. Peritoneal Dialysis International, Vol. 29, pp. 1711-1717, 3. Circulation 2004;109:369-374
4. N Engl J Med 2006;354:2773-82., 5. Peritoneal Dialysis International, Vol. 29, pp. 1711-1717

The Health Care Industry Needs a Change Model

The health care delivery system is undergoing radical transformation, technological advances are providing the infrastructure for new ways of delivering care and consumers are expecting care in a manner more conducive to meeting their needs. Today people are living longer than ever. The discovery of new technology, innovative medicines, science, and research all have a great impact. Standards of health profoundly influence economic performance and quality of life. Quality management has become a major concern in the delivery of health care. Concerns about increasing costs combined with an increasing appreciation of the variability in health care delivery practices has led to the development of strategies to better standardize health care delivery. An organization's quality system consists of the management philosophy, vision, and corporate strategies by which the organization conducts itself and allocates resources to satisfy patient requirements. To excel at meeting patient needs health care organizations must constantly improve system to serve customers.

Quality Health Care means doing the right things the right the first time. An organization's quality system consists of the management philosophy and vision by which it conducts. A quality system invokes the standards that the organization monitors to guide and regulate all of its activities that create a quality service.

Health care systems worldwide are striving to improve the quality of healthcare in an atmosphere on Evidence Based Medicine and Evidence Based Healthcare. Healthcare is Constantly Evolving sharing the strain of development in a larger world that is changing at incredible speed. Because of all the changes in healthcare, the ways in which quality is perceived, pursued, and insured continues to develop. The process of development coupled with increasing liberalization and globalisation across India has enabled consumers to realize their increasingly important role in society and governance. The consumer movement in India is as old as trade and commerce.

It is important to distinguish between quality of health (encompassing health status assessment) and quality of health care (encompassing the structures, processes, and outcomes of health care). The application of health, health care needs assessments bridges these two areas. The ultimate delivery of health care quality depends as much as on analysis of the delivery and outcomes of the health care for groups of patients (medical care epidemiology) as on analysis of the care of individuals.

India has one of the most privatised health care systems in the world; over 80% of health care expenses are paid for by individuals. Health care is also one of the most unregulated sectors. There are substantial concerns about the quality of care given, especially at the more informal end of the range of providers. This is particularly true for diseases of public health importance such as tuberculosis, malaria, and sexually transmitted infections.

Private Sector in Health is unregulated. Even where standards of care exist they are hardly ever enforced, registration of nursing homes is more often than not a very contentious issue, doctors are seldom held accountable by either their peer groups (e.g. the Indian Medical Association) or by regulatory authorities (Medical Council of India) or even through legal mechanisms such as the Indian Penal Code and the Consumer Protection Act. With an unregulated private sector and an unaccountable public sector the people face tough times ahead.

Quality is one of the major cornerstones of healthcare along with access to services and cost. Quality improvement is a continuous effort to meet and exceed the needs and expectations of the patients and other customers. Putting patients first is the key to improving the quality of health. Planners, managers, and providers can design and offer services that both meet medical standards and treat clients as they want to be treated. Adopting a client-centered approach often requires a shift in attitudes.

Private medical provision is the major constituent of health care delivery services in India. The quality of care provided by this sector is a critical issue. Professional organizations such as the Medical Council of India and local medical associations have remained ineffective in influencing the behaviour of private providers. The decision to bring private medical practice under the Consumer Protection Act (COPRA) 1986 will be effective in minimizing malpractice and negligent behavior. The medical associations have also argued that the introduction of COPRA is a step towards expensive, daunting and needless litigation. A number of other concerns have been raised by consumer forums which focus on the lack of standards for private practice, the uncertainty and risks of medicines, the effectiveness of the judiciary system, and the responsibility of proving negligence.

The poor never follow the rules of good health, we often hear. But the rules, in fact, are no guarantee of safe health in a system that is poorly regulated and unaccountable to its users.

How relevant are these concerns? Is the enactment of COPRA really appropriate to the medical sector? The paper argues that while this development is a welcome step, we need to comprehensively look into the various quality concerns. The effective implementation of COPRA presumes certain conditions, the most important being the availability of standards. QM packages should be locally developed and flexible rather than imported "off-the-shelf" packages. A QM strategy should start with a client focus. Client satisfaction is one of the most important results of good-quality care. Quality can be maintained if there exist a suitable set of laws on consumer protection, provided at least these are reasonably well implemented. In India, the two most common avenues for relief in healthcare are the Consumer Protection Act and civil courts. The various consumer commissions established under COPRA in India have begun playing a key role in protecting consumer rights, in spite of their relatively recent origin.

To achieve excellence in health care system patients, providers and systems have to be involved in employing the principals of TQM.

Standards of Practice continue to evolve. New diagnostic and therapeutic interventions are continually being developed. Benchmarking refers to the process by which performance is compared to a standard. Re-engineering refers to a fundamental rethinking and radical redesign of processes to achieve dramatic improvement in performance; when it is adapted to the healthcare delivery process, the term clinical reengineering is used.

Relatively few approaches to supporting consumers in their use of the private sector have been tested. They tend to have one or more of the following aims: to improve consumer information; to make services or products more affordable through some form of subsidy; and to create new institutions that give consumers greater authority to challenge care of poor quality.

Patient focused interventions, Regulatory involvement (acceptable standards), Incentives, IT-based interventions, Organizational interventions (culture change and Quality Management philosophy) - changing organizational behavior (clinical audit, CQI), and Healthcare delivery models (innovative interventions in resourcing, organization and delivery of services) can go a long way to improve the quality.

There are other potential approaches to strengthening the position of consumers in private medical markets - direct consumer education; information about prices; and social marketing approaches could prove useful in publicizing such information. Although regulation and accreditation can play an important role in sending clear and transparent signals to consumers about which providers are registered and meet minimum requirements in terms of structure, equipment and staff.

Regulatory approaches, including consumer protection legislation, have helped to highlight these practices but have done little to control them.

Private providers may lack access to essential diagnostic services and treatments. One approach has been to provide them with prepackaged drugs for common conditions such as malaria and sexually transmitted infections.

Social marketing, Use of vouchers and Consumer protection: Quality can be maintained if there exist a suitable set of laws on consumer protection, provided at least these are reasonably well implemented. The two most common avenues for relief in the arena of medical care are the Consumer Protection Act and various civil courts. It is not surprising that the various consumer commissions established under the Consumer Protection Act (COPRA) of 1986 have begun playing a key role in protecting consumer rights, in spite of their relatively recent origin. The main rationale for COPRA was that it could offer a quicker and cheaper way for consumers to address their grievances. Certainly, a number of cases related to insurance and medical negligence have reached these courts.

The major issue in regulation is implementation, which has typically been extremely weak. Regulation is unlikely to have had a major impact on private providers or on market structure and explains the widespread development of the informal private sector. Growth of the private sector is largely determined externally, even when enabling measures intended to support the sector are in place. Important opportunities to regulate, before the private sector becomes both politically and economically strong enough to resist, should not be missed by low-income countries. Regulation seems to be a function of the market as well as, potentially, an influence on it.

Science and technology have profoundly influenced the course of human civilization. Science promises its unlimited potential to bring revolutionary changes in human lives for better. The governments should ensure the fullest use of scientific developments for the well-being of people and whole of human kind. We must take science to the people. Research and development institutions must be managed imaginatively and efficiently to advance and utilize science and technology for health development in the best possible manner.

Quality improvement is a revolutionary idea in health care. The idea is to raise the level of care no matter how good it may already be through a continuous search for improvement. Quality improvement must become an integral and essential part of an institution. Making quality a top priority requires fundamental changes in organizational culture, in goals and guidelines, and in daily operations. QM must be driven from both the bottom and top of the health system. Persistence is crucial. It remains a challenge to find innovative approaches that improve the quality of health service delivery. Quality in health care would substantially improve if only some way could be found to secure more comprehensive and systematic uptake of the findings of biomedical research and development through implementation in everyday clinical practice. There is need to develop valid guidelines. Public health should be concerned with not only the health and health care needs of

populations but with the quality of care provided to the population. To contribute effectively to improving the quality of patient care it is important that public health physicians develop experience of the methods for achieving improvement.

The dominance of private provision in the health systems of low-income countries makes it vital to conduct more research into understanding and influencing their behavior and to experiment more with alternative strategies. In particular, research is necessary on the success of demand-side strategies, which could both complement and increase the effectiveness of interventions targeted at providers.

The organizational commitment to continuously improve the quality of the patient care is the central concern of health care institutions. CQI relates to the processes for change and institutional development, and focuses on getting the best out of your resources. Quality improvement should be a regular, expected, familiar, inevitable part of professional life. A holistic view of quality is one that emphasizes the results of addressing trends and improvements over time.

An increase in aging population is one of the most dramatic demographic trends in the world today. Many elders present many complex diseases and require complex care and disease management. The challenge also presents many opportunities in the healthcare field and a shortage of providers in rural areas.

The health care industry needs a change model that will facilitate a learning environment to enable clinicians to manage change while simultaneously developing health care workers who are knowledgeable about contemporary health care practices. Clinicians need to engage in deliberations about new models of care. This will necessitate a willingness to scrutinise closely their existing practices and not continue to attempt to apply outmoded processes and practices. There needs to be a closer alignment between the consumer's actual needs and the roles, functions and activities of nurses. This will require challenging old-world views if we are to capitalise on this opportunity for re-conceptualizing and organizing healthcare delivery.

The challenge is to find ways to improve upon the existing situation in the health sector. A potential for improvement exists in areas including the overall costs of care, financial equity, and the quality of care. A sustained improvement in these areas would play a significant role in advancing the primary goal of health policy – health, itself.

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Guest Editor

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P. D. Gulati, Editor, JIMSA

Quality Health Care for the Numerous: The Challenge of Numbers

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Abstract: The delivery of health care on a continuous basis in a progressive manner to a group of population located geographically in a certain area is a challenge by itself. Once initiated several quality issues including enhancement / expansion of services does arise. The number of beneficiaries / recipients is a crucial factor. In current times, health delivery cannot be confined to government / public sector alone as was the case for substantial period in the past. At the same time, corporate / private parties need to be monitored in relation to the practices and cost eventually payable by the patient. The uninsured need to be attended / included in the gamut. Mechanisms of partnership (PPP: public-private partnership) with a realistic approach require to be initiated / strengthened / consolidated. The degree and success is determined by continuous inputs / review / corrections. Cost control / containment has been an important consideration in developed countries' health policy as well. In matters of health there has been heterogeneity in Southeast Asian countries health policy approaches; however there have been many similarities in terms of patients / disease / issues profile as well. There is much that health policy makers, academicians, clinicians, health authority can do in the changing times more so from experiences obtained in other regions of the globe. Quality in health care is a continuous process and changes noted in the practices, feedback, outcome, cost effectiveness require to be periodically fine-tuned.

Key words: Quality. Health Care Delivery. Universal Access. Health Policy.

INTRODUCTION

The level and tier of health care has several components. The regional, environmental, spatial aspects from amongst the many influence the planning, delivery, cost and quality of health care in a given region at a certain point/phase of time. When dealing with quality in health care issues, it becomes necessary to consider the, dimension of numbers, clinical situations/ disease profile, the setup (s), partners, and Indicators.

DIMENSION OF NUMBERS

Population size indicates the numbers in different age groups that need to be attended. South and East Asia is occupied by densely populated countries¹. Despite the population stabilization programmes, it is anticipated that another equal of the existing population may be added by the year 2030. As it is the current population poses a challenge by sheer numbers belonging to different age groups and distributed in metros cities, hinterland and rural areas.

The **changing demographic profile** needs to be clearly understood. It has been rightly said that Asia is aging attributable to two factors.

1. **Better life span** both in males and females, rising from erstwhile 50 to 60+ differing in different countries. Old age² is characterized by multiple organ system disorders and has elements of chronic disease increasing complications with necessities of rehabilitative measures and care in institutional setups. Taken together, this increases the need for multiple visit attention by different members of the medical, paramedical and rehabilitative calling for care in larger necessities / requirements and adding to service volume
2. There have been some accomplishments in **reduction of IMR (infant mortality rate)** and maternal mortality rate; but still much more needs to be done. Name based tracking of pregnant women and children for Ante Natal Care and immunisation will add to accurate data from across India.

CLINICAL SITUATIONS/DISEASE PROFILE

Asia has seen a continuous change in the profile with predominance of infectious / diseases of under nutrition combined with the newer ones pertaining to lifestyle and aging.

- a). **Tropical diseases** like vector borne malaria have shown difficulties in control / eradication and morbidity / mortality may continue unabated in certain countries. Likewise, dengue / leptospirosis³ continue to affect large numbers of the population quite often on a seasonal basis particularly the months of June to October coinciding with monsoon.
- b). **Non-communicable diseases** sometimes termed as diseases of affluence

(perils of plenty) notably diabetes mellitus, hypertension, coronary artery diseases⁴ are rising in numbers with occurrence of difficulties in control and development of complications (catastrophic health payments) requiring tertiary/ super speciality care with modern technology gadgets and equipments. These have assumed the dimension of public health problem/epidemic.

- c). **Lifestyle diseases** such as HIV has been a scourge; strategic intervention has resulted into closeness to a plateau phase with several patients receiving anti retroviral therapy with reduced hospitalizations and marginally improved quality of life. Cancers attributable to dietary/ environmental factors show a demonstrable rise and demand, complex measures of chemotherapy / surgery / radiotherapy emphasizing the role on prevention for which substantial research funding is being utilized. Sound mental health is a matter of concern and the numbers clearly indicate rise in demands of psychiatry / counseling services.
- d). **Emerging diseases** such as swine flu, avian flu (facilitated by increase international travel and necessitating quarantine measures pose a challenge and demand extensive services from laboratory diagnosis, indoor services and ICU care in case of complicated situations (catastrophic health payment).
- e). **Environment related problems:** rising pollution of the environment⁵ through industrial exhaust, vehicular traffic and the effects of "Global Warming" are now visible. Flash floods, snowing, un-seasonal rains and such calamities / eventualities pose enormous demand on emergency management services and disaster management with multi agency efforts including those of immediate care and long term relief and rehabilitation. Further incidence of malaria, malnutrition, gastro intestinal diseases are anticipated to get out of control if nations do not adhere to combine all round measures in reducing the effects of global warming.

THE SETUP(S)

The modern equitable health care delivery system has as its objectives i.e. (a) adequate access; (b) sound efficiency; (c) standard quality; (d) legitimate control of cost accompanied with patients / relatives' - attendants' satisfaction. The fundamental equation is the balance between service volume and the total health spending. The demographic transitions noted above apply to individuals in a social context and under economic realities. In countries/ regions where health care setup is still at its nascent stage, the backlog shall have to be doubled in the coming 5-7 years. Conventionally there have been academic medical centers/medical schools/medical teaching institutions in large cities/state capitals which have served the purpose for substantial period of time. Coupled with these, the corporate hospitals, trust hospitals have also grown up essentially in metropolitan and large cities leaving tier 2

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cities and tier 3 towns relatively deprived/backward of medicare/health care facilities. The frenzy of fast urbanization has been enormous and cuts across all major quality of life indicators. The cities may fall well short of delivering a basic standard of living including health for their residents. The urban transformation in its scale and speed has been enormous and the slow pace of parallel development of structure such as water supply, sewerage, drainage, transport and housing shall put severe pressure on the civic body. The urban landscape forces millions of people to live under pathetic conditions (ghettos/slums) which may tend to be affected by water logging during monsoon resulting in diseases causation and spread. The WHO has launched a project called 1000 Cities, 1000 Lives offering portion of public space for physical exercise, making families friends, community health checkup, having local healthy food. The WHO launched this campaign primarily as urbanization in emerging as a major challenge for public health relating to water, environment, non-communicable disease and their risk factors-tobacco usage, unhealthy diets and communicable diseases like open Tuberculosis. In short, the setup shall have to be in (a) Metro cities; (b) vulnerable areas within the cities necessitating urban health mission programmes and (c) rural, away from hinterland relatively isolated areas having the necessity of basic health infrastructure.

Whereas in the larger cities, super speciality, high technology care, high end investigations can be carried out, it is necessary that secondary hospitals (peripheral urban health care) are developed in the above mentioned urban pockets and there need to be at least primary health unit with 30 beds in rural setup with out-patient department, provision for indoor-patient services, operation theatre, emergency/obstetrics services with a basic backup of pathology/radiology/blood bank and pharmacy services. **Tele-medicine**⁶ services can give a diagnostic advisory back up in relation to nature and urgency of treatment elsewhere.

It has been underscored that over the next 30 years virtually all population growth would be in urban areas, thereby signaling that this most defining change of urbanization is here to stay and the consequences thereof need to be anticipated from the angle of strategic planning and in particular reference to health. It thus becomes obvious that improvement in the quality of health care may have to be differential comprising of :-

- (a.) modernization and technological updating of super speciality centres / medical schools in the metropolitan / large cities,
- (b.) creating special health care provision in urban pockets (ghettos / slums) arising due to the amazing speed of urbanization without a parallel progress in infrastructural development. These efforts need to be in the nature of urban health improvement programme.
- (c.) development of medium size hospitals and related facilities in tier 2 cities and tier 3 towns,
- (d.) basic primary health care and / health facility in rural part of the country as pointed out. All the above being networked through a carefully planned referral system and networked through telemedicine⁶ / surveillance programme.

PARTNERS

Though government have been conventionally the main provider/ facilitator, it is the private sector that has now engaged in chains of hospitals at metropolitan/large cities and medical establishment needs to be undertaken in tier 3 towns and rural hinterland. In an effort for the public health care system attempting to adapt to population needs, the public-private partnership mode has to be initiated, consolidated and strengthened differentially on sound assessment.

The two most crucial issues are the reach and access. The health care provider and facilitator needs to reach the hinterland/remote part of the country so that access of citizen for urgent care, primary care/preventive care (vaccines) and checkup becomes facilitated. The overall success and the quality of health care can be judged by the availability of health care facility to the recipient in the remotest part. It shall become obvious and clear that (a.) creation (existence) of health care; (b.) enhancement to acceptable levels and (c.) addition of conveniences public health facilities in accordance to the changing times are progressive steps in the assessment of quality of

health care.

Hospital sector especially super speciality services continue to be an area of interest to private equity investors. Nationwide, private hospitals chains to the neighbourhood clinic are the line of percolation. Health "industry" appears to be rapidly latching onto multi dimensional revenue potential for health care with corporate health insurance coverage and payment potential as the key factors. There is already a lurking fear that patients become a conduit for doctors to bill money from insurance companies⁷. Threat to primacy and autonomy of the medical professional has to be averted. Though the time taken to stabilize the operations can be long, the private sector needs to be monitored. The problem of rising health cost has become key US domestic policy issue. The need for the Independent Payment Advisory Board⁸ to report on health care costs, access, quality and utilization and further recommend regarding ways of slowing the growth in private national health care expenditures, comparative-effectiveness research (CER)⁹ as a means of reducing health care cost without compromising the quality of care speaks for itself.

INDICATORS

Under National Rural Health Mission (NRHM), the Central Government has financed the addition of one lakh skilled health care providers to the public health work force. However, much more needs to be done in this direction to address the issues related to availability and quality of human resources. The Union Health Budget has increased from Rs. 8000 crores in 2004-05 to over Rs. 21,000 crores¹⁰. The Report¹⁰ includes the challenges and policy options which required a national consensus

It is stated that enhanced quality of health care contributing to better quality of life and broadly resulting in furthering the objectives of Millennium Development Goals (MDG) appears to be a natural logical sequence. Much has been said about translational medicine, broadly meaning that the results of biomedical research (*bench*) be transferred to the place of care (Outdoor-indoor critical care, OT, preventive and rehabilitative services) *bedside*. Further corollary is to see the *application* in its widest and most extensive form so that the meaningful benefits are accrued to numerous, i.e. bridging the gap between translation and application.

Undoubtedly certain issues pertaining to health care are universal. Within a given region there may exist heterogeneity, for instance in East Asia; the evolution and approaches in Japan, Korea (North and South), Singapore may be different towards financing and delivery of health care and yet there may be commonalities in relation to countries in South East Asia. The achievements of medicine in technology, diagnostics, imaging, indeed have been spectacular. Citizens all over the world have been recipients of excellent care related to the application of these developments. The quality of health care has an immense potential for further development. The scope is wide and the canvas large. However, the need to deliver service that has been barely existing and the need to have reassuring basic health care is indeed crucial. The gaps have to be bridged, the tempo has to be accelerated, the balance has to be struck for the goals of health care to the numerous being fulfilled.

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Recent Advances and Future Trends in Cardiology

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Abstract: The field of cardiac sciences has seen a lot of new developments in the last few years. We have better drugs to treat life threatening diseases. There have been significant changes in cardiology practice because of exciting new developments in the last few years. We have more potent drugs, development of new diagnostic techniques, evolution of stent technology with more complex coronary anatomy being treated percutaneously. New valve therapies for high risk patients have emerged and likely to evolve further. Advances in technology have changed the way cardiology is practiced. This article dwells upon these recent advances and what we can expect in future.

INTRODUCTION

The field of cardiac sciences has seen a lot of new developments in the last few years. We have better drugs to treat life threatening diseases. Non invasive cardiology has benefitted from ever improving technology. Invasive cardiology has not lagged behind with the most exciting developments occurring in the field of percutaneous valve therapies which continue to evolve. Gene and stem cell therapy have also shown progress. These trends give us a glimpse into the future which appears very promising.

RECENT ADVANCES

1. Clinical Cardiology

Clinical cardiology is never static. Lot of effort is put on development of better drugs. The most recent has been the approval and availability of newer thienopyridine prasugrel which is used in treatment of acute coronary syndromes for those proceeding to percutaneous interventions. There is a significant reduction in cardiovascular deaths, myocardial infarctions, stroke, stent thrombosis and urgent target vessel revascularization, but with increased risk of major life threatening bleeds¹. For management of angina we have newer drugs ivabridine and ranolazine as add on therapy. Dabigatran an oral anticoagulant is a very exciting addition in stroke and embolism prevention in patients with atrial fibrillation². The fact that it does not require INR monitoring as compared to warfarin makes it a more attractive alternative besides being superior to warfarin in reducing stroke or peripheral embolic events³. Less risk of hemorrhage is an added attraction. Newer antiarrhythmics have become available which includes drugs like dronedarone which is indicated in prevention of recurrence of atrial fibrillation. Compared to amiodarone the incidence of pulmonary, hepatic and thyroid related side effects is almost negligible⁴. Among statins post Jupiter trial rosuvastatin has been approved for prevention of coronary events in a new subset of patients who were not initially considered candidates for statin therapy by using hsCRP as a stratification tool⁵.

2. Interventional Cardiology

There have been exciting developments in the field of interventional cardiology too. On catheterization table assessment of lesion severity using FFR has gained prominence lately. In a recent analysis from FAME trial⁶ the authors concluded that coronary angiography is an inappropriate tool to identify ischemia producing stenosis as detected by FFR and this discrepancy is present not only from 50%-70% range but also in 70%-90% range. FFR represents the maximum achievable blood flow after challenge with adenosine to myocardium supplied by stenotic artery as a fraction of normal maximum value. A value of less than 0.75 identifies stenosis with inducible ischemia. The measurement is done by pressure wire⁶. Fig 1 shows FFR assessment of stenosis severity. This has made multi vessel disease angioplasty much more

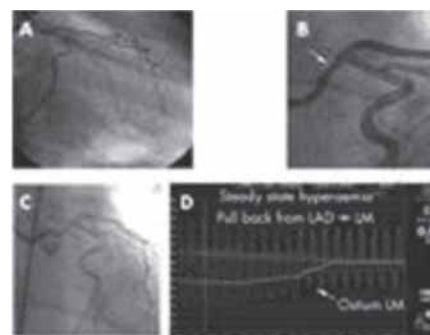


Fig 1: FFR Assessment

evidence based and unnecessary stenting in physiologically normal lesions is avoided.

The most important of recent trials have shown that coronary angiography and revascularisation within few hours after thrombolysis is safe and confers mortality benefit⁷. Hence treatment paradigms may change in future with patients being thrombolysed at a non PCI centre and then immediately shifted to a competent centre for immediate coronary angiography and revascularisation versus ischemia guided therapy⁸.

Recently lot of interest has been generated by concept of thrombus aspiration in primary percutaneous intervention. In a Bayesian meta-analysis, adjunctive thrombectomy improves early markers of reperfusion but does not substantially effect 30-day post-MI mortality, reinfarction, and stroke. The use of aspiration thrombectomy devices is not associated with a reduction in post-MI clinical outcomes. Thrombectomy is one of the rare effective preventive measures against no-reflow⁹. Fig 2 shows results of thrombectomy in acute MI.

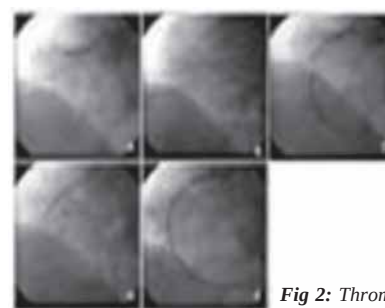


Fig 2: Thrombectomy

Local drug delivery viz Drug Eluting Balloons (DEB) have generated lots of interest lately. Rationale for the development of DEB derives mainly from the limitations of Drug Eluting Stents (DES). Nonstent-based local drug delivery using DEB maintains the antiproliferative properties of DES, but

without the limitations of DES. Moreover, DEB may be used in subsets of lesions where DES cannot be delivered or where DES do not perform well, such as in tortuous vessels, small vessels¹⁰, or long diffuse calcified lesions, which can result in stent fracture; or perhaps when scaffolding obstructs major side branches or in bifurcated lesions¹¹. The discovery that sustained drug release is not a requisite for the long-lasting antiproliferative effect of paclitaxel and the fact that the uptake of paclitaxel by vascular smooth muscle cells is rapid and can be retained up to 1 week, resulting in prolonged antiproliferation, have given rise to the concept of local paclitaxel delivery through coated balloons¹¹. The most appealing indication for paclitaxel-eluting balloons would be for the treatment of ISR¹². Fig 3 shows drug eluting balloon.

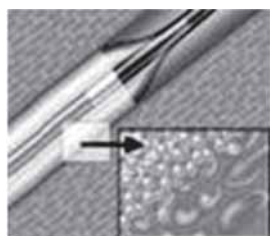


Fig 3: Drug eluting balloon

Additional potential advantages of DEB include (a) homogenous drug transfer to the entire vessel wall; (b) rapid release of high concentrations of the drug sustained in the vessel wall no longer than a week, with little impact on long-term healing; (c) absence of polymer could decrease chronic inflammation and the trigger for late thrombosis; (d) absence of a stent allows the artery's original anatomy to remain intact, notably in cases of bifurcation or small vessels, thereby diminishing abnormal flow patterns; and (e) with local drug delivery, overdependence on antiplatelet therapy could be curtailed¹¹.

Percutaneous coronary intervention (PCI) with bioabsorbable stents has created interest because the need for mechanical support for the healing artery is temporary, and beyond the first few months there are potential disadvantages of a permanent metallic prosthesis. Biodegradable stents contain a biodegradable polymer or are completely biodegradable. There are around twelve stents with biodegradable polymer. LEADERS STUDY¹³, an all comers trial, showed that biolimus eluting stent with a biodegradable polymer was non inferior when compared to sirolimus eluting stent with durable polymer at nine months, as regards safety, efficacy and angiographic outcomes. Potential advantages of having a completely biodegradable stent is that the stent would disappear from the treated site reducing or abolishing late stent thrombosis, improving lesion imaging with computed tomography or magnetic resonance, facilitation of repeat treatments (surgical or percutaneous) to the same site, restoration of vasomotion, and freedom from side-branch obstruction by struts and from strut fracture-induced restenosis. Some of completely biodegradable stents in various stages of development or trials are Igaki-Tamai Bioabsorbable Stent, BVS Everolimus-Eluting Bioabsorbable PLLA Stent, REVA Bioabsorbable Stent. Fig 4 shows pathological appearance with biodegradable stent.

Treatment of left main coronary stenosis by percutaneous means continues to evolve further. At one time a truly surgical domain is now increasingly

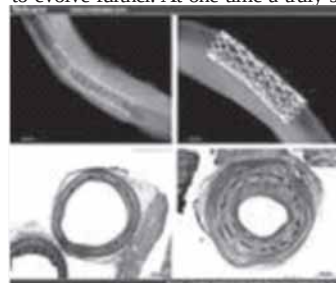


Fig 4 : Biodegradable stents

being treated with stents. In the landmark SYNTAX trial¹⁴ a subgroup of 705 patients with unprotected left main coronary artery disease (ULMCA) had similar rates of MACE, cardiac death, and MI. Stroke was significantly lower in PCI compared to CABG. However there was increased need for repeat revascularisation in the PCI subgroup. The MAIN compare¹⁵ trial also validated the findings of SYNTAX trial. The registry showed at 5 years there was no significant long term difference in death, MI or stroke but there was increased repeat revascularisation in the PCI group. However patient selection is the key to success. SYNTAX¹⁴ and EUROSORE¹⁶ systems have emerged as important tools to risk stratify patients. A SYNTAX score of more than 34 indicates patient would be better off with CABG than with PCI.

Intervention for peripheral vascular disease has also improved with further expertise. CREST trial a head to head comparison of carotid endarterectomy with carotid stenting for carotid stenosis has shown that stenting is as good as endarterectomy and perhaps in certain patients those under seventy may be better¹⁷. Patients with symptomatic or asymptomatic carotid stenosis were randomized to undergo carotid-artery stenting or carotid endarterectomy. The primary composite end point was stroke, myocardial infarction, or death from any cause during the periprocedural period or any ipsilateral stroke within 4 years after randomization. For 2502 patients over a median follow-up period of 2.5 years, there was no significant difference in the estimated 4-year rates of the primary end point between the stenting group and the endarterectomy group (7.2% and 6.8%, respectively; hazard ratio with stenting, 1.11; 95% confidence interval, 0.81 to 1.51; P=0.51).

Till now management of valvular heart disease was mostly a surgical domain. Among the valve afflictions, valvular mitral regurgitation (MR) remains largely the purview of surgery. Recently, the potential for less invasively replicating these successful surgical procedures without the need for thoracotomy or cardiopulmonary bypass has generated considerable interest. For the most part, these new approaches are modeled after established surgical strategies. The Mitraclip device (Fig 5 Evalve, Inc, Menlo Park, Calif) has proven relatively safe and often effective. Using a multiaxial transeptal catheter system, a metallic clip is used to grasp and approximate the free edges of the 2 leaflets. The ongoing EVEREST registry includes EVEREST I and nonrandomized (roll-in) EVEREST II patients. Clip implantation was successful in 89% of 104 patients with MR grade reduced to ≥ 2 in 79 (76%)¹⁸. The type of valves suitable for such procedure would be those where the cause of regurgitation is because of annular dilatation as happens in many cases of ischemic MR. Annulus reduction techniques using rings inserted through coronary sinus encircling and hence reducing the annulus size are in various stages of development or trials¹⁹.



Fig 5: mitra clip

Surgical aortic valve replacement is the reference treatment standard for patients with symptomatic severe aortic valve stenosis. Despite the fact that the prognosis with medical management is poor, many patients do not undergo surgery because of an increased anticipated operative risk, driven by comorbidities such as severe obstructive pulmonary disease, porcelain aorta, etc²⁰. The results with balloon aortic valvuloplasty are beneficial in the acute phase with clinical improvements, but unfortunately only palliative and short lived²¹. Percutaneous aortic valve replacement (PAVR or TAVI) using stent-based prostheses has emerged as a promising new option in recent years and has been used by number of operators in different centers

with incremental success in line with procedural experience²². Initially starting with 22 French systems today, PAVR using the 18F CoreValve prosthesis. (Fig 6) is feasible and reliable in experienced hands with a high acute device success rate of about 97%. PAVR has been introduced to offer a safe treatment option for candidates in whom surgical aortic valve replacement is considered not to be safe, balancing perioperative operative risk versus the natural course of the disease/medical treatment. Therefore, mortality is the key safety parameter in all present PAVR studies. The results from recent PARTNER trial²³ are very encouraging. In this study 358 patients with severe aortic stenosis, whom surgeons considered not to be suitable candidates for surgery were randomized to standard therapy (including balloon aortic valvuloplasty) or transfemoral transcatheter implantation of a balloon-expandable bovine pericardial valve (sapien valve). The primary end point was the rate of death from any cause. At 1 year, the rate of death from any cause (Kaplan–Meier analysis) was 30.7% with TAVI, as compared with 50.7% with standard therapy (hazard ratio with TAVI, 0.55; 95% confidence interval [CI], 0.40 to 0.74; $P < 0.001$). Among survivors at 1 year, the rate of cardiac symptoms (New York Heart Association class III or IV) was lower among patients who had undergone TAVI than among those who had received standard therapy (25.2% vs. 58.0%, $P < 0.001$). The conclusion of study was that in patients with severe aortic stenosis who were not suitable candidates for surgery, TAVI, as compared with standard therapy, significantly reduced the rates of death from any cause, the composite end point of death from any cause or repeat hospitalization, and cardiac symptoms, despite the higher incidence of major strokes and major vascular.

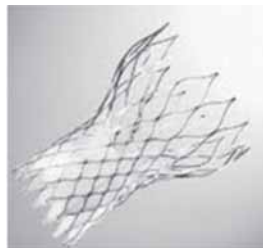


Fig 6: Core valve prosthesis

3. Stem Cell Therapy

Stem cell therapy as applied to cardiology has shown partial progress. A large number of patients with coronary artery disease experience angina with vessels that are not suitable for revascularization. The angina in so called end stage coronary artery disease is refractory to conventional medical therapy. Laboratory and preclinical studies have provided evidence for the safety and potential efficacy of autologous CD34+ stem cell therapies as treatment for angina. Clinical studies investigating intramyocardial transplantation of autologous CD34+ stem cells by catheter injection for patients with refractory angina show that this is safe and feasible. It remains unclear whether intracoronary infusion of CD34+ stem cells exerts beneficial effects in patients with angina as well. In a controlled clinical trial enrolling 112 patients²⁴ with refractory angina, no myocardial infarction was observed during intracoronary infusion. No serious adverse events occurred in either group. The reduction in the frequency of angina episodes per week 3 and 6 months after infusion was significantly higher in the treatment group (-14.6 ± 4.8 at 3 months and -15.6 ± 4.0 at 6 months) than in the control group (-4.5 ± 0.3 and -3.0 ± 1.2 , respectively; $p < 0.01$). Other efficacy parameters such as nitroglycerine usage, exercise time and the Canadian Cardiovascular Society class also showed an improvement in the treatment group compared to the control group.

The REPAIR-AMI trial²⁵ involved 204 MI patients undergoing primary PCI following which some patients were randomized to receive bone marrow stem cells. The primary end point of this study was ejection fraction at four

months. This increased significantly more in the patients who received stem-cell infusions than in those given placebo infusions. Subgroup analysis further suggested that the benefit was greatest in patients suffering larger infarcts (those with lower ejection fractions at baseline) and those treated more than five days after their MI.

Role of stem cells in heart failure is also under evaluation. The star heart study²⁶ involved 391 patients with chronic heart failure following an MI experienced three to eight years previously. Of these patients, 191 accepted the stem-cell treatment while the other 200, who did not agree to the intervention, acted as controls. The therapy involved taking bone-marrow cells from the iliac crest and isolating mononuclear cells, which were cultivated, harvested, and then re administered via an intracoronary balloon catheter directly into the infarcted zone. Results at three months, 12 months, and five years after the bone-marrow-cell therapy showed significant improvement in left ventricular ejection fraction, cardiac index, exercise capacity, oxygen uptake, and left ventricular contractility. Controls, however, showed a deterioration in LV performance. Of particular note, there appeared to be a significant decrease in long-term mortality in the stem-cell-treated patients. Within a median follow-up time of 4.6 years, average mortality rate of 0.75% per year in treatment group compared to 3.68% in control groups. Table I shows current clinical approaches in stem cell therapy.

TABLE I. Current Clinical Approaches in Cardiac Stem Cell Therapy

ABM injection (acute and chronic)
• Transcatheter
• Surgical
ABM intracoronary infusion (acute)
Stem cell mobilization/G-CSF (acute)
Myoblast injection (chronic)
• Transcatheter
• Surgical

ABM = autologous bone marrow; G-CSF = granulocyte colony stimulating factor

Still it is very early to comment on how stem cell therapy will be incorporated into treatment protocols. It is something to look forward to.

4. Cardiac Imaging

Cardiac imaging has also undergone evolution especially for evaluation of coronary artery disease. Coronary CT angiography as per trials has an excellent negative predictive value but a suboptimal positive predictive value for stenosis in 50%-70% range due to overestimation²⁷. Additional functional testing using perfusion imaging is often necessary to assess physiological significance of these intermediate lesions. Recently concern has been raised regarding radiation exposure which can be minimized by ECG gating. The value of MDCT will be enhanced in future when left ventricular function and first pass myocardial perfusion can be evaluated²⁸. Fig 7 shows a representative coronary ct angiography.

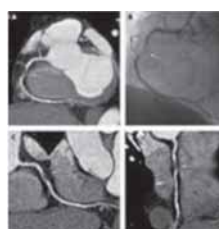


Fig 7: CT coronary angiography

FUTURE TRENDS

The future is always linked to the present. Among the technologies to be eagerly awaited the most important one is the availability and approval of completely biodegradable stents some of which are under development at present. The role of percutaneous intervention for left main stenosis may be accepted alternate to surgery in future but for that long term data is required. Another important advancement to look forward to is the refinement of trans aortic valve replacement hardware (presently 18 fr) and reduction in incidence of periprocedural strokes with further expertise. Stem cell therapy may be the answer to problem of left ventricular function recovery post primary intervention in acute myocardial infarction but needs to be proved conclusively in large scale trials.

CONCLUSION

The field of cardiology has undergone rapid changes in the last decade. We have more potent drugs, development of new diagnostic techniques, evolution of stent technology with more complex coronary anatomy being treated percutaneously. New valve therapies for high risk patients have emerged and likely to evolve further. Stem cells as always have been an area of active debate and research and continue to intrigue. It can be said that the future looks bright and there is much to look forward to.

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LITERATURE REVIEW

The incidence of renal artery stenosis in the patients referred for coronary artery bypass grafting

F. Liang, DY Hu, MY Wu, et al. *Indian Jr. of Nephrology* 2012;22: 1: 13-17

Multivessel coronary disease or peripheral arterial disease is the clinical clue to diagnosis of renal artery stenosis (RAS). RAS is considered equivalent to coronary artery disease in terms of cardiovascular risk. In this study, we evaluated the incidence of RAS in the patients who were proposed to undergo coronary artery bypass grafting (CABG). Diagnostic evaluations of coronary arteriography and renal artery angiography were performed during the same procedure; the patients who were proposed for CABG in terms of CAD anatomy and clinical manifestation were enrolled. RAS was evaluated and a diameter stenosis of $\geq 50\%$ was considered as significant RAS; significant RAS patients were divided into five groups. The five groups of RAS were as follows: (1) unilateral RAS $\geq 50-70\%$, (2) unilateral RAS $\geq 70\%$, (3) bilateral RAS $\geq 50-70\%$, (4) one-renal-artery stenosis $\geq 50-70\%$, contralateral RAS $\geq 70\%$, and (5) bilateral renal artery stenosis $\geq 70\%$. A total of 151 patients were enrolled, and RAS ($\geq 50\%$ stenosis in either or both renal arteries) was identified in 47.02% (71/151) patients. Unilateral RAS $\geq 50-70\%$ was identified in 16.6% (25/151) patients, unilateral RAS $\geq 70\%$ in 4.6% (7/151) patients, bilateral RAS $\geq 50-70\%$ in 7.9% (12/151) patients, one-renal-artery stenosis $\geq 50-70\%$ and contralateral RAS $\geq 70\%$ in 7.9% (12/151) patients, and bilateral RAS $\geq 70\%$ was in 9.9% (15/151) patients. The incidence of RAS was 29.03% (18/62) in patients aged ≤ 60 years, 60% (36/60) in patients aged >60 and ≤ 70 years, and 58.62% (17/29) in patients aged >70 years. The incidence of RAS was significantly higher in patients aged $>60 - \leq 70$, and >70 years than patients aged ≤ 60 years ($P = 0.001$ and $P = 0.007$, respectively). There was a trend that the incidence of RAS in patients with hypertension [HTN, 50.40% (64/127)] was higher than those without HTN (29.17%, 7/24), with $P = 0.056$. The incidence of RAS was 47.02% in patients who were proposed for CABG; bilateral RAS of $\geq 70\%$ was 9.9%. Older age and HTN were associated with RAS in patients who were referred for CABG. This study indicates that the incidence of RAS was high in the patients referred for CABG, and the renal function should be taken care of.

Current Status of Robotic Surgery in India

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Abstract: Robotic surgery allows the surgeon with no previous laparoscopic training to provide the patients with the advantages of minimal access surgery. For the laparoscopically trained surgeon it enables operating at a superior level with greater precision and accuracy. In India, robotic surgery is still in its infancy. There are eight robots installed in India, of which five are in New Delhi, one in Chennai, one in Nadiad and another in Pune. The All India Institute of Medical Sciences has been at the forefront of the robotic revolution in India. India now stands at the cusp of a robotic revolution. Robotic surgery in India is here to stay and it is up to us as minimally invasive surgeons across different specialties to lead the way and make maximum use of robotic surgery.

INTRODUCTION

The arrival of surgical robotics at the turn of the millennium has ushered in a new era in minimally invasive surgery. From its humble beginnings, with the introduction of primitive robots like the PUMA, PROBOT and ROBODOC (which were in-fact industrial robots adapted for medical use) to the current state-of-the-art da Vinci Si surgical system, robotic surgery has come a long way. The reason behind the unprecedented explosion in the use of robotics lies in the inherent advantages of robotic surgery over conventional laparoscopic surgery which include superior ergonomics, enhanced magnification, 3D-vision, motion scaling, tremor filtering, enhanced dexterity, precision and control of operating instruments. From the patients' perspective this translates to smaller incisions, decreased blood loss, less pain, and quicker healing time and consequently reduction in hospital stay. Rapid dissemination of the technology and technique, together with aggressive marketing has captured the imagination of the doctors and patients alike. Robotic surgery allows the surgeon with no previous laparoscopic training to provide the patients with the advantages of minimal access surgery. For the laparoscopically trained surgeon it enables operating at a superior level with greater precision and accuracy.

Among the surgical fraternity, urologists were one of the earliest to truly realize the immense potential of robotic surgery. Robotic surgery has initiated a paradigm shift in the fundamental foundations of surgery. Robotic radical prostatectomy has now become a validated treatment option for localized prostate cancer. There are now more than 1000 robots in the United States alone and there has been an exponential rise in the utilization rates. As per unpublished data released by Intuitive surgical Inc., there were more than 55,000 radical prostatectomies performed by with da Vinci robotic assistance in the United States in 2007 and more than 70,000 performed worldwide in 2008. This translates to more than 70% of radical prostatectomies being performed with robotic assistance. The increasing popularity of robot-assisted surgery has caught up in Europe, Asia and Australia and has spread to other specialties like cardiothoracic surgery, gynecology, otorhinolaryngology, surgical oncology, gastro-intestinal and bariatric surgery and general surgery. In India, robotic surgery is still in its infancy. There are eight robots installed in India, of which five are in New Delhi, one in Chennai, one in Nadiad and another in Pune. The All India Institute of Medical Sciences has been at the forefront of the robotic revolution in India. The first robotic radical prostatectomy in India was performed in A.I.I.M.S. New Delhi in July 2006. Since then over 200 robot-assisted laparoscopic radical prostatectomies have been successfully carried out. The perioperative outcome of the first 190 cases has been analyzed (Dogra PN, Javali TD et al, Indian Journal of Urology, epub. ahead of print), which is comparable to most contemporary western series. Long-term follow-up results are now available and the excellent functional and oncological outcomes are noteworthy.

Other urological procedures that have been performed with robotic assistance include extirpative oncological surgeries like radical cystectomy, anterior pelvic exenteration, radical nephrectomy, adrenalectomy and ilio-inguinal lymph node dissection. Reconstructive surgeries like pyeloplasty, vesicovaginal and ureterovaginal fistulae repairs and stone surgeries like pyelolithotomy and ureterolithotomy.

Other specialties have now hopped on to the robotic bandwagon. Using the robotic system, gynecologists are now performing radical hysterectomies and myomectomies.

ENT surgeons are performing robot-assisted surgery in the nasopharynx and oro/hypopharynx for benign and malignant lesions to achieve better

functional results compared to traditional open surgery. Many types of gastrointestinal procedures are being performed with robotic assistance. These include colorectal surgeries, esophageal fundoplication, pancreaticoduodenal procedures and bariatric surgeries. In the cardiothoracic arena, totally endoscopic coronary artery bypass grafting, mitral valve repairs, lung resections, esophagectomy and thymectomy have become commonplace.

A major reason why robotic surgery in India has not progressed at a faster rate is the financial factor. Intuitive surgical controls the monopoly in marketing. The da Vinci system sells for about \$ 1.2 million. The new da Vinci HD SI released in April, 2009 currently sells for \$1.75 million. The annual maintenance costs along with the disposable supply cost (\$ 1500 per procedure) makes it beyond the reach of many institutions and health care systems. A robotic radical prostatectomy at A.I.I.M.S. costs around INR 1.3 lakhs per case, which is much lower than the market price of Rs. 3 lakhs. The only way to tackle this and to make robotic surgery financially feasible is for multidisciplinary utilization of the robotic system to its fullest potential. The maintenance costs remains the same whether one case or 6 cases are done in a day. So it is logical that if more cases were generated out of a robotic system, the cost per case would automatically decrease. Government support is also of paramount importance to help in dissemination of robotic technology so that it becomes available to the common man at a subsidized rate. The media also has an important role to play in spreading awareness among the public about this new technology. Similarly the primary care physicians need to be made aware so that they can refer the cases to the robotic centers.

Another way to reduce costs would be to develop indigenous surgical robots. With the possibility that Intuitive surgical may run out of its patency by 2011, this is a viable alternative. However developing as sophisticated a machine as the current da Vinci system seems to be a Herculean task at the moment, although the department of biomedical engineering at the Indian Institute of Technology have made some headway in the goal of developing our very own Indian prototype.

Another major drawback with the current Indian scenario is the lack of robotic surgery fellowships in India. As robotic technology has not entered the mainstream health care system there is a lack of access to the technology and a deficit in educational opportunities. Young Indian urologists wishing to specialize in robotic surgery need to go abroad to get trained in the nuances of robotic surgery. How many of these surgeons do actually come back after their training? So robotic surgery fellowships are the need of the hour at present if we wish to take robotic surgery to the next level in India. Another drawback is the lack of evidence-based evaluation of robotic surgery outcomes from the high volume centers in India. Critical evaluation of our results is necessary to understand our shortcomings and help in progress.

Much like the robots in popular culture, the future of robotics in surgery is limited only by imagination. Newer developments include the incorporation of the TilePro™ multi-image stereo viewer which enables simultaneous display of multiple video inputs in the surgeon console, integrating display of the patient's ultrasound, CT, and MRI images; incorporation of haptic feedback and wireless technology. Newer robotic surgical platforms like miniature robotics and flexible robotics are on the horizon.

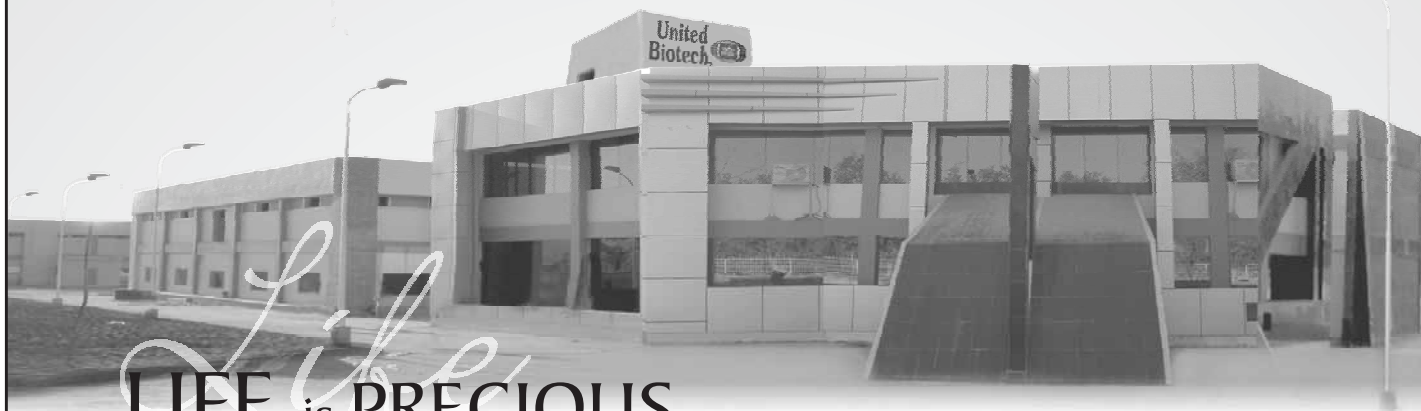
India now stands at the cusp of a robotic revolution. Robotic surgery in India is here to stay and it is up to us as minimally invasive surgeons across different specialties to lead the way and make maximum use of robotic surgery.

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Healthcare: From Good to Exceptional Governance

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Abstract: With respect to the health care dimensions of the public service, the capacity of a government to provide a good standard of health care is deemed one of the most important elements contributing to a country's standard of living. Universal access to health care, irrespective of one's ability to pay, is regarded as a basic human right in the developed world. Governance in a hospital setting concerns not only economic and financial dimensions, as there is a huge societal aspect associated with the provision of health care. In turn it could be argued that hospital governance takes a more institutional approach. As the concept of hospital governance has been broadened to include both financial and non-financial elements, its purpose is to enable a more integrated approach of supporting and supervising all hospital activities including clinical performance. Hospital governance is based on the two pillars of accountability and transparency. As the provision of health care is a 'social good' each group of stakeholders merit recognition of its interests. Resources are one of the most pressing issues in hospitals. Issues such as value for money, the reorganization of the health service and patient satisfaction has served to drive the governance process forward. These, in association with the accreditation process would appear to have put governance on the agenda of the health service and hospitals in particular.

INTRODUCTION

According to the Millennium Development Goals—access to basic health care is central to the poverty reduction worldwide. Hospitals constitute a very significant part of the overall health care sector and they provide essential services to the public. Hospitals and health systems across the country struggle with issues of governance, particularly when it comes to care standardization and quality improvement. Establishing clear channels of communication and clear lines of accountability for the numerous committees, departments, facilities and business functions of a healthcare enterprise has proven to be an ongoing challenge.

Efficient governance of hospitals requires the responsible and effective use of funds, professional management and competent governing structures. By establishing and maintaining the public's trust, being good stewards of the community's resources, and ensuring high quality care Hospital Administrators can be an important asset on the governing board in fulfilling those duties. Administrators add the perspective of the patient care process as well as a unique understanding of family issues; they grapple with overall health care concerns such as staff shortages, patient safety and quality of care; and they are the most knowledgeable about diseases and new treatment modalities, as well as being aware of the ethical dilemmas posed by new technologies.

As a result of multiple developments in health care and health care policy, hospital administrators, policy makers and researchers are increasingly challenged to reflect on the meaning of good hospital governance and how they can implement it in the hospital organisations. Due to the unique societal position of hospitals—which involves a large diversity of stakeholders—Corporate governance can provide for a comprehensive 'frame of reference', to which the hospital sector will have to give its own interpretation. The duty of Management is to: help formulate strategy; steward the expenditure of public money; ensure probity and transparency; and appoint, monitor and support top management. Good governance is crucial for effective public services and improved social outcomes.

HEALTHCARE GOVERNANCE

Governance is important work. How well it is done has significant consequences for health care organizations, the communities they serve, and their patients, medical staffs, and employees. A *technology* is a set of principles for solving problems and seizing opportunities.

Health care organization success depends on the quality of three of them: **Management technology:** Principles that help executives deploy an organization's resources in ways that accomplish goals; **Clinical technology:** Principles that help medical professionals promote health, prevent disease, and provide caring and curing services to patients; **Governance technology:**

Principles that help management effectively balance and represent the interests of stakeholders, to whom the organization belongs. Managerial and clinical technologies are far more developed and sophisticated than the technology of governing. Yet a lot is known about boards and how they can more efficiently and effectively solve problems and seize opportunities in ways that enhance an organization's success.

Charles Darwin observed that in challenging environments where resources are scarce, if an organism has even a tiny edge over others, this advantage is amplified over time. He noted, in *On the Origin of Species*, that a few grains of sand tip the balance, determining who thrives and who dies. Principle-based governance can tip a health care organization's balance toward success. Hospital Directors have to embody and express the values and ethos of the organisation and have the ability to strike the right note in a variety of situations. Nolan's principles of openness, honesty, probity and accountability are hard to improve. A hospital must have really strong clinical and corporate governance structures, led from the top but with universal reach and a performance, monitoring and reporting system that gives a comprehensive picture of clinical activity and performance. That way any adverse trends are picked up quickly and corrected.

The main obstacles to achieving good governance include unwillingness to accept challenge; tolerance of poor performance and failure to listen to what others tell you. Principles of 'good governance' could be applied to health care management to achieve excellence: knowing what governance is, achievement of strategic ends, unity of direction, unity of command, unity of accountability and responsibility, self-improvement and quality management and understanding the cost of governance.

HOSPITAL EFFICIENCY TASK FORCE

The principles of good corporate governance of hospitals include Effective and Efficient Board Structures and Processes, Long-range planning, financial oversight and Quality oversight. The importance of establishing a Strategic Plan comprising a mission and/or vision statement, a set of core values; a list of communities and health needs to be served; a description of programs and services to be offered; and plans for achieving program and service goals. The Strategic Plan and its components once adopted, management has a responsibility to develop an Operational Plan that translates into specific tactics and activities to be initiated in the next fiscal year.

BRICK BY BRICK: DELIVERING GOOD GOVERNANCE

Governance is essentially a reform package to strengthen the institutions of government and civil society with the objective of making government

more accountable, more open, transparent, more democratic and participatory. Good governance is also about effective and equitable government that promotes rule of law. Standards of Good Governance include participatory approach, sustainable, legitimate and acceptable to the people, transparent, promotes equity and equality, able to develop the resources and methods of governance, tolerates and accepts diverse perspectives, able to mobilize the resources for social purposes, strengthens indigenous mechanisms, operates by rule of law, efficient and effective in the use of resources, engenders and commands respect and trust, accountable, able to define and take ownership of national solutions, enabling and facilitative, regulatory rather than controlling, able to deal with temporal issues and service oriented.

In a healthy growth model of a free democratic society, the Government is just one of the participants. The Government exists as one of the servitors in the service of the society. Indeed the awareness that government alone can neither solve all the problems of the society nor it is the only crucial actor in addressing major societal issues has dictated the need to look beyond Government. Interdependence and need to find solutions to societal problems call for greater collaboration between the government and civil society.

MANAGEMENT OF SOCIAL CONFLICTS

No government, in the developing world, has the human and economic resources to overcome the poverty and inequality that are their legacies. If democracy and conflict free society is to be lasting, it is of the utmost importance that civil society should remain a strong component of everyday life. Governments need to build up partnerships with the private sector, NGOs, self-help groups, assistance agencies and the other organisations of civil society to define development needs and implement programmes.

During the twenty first century human survival may well depend on our ability to learn a new form of adaptation, one in which inter-group competition is largely replaced by mutual understanding and human cooperation. Curiously, a vital part of human experience – learning to live together – has been badly neglected. We have to learn to live together.

Corporate governance is the best-known form of governance and to date has focused primarily on private sector entities. More recently the governance phenomenon has spread to the public sector with particular attention being paid to resource allocation, expenditure programs and value for money. In turn, the governance processes of health care systems have also come under the spotlight. It is believed necessary to promote and ensure fairness, accountability and transparency within organizations. It has evolved continually over the years, has grown in sophistication and become more refined.

GOVERNANCE IN THE PUBLIC SECTOR

A key element of the public sector is that services are provided for the public good, suggesting that the public sector would have a higher sense of purpose in what they do than the private sector. Another difference lies in the fact that people who use public services may not be 'willing customers' as may be the case with health care. Moreover, consideration should also be given to the fact that the public sector is not concerned with economics alone. A strong societal aspect comes into play and as such many argue that governance frameworks need to be tailored accordingly to take into account the complexities of this sector.

Over the years some countries have embarked upon privatization programs in an effort to reduce the levels of expenditure on the various elements of the public sector (such as education) and improve its efficiency. Despite this attempt at 'downsizing' the public sector of a country is still perceived as hugely important and questions as to its associated costs and efficiency levels still come to the fore. There have been moves made to reform the

governance practices and procedures of the public sector in many countries.

GOVERNANCE IN HEALTH CARE

With respect to the health care dimensions of the public service, the capacity of a government to provide a good standard of health care is deemed one of the most important elements contributing to a country's standard of living. Universal access to health care, irrespective of one's ability to pay, is regarded as a basic human right in the developed world. Governance in a hospital setting concerns not only economic and financial dimensions, as there is a huge societal aspect associated with the provision of health care. In turn it could be argued that hospital governance takes a more institutional approach. As the concept of hospital governance has been broadened to include both financial and non-financial elements, its purpose is to enable a more integrated approach of supporting and supervising all hospital activities including clinical performance.

Indeed, the concept of hospital governance is relatively new. It is a shared process of top level organizational leadership, policy making and decision making of the Governing Body, CEO, senior management and clinical leaders...it's an interdependent partnership of leaders'. It is the process of steering the overall functioning and effective performance of a hospital by defining its mission, setting objectives and... having them realized at the operational level'. One of the key elements needed in order to achieve excellence in hospital governance is having a clear mission and an achievement-orientated culture in which to realise it. The key principles of governance in the development and implementation of governance models in hospitals include: knowledge of what governance is, achievement of goals, Executive Management Team relationships, unity in direction, unity of command, accountability, ownership needs, self-improvement and understanding governance costs. Clinical governance is regarded as a framework used to improve the quality of the health care service provided. Its introduction on a formalized basis means that hospitals now have to report on issues of quality whereas previously there had only been financial accountability. The concept of clinical governance tries to improve the quality of healthcare provided through integrating the financial, performance and clinical quality aspects of a hospital. The main aim of clinical governance is to accomplish continuous quality improvement in a health care setting and is designed to consolidate fragmented approaches to quality improvement. It promotes an integrated approach towards management of inputs, structures and processes to improve...clinical quality'. Four main dimensions include professional performance, resource allocation, risk management and patient satisfaction. Other elements include: Patient involvement in service delivery, Staffing and staff management, Continuous professional development, Clinical effectiveness, Education and training, Using available information and Clear lines of accountability and responsibility for clinical care. Clinical governance can be viewed as a mechanism to facilitate multi disciplinary teams all working toward the same goal – the continuous improvement of the quality of care. It is hoped that these cooperative working practices will have a positive influence on both the behaviour of medical professionals and in turn the delivery of care.

Hospital governance is based on the two pillars of accountability and transparency. As the provision of health care is a 'social good' each group of stakeholders merit recognition of its interests. Resources are one of the most pressing issues in hospitals. Issues such as value for money, the reorganization of the health service and patient satisfaction has served to drive the governance process forward. These, in association with the accreditation process would appear to have put governance on the agenda of the health service and hospitals in particular.

FROM GOOD TO EXCEPTIONAL GOVERNANCE

Providing better service; improving health care quality and patient safety; releasing information about the outcomes, costs and charges for care; securing public and stakeholder trust—these are just some of the demands on health care governing boards. There is increasing evidence that good governance at health care organizations is linked to better organizational performance. Accountability includes understanding traditional and emerging stakeholders and constituents and promoting transparency about the organization's performance. An important step while going the corporate way is changing the mindset of people. Leadership is very important here as it is necessary that the managers realise the significance of their mission and are focused towards the goal.

Though implementation of IT is still considered to be nascent in healthcare, as compared to other industries, hospitals are exploring IT to their maximum advantage. While adopting the corporate way of functioning, HR is in the forefront. This is where employees are scanned and are segregated as efficient and non-efficient. Here, hospitals are also required to find out multi-tasking employees, who can be trained further to shoulder more responsibilities and become leaders. Training the workforce is most important, so as not to waste the available manpower.

THE NEXT GENERATION OF SOLUTIONS IN MANAGING HEALTHCARE

As we enter the 'next generation' of needs in managing healthcare, our unified, focused efforts have never been more needed. The face of healthcare is constantly changing, with technological innovations, new treatments, new laws, and new types of organizations arising almost daily. In addition to negotiating the day-to-day demands of a busy and complex organization, healthcare delivery leaders must also be able to evaluate and understand the impact of alternative care delivery models. The traditional way of delivering care is no longer enough.

Healthcare services available these days deploy high technology to satisfy both internal and external customers by continuously improving various quality parameters. Quality improvement in healthcare services is a complex and multidimensional task. Although various quality management tools are routinely deployed for identifying quality issues in healthcare delivery, there is absence of an integrated approach, which can identify and analyze issues, provide solutions to resolve those issues and develop a project management framework to implement and evaluate those solutions.

There is a need to develop a web-based network, connecting all health care establishments, in both private and public sector. When fully functional, all health care transactions will be recorded electronically and this data will be available in the health data vault to authorized users when they need it and where they need it. The Knowledge Network with gigabit capabilities may provide the backbone and network infrastructure on which the Health Information Network may ride. All the district nodal data repositories will connect with a state level data bank, which in turn will connect with a central data bank.

There should be active involvement of private and public health entities to effectively address the creation of this network, portals, electronic health records, health data vault, security, privacy and other related issues in future. The ready availability of information will accrue enormous benefits to public health planning, medical education, cost control, medical research, drug development, prevention of fraud, disaster management and improved patient care.

Medical education needs to take full advantage of the power of ICT. A

well-structured health informatics curriculum needs to be made an integral part of medical education at all levels. Basic ICT facilities, such as good quality access to Internet and e-Journals, need to be made compulsory for all medical colleges in the country. For capacity building, ICT tools should be effectively deployed to train the large number of health workers.

MAKING THE HEALTH CARE DELIVERY SYSTEM ACCOUNTABLE

Accountability has become the fact of life for the health care delivery system. Appropriate measurement tools are needed to evaluate services, delivery, performance, customer satisfaction, and outcomes assessment. All employees bear responsibilities which necessitate assessment and analysis. Accountability will be accomplished when the health care industry implements quality and measurement concepts that yield the highest levels of validity and appropriateness for health care delivery. Performance measurement is fast becoming a way of life for health care providers in this age of increased accountability and outcomes reporting. A strategic plan and implementation of an effective performance measurement system will help to guide an organization to evaluate key processes and implement changes to improve patient care.

A NEW DESIGN FOR HEALTHCARE DELIVERY

There is ample evidence that better care could be provided to more people at lower cost if care delivery were organized in a more sophisticated fashion. Medical science has advanced dramatically. Pioneers have reduced rates of hospital-acquired infections, falls, medication errors, and other complications - symptoms of fragmentation - by 90 percent and more, saving thousands of lives and hundreds of millions of dollars. It requires leaders to get into the nitty-gritty of patient care, finding deficiencies in current approaches, confronting professional norms and habits that overvalue autonomy, tolerate unscientific variation in practice, and undervalue cooperative behaviors, and making continual improvements. But a strong link exists between the moral obligation of universal care and the hard work of redesigning and improving healthcare processes. The paradigm shift in health care delivery is occurring and will continue. Understandings gained from enactment and institutionalization theory can be used by managers to create the health care organization of the future. Administrators can create new environments or establish new organizational forms that will put their organization in a leading, rather than following, position.

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Concerns, Expectations and Satisfaction of Medical Tourists Attending Tertiary Care Hospitals in New Delhi, India

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Abstract: Delhi, the capital of India, has large number of hospitals providing medical services to people of neighboring states and abroad. On one hand it generates revenue to government and on the other hand big profit to private hospitals. This demands constant improvement of quality of care to remain competitive with other medical tourism destinations. Assessment of concerns, expectation and satisfaction level of medical tourists about their medical treatment is an important issue, although subjective, but one of the important methods to improve the quality of medical services. There is evidence which suggests that care, which is less than satisfactory to the patients, is also less effective and may reflect a failure to answer patients' needs, their expectations, or acceptable standard of service. From this study it is concluded that medical tourists were found to be satisfied with services provided in tertiary care hospitals of Delhi. Yet to address their overall concerns and issues, health sector needs to take some steps such as developing/strengthening facilities for follow up, in each country from where medical tourists were coming.

INTRODUCTION

Since ages people have been travelling to distant places for getting medical help. This was more common in a selected group of society. The upper social classes who sought spas, mineral baths, innovative therapies, and the fair climate, used to go for the Mediterranean as destinations to improve their health. In the early nineteenth century, when there were no restrictions on travel within Europe, people were travelling to the Swiss lakes, the Alps and special tuberculosis sanatoriums, where professional and often-specialized medical care was offered¹⁻².

Most recently, even the middle class started travelling from developed countries to those nations which have developed relatively better health care facilities, particularly to avoid treatment delays, prohibitive cost for life saving procedures, and high cost for elective surgeries.³ This is due to the fact that in last two decades globalization and advancement in technologies throughout the world including India brought many reforms in management of medical conditions. Technological advancement improved the quality but at a very high cost, which resulted in many fold increase in the cost of medical treatment throughout the world⁴⁻⁶. Whereas in comparison to the Western world the cost of these services was still lower in the developing countries. These countries could provide health services at cheaper rates because of availability of cheaper skilled professionals, resources and infrastructure⁷⁻⁹.

Asian countries like Thailand, Singapore, India, South Korea and Malaysia are attracting 1.3 million medical tourists per year from all over the world, and this number is further increasing annually. The estimated worth of medical tourism in Asia alone would be "at least \$4 billion" by 2012. India attracted an estimated 100,000 medical tourists in 2005¹⁰⁻¹¹. Confederation of Indian Industries (CII)-McKinsey report¹² states that the medical tourism market in India pegged a 30% growth in 2000. Medical tourism is likely to increase faster in the future as cost of medical care continues to increase. Delhi, the capital of India, has large number of hospitals providing medical services to people of neighboring states and abroad. On one hand it generates revenue to government and on the other hand big profit to private hospitals. This demands constant improvement of quality of care to remain competitive with other medical tourism destinations. Assessment of concerns, expectation and satisfaction level of medical tourists about their medical treatment is an important issue, although subjective, but one of the important methods to improve the quality of medical services. There is evidence which suggests that care, which is less than satisfactory to the patients, is also less effective and may reflect a failure to answer patients' needs, their expectations, or

acceptable standard of service¹³. Hence, the present study was undertaken to determine the expectation, concerns and satisfaction of medical tourists visiting Delhi for medical care.

MATERIAL AND METHODS

Research Design: The design of study was descriptive in nature.

Study Area: All tertiary Care private Hospitals of Modern system of Medicine located in Delhi those were registered with Directorate of Health Services, Government of National Capital Territory of Delhi.

Study Population: Medical Tourists of Allopathic tertiary care hospitals. Inclusion and Exclusion Criteria for Medical Tourists
Patients who had come from foreign countries primarily for treatment and were in recovery phase were included for interview.

Medical Tourists with the following criteria were excluded:

- who had come primarily as a tourist and during their stay in India, fell ill and thus sought medical care;
- who were living in India because of their Indian assignment or job or working in Embassies in India and fell ill; and
- who were seriously ill and could not provide reliable information or admitted in intensive care unit.

Period of Data Collection: The data was collected from the month of August 2008 to October 2008.

Sampling Procedure: Out of total 34 private tertiary-care hospitals, registered with Directorate of Health Services, Government of National Capital Territory of Delhi. A convenient sample of 14 hospitals was picked up by random selection. During survey of these 14 hospitals, only 8 hospitals were found to be providing health care services to medical tourists. Two hospitals out of eight didn't give permission to conduct this study in their hospitals. Hence present study was accomplished only in 6 hospitals. Among these 6 hospitals, 49 medical tourists qualified as per inclusion criteria. To collect the information from the medical tourist, a pre-tested interview schedule was used. Individual responses were recorded after obtaining a written consent from each medical tourist before starting the interview. In case of difficulty in getting information due to language problem help of interpreter, appointed by the concerned hospital or the attendant of the patient was taken. Out of 49 medical tourists, only 44 could be interviewed because 5 medical tourists didn't give their consent for interviews.

ANALYSIS

Collected data was analyzed using the software Statistical Package of Social Science (SPSS) version 16.0.

RESULTS

Forty-four among 49 medical tourists agreed to be the part of this study. Thus the response rate was 89.8%. Among the 44 medical tourists 26 (59.1%) were male and 18 (40.9%) were female. The average age was 45.3 years (± 13.7 SD) with the range between 18 years and 80 years. Of the total 44 medical tourists interviewed, 17 (38.6%) were from the SAARC countries, 12 (27.3%) were from African countries, 5 (11.4%) were from USA & Canada, 2 (4.5%) were from Gulf countries and 8 (18.2%) were from other countries that include Iraq, Dubai, Russia, and Myanmar. (Table 1) They were admitted to various in-patients departments of the selected hospitals i.e. Gastroenterology (25%), Urology (15.9%), Cardiology (13.6%), Orthopedics (11.4%), Gynecology (4.5%), Hematology (2.3%), Nephrology (2.3%), General Surgery (2.3%) and Ophthalmology (2.3%).

Table 1: Background characteristic of Medical tourists visited to New Delhi.

CHARACTERISTICS		N=44 (%)
Sex	Male	26 (59.1)
	Female	18 (40.9)
Age	Mean Year + SD)	45.3 (+13.7)
Country or Regions	SAARC	17 (38.6)
	Africa	12 (27.3)
	USA and Canada	5 (11.4)
	Gulf	2 (4.5)
	Others	8 (18.2)

EXPECTATION OF MEDICAL TOURISTS

All the 44 medical tourists had come with the expectation that they would be getting good quality of care. Majority of patients (90.9%) had expectation that they would be receiving good hospitality. This expectation was 100% among medical tourist from Africa, Gulf, USA and Canada, while this expectation was 87.5% and 82.4% respectively among medical tourists of other countries and SAARC regions. Out of 44 medical tourists, 72.7% expected skilled medical care. This expectation was high in medical tourists of SAARC (88.2%), USA & Canada (80%) but that was not a major concern for Gulf and Africa. Only 18.2% of medical tourists had expectations of less cost of treatment than their own countries. This expectation was high in medical tourists who had come from USA and Canada but not of Africa, SAARC, Gulf and Other countries (Table 2).

Table 2: Expectations of Medical Tourists

Expectations	Country/Region of medical tourists					Total N=44 (%)
	SAARC n=17 (%)	Africa n=12 (%)	Gulf n=2 (%)	USA & Canada N=5 (%)	Others N=8 (%)	
Good Quality of care	17 (100)	12 (100)	2 (100)	5 (100)	8 (100)	44 (100)
Good Hospitality	14 (82.4)	12 (100)	2 (100)	5 (100)	7 (87.5)	40 (90.9)
Skilled Care	15 (88.2)	7 (58.3)	0	4 (80)	6 (75)	32 (72.7)
Less Cost	1 (5.9)	1 (8.3)	0	4 (80)	2 (25)	8 (18.2)

CONCERNS OF MEDICAL TOURISTS

Out of 44 medical tourists who came to various hospitals for their treatments, 61.4% had concern of follow up of medical care after going back to their home countries, 27.3% were concerned about skills of doctors, 25% were concerned about their personal safety, 20.5% had concerns for the qualification of doctors and 11.4% had concerns about risk of post-operative infections. All medical tourists from Gulf Countries reported concern of follow up care

and 75% by African medical tourists. But it was not a concern from USA and Canada. Other concerns were not major for medical tourists in all the countries/regions. Overall 54.5% of medical tourists felt that they were legally protected. This is major area of concern because 45.5% of medical tourists were not feeling protected in case of any complication during or after treatment. One of the patients from USA stated that whether the hospital is having any standard operating protocol (Table 3).

Table 3: Concerns of Medical tourists

Concerns	Country/Region of medical tourists					
	SAARC n=17 (%)	Africa n=12 (%)	Gulf n=2 (%)	USA & Canada N=5 (%)	Others N=8 (%)	Total N=44 (%)
Follow up	1 (6.7)	9 (75)	2 (100)	0	5 (62.5)	27 (61.4)
Skill of Doctor	2 (11.8)	5 (41.7)	2 (100)	1 (20)	2 (25)	12 (27.3)
Personal Safety/Security	3 (17.6)	4 (33.3)	1 (50)	1 (20)	2 (25)	11 (25)
Qualification of Doctors	2 (11.8)	4 (33.3)	1 (50)	1 (20)	1 (12.5)	9 (20.5)
Infection during treatment	0	2 (16.7)	1 (50)	1 (20)	1 (12.5)	5 (11.4)
Post-op infection	Operated	1 (5.9)	1 (8.3)	1 (20)	1 (12.5)	5 (11.4)
	Not Operated	1 (5.9)	4 (33.3)	0	2 (40)	7 (15.9)
Behavior of Staff	2 (11.8)	2 (16.7)	0	2 (40)	0	5 (11.4)
HIV/AIDS risk	1 (5.9)	2 (16.7)	0	1 (20)	1 (12.5)	5 (11.4)
Behavior of Doctors	1 (5.9)	2 (16.7)	0	1 (20)	1 (12.5)	4 (9.1)
Infection during visit	0	1 (8.3)	0	1 (20)	1 (12.5)	3 (6.8)
Legal Safeguard	7 (41.2)	10 (83.3)	1 (50)	1 (20)	5 (62.5)	24 (54.5)
Standard Operating Procedure	0	0	0	1 (20)	0	1 (2.3)

Cost Concerns of Medical tourists: When the cost of treatment as compare to their own country was asked 68% of the medical tourists stated that it was in excess here. Only 15.9% of them stated that it was less than their own country and they were from USA/ Canada (100%), SAARC (5.9%) and other countries (12.5%). Cost estimates were given in advance in 34 (77.2%) out of the 44 medical tourists, but cost was more than estimated in 32.3% of the medical tourists and only 26.4% it was same as estimated. In rest of 41.1% of medical tourists the final payment of bill was less than estimated. This was found more with patients of USA/Canada (Table 4).

Table 4: Issues of Cost of treatment according to medical tourists

Cost	Country/Region of medical tourists					Total N=44 (%)
	SAARC n=17 (%)	Africa n=12 (%)	Gulf n=2 (%)	USA & Canada N=5 (%)	Others N=8 (%)	
Cost of treatment in comparison of their country						
Excessive	14 (82.3)	10 (83.4)	1 (50)	0	5 (62.5)	30 (68.2)
Same	2 (11.8)	1 (8.3)	0	0	1 (12.5)	4 (9.1)
Less	1 (5.9)	0	0	5 (100)	1 (12.5)	7 (15.9)
Don't know/ Paid by Govt	0	1 (8.3)	1 (50)	0	1 (12.5)	3 (6.8)
Was estimated cost in advance informed						
Yes	15 (88.2)	8 (66.7)	1 (50)	0	1 (12.5)	3 (6.8)
Final Cost in comparison to estimated						
More	5 (29.4)	4 (33.3)	0	1 (20)	1 (12.5)	11 (25.2)
Same	4 (23.5)	2 (16.7)	1 (50)	1 (20)	1 (12.5)	9 (20.4)
Less	6 (35.3)	2 (16.7)	0	3 (60)	3 (37.5)	14 (31.6)

PERCEPTION REGARDING THE QUALITY OF SERVICES

Reception services and Admission procedure: Reception services included provision of information at reception counter, courteousness of staff and promptness in service for any query were scored 4.27 ($SD \pm 1.04$), 4.16 ($SD \pm 1.05$), 4.18 ($SD \pm 1.14$) respectively that indicates very good to excellent grading for these services by the patients. Mean scores for admission procedures that included waiting time for admission and shifting to room were 3.95 ($SD \pm 1.25$) and 4.09 ($SD \pm 1.11$) respectively (Table 5).

Average time taken in admission procedure was 15 minutes with the range from 0 minute to 48 hours. When patients' responses were split according to time interval then it was found that

70.5% of the patients were admitted within 30 minutes time. Only in 2 cases the duration was more than 12 hours. Majority had given good and very

good scores except in some cases where grading was poor for time taken in admission (Table 5).

Waiting Time for Consultation: Waiting time for consultation was on an average of 10 minutes with wide range. In two cases they had to wait for more than 12 hours (Table 5).

Time spent during ward rounds: Time spent by consultant on each patient during the ward round was on an average of 7.5 minutes (Range from 2 minutes to 60 minutes) (Table 5).

Perception about medical service: A) Consultant: According to the average scores given by Medical Tourists the Communication skills of the treating consultant were excellent (4.45; SD±0.73). The consultant's visiting regularity for ward rounds had been rated as 4.39 (SD±0.86).

Similarly the means score for treatment satisfaction and behavior of consultant were 4.59 (SD±0.69) each (Table 5).

B) Resident Doctors: The resident doctors of the hospitals were scored for their regularity in visits, promptness of attending calls, their communication and attitude towards patients. The mean scores were 4.48 (SD±0.73), 4.50 (SD±0.73), and 4.45 (SD±0.73) respectively. All scores were graded excellent (Table 5).

Perception about Nurses: The nurses of the hospitals were scored for their promptness in attending calls, their behavior, punctuality in giving medicines to the patients and skills and efficiency in their work. The scores were as 4.34 (SD±0.80), 4.27 (SD±0.97), 4.34 (SD±0.91) and 4.39 (SD±0.81) respectively. The mean score value lie between very good and excellent. (Table 5).

Perception about rooms, toilets, electricity laundry and food Services: The cleanliness of rooms and toilets, electrical maintenance of room, interior of room and laundry services were graded as

4.36 (SD±0.81), 4.34 (SD±0.96), 4.23 (SD±0.98) and 4.45 (SD±0.79) respectively. Food quality was scored as 3.57 (SD±1.40) and timeliness of food services and food service etiquettes were graded as 4.14 (SD±0.90) and 4.25 (SD±0.84), however food taste was given less score of 2.89 (SD±1.55) indicates that quality based on taste was not rated high (Table 5).

OVERALL RATING OF THE HOSPITAL SERVICES BY MEDICAL TOURISTS

The scoring given by medical tourists for overall performance of hospital

Table 5: Perception of medical tourists about the quality of hospital services*

Perception about quality of services	Mean	SD	Range
Reception information services	4.27	1.042	1-5
Courteous Staff at reception	4.16	1.055	1-5
Promptness	4.18	1.147	1-5
Admission procedure waiting time	3.95	1.257	1-5
Shifting to room	3.95	1.257	1-5
Communication with Consultant	4.45	0.730	2-5
Visit regularity	4.39	0.868	2-5
Treatment Satisfaction	4.59	0.693	3-5
RD Visit regularity	4.48	0.731	3-5
RD Promptness	4.50	0.731	3-5
RD Communication & Attitude	4.55	0.730	2-5
NS Promptness in attn calls	4.27	0.973	1-5
NS Punctuality in giving medicine	4.34	0.914	1-5
NS Skill & Efficiency	4.39	0.813	2-5
NS Behavior	4.34	0.805	2-5
Room & Toilet Cleanliness	4.36	0.810	2-5
Room electrical maintenance	4.34	0.963	1-5
Interior of room	4.23	0.985	1-5
Laundry services	4.45	0.791	2-5
Food Taste	2.89	1.558	1-5
Food Quality	3.57	1.404	1-5
Food Service Timeliness	4.14	0.905	2-5
Service Etiquettes	4.25	0.839	3-5
Overall performance of hospital	4.48	0.698	3-5

*Source: "Satisfaction Levels of International Patients Seeking Medical Care From Tertiary Care Hospitals In New Delhi, India" International Medical Travel Journal, 2010.

was 4.48 (SD±0.69) on 5-point Likert's scale. The 4.48 score implies that overall performance of the hospitals were in between very good and excellent, indicates that they were quite satisfied with the performance.

SUGGESTIONS OF MEDICAL TOURISTS

Patients were requested to provide their suggestions to improve medical services in the hospitals.

Various suggestions given were: single window services, improvement in cleanliness and furnishing of rooms, English speaking ward boys and cleaning staff, provisions to expedite the visa process in the hospital itself, provision of transport facilities from the airport to hospital for picking and dropping the patients, advertisement about the hospital on website and photographs of inside of hospital a marketing office should be made available in their country so that more patients can be benefited from medical tourism.

DISCUSSION

India is one of the top destinations for medical tourists from all parts of the world including developed and developing nations. The present study was conducted in private tertiary care hospitals of Delhi and response rate of medical tourists was 89.7%. That can be considered very high response rate implying to high patient satisfaction according to an analysis of 210 studies where a high response rate was associated with high satisfaction levels of patients by Sitzia & Wood (1998).¹⁴ Findings of the current study indicated that majority of medical tourists expected good hospitality and skilled medical care but at a lesser cost. This expectation was high in patients from SAARC, USA & Canada but was not a major concern of patients coming from Gulf and Africa. That was because of their concern for good quality of medical care which was not available in their own country. These findings were similar to the views expressed in The Economist.¹⁵ This is well known fact that high quality of services are available in USA and Canada and major reason for patients from these countries coming to India is for availing quality treatment at lesser cost. In the present study small proportion of medical tourists expected less cost of treatment in comparison to their home countries. Incidentally number of such patients was more from USA and Canada. Similar to this finding many researchers had expressed that lesser cost is a motivating factor for patient's engagement in medical tourism.⁶

16-20

Except patients from USA and Canada, one of their major concerns (61.4%) particularly among patients from Gulf and Africa was their follow up after going back to their home countries according to the study. Similar concerns were also expressed by many reporters.²¹⁻²³ This was due to non-availability of specialists and liaison groups in their own countries. However, such facilities are available in USA and Canada. Patients were also concerned about skills of doctors and their qualifications, personal safety and risk of post-operative infections. Graves N et al (2008) had stated similar concerns of the patients particularly after undergoing surgeries.²⁴

Medical tourist's satisfaction for the services is an essential indicator of quality of health care delivery. Many factors of satisfactions such as reception services with courteous staff, promptness to attend any query, admission procedure, waiting time, nursing staff promptness to attend calls, interior of rooms and room electricity maintenance were graded excellent and very good. However, there is need of improvement in the food quality and food taste. The overall satisfaction level of the current study was consistent with the findings of medical tourism survey 2008 done in UK²⁵, revealed that the patients who traveled abroad for treatment were very much satisfied (74%) or quite satisfied (16%) and 96% of all respondents would recommend it to their friends or relatives.

CONCLUSION

From this study it is concluded that medical tourists were found to be satisfied with services provided in tertiary care hospitals of Delhi. Yet to address their

overall concerns and issues, health sector needs to take some steps such as developing/ strengthening facilities for follow up, in each country from where medical tourists were coming.

However, further research is needed not only to confirm or refute assumption regarding the areas such as legal safeguards, security, food, language etc. Compulsory accreditation of hospitals would improve overall quality of services and performance that can be further advertised and published through reputed national and International journals.

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Recent Advances and Future Trends in Obstetrics and Gynaecology

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Abstract: Medical science is ever evolving and Women's health issues have come a long way from when the patient was treated for only dire emergencies or end-stage disease to comprehensive counselling and treatment options for the whole range of related and definitive illnesses suffered spanning the prepubertal to the post menopausal age. Herein is an insight into emerging trends and advances in Obstetrics and Gynecology and their impact on improving healthcare.

Healthcare as we know it is becoming increasingly centralized and rural areas are being managed by trained midwives at various levels. Internationally a lot of focus and encouragement is being given in this view. In 2004 the SOGC Council put forward motions to encourage support for regulated Canadian midwifery programs, integration of midwifery practices into collaborative programs, optimal funding and appropriate privileges for registered midwives, and midwifery programs for Aboriginal midwives.¹

The concept of job- sharing has come to the fore where it has been considered that a physician with fewer working hours and less heavier clinical load can deliver better patient care. That is why we need to create and fill residency positions in the rural areas whilst equipping them along with adequately trained midwife staff, thus allowing a proper tier referral system and a systematic decongestion of tertiary healthcare centres. Newer horizons are unfurling and with time, Obstetrics & Gynecology can "choose a...practice ranging from primary ambulatory health care to...a focused area of specialization."²

Current clinical trends in obstetrics include:

- Increased genetic testing,
 - The prevalence of obesity in teenage and adult women
 - The steep rise in the number of caesarean deliveries,
 - The ongoing debate of vaginal birth after caesarean (VBAC) delivery, and
 - New light on causes of neonatal encephalopathy and cerebral palsy.
- Recent research on the causes of neonatal encephalopathy and cerebral palsy has found that "intrapartum hypoxia is uncommonly the sole cause of neonatal encephalopathy or cerebral palsy," according to an ACOG Task Force on Neonatal Encephalopathy and Cerebral Palsy, which published its findings in 2003. "Less than a quarter of infants with neonatal encephalopathy have evidence of hypoxia or ischemia at birth..." it stated. The Task Force set certain criteria, especially blood gas analysis, to accurately determine the timing hypoxia presented, like, close to the time of birth, during labor and delivery. Earlier, it was thought that such meconium stained liquor, non-reassuring fetal heart rate patterns, low Apgar scores, and neonatal encephalopathy were enough proof of birth asphyxia. But new evidence and more studies indicate that they are in fact "the sequelae of pathological processes established before labor." The Task Force's report says, "Criticism of the management of labor should not be confused with cerebral palsy causation because the two often may not be linked."³ This ACOG Task Force's findings have had a major impact on obstetrics litigation. These cases can now often be defended on the issue of causation.

INAPPROPRIATE TERMINOLOGY

An ACOG Committee Opinion issued in December 2005 expressed concern about ongoing use of the terms "fetal distress" and "birth

asphyxia," recommending abolition of the term "birth asphyxia" as a nonspecific diagnosis and replacing "fetal distress" with the term "non-reassuring fetal status."⁴

APGAR SCORES: NOT PREDICTIVE

Apgar scores have been used since the 1950s to describe the condition of neonates. ACOG advocates that its use be restricted to the labour & delivery room and not beyond as an indication or report of an acute intrapartum hypoxic event. Low Apgar scores at one and five minutes neither indicate hypoxia nor predict long-term neurologic outcomes.⁵

LIMITATIONS OF ELECTRONIC FETAL MONITORING

EFM has its limitations. An ACOG Practice Bulletin issued in December 2005 reviewed some of these limitations:

- The false positive rate of EFM for predicting adverse outcomes is high.
- The use of EFM is associated with an increase in the rate of operative deliveries (vacuum, forceps, and caesarean section)
- The use of EFM does not result in a reduction of cerebral palsy case rates. This same bulletin sets forth the guidelines for the frequency of reviewing EFM tracings and their retention as part of the medical record.⁶

THE 30-MINUTE INTERVAL GUIDELINE

In 1989, ACOG's Committee on Professional Standards first established "that hospitals with obstetric services should have the capability to begin a cesarean delivery within 30 minutes of the time that the decision is made to perform the procedure."

The Guidelines for Perinatal Care, published jointly by the American Academy of Pediatrics and ACOG, follows that same guideline. Research indicates a lack of evidence for improved maternal and infant outcomes even when this guideline is followed. Nevertheless, this 30-minute interval has become a medico-legal point when cesarean section is required. Bloom *et al* studied maternal and infant outcomes and found that a cesarean delivery with this 30 minutes interval guideline does not prevent all poor infant outcomes and "by no means guarantees infant safety."⁷ This is consistent with the findings of previous studies that a delay in cesarean delivery exceeding 30 minutes did not necessarily compromise infant outcomes.

HIGH RISK OBSTETRICS: THE FUTURE

There is no other physician practice area that can speak of a more volatile and unpredictable high risk environment like obstetrics. Fortunately nowadays the concept and implementation of simulation training has come to the fore to help us manage difficult and

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emergency situations- “hope for the best but be prepared for the worst”. Patient safety now has a higher profile in obstetrics as reflected in journal articles of recent years. However a need for more research is felt to promote better management to optimize more favourable patient outcomes.

Investments in obstetric patient safety maximize their return by preventing high-severity claims. Some patient safety approaches that hold promise include:

- 1.) Obstetrics Rapid Response Teams⁸
- 2.) Medical emergency preparedness strategies, such as training, stocking appropriate supplies, early warning systems, and specialized first responders⁹
- 3.) Team training using crew resource management techniques borrowed from the military and the airline industry¹⁰
- 4.) Commercially available clinical informatics systems that promote patient safety at the patient’s bedside and in real time
- 5.) Health care professionals to determine which format (send staff to a simulation center, develop in-house simulation program, develop a consortium of hospitals that run a simulation program, or use a mobile simulation program) is best for them.

In situ simulation is an effective way to develop new skills, to maintain infrequently used clinical skills even among experienced clinical teams, and to uncover and address latent safety threats in the clinical setting.¹¹ High-fidelity simulators have been developed to educate residents in anaesthesiology. Simulation settings that mimic real life crisis situations in obstetric anaesthesia have been created by coupling mannequin with computer. These modalities of training and teaching are highly effective because the risk is zero and any mistakes made are on a mannequin.¹²

EFFECTIVE ANAESTHESIA FOR OBSTETRIC PATIENTS

In various centres all throughout the world, spinal and epidural are now being favoured as the better mode of anaesthesia for delivery by caesarean section. But both are not without their negative aspects- spinal can cause profound hypotension and epidural needs careful monitoring of the patient with frequent top ups. The introduction of combined spinal-epidural anaesthesia (CSEA) offers benefits of both techniques. CSEA also offers the prospect of reducing the anaesthetic failure rate of either technique used alone.¹³

STEM CELL THERAPY AND CORD BLOOD BANKING

Stem Cell technology has taken the world by storm. The potential benefits are innumerable and newer uses are coming on over the horizon. It has already shown promise in treating over 75 diseases like the following:

- Cardiac repair
- Treatment of type II Diabetes Mellitus
- Treatment of neurological injury like- brain injury, Alzheimer’s Disease, Huntington’s Disease, Amyotrophic Lateral Sclerosis, to name a few.
- Malignancies
- Regenerative medicine- of the joint, tissue or organ
- Gene Therapy.
- Patient awareness campaigns are underway and baby’s cord blood is need to harvest these stem cells a relatively easy means of cell procurement.

Stem cell therapy will be a cornucopia of benefits to humanity, virtually unlimited in its future potential. That future begins now.¹⁴

GYNAECOLOGY

Today, gynaecological disease directly affects the quality of life of women in different ways and in varying degrees, highlighting the value and importance of patient assessed health status measures to evaluate the subjective severity and treatment efficacy of common gynaecological conditions.^{15,16} Minimally invasive surgery like laparoscopy and hysteroscopy, interventional radiographic therapy like embolization therapy, medical treatment and expectant management are replacing major gynaecological surgery for many common gynaecological complaints. For example, ectopic pregnancy is being diagnosed earlier by the use of transvaginal ultrasonography and serial quantitative measurements of human chorionic gonadotrophin concentrations. Thus women can be treated either medically as outpatients with methotrexate injections^{17,18} or by laparoscopic surgery, reducing stay in hospital and preserving tubal function in many cases^{18,19,20}.

TREATMENT OF MENORRHAGIA

A women’s lifetime risk of hysterectomy is around 20%. These days, antifibrinolytics and cyclical progestins have played a significant role in reducing the number of hysterectomies done and improving quality of life. Newer trends point to ablative therapies coming to the fore as a better treatment option.^{21,22,23,24} Several techniques are available, and despite initial concerns about safety a recent survey of more than 10 000 operations (MISTLETOE; minimally invasive surgical techniques, laser, endothermal or endoresection) showed that the techniques are safe even in inexperienced hands.²⁵ Although randomised trials have shown ablative surgery to be more effective than medical management,²⁴ the technique is invasive, requires general anaesthesia, is not without complications, and has reduced long term efficacy in women under 45 years of age.^{26,27} Recently introduced balloon devices for ablative treatment may prove to be equally efficacious, simpler, and even safer to use than ablative surgery, although further evaluation is awaited.²⁸

The **Novasure System** is the latest generation of devices that treat the entire inside of the uterus (*endometrial cavity*) at once. The procedure does not require any incisions, and does not require hospitalization. A slender device is inserted through the cervix under local anaesthesia with sedation, or general anaesthesia. Once it is in place, treatment time averages 90 seconds. Most women can resume most of their normal activities in a day or two. A major advantage of Novasure is that hormonal pre-treatment is not needed, and it can be done at any time of the cycle.

Recent randomised controlled studies showed that the efficacy of the levonorgestrel intrauterine system is comparable to that of invasive endometrial ablation²⁸ and that reduction of menstrual loss is significant in most cases.^{29,32} Studies have also shown that between 64% and 80% of women awaiting hysterectomy cancel their surgery after a 6 month trial of the device.^{29,30} The many other potential uses for the device include endometrial protection in hormone replacement therapy, the reduction of climacteric symptoms, and possibly an alternative to sterilisation in women with menorrhagia, although these uses are incompletely evaluated at present. Recent evidence has shown that the levonorgestrel intrauterine system may also reduce the risks of pelvic infection.^{29,30}

TREATMENT OF FIBROIDS

Bilateral embolisation of uterine arteries

The latest in the treatment of large symptomatic fibroids is embolisation of the uterine arteries, but it is being done in only some centres as it is still in the

evaluation phase. results have so far been promising It has been shown that embolisation of the uterine arteries with polyvinyl alcohol particles introduced transfemorally by catheter can significantly reduce the size of large fibroids (60%-65%) and produce significant symptomatic improvement or complete resolution of symptoms³³ The technique is generally well tolerated and requires only a brief admission to hospital for analgesia, although short term side effects such as pyrexia, profuse discharge, and the passage of small or large fibroids through the vagina are common. The treatment is new, and the long term safety and efficacy of fibroid shrinkage are still unknown. Significant morbidity and even mortality as a consequence of infection have resulted from embolisation of the uterine arteries, and it must therefore be considered a new treatment under evaluation until further results are available from large randomised studies. Although pregnancy has been recorded after treatment,^{34,35} embolisation of the uterine arteries is not recommended for nulliparous women until more data on fertility are available However, it may be a useful alternative for difficult or dangerous surgery, for those who decline blood transfusion, or for those who refuse surgery.

ROBOTIC MYOMECTOMY

This is an upcoming trend in the surgical management of fibroids of the uterus. An example of one such is the one done with the Da Vinci Surgical Robot. The surgeon sits at a console and looks through a 3-dimensional video camera. The hand movements in the surgeon are duplicated in the patient by the robot. Most importantly, the instruments duplicate the wrist movements of the surgeon, allowing the instruments to change angles to allow precise suturing..

HORMONE REPLACEMENT THERAPY (HRT)

HRT that can be sprayed into the nose could be the answer for women who have trouble with traditional forms of treatment. The estrogen nasal spray has been hailed the biggest breakthrough since hormone replacement therapy patches were invented 20 years ago. Research shows it is just as effective as other types of HRT but has fewer side effects. A single squirt into each nostril maintains a constant level of oestrogen in the bloodstream, which is effective for 24 hours.³⁶

IN CONTRACEPTION

ESSURE has been proven to be the most effective sterilization procedure commercially available to date.³⁷ Its motivating point is that no incision is needed and it is a relatively comfortable procedure with good results, compared to the other implants used earlier (ADIANA) which had a higher failure rate

Minor procedure units for gynaecology, with one stop investigation and treatment (including ultrasonography and hysteroscopy), and early pregnancy assessment units, where bleeding in early pregnancy can be dealt with rapidly and sympathetically, are becoming more commonplace. The prolonged life expectancy of menopausal women and their higher expectations for health have encouraged new developments in hormone replacement therapy. The increased use of such therapy has also increased surveillance and thus recognition of other common problems affecting older women. Delaying childbearing has resulted in a greater demand for effective fertility treatments and for surgical procedures that preserve fertility.

CONCLUSION

Medical Science is an dynamic cornucopia of latest and more innovative developments and improvements of current techniques and therapies. With better patient awareness and an environment of unrelenting litigation we have found ourselves strenuously trying to balance sound judgement on the part of the physician and well informed consent for

related treatment plans for the patient. So, the final word lies in the fact that ultimately the most effective way to improve healthcare is to make it more collaborative.

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Treatment Outcome with Weekly Cisplatin Concurrent with Radiation Therapy in Locally Advanced Head and Neck Squamous Cell Carcinoma.

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Abstract: This study was undertaken to investigate the feasibility of concurrent monochemotherapy with conventionally fractionated external beam radiotherapy and to assess its local response and acute toxicity patterns in patients with advanced locoregional head and neck squamous cell carcinoma (HNSCC). Between September 2005 and September 2007, a study involving 45 patients with stage III and IVA (AJCC-6th) HNSCC who met the eligibility criteria was undertaken. All 45 patients (median age 45 years) were given Cisplatin 40 mg/m² weekly before radiotherapy on every Monday. Patients received radiotherapy (66-70 Grays) to the locoregional sites on Cobalt-60 unit. **Results:** All the 45 patients who received concurrent chemoradiation were available for analysis. The locoregional response rates were as follows: an overall response rate of 88.8% (40 patients), complete response rate of 57.7% (26 patients), partial response rate of 31.1% (14 patients) and stable disease in 11% (5 patients). Only 2 (4.4%) patients were reported dead at the time of evaluation. The survived patients enjoyed good quality of life. **Conclusion:** Patients responded better with concurrent chemoradiotherapy with benefit in terms of survival and good organ preservation along with acceptable and manageable occurrence of schedule and dose related adverse effects.

Keywords: concurrent chemoradiotherapy; inoperable head and neck cancer

INTRODUCTION

Head and neck cancer comprises a huge burden of disease worldwide. It is the fifth most common malignancy globally among adults¹. It comprises 5% of all malignancies worldwide². More than 500,000 new cases are projected annually, globally³.

Loco regionally advanced stage III or IV cancers comprise $\geq 60\%$ of these tumors for which cure rates have been $< 30\%$, with notably high morbidity for surgical as well non-surgical treatment and therefore prognosis has remained poor in this group of patients and this has remained unchanged over the past 30 years.

The treatment of patients with locally advanced unresectable head and neck cancer remains a challenge with poor locoregional tumor control and limited survival when surgery, radiotherapy or both are used. Although radiation and surgery have been the standard of care, the addition of chemotherapy has demonstrated superior locoregional tumor control while showing promise to improve patient survival. In patients with advanced inoperable or unresectable disease, Paccagnella et al demonstrated improved survival after treatment with induction chemotherapy and definitive radiotherapy compared with controls treated with radiation alone. Concurrent chemoradiation has been investigated to take advantage of the radiosensitive capability of many drugs for patients with head and neck cancers to attain an increase in the locoregional control, which would translate into increased survival. The mechanism for enhanced cell kill with concurrent chemoradiation is due to interference with repair process after sub lethal and potentially lethal damage caused by drugs and tumor cell synchronization may also prevent or decrease the emergence of resistant clonogenes⁴.

There are many drugs, which have been investigated as radiosensitising agents such as bleomycin, methotrexate, mitomycin, 5-fluorouracil, cisplatin and paclitaxel. Cisplatin is one of the favored drugs because of its proved radiosensitising effect and its different toxicity profile. This drug has been most extensively studied in the management of HNSCC which can be used alone or in combined with variety of other drugs and has shown improved overall response rate ranging from 23% to 71% with a cumulative rate of 28%. This study was conducted to assess the role of concurrent cisplatin with conventional external beam radiotherapy in patients with locally advanced inoperable head and neck cancers. The objective of this study was to evaluate the response rate, locoregional control, disease free survival and

overall survival in previously untreated, inoperable head and neck cancer patients. The Institute ethical committee reviewed the study design and allowed to carry out the study.

METHODS

From September 2005 to September 2007, 45 patients of locally advanced head and neck cancer attending the department of Radiotherapy, Sher-i-Kashmir Institute of Medical Sciences, Srinagar were included in a prospective non-randomized trial of concurrent chemoradiotherapy. The inclusion criteria were as follows:

- Histopathologically confirmed squamous cell carcinoma of head and neck.
- Only locally advanced tumors (stage III and stage IV-A : Staging by AJCC) only.
- Patients not exposed to surgery, chemotherapy and radiotherapy for current disease.
- Performance status < 2 (ECOG) with any age group.
- No associated co-morbidity with contraindication to chemotherapy.
- Normal renal and liver function.
- Normal Hemogram.
- Written informed consent.

Patient characteristics are shown in table1. Site and size of primary disease was assessed by inspection, direct and indirect laryngoscopy, and by other appropriate studies if required e.g. CAT scan. Clinically lymph node status was assessed and TNM staging was done as per UICC criteria. Complete blood profile, blood urea, serum creatinine was done before each course of chemotherapy.

Table 1: Epidemiological characteristics of all patients

Characteristic	No. of patients	Percentage
Age		
10-20	1	2.2%
21-30	5	11.1%
31-40	5	11.1%
41-50	8	17.7%
51-60	12	26.6%
61-70	11	24.4%
71-80	2	4.4%
81-90	1	2.2%

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	Sex	
Male	35	77.7%
Female	10	22.2%
	Addiction	
Smoke	31	68.8%
Smoke + Other (Alcohol+Snuff+Ganja+Tobacco)	7	15.5%
No Addiction	7	15.5%
	Primary Site	
Larynx	19	42.2%
Hypopharynx	7	15.5%
Nasopharynx	4	8.8%
Oropharynx	7	15.5%
Oral Cavity	8	17.7%
	Stage	
III	20	44.4%
IV-A	25	55.5%

TREATMENT DESIGN

Treatment schedule was designed to optimize clinical efficacy and minimize the occurrence of schedule and dose related adverse events in patients. After proper evaluation, all patients received concurrent Cisplatin 40 mg/m² on the first day of every week before radiotherapy, which extended for four weeks in the initial treatment followed by two more weeks of treatment with supplementary radiation. Cisplatin was given by intravenous infusion in normal saline after proper hydration. Patients received potassium chloride, magnesium sulfate and mannitol infusion.

All patients received external beam radiation therapy on a telecobalt60 unit (Theratron 780E), five fractions a week for four weeks to the local site including neck nodes to a total dose of 45 Grays in the initial treatment. This was followed by supplementary radiation therapy of 25 Grays in ten fractions with reduced portals taking the total dose of radiation to 70 Grays excluding spinal cord and other structures wherever necessary.

EVALUATION AND FOLLOW UP

Before each course of concurrent chemotherapy, patients were evaluated and during treatment they were seen weekly by radiation oncologist for normal tissue reaction and tumor response. Routine investigations were performed and if required supportive treatment was given. As per RTOG toxicity criteria, adverse reactions were documented.

Patients were examined at the time of completion of radiotherapy, 6 weeks after completion of treatment and 3 monthly thereafter by radiation oncologist and by otorhinolaryngologist.

RESPONSE

If there was complete disappearance of all viable and palpable tumor without evidence of distant metastasis after completion of concurrent chemoradiotherapy these were considered as having complete response (CR) and where there was >50% regression of the longest perpendicular dimensions of the lesion or nodes, they were grouped under partial response (PR). Rest were considered as having stable disease (SD) or progression of disease (PD).

RESULTS

Tumor response to treatment was recorded in all 45 patients. This included a complete response in 26 patients (57.7%) and partial response in 14 (31.1%) and in 5 (11.1%) the disease remained stable. Among the 26

patients in whom complete response was achieved, recurrence was observed in 4 (15.3%). In two patients failure occurred at the locoregional area and in the other two distant metastasis was observed. These recurrences were observed within a mean follow up of 8 months from the time of local control. With respect to the site, the best response rate was achieved in hypopharyngeal tumors with a complete response rate of 71.4% followed by larynx (63.1%). Table 2 shows the response distribution in each subgroup of patients.

Table 2: Response rates in each subgroup of patients

Site	Patient No.	PR	CR	SD	OR
Larynx	19	6 (31.5%)	12 (63.1%)	1 (5.2%)	18 (94.7%)
Hypopharynx	7	1 (14.2%)	5 (71.4%)	1 (14.2%)	16 (85.7%)
Nasopharynx	4	2 (50%)	2 (50%)	0 (0%)	4 (100%)
Oropharynx	7	1 (14.2%)	4 (57.1%)	2 (28.5%)	5 (71.4%)
Oral Cavity	8	4 (50%)	3 (37.5%)	1 (12%)	7 (87.5%)
Total	45	14 (31.1%)	26 (57.7%)	5 (11.1%)	40 (88.8%)

At one year follow up, only 2 (4.4%) patients were reported dead. Survival was assessed (Table 3) with respect to the gender, age, site of primary tumor, stage, performance score of the patient, T, N and overall stage of the tumor and histopathological differentiation. No significant impact of T, N stage was observed as far as survival of the patients is concerned.

Table 3: Survival relative to patient characteristics

Patient Characteristic	Median survival in months (Kaplan Meier)	Result
Gender	Male	13
	Female	14
Performance Score	0	17
	1	14
	2	11
Age	≤45	15
	>45	12
Site	Larynx	13
	Hypopharynx	11
	Nasopharynx	14
	Oropharynx	14
T Stage	Oral Cavity	8
	1	17
	2	11
	3	15
N Stage	4	12
	0	14
	1	10
	2	14
Overall Stage	3	14
	III	13
	IV	14
HPE Differentiation	WD	11
	MD	15
	PD	14
	UD	17

ACUTE TOXICITY

Patients were assessed as per the Radiation Therapy Oncology Group (RTOG) toxicity criteria. Overall, the treatment was well tolerated by majority of patients. Vomiting occurred in 30% of patients, 14 (31%) patients were reported to have some degree of hematological toxicity and out of these 13 (93%) patients developed mild grade 1 or 2 leucopenia; out of all 45 patients only 1 (2.2%) developed severe toxicity, in the form of grade 3 thrombocytopenia. With a dose of 40 mg/m², no significant renal toxicity was observed in our study. Mucositis was observed in 42 (93%) patients in total. Chronic grade 1 and 2 xerostomia was observed in 28 (62%) of patients. Only 2 (4.4%) patients were reported dead in our study.

DISCUSSION

In developing countries like India, more than 60% of head and neck squamous cell cancers present with advanced disease and carry a poor prognosis which has remained unchanged over the past 30 years. When presenting disease is either inoperable or patients refuse surgical management, role of radiotherapy is limited and remain a challenging problem for the radiation oncologist. With primary radiotherapy given in maximum tolerable doses, locoregional recurrence remains the major pattern of treatment failure. Whether improvement in locoregional control will ultimately be translated to increase survival or not, is a matter of considerable debate⁵.

In patients who have locally advanced and inoperable cancer of the head and neck, the achievement of initial local control (complete response) of the disease with initial definitive treatment with radiotherapy with or without chemotherapy, is an important prognostic factor for overall survival. Complete response was found to be 69% in patients who had received cisplatin 100 mg/m² three weekly concurrently with definitive radiotherapy and the authors of the study concluded that the combination of cisplatin and radiotherapy is an effective and safe treatment in patients with advanced head and neck cancer⁶.

Laboratory data points towards increased radiation sensitivity, particularly under hypoxic conditions when cisplatin is used⁷. Cisplatin has been found to be inhibitive to the repair of sublethal damage.

In our study, where 44.4% of the patients had stage III and 55.5% had stage IV locally advanced cancer, the clinical response was very encouraging. Complete response was achieved in 57.7% of patients with an overall response rate of 88.8% when all the subsites of the head and neck cancer patients were combined. Highest combined response rate was seen in hypopharyngeal cancers where 71.4% achieved such response, lowest response rate was seen in oral cavity group where only 37.5% achieved complete response but overall response rate was 87.5%. Of the 4 patients of nasopharyngeal cancer 2 had complete response and the remaining 2 had partial response (overall response 100%). These two patients were treated with 6 cycles of combination chemotherapy of cisplatin plus 5-fluorouracil to take the complete response to 75%. Among the patients with laryngeal carcinoma, overall response rate was high (94.7%), whereas 63.1% achieved complete response. The patients with partial response were offered surgery but only one patient could be salvaged with such treatment.

Though the use of concurrent chemoradiation in head and neck cancer improves the local control of the tumor but at the cost of markedly increased toxicity due to combined radiotherapy and chemotherapy. Taylor et al⁸ used cisplatin 60 mg/m² and 5-fluorouracil 800 mg/m² in 14-day cycles with conventional radiotherapy. They demonstrated an improved freedom from recurrence in patients treated with chemoradiotherapy compared to induction

chemotherapy. There was, however, an increase in mucositis requiring supportive care in the concurrent group.

A recently completed intergroup study randomized patients with unresectable squamous cell cancers of the head and neck to radiotherapy alone, radiotherapy plus bolus cisplatin, or split course radiotherapy with first and third cycles of cisplatin and 5-fluorouracil. The 2 and 3 year actuarial survival rates were 23% for radiotherapy alone, 35% for radiotherapy plus cisplatin (P=0.016), and 27% for split course radiation plus cisplatin and 5-fluorouracil (P=0.13)⁹. At the time of evaluation of our study, 43 out of 45 (95%) patients were alive with a median survival of 14 months. T and N stage did not significantly affect the survival but it is presumed that appropriate survival analysis is undeserved owing to the early evaluation of results. However, the two patients who died had higher T and N stage.

The use of cisplatin weekly as an outpatient treatment is an extremely attractive schedule from the standpoint of delivery, tolerance, compliance and cost-effectiveness. The radiosensitive effects of cisplatin are evident from both the increase in toxicity as well as complete responses. Mucositis was the predominant toxicity occurring in majority of patients and requiring interruptions in radiotherapy and chemotherapy dose modifications. Concurrent chemoradiotherapy has been proved effective in the management of HNSCC because survived patients offered a good quality of life without any significant financial or cosmetic deficit.

CONCLUSION

Treatment of patients with advanced inoperable head and neck cancers with concurrent weekly cisplatin and conventional external beam radiotherapy is feasible. Mucositis was the most predominant and commonly seen toxicity. While survival data are too early to evaluate, the overall response rate and the high frequency of complete response rates are encouraging.

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The present issue marks the 25th year of publication of the Journal International Medical Sciences Academy. It is a matter of pride for all fellows/members that Journal Selection Committee (constituted by ICMR), in its meeting held on August 3, 2011, has approved the indexing of JIMSA in IndMED, the best known Indian Medical Database <http://indmed.nic.in>. The Journal will host full text of the articles at MedIND <http://medind.nic.in> and the readers will have access to the full text of articles from January-March 2003 onwards. These articles will be linked for IndMED to JIMSA website.

I wish to express my gratitude for the help and guidance received from the Members of Board of Trustees and the Central Executive Committee members, of International Medical Sciences Academy, World Headquarters, New Delhi. I am also grateful for the valuable cooperation extended by the members of JIMSA Editorial and Advisory Boards; and also the peer reviewers, for their consistent and continuous effort and support to maintain a high standard of quality of the articles published in the journal.

Friends, this is an important milestone in the history of our journal; this will broaden accessibility to all published articles. The journal should now attract original articles of even better quality. We should enforce rigorous peer review of the submitted articles and also on time publication of the issue, every quarter.

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Professional Nursing: Trends and Adjustments

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Abstract: The second half of the twentieth century has witnessed phenomenal changes in the health care systems of almost all the countries. The three broad movements, each having a pre-eminent concern and currently seeking to change the world of medicine, are the proponents of evidence-based medicine are mainly concerned with ensuring that strategies of proven clinical effectiveness are adopted, the health economists are mainly concerned with establishing that cost-effectiveness and not clinical effectiveness is the criterion used in determining option selection; and a variety of patient support and public interest groups are mainly concerned with ensuring that patient and public preferences drive clinical and policy decisions. Rapid change in the nursing and health care delivery environment has created an irresolvable dilemma for the nursing services. These changes include a major reconfiguration of the health care delivery system, unprecedented technological advances, and enormous changes in the expectations of the health care consumer. Enormous advances in the use of technology have been incorporated into the delivery of health care services. With acceptance of the World Wide Web, many health care organizations implemented mechanisms for using this technology to enhance access to health care services and to provide more efficient care to those whose access to the traditional system is limited by distance and other factors.

INTRODUCTION

Nursing is a caring profession. Caring encompasses empathy for and connection with people. Teaching and role-modeling caring is a nursing curriculum challenge. Caring is best demonstrated by a nurse's ability to embody the five core values of professional nursing. Core nursing values essential to baccalaureate education include human dignity, integrity, autonomy, altruism, and social justice. The caring professional nurse integrates these values in clinical practice. Strategies for integrating and teaching core values are outlined and outcomes of value-based nursing education are described. Carefully integrated values education ensures that the legacy of caring behavior embodied by nurses is strengthened for the future nursing workforce.

Nursing has long been described as an art and a science. Nurses represent the major personnel expense in any hospital and are the most directly responsible for using supplies for patients. The nurse assumes the major role in determining and implementing acceptable standards of clinical nursing practice, management, research and education. The nurse, in providing care, ensures that use of technology and scientific advances are compatible with the safety, dignity and rights of people.

The identified key issues are education, scope of practice, specialty practice, reimbursement, titling, prescriptive authority, legal status, regulation, and credentialing issues. And, indeed these issues are still importance to the practice of advanced practice nurses. Even though most of the hard work was done to promote the path to independency and uniformity for advanced practice nursing, but several issues remain to be solved especially in the areas of credentialing and regulation. Many nursing organization is working aggressively to put a new regulatory model in place to promote a system of mutual regulatory recognition. The field in advanced practice nursing is evolving and changing rapidly, especially in the areas of advanced practice nursing specialties. As a result of this complex change, policymakers and regulators face many challenges and obstacles to ensure development of broad-based practice standards. At the same time this challenge also presents many new opportunities for advancing practice nursing; thus APNs continue to prove themselves as safe and cost-effective providers to the members of society and to move forward to a better professional future.

At present, consumers are more informed about health care services, given the ease of access to information using the electronic media. Therefore, consumers expect the most current treatment regardless of expense or geographic location of the service. The health care sector is feeling the impact of rising consumer demand for services. This is a result of, among other factors, an ageing population, and it is struggling to provide services in an environment that was not designed to meet the current demands and the

many changes that have occurred within the industry.

There has been unrelenting change within the health care system over the past decade as a result of the increased use of biomedical technology, advances in science that are reflected in the medical management of patients, continuing development of information technology, and ongoing economic rationalism. There is a lack of co-ordinated, streamlined approaches and limited consensus on approaches to managing the health care environment and patient care practices. There have been blocks to achieving efficiency and a level of efficacy that has resulted from fragmentation of services, which is reflected in a non-streamlined approach to patient care. The resulting lack of a continuum of care for patients, from point of entry into the health care system to discharge, does not facilitate the provision of optimum patient care or appropriate use of the services. Current information systems are inadequate, there is duplication of costs as a result of the uncoordinated approach to patient care provided by health service personnel, and the demand for hospital beds is at a premium when often they are being used inappropriately.

Given that change has occurred haphazardly over a period of time, the changes have been ill defined, largely poorly managed and not evaluated for their effect on either the service or on patient outcomes. The implementation of changes that are advocated within the health care systems worldwide has generally not been coordinated, formally acknowledged or managed, but rather has often been allowed to unfold with little or no support for the health care workers. And yet, Health Departments expect that the changes in the sector be driven and managed by clinicians. To enable the health care workforce to meet the demand for its services, changes to the roles and functions of health care personnel need to be examined and a more coordinated approach to patient care developed for effective and efficient utilisation of the health care system. Because nurses are the largest group of clinicians within the system and provide a service across the 24 hours in a day, it is reasonable to expect that those nurses will be instrumental in facilitating changes within the health care environment.

If nurses are to be instrumental in bringing about the changes that are necessary to align health care services with patient care, there is also a need to address the current significant attrition rate from nursing. The development of new models of care might be invaluable in assisting with this challenge as health care organisational forces determine the conditions under which nurses work. Studies have identified organisational culture and a lack of autonomy in decision making and change as contributing stressors for nurses. Advances in technology have also been cited as impacting on the nurse's role.

Consideration therefore needs to be given to whether or not the roles and functions of nurses in a range of contexts of practice have changed or need

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to change. Perhaps greater emphasis needs to be placed on different functions in particular situations, because of changing patient care needs and the reduced timeframe in which care is expected to be provided. The feasibility and practicality of delivering total patient care has to be questioned in a range of contexts of practice. Nurses have to be very clear about whether or not their practice is consumer oriented. Any desired change in the culture within the sector and the experiences of nurses will not occur overnight. However, this is an opportunity for nurses to demonstrate their skills in making a difference to outcomes for their clients. In a way, it is a chance to invest in our profession.

It is imperative that nurses are involved in the development of new models of care and the broad change processes. By maximising the contribution that nurses make, we can reduce the potential for further stress in the workplace. However, this will require a new level of insight and forward planning for the development of approaches to practices that meet the needs of patients within a complex and changing health care environment and society at large, rather than waiting for change to be imposed upon us.

To achieve sustainable change in today's complex health care environment, it is essential to have nurses with well-developed leadership qualities, a sound grounding in nursing practices, and clear identification and understanding of the contemporary environment. To determine the appropriateness of various configurations of roles and functions within a range of models of care, nurses themselves need to assume responsibility for proposing strategies for change that are realistic and effective at the coalface.

RESTRUCTURING OF THE HEALTH CARE DELIVERY SYSTEM

Rapid change in the nursing and health care delivery environment has created an irresolvable dilemma for the nursing services. These changes include a major reconfiguration of the health care delivery system, unprecedented technological advances, and enormous changes in the expectations of the health care consumer. Enormous advances in the use of technology have been incorporated into the delivery of health care services. With acceptance of the World Wide Web, many health care organizations implemented mechanisms for using this technology to enhance access to health care services and to provide more efficient care to those whose access to the traditional system is limited by distance and other factors. Although telemedicine has become an accepted term for provision of medical care across distance using electronic means, telenursing has been variously defined by a number of different groups. The Telenursing refers to "the practice of nursing over distance using telecommunications technology". Historically, telemedicine discussions have centered on consultation or other situations in which a licensed physician is in direct contact with another licensed physician, each maintaining a license in the state of practice. However, with the explosive increase in electronic nursing practice, the most typical pattern is that the nurse is direct contact with a patient.

Some might ask whether using electronic technology to provide care indeed constitutes the practice of nursing. In fact, there are those who suggest that, since electronic care does not include hands on care and that typically telephone triage nurses use physician approved protocols for reference, this practice is not in fact nursing practice. Nurse Practice Acts in all states define nursing more broadly than "hands-on care," therefore, a consensus has been reached by boards of nursing that a nurse utilizing the knowledge, skill, assessment, judgment and decision making inherent in nursing education and licensure is indeed practicing nursing.

CHANGES IN THE EXPECTATIONS OF CONSUMER

An important factor in the evolution of 21st century health care is the demand by consumers to be involved in decisions about their care. With acceptance of the World Wide Web, people have unprecedented access to

information about the diagnosis and treatment of illness, often without appropriate safeguards to determine the accuracy or efficacy of the information or mechanisms to determine whether the information is appropriate for their particular need. Popular media and literature have flooded consumers with "disease of the month" stories and encouraged greater consumer involvement in health care decisions. The result of this paradigm shift is that consumers now expect to be a participant in determining appropriate treatment. The implications of this consumerism are profound:

- Consumers will demand care when and where they want it.
- Consumers will demand to be included in decisions about their own health care
- Consumers are increasingly comfortable using technology to access health care information
- Society will expect increased emphasis on health and healthy behavior.

Any one of these factors individually might have allowed health care delivery, as well as nursing regulation, to nurture the illusion of "maintaining business as usual." However, as these factors merge into a radically reformed expectation of health care providers, the question of whether current licensure (defined as the granting of legal authority to engage in certain practices) and nursing regulation (defined as the system of laws and rules that govern nursing practice) will be able to ensure public protection within a radically different structure arises.

States do not have the ability to grant a nurse authority to practice in other states. Thus, a dilemma has been created by the collision of the historical state-based licensure system and the recent transformation of the health care delivery system that is not confined to state boundaries. With the rapid escalation in electronic practice, especially across state lines, other questions have generated intense dialogue among health care providers as well as legal experts.

One issue, as yet undecided by case law, is whether care occurs at the location of the patient, at the location of the health care provider or both. Some speculate that since medical or nursing measures are generated by the provider, care must therefore occur at the location of the provider.

THE ICN CODE OF ETHICS FOR NURSES

Nurses have four fundamental responsibilities: to promote health, to prevent illness, to restore health and to alleviate suffering. The need for nursing is universal. Inherent in nursing is respect for human rights, including cultural rights, the right to life and choice, to dignity and to be treated with respect. Nursing care is respectful of and unrestricted by consideration of age, colour, creed, culture, disability or illness, gender, sexual orientation, nationality, politics, race or social status. Nurses render health services to the individual, the family and the community and co-ordinate their services with those of related groups.

The *ICN Code of Ethics for Nurses* has four principal elements that outline the standards of ethical conduct.

The nurse's primary professional responsibility is to people requiring nursing care. In providing care, the nurse promotes an environment in which the human rights, values, customs and spiritual beliefs of the individual, family and community are respected. The nurse ensures that the individual receives sufficient information on which to base consent for care and related treatment. The nurse holds in confidence personal information and uses judgement in sharing this information. The nurse shares with society the responsibility for initiating and supporting action to meet the health and social needs of the public, in particular those of vulnerable populations. The nurse also shares responsibility to sustain and protect the natural environment from depletion, pollution, degradation and destruction.

NURSES AND PRACTICE

The nurse carries personal responsibility and accountability for nursing practice, and for maintaining competence by continual learning. The nurse

maintains a standard of personal health such that the ability to provide care is not compromised. The nurse uses judgement regarding individual competence when accepting and delegating responsibility. The nurse at all times maintains standards of personal conduct which reflect well on the profession and enhance public confidence. The nurse, in providing care, ensures that use of technology and scientific advances are compatible with the safety, dignity and rights of people.

The nurse assumes the major role in determining and implementing acceptable standards of clinical nursing practice, management, research and education. The nurse is active in developing a core of research-based professional knowledge. The nurse, acting through the professional organisation, participates in creating and maintaining safe, equitable social and economic working conditions in nursing.

The nurse sustains a co-operative relationship with co-workers in nursing and other fields. The nurse takes appropriate action to safeguard individuals, families and communities when their health is endangered by a coworker or any other person.

Provide care that respects human rights and is sensitive to the values, customs and beliefs of all people. Provide continuing education in ethical issues. Provide sufficient information to permit informed consent and the right to choose or refuse treatment. Use recording and information management systems that ensure confidentiality. Develop and monitor environmental safety in the workplace.

NURSING INFORMATICS

The implementation of information technologies in nursing care settings is on the rise. Informatics competencies are increasingly considered a basic skill for every nurse. Health care informatics has been defined as, "the integration of health sciences, computer science, information science, and cognitive science to assist in the management of health care information". Health care informatics may be decided in to specialties like:

- medical informatics,
- health informatics,
- dental informatics, and
- nursing informatics

Medical informatics refers to information technologies that concern patient care and the medical decision-making process. Health informatics refers to educational technology for health care clients or the general public. Nursing informatics refers to electronic information combined with nursing and any aspect of clinical practice, administration, research, or education. Nursing informatics is a developing field of study that is highly interdisciplinary. It is strongly connected to education, business, and computer science.

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DRUG PROFILE

Bromocriptine

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Contraindications: Bromocriptine is contraindicated in patients with known hypersensitivity to ergot-related drugs, in patients with syncopal migraine causes hypotensive episode; may reflect dopamine receptor hypersensitivity. It is also contraindicated in nursing women. Bromocriptine may inhibit lactation. **Side effects**: The most common adverse events associated with bromocriptine mesylate are nausea, fatigue, dizziness, vomiting and headache. The incidence of hypoglycemia is 6.9% among bromocriptine mesylate-treated patients compared with 5.3% of patients receiving placebo. **Precautions/Interactions**: (i) Interaction with dopamine antagonists: Concomitant use with dopamine antagonists as neuroleptic agents may diminish the effectiveness of both drugs. (ii) Assess orthostatic vital signs prior to initiation of Bromocriptine and periodically thereafter. (iii) Use in patients with severe psychotic disorders is not recommended. (iv) May increase ergot-related side effects or reduce ergot effectiveness for migraines if administered within 6 hours of ergot-related drugs. (v) Extensively metabolized by CYP3A4. Use caution when co administering strong inhibitors, inducers, or substrates for CYP3A4."



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Comparative Analysis of Various Diagnostic Techniques for Tubercular Lymphadenitis: A Pilot Study from a Resource Poor Country

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Abstract: Background: Tuberculosis lymphadenitis (LNTB) is the most common presentation of extra pulmonary tuberculosis. The main causative agents reported were predominantly *Mycobacterium tuberculosis* (*M.tb*), closely related *Mycobacterium bovis* (*M.bovis*) and non-tuberculous mycobacteria (NTM). Over the past decade, a set of tedious cytological and microbiological diagnostic tests i.e. fine needle aspiration cytology (FNAC), microscopic smear examination & culture were used. Although FNAC & smear examination were rapid, but none of these techniques were able to differentiate between *M.tb* and other members of *Mycobacterium* spp., which is highly essential for planning anti-microbial therapy programme. Methodology In the present study, smear, FNAC, culture and *hupB* gene (*Rv2986c*) based PCR, were applied and each method was analyzed in terms of sensitivity, specificity, along with reliability and cost effectiveness. Results Considering culture as a gold standard, all other diagnostic methods were compared. Direct PCR, showed the sensitivity & specificity of 47% & 75% whereas when performed on culture isolates, the sensitivity rose to 76%. The sensitivity & specificity of FNAC were 60% & 49% respectively whereas of direct smear examination was 50% and 70% respectively. Conclusion: we conclude that smear and FNAC are rapid, cost effective, easily available, but has lower specificity and may not be able to differentiate tubercular lymphadenitis from non tubercular lymphadenitis. PCR(*hupB* gene based) being a singular target for *M.tb* showed reliability and potential to rapidly detect & identify causative agent of LNTB, can help clinician to initiate correct and timely treatment.

Keywords: Tuberculosis lymphadenitis, culture, *hupB* gene, fine needle aspiration cytology (FNAC)

INTRODUCTION

Tuberculous lymphadenitis (LNTB) being one of the most frequent cause of lymphadenopathy¹, accounted for about a half of 2,19,945 of total extra-pulmonary TB cases reported in the year 2008 in India². An Indian pediatric study showed prevalence of peripheral lymphadenopathy as 27.2/1000 children and that of LNTB as 4.43/1000³. Although *Mycobacterium tuberculosis* complex (MTC) organisms i.e. *Mycobacterium tuberculosis* (*M.tb*), *Mycobacterium bovis* (*M.bovis*), *Mycobacterium africanum* and *Mycobacterium microti* were the main cause of mycobacterial lymphadenitis cases, nontuberculous mycobacterial (NTM) lymphadenitis (NTM-LN) with high frequency in human immunodeficiency virus type 1 (HIV-1)-infected individuals⁴ reported to be an emerging causative agent. Cervicofacial lymphadenitis, the most frequent head and neck manifestation of NTM infection, often presents as chronic, unilateral lymphadenopathy with characteristic violaceous overlying skin changes. Lymphadenitis due to infection with the MTC is more chronic in nature, while NTM-LN often has a more rapid course⁵ and their treatment follow-up were also different as tuberculous adenitis is best treated as a systemic disease with anti-tuberculosis medication whereas NTM infections can be addressed as local infections and are amenable to surgical therapy. Therefore, species identification is also of paramount importance.

Over the past decade, The efficacy of fine needle aspiration cytology (FNAC) and direct microscopical screening of stained slides for AFB were validated as a diagnostic tool for LNTB because of their simplicity, rapidity, and performance friendly nature, but have their own limitations^{6,7}. Mycobacterial culture technique although being more sensitive & specific, requires 6-8 weeks before a positive visual result is obtained⁸. The main shortcoming of these parameters was that none of these were able to perform speciation of the genus mycobacteria thus causing misery to the clinician to initiate therapy.

After considering these limitations of existing diagnostic tools, molecular techniques like polymerase chain reaction (PCR) based on the amplification of target sequences were introduced to rapidly detect and identify mycobacterial agent in clinical samples at the genus, complex, and species levels⁹. Various targets like IS6110 insertion element¹⁰, *hupB*¹¹⁻¹³, *katG*¹⁴,

*prnA*¹⁵ genes and even peripheral blood mononuclear cells¹⁶ etc were used to differentiate *M. tb* from other members of mycobacterium group. The various diagnostic tools are available to diagnose LNTB, but it has only added to already existing confusion regarding diagnosis. In this study, we have tried to compare already available diagnostic tools and suggest in terms of sensitivity, specificity, reliability and cost effectiveness and tried to suggest the better method to help clinician initiate timely and correct therapy to tubercular lymphadenitis patients. We have used *hupB* gene (*Rv2986c*) encoding a histone-like protein of *M. tb*, based PCR on clinical aspirates to identify the causative agent in LNTB as a target for detection and identification of *M. tb* and closely related *M. bovis* from other members of the MTC and NTM. Sequence analysis of *M. tb* and *M.bovis* has shown that *M.bovis* lacks the 12.7 kb fragment containing the *mce3* operon¹⁷, whereas all *M. tb* isolates examined showed the presence of the 12.7 kb fragment, while all the *M.bovis* strains lacked this fragment. We exploited the differences in the organization of the *mce3* operon in the two species.

METHODS

A collaborated pilot study was undertaken at Department of Histopathology and Microbiology, at Vardhman Mahavir Medical College & Safdarjung Hospital (VMMC & SJH), New Delhi, and Department of Biotechnology, at All India Institute of Medical Sciences (AIIMS), New Delhi, India during Jan.2009 to August 2009. The study was divided in two parts. First phase involved patient registration, sample (aspirates) collection, smear preparation and staining and culture by both solid Lowenstein Jensen (L J) & Liquid broth based BacT/ALERT 3D automation and was performed at Safdarjung Hospital. The second phase involved DNA extraction & PCR from clinical aspirates and was performed in AIIMS.

In this study, 89 clinical suspected patients (52 male and 37 female) of tubercular lymphadenitis were included, after taking ethical clearance and informed written consent from patients or from parents (in case of children). There were 23 (25.8%) cases of children <15 yrs. The duration of lymph adenopathy varied from 10 days to 20 months.

Fine needle aspirations (approx. volume 0.5-2 ml) from all enrolled patients were performed in the Department of Histopathology under sterile aseptic conditions on the suspected lymph nodes. Two smears were prepared and

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stained by Giemsa stain and acid fast staining by Ziehl Neelsen (Z N) method as per the approved guidelines¹⁸ and the findings were recorded.

0.1-0.2 ml aspirate was inoculated on Lowenstein-Jensen (LJ) slant & 0.2-0.5 ml (depending upon total volume of sample aspirated) was put into BacT/ALERT enriched bottles for cultivation of bacilli. The growth on LJ slant was checked everyday in first week to look for rapid growers bacteria and thereafter on weekly basis till sixth week. The growth was finally confirmed by ZN stain for the presence of AFB. In the same way, when BacT/ALERT system flashes positive signal, the bottle was taken out and smear was made to confirm TB bacilli.

DNA Extraction and PCR: DNA extraction and PCR were performed as per in-house protocol developed in the Department of biotechnology, AIIMS, New Delhi¹¹.

Three primers were used: Forward primer CMB-F common to *M. tb.* and *M.bovis*, and 2 reverse primers N-tb & BMB-R specific for *M. tb.* and *M.bovis* respectively. The assay mixture (25µl reaction) contained: forward primer FP (0.625µM), the reverse primers N-tb & BMB-R (0.325µM each), 1x PCR buffer (100mM Tris/HCl, pH 8.8, 500mM KCl, 0.8% nonidet-P40), 2.5mM MgCl₂, 0.3mM dNTPs and 1.25U Taq DNA polymerase. The thermal cycle parameters were 95°C for 10 min and 40 cycle of each, of 45 sec at 95°C, 45 sec at 58°C and 45 sec 72°C and final extension at 72°C for 10 min. The Forward primer i.e CMB-F used was common to both *M. tb* & *M.bovis*; whereas reverse primers, N-tb has been derived from the 12.7 kb fragment and BMB-R from the region adjacent to the 12.7 kb fragment (Fig.1). N-tb primer was specific for *M. tb*; while the sequence of the BMB-R reverse primer was present in both *M. tb* and *M.bovis*. However amplification occurs in case of *M.bovis* with the CMB-F & BMB-R exclusively and not in case of *M. tb*, as the 12.7 kb insert prevents Taq polymerase mediated amplification.

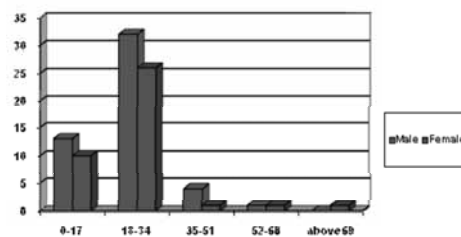


Table 1: Age & gender of patients studied

The standardized assay was used for detection of *M. tb.* as well as *M.bovis* in clinical samples. The amplified product obtained in CM-PCR assay is 162 & 127bp for *M. tb.* & *M.bovis* respectively (Table-2).

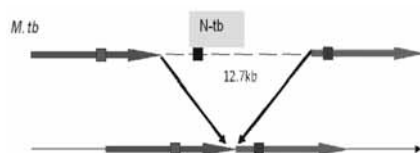


Table-2: Primers used

RESULTS

The aspirated lymph nodes included cervical (67%), supraclavicular (11 %), submandibular (6 %), auricular (11%), submental (5%) of the total cases. The final diagnosis was made if FNAC showed epithelial cell granuloma with necrosis and/or smear positivity for AFB and/or growth on LJ or bactec, were seen⁷. Based on this, 54 cases were termed as positive. Considering culture as a gold standard, this assay when applied directly on clinical aspirates, showed the sensitivity & specificity of 47% & 75% whereas when performed on culture isolates, the sensitivity rises to 76%. The sensitivity & specificity

of FNAC were 60% & 49% respectively. The overall acid-fast bacilli positivity in fine needle aspiration smears was 38.4% of the total cases and in 50% of all culture-positive aspirates whereas of direct smear examination was 50% and 70% respectively (Table 3). LN-PCR was positive in 47% of the aspirates from patients, while PCR on culture isolates, showed sensitivity **Table 3: Comparison of sensitivity, specificity of PCR & other tests with culture**

Test	Sensitivity	Specificity
PCR(Clinical samples)	47%	75%
PCR(Culture isolates)	76%	N.A *
FNAC	60%	49%
Smear	50%	70%

* Can't calculate as it is performed only on positive culture isolates

to 76%.

DISCUSSION

In endemic areas like India, the detection of LNTB with traditional diagnostic tools is always a major challenge. In the past decade, various studies describing lymph node PCRs from fine needle aspirates or biopsy specimens have consistently shown improved sensitivity (61-78%) when compared with conventional microbiologic methods^{10,12,13,19-21}. The PCR assay described in the study is based on the *hupB* gene of *M. bovis* and *M. tb*. The specificity of the *hupB*-based PCR assay to detect and identify *M. bovis* and *M. tb* has been established and the sensitivity were reported to detect as low as 10 - 20 picogram DNA of the tubercle bacilli¹¹⁻¹³.

In the present study, the LN-PCR was positive in 47% of the aspirates from patients. This lower sensitivity may be attributed either to the small volume of aspirate remaining after distributing the sample for the microbiological and cytological assays or due to presence of PCR inhibitors¹². To confirm the cause, we again performed PCR on culture isolates, the PCR sensitivity then jumps to 76%. This was expected as inadequate sampling predominantly influences the assay. We performed PCR from the leftover aspirate after performing conventional parameters and identified *M.tb* in the vast majority of positive cases whereas *M.bovis* was not found. There were three pediatric cases in which only culture & PCR came positive whereas both FNAC & smear microscopic were negative. These results indicate that culture-enhanced PCR is a highly sensitive and specific method for the detection of *M. tb* in extrapulmonary specimens especially in children and would diminish the chance of open biopsy.

The only limitation found was unlike culture, the PCR technique does not distinguish between live and dead mycobacteria, a feature that is of the utmost importance when screening for viable mycobacteria in samples such as dairy products following pasteurization or pre-exposure of broad spectrum antibiotics such as amoxicillin-clavulanic acid & fluoroquinolones known to inhibit *M.tb*²³.

Revised National Tuberculosis Control Programme (RNTCP) mainly recommends cytology & ZN smear microscopy for the diagnosis of LNTB²⁴. In FNAC, diagnosis is based on the presence of granulomas, central necrosis and if possible, demonstration of acid-fast bacilli by staining. Cytology has a sensitivity of approximately 32-59%^{6,25}. In our study, it was 60%. But when compared with culture, FNAC showed low specificity (49%). However, absence of specific cytologic findings of granulomatous lymphadenitis or negative acid-fast bacilli (AFB) smears requires additional open biopsy or repeated FNAC, thus this method has limitations in clinical situations. Another shortcoming of FNAC lies in the difficulty of differentiating tuberculosis from other granulomatous diseases or nontuberculous mycobacterial. Lymphadenitis caused by nontuberculous mycobacterial species usually resistant to anti-tubercular drugs and they would be misdiagnosed as multi-drug resistant tuberculosis (MDR-TB)²⁶. However, this technique

provides an easy way for collecting materials for bacteriological examination. The concentration of organisms in the clinical specimen has a direct relationship with the sensitivity of the ZN stain and a concentration of $\geq 10^4$ organisms/ml would normally guarantee a positive smear. The overall acid-fast bacilli positivity in fine needle aspiration smears can vary from 37.4% to 59.4%^{6,7,25}. In the present study, it was 38.4% of the total cases and in 50% of all culture-positive aspirates. The low sensitivity was probably due to the low concentration of mycobacteria in the aspirate.

Culture reports from different studies^{1,8} detect fine needle aspirates between 39 to 80% positive in the clinically suspected TB-L cases. Our observation also falls in between the reported range (43.1%). However, low sensitivity and extensive time requirements of culture studies limit its usual application. Traditionally, culture followed by a panel of biochemical tests has been used for speciation of mycobacteria but has inherent shortcomings⁹. In the present study, the time consumed for primary isolation on L J media ranges from 4 to 6 weeks and 2-3 weeks by liquid broth based automated BacT/ALERT system. Although BacT Alert 3D system recovers mycobacteria rapidly even this is too long as it is necessary to commence treatment as soon as possible.

These results confirm that PCR from the remainder of fine-needle aspirate could be a good initial diagnostic tool. Given the availability of a thermal cycler, the rest of the procedure has a cost similar to other routine assays for LNTB diagnosis. Therefore, this PCR assay could be of immense utility in redefining research priorities and public health strategies for control and prevention of both human and bovine tuberculosis and it can reduce the need for more invasive diagnostic approaches.

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LITERATURE REVIEW

Maternal Obesity and Pregnancy Outcome: A Prospective Analysis

Debasmita Mandal, Saroj Mandal, Abhijit Rakshit, et al; Department of Obst and Gynae, IPGME and R, Department of Cardiology, IPGME and R, 244 AJC Bose Road, Kolkata-700 020 JAPI:August 2011;Vol.xx:Pg. 486-488

Objective: To analyze whether the obese women have an increased risk of pregnancy complications and adverse fetal outcome.

Methods: The longitudinal prospective study was carried out in the Obst and Gynae department, IPGME and R, Kolkata. The study enrolled 422 pre-pregnant obese women with pregnancy as study population and equal number of non obese pregnant mothers as controls. Body mass index (BMI) was $\geq 30.0 \text{ kg/m}^2$ and 20-22 kg/m^2 in obese and control group respectively. Results: In comparison to average weight pregnant women, obese pregnant women were at increased risk of gestational diabetes mellitus (19.43 vs 3.79%; $p < 0.001$), pregnancy induced hypertension (12.32 vs 2.36%; $p < 0.001$), pre-eclampsia (8.76 vs 3.31%; $p < 0.001$), preterm labor in less than 34 week gestation (7.58 vs 3.55%; $p < 0.001$), cesarean section (36.72 vs 17.53%; $p < 0.001$), instrumental deliveries (12.32 vs 5.21%; $p < 0.001$) and postpartum infection morbidities (9.95 vs 3.79%; $p < 0.001$). These women were more prone to develop overt diabetes (2.36% vs 0) and chronic hypertension (5.21 vs .47%) in future as well. Neonates of obese women were mostly large for gestational age, macrosomic and they had high incidences of birth injuries, shoulder dystocia, premature deliveries, late fetal deaths and congenital malformations particularly spina bifida, cleft lip, cleft palate and heart defect. Conclusion: As obesity is considered to be a modifiable risk factor, preconception counseling and creating awareness regarding health risks associated with over weight and obesity should be encouraged.

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Recent Advances in Management of Diabetes Mellitus

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Abstract: Diabetes mellitus is characterized by chronic hyperglycemia with disturbances of carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion, insulin action, or both. The prevalence of diabetes is rapidly rising all over the globe at an alarming rate. There is an increase in the prevalence of type 1 diabetes also, but main cause of diabetic epidemic is type 2 diabetes mellitus, which accounts for more than 90 percent of all diabetes cases. Future drug therapy of T1DM will depend on the success of ongoing and planned intervention trials. Immunomodulation alone, or possibly combined with immunosuppressive therapy, seems to be promising in reducing the loss of C-peptides after diagnosis. Studies of the function of the human immune system lag behind that of the mouse and rat. Since 2001, Trial Net, an international network of clinical research groups supported by the National Institutes of Health, has established an infrastructure for trials for predicting and preventing T1DM.

INTRODUCTION

Diabetes mellitus is characterized by chronic hyperglycemia with disturbances of carbohydrate, fat, and protein metabolism resulting from defects in insulin secretion, insulin action, or both. The prevalence of diabetes is rapidly rising all over the globe at an alarming rate. There is an increase in the prevalence of type 1 diabetes also, but main cause of diabetic epidemic is type 2 diabetes mellitus, which accounts for more than 90 percent of all diabetes cases. According to World Health Organization (WHO) reports, India had 32 million diabetic people in the year 2000¹. The International Diabetes Federation (IDF) estimates the total number of diabetic subjects to be around 40.9 million in India and this is further set to rise to 69.9 million by the year 2025². The majority of cases of diabetes fall into two broad etiopathogenetic categories now called type 1 and T2 DM.

The etiologic classification of diabetes mellitus currently recommended by WHO and the ADA in 1997.

DIAGNOSIS AND CLINICAL PRESENTATION

Type 1 DM: Type 1 diabetes mellitus, results from insulin deficiency following destruction of the insulin-producing pancreatic beta cells. It most commonly presents in childhood but one-fourth of cases are diagnosed in adults. The incidence of type 1 diabetes varies depending upon various factors like age, family history, environmental factors etc. Incidence rates in children <14 years ranging from 0.1/100,000 per year in China to 37/100,000 per year in Finland³. The incidence of childhood type 1 disease is rising worldwide, with reported annual increases of 2 to 5 percent in Europe, the Middle East, and Australia⁴. Type 1A diabetes mellitus results from autoimmune destruction of the insulin-producing beta cells in the islets of Langerhans. In genetically susceptible subject, this process is probably triggered by one or more environmental agents. Type 1B diabetes mellitus refers to non-autoimmune islet destruction.

Type 1 diabetes can present in several different ways⁵. Classic new onset, diabetic ketoacidosis or as asymptomatic incidentally discovered diabetes. Classic new onset presents as hyperglycemia without acidosis. Symptoms are caused by hyperglycemia and include polyuria, polydipsia, and weight loss despite increased appetite initially. Children with type 1 diabetes often present with diabetic ketoacidosis (hyperglycemia and ketoacidosis). The International Society for Pediatric and Adolescent Diabetes (ISPAD) in 2007 defined the following biochemical criteria for the diagnosis of DKA⁶; Hyperglycemia, blood glucose of >200 mg/dL (11 mmol/L) a metabolic acidosis, defined as a venous pH <7.3 and/or plasma bicarbonate <15 meq/L (15 mmol/L). These abnormalities are accompanied by hyperketosis

(concentration of total ketone bodies >5 mmol/L) and hyperosmolality. Some children will be diagnosed with type 1 diabetes before the onset of clinical symptoms.

Type 2 DM: T2 DM mellitus (T2DM) is the most common form of diabetes. It is characterized by disorders of insulin action and insulin secretion, either of which may be the predominant feature. The risk of developing T2 DM increases with age, obesity, and physical inactivity. T2DM shows strong familial aggregation, so that persons with a parent or sibling with the disease are at increased risk, other individuals with obesity, hypertension, or dyslipidemia and women with a history of gestational diabetes are also at increased risk of developing T2 DM. T2 DM is now considered to be a facet of Syndrome X (Reaven's syndrome) comprising of hyperinsulinemia, dyslipidemia, hypertension and hyperglycemia.

T2DM frequently goes undiagnosed for many years because the hyperglycemia develops gradually and in the earlier stages is not severe enough to produce the classic symptoms of diabetes; however, such patients are at increased risk of developing macrovascular and microvascular complications. The classic symptoms of polyuria, thirst, recurrent blurred vision, paresthesias, and fatigue are manifestations of hyperglycemia and osmotic diuresis and are present late in the course of disease. Diabetes should be suspected in women with chronic candidal vulvovaginitis as well as in those who have delivered large infants (4.1 kg) or have had polyhydramnios, pre-eclampsia, or unexplained fetal losses.

MONITORING OF BLOOD GLUCOSE

Blood glucose testing: The glucose concentration is 10-15 % higher in plasma or serum than in whole blood because structural components of blood cells are absent.

Venous blood sample: The laboratory methods commonly used for determining plasma glucose utilize enzymatic methods, colorimetric methods or automated methods.

Capillary blood samples: Several strip based portable, battery operated meters utilize glucose oxidase method. Latest generation devices represent a noninvasive method relying on infrared absorption spectra.

TESTING FOR KETONURIA / KETONEMIA

Most strips utilize a nitroprusside re-action that measures only acetone and acetoacetate. Although these tests do not detect β -hydroxybutyric acid, the semi quantitative estimation of the other ketone bodies is nonetheless usually adequate for clinical assessment of ketonuria.

GLYCOSYLATED HEMOGLOBIN

The major form of glycohemoglobin (HbA_{1c}) is abnormally elevated in

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diabetics. Glyco-hemoglobin generally reflects the state of glycemia over the preceding 8-12 weeks, thereby providing a method of assessing chronic diabetic control⁷.

DIAGNOSTIC CRITERIA

The diagnosis of diabetes mellitus is based on measuring venous plasma glucose in the fasting state and 2 hours after a 75 gram glucose load (recommended by the WHO). The details of the diagnostic criteria are given in Table 1^{8,9}.

- All values are venous plasma glucose
- To convert mg/dl to mmol/L, divide by 18.
- In case of an abnormal test result, the test should be repeated on a different day.

Oral glucose tolerance test (OGTT) is recommended by WHO and not by ADA for epidemiological purposes.

Table 1: Diagnostic criteria for Diagnosis of Diabetes mellitus

Category	WHO	ADA
Impaired fasting glucose (IFG)	BGF=100 to < 126 mg/dl	BGF=100 to < 126 mg/dl
Impaired glucose tolerance (IGT)	2 hr post glucose > 140 mg/dl and < 200 mg/dl	-
Diabetes mellitus (DM)	BGF $\geq$ 126 mg /dl or 2 hr Post glucose $\geq$ 200 mg/dl (OGTT)	BGF $\geq$ 126 mg /dl or Casual = 200 mg/dl + Osmotic Symptoms
Normal	FPG=100 mg/dl and PP $\leq$ 140 mg/dl	FPG=100 mg/dl and PP $\leq$ 140 mg/dl

MANAGEMENT OF DIABETES MELLITUS

Diabetes mellitus is condition associated with number of complications including coronary heart disease, retinopathy, neuropathy etc. It is now clear that tight control of blood glucose significantly reduces the risk of complications of diabetes. Therefore, multidisciplinary approach, involving dieticians, endocrinologists /diabetologists, cardiologists, nephrologists, ophthalmologists, chiropractors etc. is needed for management of diabetes mellitus.

MANAGEMENT OF TYPE 2 DIABETES MELLITUS

Non-pharmacological Therapy: Non-pharmacological measures including diet, exercise and stress alleviation are as important interventions for the management of diabetes.

Medical Nutrition Therapy (MNT): A proper diet is important component of therapy in all patients with diabetes. In patients with T2 DM recommendations for caloric distribution is as follows: 55-60% energy from carbohydrate, 10-15% from protein and 20-25% from fats. This dietary distribution is also indicated in patients with type 1 diabetes on intensive insulin regimens in whom near-normoglycemic control is less achievable on diets higher in carbohydrate content.

Dietary Fiber: Fibers such as cellulose or hemicelluloses, as found in bran, termed as insoluble fibers increases intestinal transit time and may have beneficial effects on colonic function. Soluble fibers such as gums and pectin's, as found in beans, oatmeal, or apple skin, tend to decrease gastric and intestinal transit slowing glucose absorption thus decreasing hyperglycemia.

Artificial Sweeteners: The nonnutritive sweetener saccharin is widely used as a sugar substitute. Aspartame may prove to be the safest sweetener for use in diabetics which is 180 times as sweet as sucrose. A major limitation is its heat lability, which precludes its use in baking or cooking. These should be used in moderation.

Fruits: Fruits (whole) should be taken in moderation. However, very sweet fruits and fruit juices can be avoided.

Alcohol: Alcohol intake is best avoided and if used must be in moderation as it may worsen the dyslipidemia, neuropathy and glycemic control.

Common Salt: Up to 6 gms /day of are permitted. Restrict pickles, papad, chatni and salty processed foods.

Tobacco: Smoking and the use of tobacco in any form should be prohibited.

Physical activity: In T2 DM exercise programme to achieve weight reduction and calorie counting is central to the management. The best form of exercise is a stepwise increase in aerobic exercises. All diabetics need to be evaluated to rule out any contraindication like CAD, proliferative diabetic retinopathy, autonomic neuropathy etc. before any exercise programme. Brisk walking for 30-60 minutes or equivalent should be enforced regularly. Yoga, a traditional Indian system, has been demonstrated to have beneficial effect in diabetes. Some aspects of Yoga like, Asanas (involving postures), Pranayama (involving breath), Dhayana (meditation) and Bhavana (visualization) are beneficial but need to be learnt under expert guidance⁽¹⁰⁾.

PHARMACOLOGICAL THERAPY

Oral agents for the treatment of hyperglycemia (Table 2).

The drugs for treating T2 DM can be divided into three categories⁽¹¹⁾.

1. Drugs that primarily stimulate insulin secretion, known as insulin secretagogues.
2. Drugs that sensitize tissues (primarily liver and adipose tissue) to the action of insulin named as insulin sensitizers.
3. There are drugs that principally affect absorption of glucose by retarding the

Table 2: Characteristics of oral antidiabetic drugs

Sulfonylureas			Commonly used, lower cost, effective in severe hyperglycemia. Can be used in combinations. S/E: Hypoglycemia, wt gain. Contra-indicated if S Cr. >2 mg/dl.
Glibenclamide	1.25- 20 mg OD / BID	Up to 24 hours	
Gliclazide	80-320 mg / BID	Up to 24 hours	
Glipizide	2.5-40 mg / OD/BID	6-12 hours	
Glimeperide	1-8 mg / OD	Up to 24 hours	
Meglitinide analogues			For mild hyperglycemia, variable meal schedule, post-prandial hyperglycemia and renal insufficiency. High cost
Repaglinide	0.5 - 4 mg / before major meals	3 hours	
Nateglinide	60-240 mg / before major meals		
Biguanides			No hypoglycemia. Weight neutral, post meal hyperglycemia; can be combined. S/E: GI, CI if S Cr >1.5 mg/dl; age > 70 yrs; systemic diseases.
Metformin	1-2.5 g with meals / 2 or 3 times daily	7-12 hours	
Thiazolidinediones			Beneficial in dyslipidemia; can be used in combinations. S/E: hepatotoxicity, wt gain, anemia.
Rosiglitazone	4-8 mg / OD/BID	24-30 hours	
Pioglitazone	15-45 mg / OD	30 hours	
Alpha-glucosidase inhibitors			S/E=GI. Hypoglycemia in combination with other agents, less potent and costly. Better for post meal, erratic meal schedule and combinations.
Acarbose	75-300 mg / in 3 divided doses with first bite of food	4 hours	
Voglibose	75-300 mg in divided doses with first bite of food	4 hours	

* Tolbutamide, chlorpropamide, acetohexamide and tolazamide are no longer in routine clinical use.

INSULIN SECRETOGOGUES

Sulfonylureas: The proposed mechanisms of action of the sulfonylureas include: (a) augmentation of insulin release from pancreatic β cells and (b) potentiating of insulin action on its target cells.

Pancreatic β cells have specific receptors, consisting of two proteins, one that binds the sulfonylurea (SUR) and the other which is an ATP-sensitive potassium channel (Kir6.2). It has been shown that activation of these receptors closes potassium channels, resulting in de-polarization of the β cell. This depolarization allows calcium to enter the cell and actively promote insulin release. Table 2, enlists various sulfonylureas along with their characteristics.

The earlier generation sulfonylurea's, like glibenclamide and chlorpropamide, have a long duration of action and high probability of inducing hypoglycemia. Glipizide and gliclazide have short duration of action and thus need more frequent dosing. Glimeperide, is the newer generation sulfonylurea, it is given as monotherapy or in combination with other oral agents or insulin in a single daily dose. (Max.dose is 4 mg)¹¹ for each sulfonylurea the decline in blood glucose for each unit increment in the dose is best seen till the half-maximal dose of the drug is reached. After half maximal dose is achieved, further increase in the dose results in a smaller decline in blood glucose.

There has been concern of possible cardiovascular effects of sulfonylureas, because the ATP sensitive K⁺ channel, which is responsive to sulfonylurea

action, is ubiquitous in its distribution. Some animal experiments and short term human studies have suggested that earlier sulfonylurea's like glibenclamide and tolbutamide may have adverse cardiovascular effects but many large trials using sulfonylureas have not provided any evidence for cardiovascular risk. Since most sulfonylureas are metabolized in the liver and excreted through the kidney their use is prohibited in case of liver dysfunction and renal failure.

MEGLITINIDES

This is another class of secretagogues. They are similar to sulfonylureas in their mechanism of action but lack the sulfonic acid-urea moiety products. Repaglinide is given three times a day 15 minutes before each meal (max. dose of 16 mg/day); nateglinide is given 60 mg three times a day. The drug may be useful for postprandial hyperglycemia, elderly and in patients with renal impairment. There are less chances of hypoglycemia and useful in patients who have an inconsistent daily schedule with long gaps between meals⁽¹²⁾. Several novel insulin secretagogues have been reported to act by closing the K-ATP channels. The meglitinide derivative mitiglinide (KAD-1229) appears to bind at the benzamide site on SUR1¹³.

INSULIN SENSITIZERS

Biguanides

Phenformin has been discontinued because of its association with the development of lactic acidosis in patients with coexisting liver or kidney disease. Metformin (1, 1-dimethylbiguanide hydrochloride) was introduced in France in 1957 as an oral agent for therapy of T2 DM, either alone or in combination with sulfonylureas. In 1995 FDA approved its use in the United States but has been used in most of the countries, including India, for over 4 decades. The exact mechanism of action of metformin is not clear but it may reduce hepatic gluconeogenesis, slow down gastrointestinal absorption of glucose and increase up-take by skeletal muscle. It can be used as monotherapy, an adjunct to diet, sulfonylurea's, thiazolidinediones or insulin. Metformin is relatively contraindicated in patients with cardiorespiratory insufficiency, impaired renal function, any state likely to be associated with tissue hypoxia, general anesthesia, use of radiographic contrast media, and age of 70 years. Maximum dose of metformin is 2550 mg daily. Common side effects of metformin are gastrointestinal symptoms (anorexia nausea vomiting, abdominal discomfort, diarrhea. Lactic acidosis, though uncommon with metformin in contrast to phenformin, is reported in cases with associated risk factors such as renal, hepatic, or cardiorespiratory insufficiency, alcoholism and advanced age¹⁴.

Thiazolidinediones

These agents sensitize peripheral tissues to insulin by binding to a nuclear receptor called peroxisome proliferators-activated receptor-gamma (PPAR- γ). Other effects including, increased glucose transporter expression (GLUT 1 and GLUT 4), decreased free fatty acid levels, decreased hepatic glucose output, and increased differentiation of preadipocytes into adipocytes have also been observed. Troglitazone, was withdrawn because it caused acute liver failure. Rosiglitazone and pioglitazone are used as monotherapy, or in combination with sulfonylurea's, metformin, and insulin. Common side effect is weight gain, especially when the drug is combined with a sulfonylurea or with insulin. The dosage of rosiglitazone is 4-8 mg daily and of pioglitazone 15-45 mg daily. The Thiazolidinediones should not be given to patients if ALT is 2.5 times greater than the upper limit of normal, and liver function tests should be performed once every 2 months for the first year and periodically thereafter¹⁵. Recently Rosiglitazone is withdrawn from India and most other countries due to cardiac safety.

INHIBITORS OF INTESTINAL CARBOHYDRATE ABSORPTION

Alpha-Glucosidase Inhibitors

Acarbose and miglitol are competitive inhibitors of intestinal brush border

alpha-glucosidases, thus delaying the absorption of carbohydrates and reduce postprandial glycemic excursion. Both of these agents are potent inhibitors of glucoamylase, α -amylase, and sucrase. They are less effective on isomaltase and are ineffective on trehalase and lactase. The common adverse effect is flatulence. Troublesome diarrhea seen in 3% of cases. The starting dose of acarbose is 25 mg twice daily and can be gradually increased to 100 mg three times daily. A slight rise in hepatic aminotransferases has been noted in clinical trials (5% versus 2% in placebo controls, and particularly with doses greater than 300 mg/d). Miglitol is structurally similar to glucose, is absorbable and is similar to acarbose in terms of its clinical effects. Miglitol should not be used in renal failure since its clearance is impaired in this setting¹⁶.

INCRETIN MIMETICS: Insulin has been shown to be released more effectively through an oral glucose load than intravenously and this is known as the incretin effect. This incretin effect is mediated by number of peptides released from intestine. Insulin stimulating benefits of peptides such as GLP-1 are rapidly diminished as GLP-1 is rapidly metabolised by the glycoprotein dipeptidyl peptidase (DPP-IV). It is possible to enhance incretin effect either by increasing the effect of GLP-1 or by slowing its breakdown.

Glucagon-like polypeptide 1 analogues: Exenatide is the first synthetic agent belonging to the class of GLP-1 agonists. It augments insulin release in response to ingested glucose. In addition, GLP-1 suppresses inappropriately high glucagon values which in turn suppress hepatic glucose output. It also reduces the rate of gastric emptying, thus promoting satiety, resulting in reduced caloric intake and weight reduction^{15pmj}. It has also been shown that GLP-1 analogues may preserve β cell reserves. The recently published data on subjects completing over 2 years of treatment with exenatide showed a sustained reduction in HbA1c and weight after 104 weeks of treatment.

Dipeptidyl peptidase inhibitors: This class of drugs act slowing breakdown of GLP-1 analogues. These agents work by enhancing the sensitivity of β cells to glucose, which causes enhanced glucose dependent insulin secretion. Many studies using sitagliptin and vildagliptin alone or in combination have shown a positive effect on values of HbA1c¹⁷.

Phosphodiesterase inhibitors and other approaches: The β - cell expresses several phosphodiesterases (PDEs) that degrade cAMP and so reduce insulin release. Transient inhibition of these enzymes in β - cells, especially isoform PDE - 3B, which exerts most influence on glucose induced insulin secretion, could be a possible intervention¹³.

Peroxisome proliferator activated receptor agonists: current, thiazolidinediones (pioglitazone and rosiglitazone) exert their "insulin sensitizing" effects largely by stimulating the peroxisome proliferator activated receptor γ . Stimulation of these receptor increase adipogenesis, enhance insulin sensitivity. Additional thiazolidinediones that stimulate PPAR γ are being developed (e.g. rivoglitazone), and non thiazolidinedione PPAR γ agonists have been reported¹³.

Other peroxisome proliferator activated receptor agonists: To take advantage of the blood lipid lowering and anti-inflammatory effects of low affinity binding to PPAR α various thiazolidinediones and non - thiazolidinedione molecules have been described with binding affinities for both PPAR α and PPAR α so called dual PPAR α / γ agonists (glitazars). The two glitazars (muraglitazar, tesaglitazar) were discontinued because of side effects. Pan PPAR agonist or SPPARM selective PPAR modulator could offer therapeutic advantages¹³.

Vitamins and Minerals: Whether supplementation of the antioxidant vitamins C (ascorbic acid), E (α -tocopherol) and β -carotene can measurably benefit insulin sensitivity and reduce cardiovascular risk is not clear. Vitamin D3, appears to be necessary for normal insulin production and secretion, and may be required for normal insulin action. Diabetic patients are often deficient in circulating vitamin D3 and preliminary data suggest that vitamin D supplementation in deficient individuals might benefit glycemic control. Insulin like antidiabetic effects has been reported for zinc, lithium, selenium, molybdenum, tungsten, mercury and cadmium¹³.

Other potentiators of insulin action: Bromocriptine: The dopamine D2 receptor agonist bromocriptine, used in the treatment of Parkinson disease, galactorrhea and prolactinomas, has long been known to improve insulin sensitivity and glycemic control in T2DM. Bromocriptine as monotherapy or an adjunct to other antidiabetic agents for up to 1 year has reduced HbA1c

by 0.5 – 1.2%, reduced triglyceride, reduced some cardiovascular events, has not caused serious hypoglycaemia¹⁸.

Lipoic acid, isoferulic acid and angiotensin-converting enzyme inhibitors: The antioxidant α - lipoic acid, used in some countries to treat diabetic neuropathy, increases insulin sensitivity and improves glycemic control. Isoferulic acid increases expression of GLUT - 4 and decreases gluconeogenesis. Modest improvements of insulin sensitivity have been seen during treatment with angiotensin converting enzyme (ACE) inhibitors, possibly because of improved hemodynamics resulting from increased bradykinin¹⁹.

Anti-obesity agents: Several centrally acting appetite suppressing and satiety inducing anti - obesity agents also exert peripheral effects that improve some actions of insulin and assist glycemic control in overweight patients.

Sibutramine and Rimobant: has already been withdrawn because of side effects²⁰.

β - 3 Adrenoceptor agonists: Various β -3 adrenoceptor agonists have been shown to stimulate insulin release, improve insulin mediated glucose disposal and improve glycemic control in obese diabetic rodents, but adequate efficacy have yet to be demonstrated in humans¹³.

Sodium glucose cotransporter 2 inhibitors: Glucose is filtered through the renal glomeruli and all that has been filtered is reabsorbed in the proximal tubules. Reabsorption is mediated mostly via the sodium glucose co-transporter 2 (SGLT2) systems. Thus, specific inhibition of these transporters reduces hyperglycemia by elimination of excess glucose in the urine. Selective inhibitors of SGLT2 (termed "gliflozins") have been developed recently²¹. Possible adverse effects of osmotic diuresis during SGLT2 inhibition include risk of dehydration and electrolyte imbalance, as well as infection in the urinary tract and urogenital region.

Sirtuins: Sirtuins comprise a group of seven enzymes that are nicotina mide-adenine-dinucleotide(NAD)-dependent-histone deacetylases and/orADP ribosyltransferases. Sirtuin SIRT1 is widely expressed in mammalian tissues including liver, muscle and fat, and appears to promote mitochondrial biogenesis and activity in some tissues, increasing thermogenesis and reducing susceptibility to weight gain, diabetes and cardiovascular disease. SIRT1 in pancreatic β - cells may also facilitate insulin secretion. Several small molecule activators of SIRT1 have been studied in animal models²².

COUNTER REGULATORY HORMONES

These hormones increases blood glucose by stimulating hepatic glycogenolysis and gluconeogenesis. Agents that interfere with the secretion or action of counter regulatory hormones could potentially be therapeutically useful¹³.

Glucocorticoid antagonists: Increased glucocorticoid concentrations can result in truncal obesity, insulin resistance and hyperglycemia, any approach to reduce the glucocorticoid action will reduce these adverse effects. Selective inhibitors of 11 β - HSD1 have been shown to improve insulin sensitivity, glycemic control and plasma lipids in obese diabetic rodents²³.

Insulin: Insulin is required in patients with T2 DM who have developed sulfonylurea failure or those who are undergoing an acute infective or operative event.

CONCLUSIONS

Previously available treatments for T2DM have improved glycaemic control but have been accompanied by weight gain and increased risk of hypoglycaemia. T2DM is a progressive disease and more conventional agents do not address the decline of β cell function. Newer agents thus add to the choice of treatment options already available for T2DM and are welcome, especially in light of the recent safety concerns with some of the more modern agents.

Management of type 1 diabetes mellitus

Insulin is the only therapy available for patients with type 1 diabetes. Insulin replacement in patients with type 1 diabetes has been less than optimal because it is not possible to completely reproduce the normal physio-logic pattern of insulin secretion into the portal vein. The problem of achieving optimal insulin delivery remains unsolved with the present state of technology.

Immunogenicity has been markedly reduced with the use of highly purified human insulin preparations, thereby reducing complications associated with impure insulins.

Human insulin is now been produced by recombinant DNA technology. "Purified" insulin is defined as containing less than 10 ppm of proinsulin, whether extracted from animal pancreas or produced from biosynthetic proinsulin. All human and pork insulins currently available contain less than 10 ppm of pro insulin and are labeled as "purified." The more highly purified insulins currently in use preserve their potency quite well; therefore, refrigeration while in use is not necessary. At present, insulins in the USA are available only in a concentration of 100 units/ml (U 100) while in India both U 100 and U40 are available and dispensed in 10-mL vials. Four principal types of insulin are available: (a) Ultra short-acting insulin, with very rapid onset and short duration of action; (b) short-acting insulin, with rapid onset of action; (c) intermediate-acting insulin; and (d) long-acting insulin, with slow onset of action (Table 3)²⁴.

Table 3: Characteristics of currently used preparations of human insulin and insulin analogues

Type of insulin	Onset of action	Peak effect	Dosing interval	Time point to monitor effect
Mealtime	(min)	(min)		
Lispro (rapid acting)	5-15	30-90	At meal	2 hr
Aspart(rapid acting)	5-15	60-120	At meal	2-3 hr
Regular(short acting)	30-60	120-240	30-45 min premeal	4 hr
Background	(hrs)	(hrs)		
NPH(intermediate acting)	2-4	4-6	Twice daily	8-12 hr
Ultralente (long acting)	3-5	Limited peak	Twice daily	10-12 hr
Glargine (long acting)	2-4	Peakless	Once daily	Fasting glucose
Detemir	2-4	Peakless	Twice daily	Fasting glucose

Ultra-short-acting and short-acting insulins are dispensed as clear solutions at neutral pH. All other commercial insulins have been specifically modified to obtain more prolonged action.

Rapid and long-acting insulin analogs: Rapid-acting insulin analogs, such as insulin aspart, insulin glulisine and insulin lispro have a faster onset of action, sharper and earlier peak activity and more rapid return to baseline levels than regular human insulin. Given before the evening meal, large doses of regular insulin increase the risk of nocturnal hypoglycemia. These problems are reduced with rapid-acting insulin analogs²⁵.

Long-acting insulin analogs, detemir and glargine, the first soluble insulin analogs have a flat and prolonged time action profile. Bolus/basal therapy that combines premeal aspart or lispro with glargine or detemir insulin has emerged as the 'gold standard' for intensive injection therapy provided through multiple daily injections (MDI) in adults with T1DM²⁶.

METHODS OF INSULIN ADMINISTRATION

A. Insulin Syringes and Needles

Single unit syringes (those with a needle fixed to the syringe to minimize dead space) are available for injection of insulin. 27- or 28-gauge, and more recently even 30- gauge attached needles have greatly reduced the pain of injections. Disposable syringes may be reused until blunting of the needle occurs (usually after three to five injections).

B. Pen devices

Pen devices contain cartridges of U 100 regular human insulin and retractable needles. Cartridges containing insulin lispro; regular insulin, NPH insulin and pre-mixed insulin are available for use with these pens²⁷.

C. Sites for Injection

Any part of the body covered by loose skin can be used as an injection site, including the abdomen, thighs, upper arms, flanks, and upper outer quadrants of the buttocks. Exercise facilitates insulin absorption when the injection site is adjacent to the exercising muscle. Rotation of sites is advised to avoid delayed absorption when fibrosis or lipohypertrophy occurs owing to repeated use of

a single site. For most patients the abdomen is the recommended site for injection, since it provides a considerable area in which to rotate sites and there may be less variability of absorption with exercise than when the thigh or deltoid areas are used.

NEW AND IMPROVED INSULIN DELIVERY DEVICES

Advances in diabetes technology have helped to improve the outcomes of management of T1DM in last three decades.

Intranasal: soluble insulin administered intranasally is rapidly absorbed when given along with a detergent substance to facilitate adsorption. Preliminary clinical trials have demonstrated its efficacy in reducing post-prandial hyperglycemia in subjects with type 1 diabetes. However, its absorption is limited to less than 10% of the administered nasal dose. This reduces its cost-effectiveness, and most manufacturers have discontinued clinical trials until more progress is made in improving its bioavailability. Inhalers that can provide more precise delivery of drugs have been developed, and inhaled insulin is currently in phase III trials.

Insulin pumps and continuous subcutaneous insulin infusion: insulin pump devices have become smaller and increasingly more sophisticated in their functionality. Insulin is delivered through a cannula placed subcutaneously and replaced with a 72 h frequency. A continuous basal rate is programmed into the pump and additional boluses of insulin can be administered 'at the push of a button'. Smart pumps have a more sophisticated computer incorporated into the insulin pump. The delivery of CSII through insulin pumps has been extensively investigated in the paediatric and young adult population²⁸.

Continuous glucose monitoring (CGM) systems: This system, through which a subcutaneous, glucose oxidase coated sensor measures interstitial fluid glucose concentrations and converts them to a plasma glucose estimate, provides a promising modality for future management of type 1 diabetes. A plot of plasma glucose concentrations over a 24-h period are produced and can enable insulin adjustment to identify episodes of hyper or hypoglycaemia that may not have been identified using conventional capillary glucose monitoring. More recently, real-time CGM and CSII technologies have been combined in a single device and this exciting technology may represent a step towards an 'artificial pancreas'²⁹. However, despite advances, this technology is in its infancy and its current role in the management of type 1 diabetes is unclear.

Other modes of therapy in T1dm: Amylin analogues: Pramlintide is a synthetic analogue of amylin, a polypeptide hormone, co-secreted with insulin from pancreatic β cells. It is injected pre-prandially in addition to insulin and has shown modest improvements in post-prandial hyperglycaemia with 20-30% decrease of insulin dose³⁰. Treatment of type 1 diabetes with pramlintide is associated with fewer hypoglycaemic episodes and significant weight loss. Its use is limited by nausea and additional prick required besides insulin.

Pancreatic and islet transplantation: Whole-organ pancreatic transplantation for the treatment of type 1 diabetes has largely been reserved for those undergoing renal transplantation for end-stage diabetic nephropathy. While normalization of glycaemic control is achieved following successful transplantation, but this therapy carries the risk of pancreatic graft rejection and side effects of immunosuppression³¹.

Islet cell transplantation provides a promising treatment option for type 1 diabetes. β -cells isolated from a donor pancreas are injected into the portal venous system where they then lodge within liver sinusoids. These β cells remain glucose sensitive and secrete insulin into the portal system, in the same way as occurs in the physiological situation³². Variable β -cell yield using this isolation technique requires harvest from more than one pancreas to provide sufficient tissue for successful transplantation. Nonetheless, with the future promise of engineered β cells using stem cell differentiation methods, this technique of cell delivery/transplantation may provide a successful long-term treatment of glycaemia in type 1 diabetes.

IMMUNOTHERAPY

Pancreatic β -cell preservation using immune suppression or immune tolerance has been disappointing. When used as secondary prevention of type 1

diabetes, ciclosporin and anti-CD3 antibodies reduce the required insulin dose and prolong β -cell survival, as assessed by fasting and stimulated serum C-peptide concentrations³³. However, both of these treatment modalities have unacceptable side-effect profiles, particularly given the age of the target population. GAD-alum immunization in an attempt to promote immune tolerance in subjects with diagnosed type 1 diabetes did not significantly reduce the requirement for insulin or improve fasting serum C-peptide concentrations³⁴. The use of these therapies requires more research before their introduction as mainstream approaches to prevention of type 1 diabetes mellitus.

CONCLUSION

Future drug therapy of T1DM will depend on the success of ongoing and planned intervention trials. Immunomodulation alone, or possibly combined with immunosuppressive therapy, seems to be promising in reducing the loss of C-peptides after diagnosis. Studies of the function of the human immune system lag behind that of the mouse and rat. Since 2001, Trial Net, an international network of clinical research groups supported by the National Institutes of Health, has established an infrastructure for trials for predicting and preventing T1DM.

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Cost Analysis of a Dialysis Unit at a Tertiary Care Multi Specialty Teaching Hospital

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Abstract: The supply of dialysis therapy for patients with renal failure in the developing world is still inadequate. A complex business like healthcare requires frequent information about operations in order to plan for the future, to control present activities, and to evaluate the past performance of the organization. For a health care provider, dialysis facility becomes a profitable venture only if he has the knowledge and control on the cost of all the inputs that goes into providing the facility. A costing study gives the provider the necessary information required to carry out cost cutting exercise. Strategic cost-cutting must be planned carefully, as not all cost reduction techniques yield the same benefits.

INTRODUCTION

Dialysis and transplantation have become effective in prolonging the lives of patients with renal insufficiency. Conservative medical management of the patient and dialysis are the mainstay of therapy to acute renal patient¹.

The incidence of chronic renal disease is growing fuelled largely by diseases associated with an aging population, hypertension and increasing rates of diabetes largely related to obesity¹.

About 20% of patients with chronic renal failure are totally rehabilitated by dialysis, and another 30 to 40% of non-diabetics may be expected to be rehabilitated to functional level¹.

Recording the number of kidney patients undergoing haemodialysis worldwide show that around 1.7 million patients are currently kept alive by such a therapy³.

The dialysis market has seen a robust growth in the past 5 years. What makes this market more interesting and challenging is its customer base, which is relatively small yet of high value⁴.

It is among the most lucrative markets in per capita terms. Indian market for dialysis equipment and consumables was valued at Rs.231 Crore in 2008⁴.

As the number of people with end stage renal disease grows, the market for hemodialysis equipment and services is expected to expand, generating increased revenues throughout the forecast period⁴.

Hospital costs to patients are rising to unprecedented heights, and the estimates of expenses always seem to be higher than the income generated. Users expect that hospitals should base their rates on direct patient care alone. But this approach cannot permit the hospital to survive on a long term basis⁵.

Revenues of hospitals in the voluntary sector should not only cover the traditional direct patient expenses, but must also contribute towards, providing sufficient finances to meet current obligations, covering the costs of service to indigent patients and generating funds for up gradation and expansion of existing facility⁵.

Patients undergoing treatment receive services of varied nature from different departments. The hospital has to recover the expenses of the direct departments as also of the support departments from the patients availing these services⁶.

The cost of providing a service becomes evident after cost finding studies. The departmental charges should be set at least to equal these costs⁵.

The cost analysis is a tool which is useful in setting priorities for various courses of action to meet objectives, and provide an estimate of the net

financial value associated with each course of action (e.g. manpower and labour, material and equipment, facilities)⁵.

Aim: Economic evaluation of a dialysis unit using cost analysis as a tool.

METHODOLOGY

A prospective study was carried out in the dialysis unit, for estimating the cost incurred by the hospital for providing the service. The costs were considered under direct and indirect costs incurred per procedure. Direct costs included direct labour, direct material cost, depreciation and repair & maintenance cost of the equipment. Indirect costs included indirect labour, building and electrical maintenance and electrical consumption. Overhead cost was taken as 5 % of the total cost i.e. direct plus indirect costs.

RESULT AND ANALYSIS

Direct cost per procedure	
Direct material cost	963.73
Direct labour	241.83
Depreciation and maintenance cost of equipment	59.08
Electricity cost	37.4
Water consumption cost	9.6
Linen and laundry cost	4.6
Total Direct Cost	1,316.24

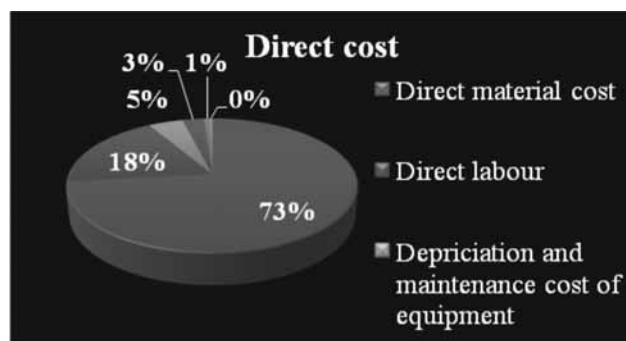


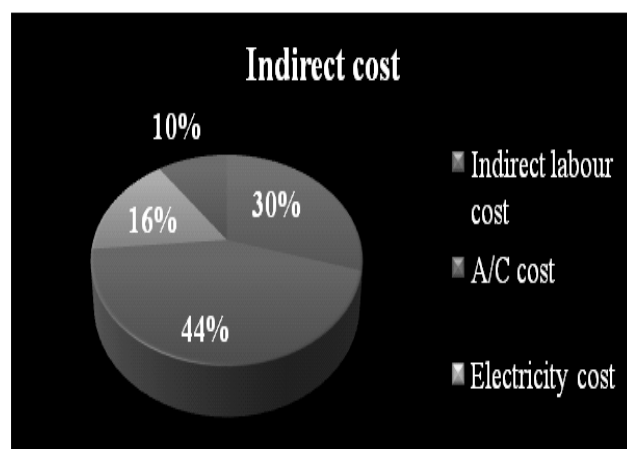
Fig 1: Direct material cost includes pharmacy and general store consumption.

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From the above chart it is evident that material cost followed by labour cost formed a major part of the direct cost.

From the above chart it is evident that material cost followed by labour cost formed a major part of the direct cost.

Indirect cost per procedure	
Indirect labour cost	40.8
A/C cost	60.48
Electricity and maintenance cost	22.6
Depreciation of building	13.7
Total Indirect Cost	137.58



Air conditioning charges and labour cost formed a major part of the indirect cost.

Unit Price/Cost per procedure	
Direct cost	1,316.24
Indirect cost	137.58
Overheads	72.69
Total Unit Price	1,526.51

The actual cost incurred by the hospital to provide dialysis service is Rs.1,526.51. The direct costs account for 86 percent of the total cost, while the indirect cost account for 9 percent and overhead cost being 5 percent of the total.

Profit	
Sale price per procedure	1,613
Cost per procedure	1,526.51
Profit per procedure	86.49

In the hospital the patients are charged Rs. 1613 per procedure.

DISCUSSION

The study was carried out with the aim to calculate the cost per dialysis procedure and the result suggests that the cost incurred per procedure was Rs. 1,526.51 and Rs.86.49 was the profit obtained by the hospital per procedure. It is evident from the study that material cost, labour cost and air conditioning cost are the major inputs to the dialysis unit. The average numbers of procedures carried out in the dialysis unit per day are 52 and this includes both inpatients as well as outpatients. So the profit made by the dialysis unit per day is Rs. 4,497.48.

Hospital cost information is derived by relating the inputs of resources in monetary terms to the outputs of services provided by the hospital. Cost information is part of the basic information needed by managers and policy makers for making decisions about how to improve the performance of a hospital, where to allocate the resources within or among hospitals, or to compare the performance of different hospitals to one another. Some of the basic reasons for wanting cost information are to improve efficiency, increase effectiveness, enhance sustainability, and improve quality.

CONCLUSION

Cost information is part of the basic information needed by managers and policy makers for making decisions about how to improve the performance of a hospital and where to allocate the resources within or among hospitals. Cost data are not always available from routine data systems, due to poor information systems and lack of resources devoted to hospital management. Without quality cost data it is not possible to make accurate projections, improve technical efficiency, control expenditure and enhance accountability of managers. A scientific costing system is a very important tool for managements to fulfil these needs and hence, is imperative for the successful running of a hospital.

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Study of Patient Satisfaction at Cardio Thoracic and Neurosciences Centre at AIIMS, New Delhi, India

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Abstract: Hospitals have evolved from being an isolated sanatorium to a five star facilities. The patients and their relatives coming to the hospital not only expect word- class treatment, but also other facilities to make their stay comfortable in the hospital. This change in expectation has come due to tremendous growth of media and its exposure, as well as commercialization & improvement in the facilities. The study was conducted by distributing 50 structured questionnaires amongst patients and their relatives to find out the factors which satisfy patients and their relatives in a tertiary care teaching hospital.

Key Words: Hospital, Expectation, Patient's satisfaction, Satisfiers, dissatisfiers

INTRODUCTION

Patient Satisfaction refers to fulfillment or meeting of expectation of a person from a service or product. When a patient comes to a hospital, he has a pre set image of the various aspects of the hospital as per the reputation and cost involved. Although their main expectation is getting cured and going back to their work, but there are other factors, which affects their satisfaction. Sometimes they might have rated a hospital very low on the basis of information they have got from different sources, but they find it above their expectation and they are satisfied. Similarly if they have got a very high expectation from a hospital, but if they find it below their expectation, they will not be satisfied.

Hospitals have expanded in terms of availability of specialties, improved technologies, facilities and increased competition, the expectations of patients and their relatives have increased many fold. Consumer expectation in any medical experience influence how soon and how often they seek care from which medical facility. High expectation from a medical organization is a positive indicator of its reputation in the society and is very important for attracting patients, where as low expectation deters patients from taking a timely medical help, thus negatively affecting himself as well as the medical care provider. However a very high and unrealistic expectation may lead to dissatisfaction despite reasonable good standards of medical practice.

Previously there were very few Government hospitals with no charge to the patients. Hence the expectations were also very minimal. But now the scenario has changed. The hospitals (even government) have started charging to the patient in the name of user charges, private hospital care cost has gone very high. With the advent of Consumer Protection Act (1986) the patient's expectation has also gone very high. Now hospitals have to be very careful about patient dissatisfaction to avoid any unnecessary litigation. Knowledge of expectation and the factors affecting them, combined with knowledge of actual and perceived health care quality, provides the necessary information for designing and implementing programs to satisfy patients. Human satisfaction is a very complex concept that is affected by a number of factors like life style, past experience, future expectation and the values of individual and society in terms of ethical and economical standings. Maslow in 1954 gave hierarchy of needs for satisfaction and motivation of individuals. According to him, needs generally have priority in following order: Physiological, Safety & security, Sense of belonging, Esteem and Self actualization.

REVIEW OF LITERATURE

Currently available national and international literature was reviewed to understand the concept of patient satisfaction.

Codmans¹ "Assessment of the outcomes of care" investigated four aspects of care for each case received (1) The physicians' or surgeons' input (2) The hospitals contribution (3) The patients' disease or condition and (4) The factors which deterred patient's co- operation. Pathology reports help determine whether surgery was indicated in a case of Appendectomy or not. They have had a wide application in the evaluation of quality of care. Ovariectomies and Hysterectomies were examined by Doyle². Because many of these outcome measures do not assess the overall performance of the organization, Roemer had developed a method to adjust hospital death rates (which were calculated for all patients and all conditions), so that they could be used as an over all measure of the quality of care. He called his index as " Surgery adjusted Death Rate" (SADR). SADR tried to overcome the distortion when hospital death rates are compared which are not adjusted for patient mix and particularly severity of illness of the hospital's patient population.

Hendrickson³ examined effects of implementing nursing information computer system in 17 Hospitals in New Jersey, USA. They observed that staff impression of the effects of system was positive; documentation was better (more readable). "Effects of a hospital based managed care on the cost and quality of care" was studied by Bregan, MA et al⁴ on women delivered by Caesarean in the maternity unit at a tertiary level university hospital of Iowa, USA . They found decrease in ALS (Average length of stay) by 13.5 % and the average cost decreased by 13.1 %, patients' perception quality of care increased from 4.26 to 4.41 on a 1-5 scale.

Cock DJ et al⁵, conducted a "continuous quality improvement study" in their medicine department of Mc Master University, Faculty of Health Sciences, Ontario by monitoring patterns in Medical teaching ward. They found that in 68 % of cases, oxygen therapy was initiated by house staff, nurse initiated therapy in 18 % of cases, but discontinued it more often than any other health worker. 30% of patients on oxygen did not meet the criteria set by American College of Chest Physician. This showed that practice guidelines based on best available evidence are needed to increase the efficiency of Oxygen use.

Houston and Pasanen⁶ employed a patient satisfaction questionnaire with patients recently discharged after at least 2 days stay at a large hospital. Care was evaluated extremely favorable with the highest rating given to physician and nursing care. Most dissatisfaction was due to that the physicians did not disclose details of their illness. 17.1% were reluctant to return to the medical care facility.

Khosla et al.⁷ found in their study, emphasis by the patients of two Delhi Hospital on varying needs according to their income groups:

- Low Income Group- improved physical facilities, improved diet

and relaxation of visiting hours, better service by class IV staff, human and sympathetic behaviour and transport facilities after discharge.

- Middle and High Income group- personal and prompt attention of doctors, better behaviour by class IV staff, improved physical facilities, relaxation of visiting hours.

Jain & Prasad⁸ adopting interview techniques studied the opinions of 400 patients admitted to medical wards of Gandhi memorial College and associated hospitals and reported about patient satisfaction as shown below:-

Factor	Satisfied	Unsatisfied
1. Diet	66.4%	33.6%
2. Doctor- patient relationship	70%	30%
3. Nurse- patient relationship	78.3%	21.7%
4. Ward boys and sweeper	43%	57%
5. Reaction towards medical treatment	61.15%	38.5%

Bhatia⁹, in his study among orthopedic patients found that the dissatisfaction was usually with food, entertainment, visiting hours and lack of proper interaction with the staff i.e. doctors, nurses etc. The patients also complained of lack of privacy.

Timmappaya et al¹⁰ through a hypothesized model, studied a relationship between patient satisfaction, hospital status, employee satisfaction and service. This model assumes that the performance of the hospital will depend upon proper functioning of its social system, because practically every person working in the hospital depend upon some other person, since there is extensive diversion of labor and highly specialized work of each person. Doctors, nurses and others cannot function separately or independent of one another. Their work is mutually supplementary, interlocking and interdependent. If the system has to function properly and has to attain its objectives, its members and departments have to be highly co-ordinate. Job satisfaction is one of the conditions for better patient co- ordination and workers morale. Better co- ordination and job satisfaction of the employees will result into better patient care and satisfaction and consequently it will earn a better reputation for the hospital in the community. Good reputation of the hospital improves the status of its employees, which also contributes to their job satisfaction. Job satisfaction again via services leads to patient satisfaction to hospital reputation etc.

As a part of this study Chopra et al¹¹ carried out participant's observation in patient role in a hospital and confirmed through a flow chart that the aforesaid two factors led to the better out put i.e. recovery, which in turn led to patient satisfaction. In their report, hospital food, communication, discharge policy, use of influence, nursing orderly and sweepers were identified as dissatisfying factors. However, it was concluded that best possible hospital services might take care of patient dissatisfaction but to attain positive satisfaction patients must have a good medical care.

METHODOLOGY

The study was conducted by Review of available national and international literature on the subject, carrying out survey amongst patients and their relatives at Cardio Thoracic and Neurosciences Centre by using structured questionnaire and by analyzing the data using appropriate statistical methods.

OBSERVATION

The study about patient satisfaction in Cardio Thoracic and Neurosciences Centre was conducted by circulation of structured questionnaires amongst 50 patients and relatives of private and general wards. The questions asked were about the process of patient getting admitted, their reception in the ward, room preparation, behavior of doctors, nurses, orderlies, food services, cleanliness of toilet etc. The questions were given same scale from excellent

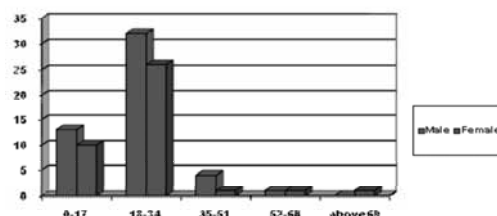
to poor for uniformity of comparison. There were two open ended questions for their opinion about the problems and suggestions for improvement of services.

1. **Admission & Reception**- There is a long queue of patients waiting for admissions causing delay in admissions of seriously ill patients. There is procedure of issuing only one attendant's pass. However if a patient is sick or attendant is a lady and the attendant has to go out to get any medicines etc, then he has problem. 17% patients felt it was excellent, 25% patients felt it was very good, 40% felt good, 18% felt it was average. None of them said it to be poor. Overall 82% people were satisfied with the services at admission counter.
2. **Room preparation at the time of admission**- 7% patients felt it was excellent, 48% patients felt very good, 25% felt good, 20 % felt it was average. 8 % of them said it to be poor. As a whole 81% people were satisfied with the room preparation at the time of admission.
3. **Nursing services** - 7% patients felt it was excellent, 48% patients felt very good, 25 % felt good, 20% felt it was average. 1 of them said it to be poor. So on a whole 80% people were satisfied with the Nursing services.
4. **Cleanliness of toilets** - None of the patient felt it was excellent, 7 % patients felt very good, 42% felt good, 42% felt it was average. 9 % of them said it to be poor. On a whole only 49% people were satisfied with the cleanliness of the toilets.
5. **Briefing about Policies, rules and regulations**- 3% patients felt it was excellent, 13% patients felt very good, 50 % felt good, 14% felt it was average. 20 % of them said it to be poor. So on a whole 76 % people were satisfied with the briefing about rules and regulations at the time of admission. It was observed that the briefing about the rules and regulations of hospital had got 40 % average and 22 % of poor response. It was the biggest dissatisfier.
6. **Doctors**- 37% patients felt it was excellent, 40% patients felt very good, 17% felt good, 3 % felt it was average. 3% of them said it to be poor. On total 94 % people were satisfied with the explanation about disease and treatment by doctors.
7. **Diet services**- 3 % patients felt it was excellent, 35% patients felt very good, 40 % felt good, 22% felt it was average. None of them said it to be poor. Food services have got 22 % average response. It was the second major dissatisfier. Overall, only 78% people were satisfied with the quality of food served in the hospital.
8. **Behavior of Nurses**- 10 % patients/ attendants felt it was excellent, 42% patients felt very good, 42 % felt good, 6 % felt it was average. None of them said it to be poor. On a whole 92% people were satisfied with the behavior of Nurses.
9. **Behaviour of Doctors**- 50% patients/ attendants felt it was excellent, 30% patients felt very good, 17% felt it was good. Only one of them (3%) said it to be poor. Some people felt that the doctors have become less sensitive and empathetic to their problems. The new generations of doctors should be trained in soft skills and value of empathic care must be reemphasized. However 92 % people were satisfied with the behavior of Doctors.
10. **Behaviour of Orderlies/ sweeper**- 13% patients/ attendants felt it was excellent, 26% patients felt very good, 42 % felt it was good. 19% average, 13 % of them said it to be poor. It was felt that there is less sensitivity about protocols to avoid cross infection amongst staff. Some people complained about the bad behavior of Hospital and Sanitary attendants, although they did not give in writing. The shortage of Hospital attendants for taking the patient for investigations was also reported. On a whole 83% people were satisfied with the behavior of Orderlies/ sweeper.

RECOMMENDATIONS

On interaction with patients and their attendants, following suggestions

Services	Excellent	Very Good	Good	Average	Poor
Admission & Reception	17	25	40	18	
Room Preparation		7	48	25	20
Nursing		7	48	25	20
Cleanliness	0	7	42	42	9
Briefing about rules	3	13	50	14	20
Medical care		37	40	17	3
Diet services	3	35	40	22	
Behavior of Nurses		10	42	42	6
Behavior of Doctors		50	30	17	
Behavior of Orderlies	13	26	42	19	13



came out for improvement:

- Admission:** There is procedure of issuing only one attendant's pass. However if a patient is sick or attendant is a lady and the attendant has to go out to get any medicines etc, then he has problem. The policy of issuing two passes may have to be reconsidered. There is a long queue of patients waiting for admissions causing delay in admissions of seriously ill patients. Criteria of admissions should be clearly defined and told to all the doctors. The reception counter should have facility for photocopier with charges as the patients have to go to distant places for the same before getting discharge.
- Room preparation:** there were many complaints of cockroaches and rodents in the ward. The pest control department should do regular sprays and take effective measures for controlling them. Room preparation should be improved by more cleaning, anti pest and anti rodent measures. The quality of washing of bed sheets etc should be improved.
- Nurses' cooperation:** Over the years many nurses have been promoted to supervisor grades. Hence the working number of staff nurses has decreased. This has started showing in their efficiency and behavior. More number of staff nurses should be posted for patient care.
- Toilets:** the cleanliness of toilets should be improved. It may be done twice a day. Frequent and surprise checks by sanitary inspectors and administrators will instill a sense of responsibility and alertness in sanitary attendants.
- It was observed that the **briefing about the rules** and regulations of hospital had got 40 % average and 22 % of poor response. It was the biggest dissatisfier. Although smoking is strictly prohibited in the hospital, still some people including staff are found openly smoking in the hospital. The patients and their relatives should be clearly informed in writing about the rules and regulation. This should be available in Hindi also.
- Explanation about disease and treatment by doctors:** All tests to be carried out were not told at the time admission, which caused frequent delay in treatment and procedures. Patients require more information about their disease and treatment. Patient should be explained in detail about the tests and procedures to be carried out and these should be pre planned and if possible may be got done from the OPD itself. There were no guidelines for attendants about care of postoperative patients.
- Food services** have got 22 % average response. It was the second major dissatisfier. The quality of food, especially quality of chapattis, and its presentation should be improved.
- Behaviour of Nurses:** Over the years number of senior nurses have increased and working staff nurses have decreased. This is causing increased stress amongst them leading to some downfall in

their behavior.

- Behaviour of Doctors:** Although 100% of responses showed that the doctors at CNC AIIMS were above good level, yet some (2%) people felt that the doctors have become less sensitive and empathetic to their problems. The new generations of doctors should be trained and value of empathic care must be re-emphasized.
- Behaviour of Orderlies/ sweeper:** the patients were disturbed by frequency of visits by different staff at different time. The timing for activities like nursing, cleaning, ward rounds should be fixed, so that the patient is mentally prepared for the same and can take rest at other time. Some people complained about the bad behavior of hospital and sanitary attendants. There is no sensitivity about avoiding cross infection in staff like washing of hands. They should be trained about the importance of hand washing and other universal precautions, before and after touching any patient. They should be regularly trained and sensitized about how to improve their image and behavior.
- With the introduction of **consumer charges**, the hospital services have become costly for poor people. Being a government hospital, people expect it to be free of cost. This should be explained to the patient before getting admitted in the hospital. However this policy of revising rates may be looked into.
- There should be **package charges** for all procedures to avoid running around by patient's attendant for minor requirements. The prescriptions should be given at least for 3 days with condition of return ability in case of non- utilization.
- Media:** One patient observed that there are many **negative articles about AIIMS**, in the newspapers. They should cover positive achievements also. The media coverage should be improved the image of the institute by giving more publicity to the good work being done.

CONCLUSION

It was found in the present study that most of the patients are satisfied with most of the services in the Cardio Thoracic and Neurosciences Centre of AIIMS, New Delhi.

Five major satisfiers were:

- Behaviour of doctors
- Explanation about disease and treatment
- Courtesy of staff at admission counter
- Behaviour of nurses
- Cooperation of nurses.

Five major dissatisfiers were:

- Cleanliness of the toilet
- Quality of the food
- Explanation about rules and regulations.
- Behaviour of Hospital and sanitary attendants
- Room preparation

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Analysis of Inventory of Drug and Pharmacy Department of a Tertiary care Hospital

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Abstract: The health care in modern days has become more complex sophisticated and more expensive in terms of cost of drugs, surgical equipment and hospital stay. The study was undertaken with the prime objective of studying the drugs stored in pharmacy department according to their cost and criticality. To access the inventory of drugs at SKIMS, the area of study included- main drug and pharmacy store. It was a retrospective study carried out for a period of one year from 1-4-2005 to 31-3-2006. The study revealed that 156 items in total were stored during the study period. The value of annual consumption of the inventory was worked out to be Rs.9303507. Out of these drugs, 15.38% consumed 70% of annual drug expenditure comprising group 'A' items. 22.43% consumed 20% of annual drug expenditure forming group 'B' items. Rest 62.17% items consumed only 10% of total budget, classified as group 'C' items. VED classification of the inventory revealed that out of 156 items stored, 19.23% were considered 'Vital' by the constituted medical panel; 39.10% were 'Essential' and the rest, 41.66% were considered 'Desirable'. The results of the study are expected to guide the management to delegate the responsibility to different officers and apply the "Principle of Management by Exception". Moreover it will facilitate the management in controlling the cost and ensure the availability of vital and essential items in the hospital which will be in the interest of patients and the administration.

INTRODUCTION

The health care in modern days has become more complex sophisticated and more expensive in terms of cost of drugs, surgical equipment and hospital stay. With rise in per capita income of general population and also with rise in the level of general information and education of people, the demand for more sophisticated medical care has come up. However, the rise in hospital costs has been substantially more than the rise in general consumer price. "Since 1950, the cost of one day's stay in a hospital has increased more than 1,000 percent compared with 135 percent climb in the consumer price index".¹

Economics of materials control is a matter of self presentation in today's competitive environment. Materials control is a matter of rupee control; it is axiomatic that stringent controls must be placed on higher value items. The management of inventory paves the avenues for optimizing the costs of Medicare services besides making available materials to the patients which increase the quality of health care services.

Out of materials, drugs consume a major portion of hospital budget. The basic social issue confronting medical practice today is how to improve the organization of utilization of the fruits of medical knowledge, the technological advancement and managerial innovation in Health Care Institutions on most economical terms. The rising hospital cost and methods to contain this have attracted the attention of one and all be it the professionals, the public and private sector management and even the trade union activist.² The hospital management has to ensure the availability of various drugs round the clock as these are essential and vital for patient care. The Pharmacy Departments are most often charged with responsibility for managing drug and delivery system costs. Systems should develop to utilize drug and delivery resources in a cost effective fashion. The pharmacy management team should focus on developing effective strategies to maximize leverage of drugs and human resource cost.

Since there is widespread concern about the cost of health care, a variety of cost containment initiatives have been pursued.

The main health concern now-a-days is allocation of resources on a rationale basis. Management must therefore lay stress on the cost analysis and formulate guidelines for the definitions of cost and established standards through cost analysis. Cost analysis is a research tool for the financial management in a hospital. The objective of the study was to analyze the drugs stored in Drug and Pharmacy of Sher-i-Kashmir institute of Medical sciences according to

their cost and criticality (ABC and VED analysis).

MATERIAL & METHODS

It was a retrospective study carried out for a period of one year from 1-4-2005 to 31-3-2006. The data was collected by checking the stock registers and the bills of the supplies of main drug store. The data included only those drugs which were provided to the patients by the hospital and does not include the drugs for sales counter, surgical items, disposables, and dressing items. The researcher visited the main drug store daily on working days and the items were recorded on predesigned and pretested proforma developed for the same purpose. The proforma enlisted the inventory of drugs stored for the study period as well as additional characteristics like cost per unit, units stored as well as the total cost for each drug. The proforma also categorized drugs in accordance with VED analysis. The total cost of the drugs stored was entered on the proforma in descending order with highest cost item at the top and lowest cost item at the bottom. The cumulative cost was calculated and entered on the same proforma. Cumulative cost of the drugs was compared with actual no. of drugs and the results drawn on a graph showing percentage of A, B and C category drugs.

A-category being the highest cost items.

B-category the intermediate cost items and

C-category the lowest cost items.

To study the inventory of drugs on the basis of their criticality (VED analysis), a team of five medical experts including a physician, a surgeon, a cardiothoracic surgeon, a gastroenterologist and a cardiologist was constituted. The inventory of drugs stored for the study period was presented to each member of the team for categorization of drugs on the basis of VED analysis.

The final list of drugs arranged on the basis of VED analysis by medical experts was analyzed for concurrence of opinion regarding classification. Up to 60% concurrence was taken as cutoff limit. Drugs having concurrence of opinion less than 60% were not considered for the category.

RESULTS

Cost accounting has become an essential part of healthcare management. The increasing costs have forced the healthcare managers to know the costs of different alternatives, approaches to providing care. These costs can only be known if the organization has the knowledge and capability to measure.³ With the advent of advanced medical technology and drugs, the

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expenditure on health-care delivery is increasing disproportionately as compared to the resources available. Armed forces medical services (AFMS) provide state of art medical care through a network of over 100 hospitals with a central procurement system. In one of their studies, they found that the drugs consume approximately 60% of the total consumable budget.^{4,5} This necessitates effective and efficient management of medical stores. Efficient priority setting, decision making in purchases and distribution of specific drugs, close supervision of drugs belonging to important categories, and prevention of pilferage depends on drug and inventory management. In a study from a large state funded hospital, control measures for expensive drugs have resulted in 20% savings.⁶

Inventory control is the tool of management which is used to maintain an economic minimum investment in materials and products for the purpose of obtaining a maximum financial return. ABC analysis is the analysis of stores on cost criteria. VED analysis analyses inventory on the basis of criticality in relation to the functioning of the hospital. The study revealed that 156 items in total were stored during the study period. These items included the drugs provided by the hospital to the patients and does not include the drugs for sales counter, surgical items, disposables and dressing materials. The value of annual consumption of the inventory was worked out to be Rs.9303507/-.

This amount does not include the inventory carrying cost, inventory storage cost and inventory acquisition/replacement costs.

Out of these drugs, 24 items (15.38%) consumed 70% (Rupees 6512454) of annual drug expenditure comprising group 'A' items. 35 items (22.43%) consumed 20% (Rs.1860701) of annual drug expenditure forming group 'B' items. Rest 97 items (62.17%) consumed only 10% (Rs.930350) of total budget, classified as group 'C' items- Table 1.

Table-1: ABC analysis of drugs at SKIMS Drug and pharmacy deptt.

Drug analysis	Category			Total
	A	B	C	
Total annual consumption(%)	70	20	10	100
Value of annual consumption(Rs)	6512454.9	1860701.4	930350.7	9303507
No. of items	24	35	97	156
%age of items	15.38	22.43	62.17	100

The annual drug consumption in terms of rupees was plotted against the inventory of items stored during the study period and is depicted in Fig-1.

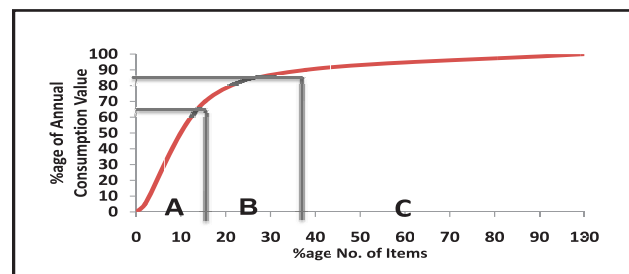


Figure 1: ABC Analysis of drugs at SKIMS Drug & Pharmacy Department

For ABC analysis it is the annual value of consumption which is taken into consideration and has nothing to do with the unit cost of the item.

The curve clearly depicts the percentage no. of items (A=15.38%, B=22.43, C=62.70%) and their percentage annual consumption value (A=70%, B=20%, and C=10%).

VED classification of the inventory depicted in Table-2 revealed that out of 156 items stored 30 items(19.23%) were considered 'Vital' by the constituted medical panel; 61 items (39.10%) were 'Essential' and the rest 65 items (41.66%) were considered 'Desirable'. Out of 30 vital items, 10

items had 100% concurrence of opinion of the medical panel, 7 items had 80% concurrence while 13 items had 60% concurrence of opinion on drug classification. 61 items which were considered essential, 25 items had 100% concurrence of opinion of medical panel for being included as 'Essential items'. Only 33 items of the remaining 65 items considered desirable had 100% concurrence of opinion of the medical panel.

Table-2: Distribution of drugs into VED classification.

Category of drugs	No. of drugs	% of drugs	Concurrence of medical panel on drug classification		
			100%	80%	60%
Vital	30	19.23	10	7	13
Essential	61	39.10	25	20	16
Desirable	65	41.66	33	20	12
Total	156	100	68	47	41

The ABC-VED matrix classification of the inventory depicted in Table-3 reveals that 49 items (31.41%) out of 156 items constituted Category-I items. 10 items of Category-I items were both high cost and vital, 11 items were high cost and essential, 8 items were high cost and desirable. Category-II items (39.10%) was constituted by intermediate cost and essential items numbering 17, intermediate cost and desirable items numbering 11 while 33 items were low cost and essential.

Table-3: Showing ABC-VED matrix

Category of Drugs	V	E	D	Matrix Classification
A	(AV) 10	(AE) 11	(AD) 8	Category-I (31.41%)
B	(BV) 9	(BE) 17	(BD) 11	Category- II (39.10%)
C	(CV) 11	(CE) 33	(CD) 46	Category -III (29.48%)

Category-III, items (29.48%) numbered 46, were low cost and desirable items.

DISCUSSION

The rising cost of the health care has become a matter of great concern all over the world. Today's healthcare is more complex, more sophisticated and it is hoped to be more effective. Increase in costs of hospital care, modern technology, inflation, increasing demands and expectations of public are necessitating the development of financial policies and mechanisms. The main healthcare concern nowadays is development of resources on rationale basis.

Approximately 35% of the annual hospital budget is spent on buying materials including drugs. This necessitates effective and efficient management of medical stores. Efficient priority setting, decision making in purchase and distribution of specific drugs, close supervision on drugs belonging to important categories, and prevention of pilferage depend on the drug and inventory management.

ABC analysis of the drugs stored at Drug and Pharmacy deptt. of SKIMS revealed that 156 items were stored in total during the period of study. The annual value of consumption for the inventory worked out to be Rs.9303507. Of these drugs 15.38% items (n=24) consumed 70% of annual drug expenditure comprising group "A" items. 22.43% items (n=35) consumed 20% of annual drug expenditure, forming group "B" items. Rest 62.17% inventory consumed only 10% of the annual budget and were classified as group "C" items.

Research by Lt.Col.R Gupta et al in 2007, studied ABC and VED analysis in medical stores of a 190 bedded hospital. The results of the study showed that 14.4% (n=47) items consumed 70% of annual drug consumption comprising group "A", 22.46% (n=73) items 20% of annual drug consumption forming group "B" items and rest 205 (63.7%) drugs merely consumed 10% of the annual drug expenditure, grouped as "C" items. The findings of the study are

in complete agreement with the findings of the present study.

Another study inline with the findings of present study by Ridhi Prakash Doshi et al observed that about 70% of the annual drug expenditure was on 35 drugs, 20% on 56 drugs and 10% on 308 drugs.⁷

The drugs belonging to group "A" category should be controlled strictly by top management of the institution. The group "B" items require a moderate control by the middle level managers while the "C" items can be left for the lower management as it requires lesser control measures for order and purchase. Also in line with the findings of the present study, research by Ashraf Khan et al at a tertiary care institute revealed that cumulative cost of Rs.87 lac was spent on 198 items stored during the period of study.⁸

Most of drug budget was spent on "A" items which was 75% and rest 25% on "B" and "C" items which was found as 18% and 7% respectively. Further in comparison with the results of present study, research by D Mario et al observed that 822 drugs were stored during the period of study. Out of 822 drugs, 10.83% were classified as "A" category and consumed around 69.82% of the annual budget. "B" category items constituted 20% and consumed 20.13% of annual consumption budget. Group "C" items constituted 69.10% of the total inventory and consumed 10.05% of the annual budget.

VED classification of the inventory revealed that out of 156 items stored, 30 items (19.23%) were considered "Vital" by the constituted medical panel; 61 items (39.10%) were "Essential" and the rest 65 items (41.66%) were considered "Desirable". Out of 30 vital items, 10 items had 100% concurrence of opinion of the medical panel, 7 items had 80% concurrence while 13 items had 60% concurrence of opinion of the constituted medical panel on drug classification. 61 items which were considered essential, 25 items had 100% concurrence of opinion of the medical panel for being included as essential items.

Only 33 items of the remaining 65 items considered desirable had 100% concurrence of opinion of the medical panel. Lt.col.Gupta et al in their research observed that 24 (7.3%) items constituted vital, 160 (49.3%) items were considered essential and the rest 141 (43.4%) were considered desirable. Inline with the findings of the present study, Ridhi Prakash Doshi et al also observed that 13% (n=54) drugs were vital for the patients life, 51% (n=203) drugs were essential and 36% (n=142) were considered desirable.

The ABC-VED matrix revealed that 10 items of Category-I drugs were both high cost and vital, 11 items were high cost and essential and 8 items were high cost and desirable.

Category-II items were constituted by intermediate cost and essential items (n=17), intermediate cost and desirable items (n=11), and 33 items were low

cost and essential.

The Category-III items were both low cost and desirable. Inline with the findings of the present study, Lt.Col.Gupta et al observed that 68 items were classified as Class-I items, 159 items constituted Class-II, while 98 items were constituted as Class-III.

In a comparable study by Sikder SK et al ABC-VED matrix shows that out of 292 items, 63 (21%) items were Class-I, 164 items (56%) Class-II and 65 items (22%) were Class-III. In agreement with the findings of the present study, research by Ridhi Prakash et al showed that Category-X consists of expensive and vital drugs accounting for 20.6% of drugs. Category-Y consists of less expensive and essential drugs accounting for 50.9% and Category-Z consists of cheap and non-essential drugs accounting for 28.6%.

CONCLUSION

The study has analyzed the inventory of drugs as per their cost and criticality. It is expected to guide the management to delegate the responsibility to different officers and apply the "**Principle of Management by Exception**". Moreover it will facilitate the management in controlling the cost and ensure the availability of vital and essential items in the hospital which will be in the interest of patients and the administration. It is also suggested that the sales counter inventory be also analyzed which involves more costly drugs and have much more financial implications.

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Future Medicine: Nanomedicine

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Abstract: Nanotechnology is a field of applied science focused on the design, synthesis, characterization and application of materials and devices on the nanoscale. The application of nanotechnology within medicine has the ability to revolutionize the cure, alleviation and prevention of disease drastically, and ultimately reinforce the restoration and preservation of health through the design, characterization, production and application of nano sized, intelligent materials.

Nanomedicine is the preservation and improvement of human health using molecular tools and molecular knowledge of the human body. Nanomedicine will have extraordinary and far-reaching implications for the medical profession, for the definition of disease, for the diagnosis and treatment of medical conditions including aging, and ultimately for the improvement and extension of natural human biological structure and function. As the science and technology of nanomedicine speed ahead, ethics, policy and the law are struggling to keep up. It is important to proactively address the ethical, social and regulatory aspects of nanomedicine in order to minimize its adverse impacts on the environment and public health and also to avoid a public backlash. At present, the most significant concerns involve risk assessment, risk management of engineered nanomaterials and risk communication. Future applications of nanomedicine will be based on the ability to build nanorobots. These nanorobots could actually be programmed to repair specific diseased cells, functioning in a similar way to antibodies in our natural healing processes. Human health has always been determined on the nanometer scale; this is where the structure and properties of the machines of life work in every one of the cells in every living thing. The practical impact of nanoscience on human health will be huge.

INTRODUCTION

Nanotechnology consists of the processing of, separation, consolidation, and deformation of materials by one atom or one molecule. More broadly, nanotechnology includes the many techniques used to create structures at a size scale below 100 nm. The biological and medical research communities have exploited the unique properties of nanomaterials for various applications (e.g., contrast agents for cell imaging and therapeutics for treating cancer). Terms such as biomedical nanotechnology, bionanotechnology, and nanomedicine are used to describe this hybrid field. Functionalities can be added to nanomaterials by interfacing them with biological molecules or structures. Nanomaterials can be useful for both in vivo and in vitro biomedical research and applications. The integration of nanomaterials with biology has led to the development of diagnostic devices, contrast agents, analytical tools, physical therapy applications, and drug-delivery vehicles.

NANOMEDICINE

Nanotechnology has become a new advent of medicine (nano-medicine). The use of nanotechnology in medicine offers some exciting possibilities. Some techniques are only imagined, while others are at various stages of testing, or actually being used today. Two main approaches are used in nanotechnology: one is a "bottom-up" approach where materials and devices are built up atom by atom, the other a "top-down" approach where they are synthesized or constructed by removing existing material from larger entities. Nanotechnology in medicine involves applications of nanoparticles currently under development, as well as longer ranges research that involves the use of manufactured nano-robots to make repairs at the cellular level (referred to as nanomedicine). Nanotechnology-on-a-chip is one more dimension of lab-on-a-chip technology. Biological tests measuring the presence or activity of selected substances become quicker, more sensitive and more flexible when certain nanoscale particles are put to work as tags or labels. The overall drug consumption and side-effects can be lowered significantly by depositing the active agent in the morbid region only and in no higher dose than needed. This highly selective approach reduces costs and human suffering. A targeted or personalized medicine reduces the drug consumption and treatment expenses resulting in an overall societal benefit by reducing the costs to the public health system. Nanotechnology can help to reproduce or to repair damaged tissue. This so

called "tissue engineering" makes use of artificially stimulated cell proliferation by using suitable nanomaterial-based scaffolds and growth factors. Tissue engineering might replace today's conventional treatments, e.g. transplantation of organs or artificial implants. There are four entry routes for nanoparticles into the body: they can be inhaled, swallowed, absorbed through skin or be deliberately injected during medical procedures (or released from implants). Once within the body they are highly mobile and in some instances can even cross the blood-brain barrier.

TYPES OF NANOPARTICLES

Nanoparticle contrast agents are compounds that enhance MRI and ultrasound results in biomedical applications of in vivo imaging. These particles typically contain metals whose properties are dramatically altered at the nano-scale. Gold "nanoshells" are useful in the fight against cancer, particularly soft-tissue tumors, because of their ability to absorb radiation at certain wavelengths. Once the nanoshells enter tumor cells and radiation treatment is applied, they absorb the energy and heat up enough to kill the cancer cells. Positively-charged silver nanoparticles adsorb onto single-stranded DNA and are used for its detection. Many other tools and devices for in vivo imaging (fluorescence detection systems), and to improve contrast in ultrasound and MRI images, are being developed.

In the case of cancer therapies, drug delivery properties are combined with imaging technologies, so that cancer cells can be visually located while undergoing treatment. The predominant strategy is to target specific cells by linking antigens or other biosensors (e.g. RNA strands) to the surface of the nanoparticles that detect specialized properties of the cell walls. Once the target cell has been identified, the nanoparticles will adhere to the cell surface, or enter the cell, via a specially designed mechanism, and deliver its payload.

Once the drug is delivered, if the nanoparticle is also an imaging agent, doctors can follow its progress and the distribution of the cancer cell is known. Such specific targeting and detection will aid in treating late-phase metastasized cancers and hard-to-reach tumors and give indications of the spread of those and other diseases. It also prolongs the life of certain drugs that have been found to last longer inside a nanoparticle than when the tumor was directly injected, since often drugs that have been injected into a tumor diffuse away before effectively killing the tumor cells.

Molecular nanotechnology refers to the three-dimensional positional control of molecular structure to create materials and devices to molecular

precision. The human body is comprised of molecules, hence the availability of molecular nanotechnology will permit dramatic progress in human medical services. More than just an extension of “molecular medicine,” nanomedicine will employ molecular machine systems to address medical problems, and will use molecular knowledge to maintain and improve human health at the molecular scale. Nanomedicine will have extraordinary and far-reaching implications for the medical profession, for the definition of disease, for the diagnosis and treatment of medical conditions including aging, and ultimately for the improvement and extension of natural human biological structure and function. Nanomedicine is the preservation and improvement of human health using molecular tools and molecular knowledge of the human body.

APPLICATIONS OF MEDICAL NANOTECHNOLOGY

Applications of medical nanotechnology span across a variety of areas such as in Drugs, Medicines, Therapeutics; in Diagnostics of diseases, abnormal conditions etc., in Surgery, in Medical Robotics, in the general sake of increasing knowledge of the human body, etc.



Nanoparticles are taking over the world of biomedicine

Applications in Drugs and Medicine

Nanotechnology can deliver medicine or drugs into specific parts of the human body, thereby making them more effective and less harmful to the other parts of the body. Anti-cancer gold nanoparticles have been found very effective. Gold “nanoshells” are useful to fight cancer because of their ability to absorb radiation at certain wavelengths. Once the nanoshells enter tumor cells and radiation treatment is applied, they absorb the energy and heat up enough to kill the cancer cells. Not only gold but other elements can also be used.

Applications in Surgery

With nanotechnology, minute surgical instruments and robots can be made which can be used to perform microsurgeries on any part of the body. Instead of damaging a large amount of the body, these instruments would be precise and accurate, targeting only the area where surgery should be done. Visualization of surgery can also be improved. Instead of a surgeon holding the instrument, computers can be used to control the nano-sized surgical instruments. “Nanocameras” can provide close up visualization of the surgery. There is less chance of any mistakes or faults. Surgery could also be done on tissue, genetic and cellular levels.

Nano-robotics, although having many applications in other areas, have the most useful and variety of uses in medical fields. Future medical nanotechnology expected to employ nanorobots injected into the patient to perform treatment on a cellular level.

The workings of cells, bacteria, viruses etc can be better explored. The causes of relatively new diseases can be found and prevented.

Restore vision. Genome sequencing can be made much easier. Biological causes of mental diseases can be monitored and identified. Simple curiosities can be answered.

Tissue engineering could also be done using nano-materials. Tissue engineering makes use of artificially stimulated cell proliferation by using suitable nanomaterial-based scaffolds and growth factors. Advances in nanotechnology-based tissue engineering could also lead to life extension in humans and other animals.

Potential risks

Potential risks of nanotechnology can broadly be grouped into three areas:

the risk to health and environment from nanoparticles and nanomaterials; the risk posed by molecular manufacturing (or advanced nanotechnology); and societal risks.

Economical Issues

Will “nanomedicine” widen the gap between the rich and the poor in its initial stages like many disruptive technologies of the past? Is there a certain patent for nanomedicine? How much will the ideas of nanomedicine sell for? Will the poor get equal access to nanomedicine and other nanomedicinal technologies?

THE FUTURE OF MEDICINE

Study of medical history reveals a long, hard struggle to improve human health, a struggle that will ultimately culminate in a grand victory; the elimination of ill health and suffering in the 21st Century. Assuming that the approximately ten billion people who have ever lived survived an average of 40 years and spent just 2% of their lives in misery and sickness from disease, and then a not inconsiderable price of ~70 trillion man-hours of human suffering will have been paid to achieve this end.

Biotechnology and genetic engineering are comparatively well-known because of their many important successes over the last several decades. But advocates of these approaches often ignore a future post-biotechnology discipline, just now appearing on the 2-3 decade R&D horizon, that can almost guarantee whole-body elimination of biological senescence and the indefinite maintenance of healthy mind and body, while producing few if any unwanted medical side effects. This new technology involves the application of molecular nanotechnology and nanorobotics to human health care. In near future, it will become increasingly clear that all of biotechnology is but a small subset – albeit an important subset – of nanotechnology. Indeed, the 21st century will be dominated by nanotechnology – the engineering and manufacturing of objects with atomic-scale precision – not biotechnology. Humanity is poised at the brink of completion of one of its greatest and most noble enterprises. Early in the 21st century, our growing abilities to swiftly repair most traumatic physical injuries, eliminate pathogens, and alleviate suffering using molecular tools will begin to coalesce in a new medical paradigm called nanomedicine. Nanomedicine may be broadly defined as the comprehensive monitoring, control, construction, repair, defense, and improvement of all human biological systems, working from the molecular level, using engineered nanodevices and nanostructures, molecular machine systems, and – ultimately – nanorobots too small for the eye to see.

Molecular nanotechnology refers to the three-dimensional positional control of molecular structure to create materials and devices to molecular precision. The human body is comprised of molecules; hence the availability of molecular nanotechnology will permit dramatic progress in human medical services. More than just an extension of “molecular medicine,” nanomedicine will employ molecular machine systems to address medical problems, and will use molecular knowledge to maintain and improve human health at the molecular scale. The body is constantly under assault from the environment, and the immune system is continually waging a silent war against these threats. Toxins, bacteria, fungi, parasites and viruses are all constantly attacking the body and trying to do it harm. Many nanotechnological techniques imagined only a few years ago are today already making remarkable progress toward becoming reality. Scientists are currently exploring how to put to use dendrimers, (branched spherical molecules) carbon buckyballs, and other specifically engineered nanoparticle drugs to combat everything from bacteria and viruses to cancer. Nanoshells could also be used to concentrate infrared (laser) light to heat, and thereby selectively destroy cancerous cells. It may become possible to orally administer drugs that can currently only be delivered by injection. Nanoparticle encapsulation of the drug will help it to easily pass through the stomach lining and into the bloodstream where its payload would be released. Inhaled nanofibers can even stimulate the regeneration of cartilage in damaged joints.

The true potential power of nanomedicine, however, lies in still theoretical,

tiny medical **nanorobots**. “Nanobots” will be devices as small as a microbe, but they will not possess the ability to self-replicate. These engineered nanodevices, or nanomachines, will repair the damage that accumulates as a result of metabolism (being alive) by performing nanorobotic therapeutic procedures on each of the ~75 trillion cells that comprise the human body. They will contain various substructures such as an onboard power supply, nanocomputer, sensors, manipulators, pumps, and pressure tanks. By the early 2020s, molecular manufacturing - the ability to manufacture objects chiefly out of carbon with atomic precision, in very large numbers (through massively parallel assembly) using nanofactories - will enable the first nanobots to be inexpensively produced for use in medicine. Researchers are already beginning to tackle the problem of how to construct such devices.

As doctors begin to use medical nanobots in their daily practice, they will gain the ability to rapidly repair almost any physical injury, cure virtually every known disease that disables and kills people today, and vastly extend human life and health span.

Respirocytes are a design for an artificial red blood cell. The human body contains approximately 30 trillion natural red blood cells which circulate in the bloodstream and occupy roughly half of the blood volume. A single disc-shaped red blood cell measures around 6-8 μm in diameter and 2-3 μm thick. Respirocytes will be much smaller - an entire respirocyte will be a ‘perfect’ sphere measuring only a single μm in diameter - about the same size as a bacterium. A respirocyte will be an atomically-precise arrangement of 18 billion structural atoms. An onboard nanocomputer controls the loading/unloading of oxygen and carbon dioxide molecules to and from microscopic pressure tanks made of diamondoid crystal via thousands of molecular-scale pumps arranged over its surface. Just 5 ml (or one thousandth of our total blood volume) worth of respirocytes added to a person’s blood could double their natural oxygen-carrying and carbon dioxide removing capacity. A single respirocyte will be capable of transporting hundreds of times more bioavailable oxygen than a natural red blood cell, at only a fraction the size. Half a liter - the most respirocytes that could be safely added to a person’s blood - would allow them to sprint at top speed for twelve minutes, or remain underwater for up to four hours without taking a single breath. Alternatively, respirocytes would buy valuable time in the event of a heart attack, or drowning, and due to their diminutive form factor they would be able to supply needed oxygen to cells that would otherwise be starved following a crushing or other accident that constricts blood flow.

Microbivores, or nanorobotic phagocytes (artificial white blood cells) introduced into the bloodstream would form a synthetic immune system, a search and destroy task-force constantly on patrol for pathogenic microbes, viruses and fungi. Multiple-drug resistant strains of bacteria stand no chance against the microbivore. Even the deadliest of infectious pathogens could be completely cleared from the system within just minutes or hours with no negative effect to the patient, and using only a few milliliters of microbivores. Contrast this with the weeks or months required to achieve similar results (best case scenario) with current antibiotics. Microbivores are expected to be on the order of a thousand times faster acting than even antibiotic-aided natural phagocytes. With additional programming, similar nanobots could be used to detect and selectively destroy cancerous cells, or even clear obstructions from the bloodstream in just minutes, preventing ischemic damage in the event of a stroke.

Chromalloytes, one variety of cell-repair nanobot, would enter the nucleus of a cell and extract all of the genetic material (chromosomes) and replace it with a synthetically produced copy of the original that has been manufactured in a laboratory to contain only non-defective base-pairs. The result of this cytosurgical “Chromosome Replacement Therapy” (CRT) process would be the removal of all inherited defective genes, reprogramming of cancerous cells back to a healthy state, and a permanent cure for all genetic diseases, or any combination thereof desired by the patient. CRT will enable us to exchange our old defective chromosomes with digitally-precise new copies of our genes, manufactured in a laboratory by a benchtop size production device, using the patient’s genome as the blueprint. By installing new DNA in every tissue cell in the body, this technology will make it possible to arrest and even reverse the effects that aging has on our

biology, and most current causes of natural human death - forever severing the link between calendar age and physiological health. If you are biologically old, and do not wish to be, then for you, aging/being old is a disease, that you deserve to be cured of. Through a combination of nanobot therapies, say once a year or less frequently, accumulated metabolic toxins and other nondegradable material will be cleansed from your body, while chromalloytes delete any genetic mutations or damage. Any remaining structural damage to cells that they are unable to auto-repair such as disabled or enlarged mitochondria will be dealt with using dedicated cellular repair nanobots. These rejuvenation procedures will need to be repeated once a year (or less frequently) to revert all of the damage that occurs on a continual basis as a result of metabolism.

Clottocytes are a design for micron-scale, oxygen/glucose-powered, artificial mechanical platelets. Clottocytes would be 100 to 1,000 times faster in response than the body’s natural platelets, stopping bleeding almost instantly (within about one second) even in the event of fairly large wounds. The clottocyte is conceived as a two micron diameter, spheroidal nanobot that contains a tightly-folded (biodegradable) fiber mesh payload which, when commanded by its internal nanocomputer, deploys in the general vicinity of a damaged blood vessel. Certain parts of the mesh are designed to dissolve exposing sticky sections upon contact with water in the blood plasma. The overlapping nettings of multiple activated clottocytes trap blood cells and stop bleeding immediately. The clotting function performed by clottocytes is essentially equivalent to that of biological platelets, albeit at just 1/10,000th the concentration in the bloodstream, (or approximately 20 nanobots/cubic centimeter of blood,) and much quicker acting.

DNA can be considered to be biological nanosoftware; ribosomes, large scale molecular constructors. Enzymes are what Nature chose as truly functional molecular sized assemblers. Genetic engineers are not creating new tools per se, but rather, adapting and improvising from what Nature has already provided. Future generations of engineers, armed with molecular engineering techniques, will have a real chance of imitating and perhaps improving upon Nature.

Nanobots can also be designed and constructed with absolute atomic precision - a level of perfection that is actually beyond that which say, an entire natural cell operates on. Practically every atom in a nanobot will have a particular function in the overall structure. Intelligent design of the human variety can now be much more direct and efficient than nature - but it took nature to get us this far.

THE END OF AGING AND DISEASE

The result of these technological advances will be the effective end of aging as well as the reversal of one’s current biological age to any new age that is desired. These procedures are anticipated to become commonplace as the technology evolves, a few decades hence. With routine annual checkups/repairs, and the occasional major tune-up, you could remain virtually constantly your ideal biological age. Most people will probably choose to remain perpetually in the prime of their lives - their early twenties - physiologically. People will still die at some point, however most deaths will likely become accidental, rather than “natural.” Even if such procedures can keep you “clinically immortal,” if you’re hit by a flying car, you may still die, though cell repair nanobots and other advanced future medical techniques will be able to repair much more extensive injuries than are now possible. Based on projected rates of accidental death and suicide, a life expectancy of at least one thousand years is expected - if we don’t annihilate ourselves in the interim.

Perhaps the most significant danger in curing aging is in the cultural and intellectual stagnation of humankind that may result if the current generation were stopped in time. Aging and Disease result from the molecules in our tissues sliding into disorder, first destroying health, and eventually taking life itself. Nanotechnology will give us numerous novel approaches to repair our aging bodies and undo the disastrous results of the ravages of time. The advancements anticipated in the Nano age offer the first promising hope of a science-based fountain of youth. Radical life (and health) extension will become commonplace.

DIAGNOSTICS

The high-tech, cutting edge tools required by medicine (especially medical research) are presently very expensive to produce. Building with individual atoms makes it possible to produce entire tools that are incredibly small. Sensors, and indeed entire nanobots, will be made that are tiny enough to fit within living cells.

The complexity of the human body dictates that determination of its state requires the collection of large volumes of data. An analysis of these data will even be available in real-time, (crunched by integrated nanocomputers millions of times faster than current-day computers.) Monitoring the patient's condition continuously, they will construct a detailed model of the patient's body, and apply a predictive approach to both the course of the disease or other ailment and any possible course of action in treating the condition. The sensors/nanocomputers could even provide recommendations based on computation of the probabilities of various potential treatments. The small size and low cost of nanosensors will, for the first time, make gathering this information possible, even in routine diagnosis. With real-time monitoring of a patient's systems, it becomes possible to identify problems much earlier, allowing for a more aggressive and experimental treatment approach. Thousands of medical tests will be combined into a single, inexpensive, hand-held device. This will make diagnosis much more reliable, hence increasing accuracy while reducing malpractice/insurance liability.

INVINCIBLE MENTAL HEALTH

The single most exciting prospect of molecular nanotechnology is the potential to rewrite the very subjective quality of every moment of our experience itself into something infinitely more fulfilling. Aldous Huxley once said, "If we could sniff or swallow something that would, for five or six hours each day, abolish our solitude as individuals, atone us with our fellows in a glowing exaltation of affection and make life in all its aspects seem not only worth living, but divinely beautiful and significant, and if this heavenly, world-transfiguring drug were of such a kind that we could wake up next morning with a clear head and an undamaged constitution-then, it seems to me, all our problems (and not merely the one small problem of discovering a novel pleasure) would be wholly solved and earth would become paradise." It is possible that our super intelligent posthuman descendants (or perhaps even our future selves) will be animated by gradients of bliss that are literally billions of times richer than anything biologically accessible today.

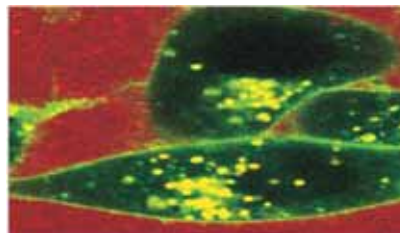
REENGINEERING THE MAN MADE WORLD

Huge aspirations are coupled to nanotechnological developments in modern medicine (Nanotechnology, Biotechnology, Information Technology & Cognitive Science - NBIC developments). The potential medical applications are predominantly in diagnostics (disease diagnosis and imaging), monitoring, the availability of more durable and better prosthetics, and new drug-delivery systems for potentially harmful drugs.

Nano medicine provides a new avenue for developing ways of combating these stumbling blocks. For instance for many ailments surgery is an inevitability, but surgery can be very damaging to the body. Many patients may have complications after surgery or reductions in quality of life. With Nanotechnology it may be possible to treat disease in a non-invasive way. A prime example of this is the treatment of tumors with a reduction in side-effects, through the development of targeted drug delivery systems negating the need for the poison, slash and burn techniques currently used in medicine for their treatment.

Nanomedicine makes use of various different engineered nanoparticle types and encompasses areas such as nanoparticle drug/ vaccine delivery and in vivo imaging. Nanomedicine also refers to the field of molecular nanotechnology in which nanorobots such as neuro-electronic interfaces and cell repair machines will be used in therapies and surgeries.

The advent of nanotechnology is considered to be the biggest engineering innovation since the Industrial Revolution. Proponents of this new technology promise to re-engineer the man-made world, molecule by



Bright green/yellow showing cancer drug entering a cancerous cell from purdue.edu

molecule, sparking a wave of novel revolutionary commercial products from machines to medicine. Nanotechnology opens up a huge range of possibilities for humans but it will also bring huge risks (i.e. misuse and malfunctioning) so there is a need for strong regulation by Governments and International Institutions.

NANOMATERIALS

There are different kinds of nanoparticles which are suitable to be applicable in drug- and gene- delivery, probing DNA structures, etc, and are categorized as: liposomes, polymer nanoparticles (nanospheres and nanocapsules), solid lipid nanoparticles, nanocrystals, polymer therapeutics such as dendrimers, fullerenes (most common as C60 or buckyball, similar in size of hormones and peptide α -helices), inorganic nanoparticles (e.g. gold and magnetic nanoparticles).

Nanoparticles, being the fundamental elements of nanotechnology, can be applied in various ways such as fluorescent biological markers, as markers for detection of proteins, probing of DNA structures and for separation and purification of biological molecules and cells, and they can also be used for magnetic resonance imaging enhancement, tumour destruction via heating, tissue engineering and drug, gene delivery. Two kinds of nanoparticles that are suitable to be applicable at least in drug-delivery include gold nanoparticles (3-20 nm), that are gold composites with dielectrical cores and golden shells. By choosing the right ratio of core to shell diameters the particle can be tuned to absorb highly in the near infrared, and by irradiation with such wavelength can be heated, even in deeper skin areas. If the particles are embedded in a temperature sensible hydrogen matrix, the matrix will collapse and the included agents will be released at a critical temperature and second, magnetic nanoparticles, with controllable sizes between 2-30 nm that can be coated with biological molecules to make them interact with or bind to a biological entity. They can be made to deliver a package (an anticancer drug, or a cohort of radionuclide atoms) to a targeted region of the body. The magnetic particles can be provided with energy from the exciting external field, and can be heated up making them good hyperthermia agents, delivering toxic amounts of thermal energy to targeted bodies, such as tumours.

For applications to medicine and physiology, these nanomaterials, nanoparticles and devices can be designed to interact with cells and tissues at a molecular (i.e., subcellular) level with a high degree of functional specificity, thus allowing a degree of integration between technology and biological systems not previously attainable. Due to advances in biochemical research and molecular biology diseases can put down to molecular abnormalities. Molecular imaging should detect the corresponding molecular signatures of diseases and use it for medical diagnosis. This should ideally lead to diagnosis and therapy before occurrence of symptoms. In molecular imaging, an imaging molecule is coupled to a transport molecule or particle, which possesses a targeting unit (e.g. special receptors, or peptides). The target finding system should be a specific molecular marker of a certain disease thus the contrast medium accumulates within the sick tissue. Molecular imaging is developed for several diagnostic procedures such as magnetic resonance, ultrasonic imaging, as well as nuclear and optical imaging technologies.

NANOTECHNOLOGY TOOLS

Different methods for the synthesis of nanoengineered materials and devices can accommodate precursors from solid, liquid or gas phases and encompass a tremendously varied set of experimental techniques. Most synthetic

methods can be classified into two main approaches: “top-down” and “bottom-up” approaches and combinations of them. “Top-down” (photolithography, microcontact printing) techniques begin with a macroscopic material or group of materials and incorporate smaller-scale details into them, whereas “bottom-up” (organic- synthesis, self-assembly) approaches, begin by designing and synthesizing custom-made molecules that have the ability to self-assemble or self-organize into higher order mesoscale and macroscale structures.

Other advanced applications of micro- and nanotechnology in medicine are the microchip-based drug delivery systems, which are devices incorporating micrometer-scale pumps, valves and flow channels. They allow controlled release of single or multiple drugs on demand. Micro- and nanotechnology-based methods (e.g., UV-photolithography, reactive ion etching, chemical vapour deposition, electron beam evaporation) can be used for the fabrication of these silicon-based chips.

Imaging is becoming an ever more important tool in the diagnosis of human diseases. Imaging at cellular, and even sub-cellular and molecular level, is still largely a domain of basic research. However, it is anticipated that these techniques will find their way into routine clinical use. Atomic force microscopy (AFM) and AFM-related techniques (e.g. Scanning Near-Field Optical Microscopy-SNOM) have become sophisticated tools, not only to image surfaces of molecules or sub-cellular compartments, but also to measure molecular forces between molecules. This is substantially increasing our knowledge of molecular interactions.

APPLICATIONS OF NANOMEDICINE

Nanotechnology provides extraordinary opportunities not only to improve materials and medical devices but also to create new “smart” devices and technologies where existing and more conventional technologies may be reaching their limits.

Nanorobots and nanodevices

The “respirocyte” is expected to be able to deliver more oxygen to the tissues than natural red blood cells and to manage carbonic acidity. Primary medical applications of respirocytes would include transfusable blood substitution; partial treatment for anemia, lung disorders, enhancement of cardiovascular/neurovascular procedures, tumour therapies and diagnostics, prevention of asphyxia, artificial breathing, and a variety of sports, veterinary and battlefield. Microbivores are expected to be up to 1000 times faster acting than either unaided natural or antibiotic assisted biologic phagocytic defenses and able to extend the therapeutic competence of the physician to the entire range of potential bacterial threats, including locally dense infections. Medical “nanorobots” may also be able to intervene at the cellular level, performing in-vivo cytotoxicity. The most likely site of pathologic function in the cell is the nucleus – more specifically, the chromosomes. In one simple cytosurgical procedure called “chromosome replacement therapy”, a “nanorobot” controlled by a physician would extract existing chromosomes from a particular diseased cell and insert new ones in their place, in that same cell. If the patient chooses, inherited defective genes could be replaced with non defective base-pair sequences, permanently curing a genetic disease. Engineered bacterial “biobots” (synthetic microbes) may be designed to produce useful vitamins, hormones, enzymes or cytokines in which a patient’s body was deficient or to selectively absorb and metabolize harmful substances such as poisons toxins etc into harmless end products.

Biocompatibility and Orthopedic implants

An important field of application for nanotechnology in medicine is the biomaterials, used for example in orthopedic implants or as scaffolds for tissue engineered products. If the design of a hip implant, for instance, is carried out at nanolevel, it might become possible to construct an implant which closely mimics the mechanical properties of human bone, preventing stress-shielding and the subsequent loss of surrounding bone tissue. Extracellular matrix (ECM) provides an excellent three-dimensional web of

intricate nanofibers to support cells and present an instructive background to guide their behavior. It takes a variety of forms in different tissues and at different stages of development in the same tissue. Nanostructuring of materials provides a powerful mechanism to encourage and direct cell behaviour, ranging from cell adhesion to gene expression, thus enhancing their biocompatibility, by dictating the desirable interactions between cells and materials.

Nanotechnology in Cardiology

Minimally invasive treatments for heart disease, diabetes and other diseases is a desirable goal for scientists, and there is hope for it, because of the use of nanotechnology. Cardiovascular gene therapy could be realized roughly as follows: identification of a protein whose presence causes blood vessels to form, production and packaging of strands of DNA that contain the gene for making the protein and deliverance of the DNA to heart muscle. Of those steps, the last is the most challenging. “Biobots” (a kind of nanorobots), another application of nanotechnology, is the creation of muscle-powered nanoparticles having the ability to transfer information into cells, gives the potential of replacing lost biological function of many tissues such as sinoatrial node. This effect can lead to treatment of diseases which otherwise would be fatal or difficult to cure for human beings and Coronary Artery disease (CAD), by improving the biocompatibility of intracoronary stents and by regulating the main limit factors for Percutaneous Transluminal Coronary Angioplasty (PTCA) at a molecular level via nanoparticles.

Various inhibitors of growth factors secreted by activated platelets such as PDGF, IL-1, TGF- β and inhibitors of proinflammatory agents released by leucocytes upon activation (e.g monocyte chemoattractant protein-1) could be used as antithrombotic and antirestenotic agents. It can be concluded that a highly effective molecular coronary intervention by means of nanotechnology may eliminate the need for stents themselves.

Diagnosis of cardiovascular diseases is an application of recent advances in nanotechnology as well. Many monoclonal antibodies, peptides and carbohydrates for non-invasive targeting of atherosclerotic lesions, myocardial necrosis, brain infarction and various tumours can be used for their detection.

The detection of the complementary DNA strand is another application of nanotechnology in the field of cardiology, that is based on the discovery of complexes of single-walled Carbon nanotubes with single-stranded DNA. If a single nucleotide alteration occurs, the association between the carbon nanotube and the complementary DNA strand will be changed, resulting in the detection of single-nucleotide polymorphisms (SNPs). SNPs are sites in the human genome where individuals differ in their DNA sequence, often by a single base. These slight variations in DNA sequences can have a major impact on whether or not a person may develop a disease and even influence the response to drug regimens.

Researchers in public and private sectors are generating SNPs maps which can occur in genes as well as in noncoding regions. Scientists believe that these maps will be used for the identification of the multiple genes associated with complex diseases such as Coronary Artery Disease (for example, ABCA1 gene is susceptible for CAD), hyperlipidaemia, cancer, diabetes mellitus and to detect humans with genetic predisposition to these diseases. By screening tests which are based on the above application of Nanomedicine, individuals that are prone to develop atherosclerosis might be detected and by controlling the main risk factors for CAD (hypertension, diabetes mellitus, smoking, hyperlipidaemia, obesity) a long-term acute coronary syndrome may be avoided.

Nanotechnology against Cancer

Nanotechnology may have an impact on the key challenges in cancer diagnosis and therapy. Diagnosing, treating, and tracking the progress of therapy for each type of cancer has long been a dream among oncologists, and one that has grown closer thanks to parallel revolutions in genomics, proteomics and cell biology. Nanotechnology’s greatest advantage over conventional therapies may be the ability to combine more than one

function.

Recently, there is a lot of research going on to design novel nanodevices capable of detecting cancer at its earliest stages, pinpointing its location within the human body and delivering chemotherapeutic drugs against malignant cells. The major areas in which nanomedicine is being developed in cancer involve: a) early detection of tumour (developing "smart" collection platforms for simultaneous analysis of cancer-associated markers and designing contrast agents that improve the resolution of tumour area comparing with the nearby normal tissues), and b) cancer treatment (creating nanodevices that can release chemotherapeutic agents).

Tumour diagnostics and prevention is the best cure for cancer, but failing that, early detection will greatly increase survival rates with the reasonable assumption that an in situ tumour will be easier to eradicate than one that has metastasized. Nanodevices and especially nanowires can detect cancer-related molecules, contributing to the early diagnosis of tumour. Nanowires having the unique properties of selectivity and specificity, can be designed to sense molecular markers of malignant cells. They are laid down across a microfluidic channel and they allow cells or particles to flow through it.

Nanowires can be coated with a probe such as an antibody or oligonucleotide, a short stretch of DNA that can be used to recognize specific RNA sequences. Proteins that bind to the antibody will change the nanowire's electrical conductance and this can be measured by a detector. As a result, proteins produced by cancer cells can be detected and earlier diagnosis of tumour can be achieved.

Nanoparticle contrast agents are being developed for tumor detection purposes. Labeled and non-labeled nanoparticles are already being tested as imaging agents in diagnostic procedures such as nuclear magnetic resonance imaging²⁴. Such nanoparticles are paramagnetic ones, consisting of an inorganic core of iron oxide coated or not with polymers like dextran. There are two main groups of nanoparticles: 1) superparamagnetic iron oxides whose diameter size is greater than 50 nm, 2) ultrasmall superparamagnetic iron oxides whose nanoparticles are smaller than 50nm²⁵. Moreover, quantum dots being the nanoscale crystals of a semiconductor material such as cadmium selenide, can be used to measure levels of cancer markers such as breast cancer marker Her-2, actin, microfibril proteins and nuclear antigens. Tumour treatment can be succeeded with nanoscale devices (such as dendrimers, silica-coated micelles, ceramic nanoparticles, liposomes). These devices can serve as targeted drug-delivery vehicles capable of carrying chemotherapeutic agents or therapeutic genes into malignant cells.

The nanoshell-assisted photo-thermal therapy (NAPT), is a non-invasive procedure for selective photo-thermal tumour destruction. It is based on nanoshells that absorb light in the near infrared (NIR) region, which is the wavelength that optimally penetrates tissues. These nanoshells have a core of silica coated with a metallic layer, usually of gold. The metal shell converts the absorbed light into heat with great efficacy. Further specificity can be engineered by attaching antigens on the nanoshells which are specifically recognized by the cancer cells. By supplying a light in NIR from a laser, the particles produce heat, which destroy the tumour. It has been found that, the temperature within the nanoshell-treated tumours rose by about 40oC compared to a rise in 10oC in tissues treated with NIR light alone. The benefit of thermal therapeutics is that most procedures are non-invasive and have the potential to treat tumours which can not be surgically treated.

Gene-, Protein-, Lab-on-a-chip Devices, "Theranostics": Medical devices for in-vitro diagnostics, such as gene-, protein- or lab-on-a-chip devices, do not have any of the safety concerns associated with nanoparticles introduced into the body. Numerous devices and systems for sequencing single molecules of DNA are feasible. Nanopores are finding use as new nanoscale technology for cancer detection enabling ultrarapid and real time DNA sequencers. In general, developments in protein-chips and lab-on-a-chip devices are more challenging compared to gene-chips. These devices are anticipated to play an important role in medicine of the future, as they will be personalised and will combine diagnostics with therapeutics into a new emerging medical area called "theranostics".

The applications of special relevance to improving health and enhancing human physical abilities include the use of virtual environments for training, education, and interactive teaching. This will provide new ways for medical students to visualize, touch, enter, smell, and hear the human anatomy, physiological functions, and medical procedures, as if they were either the

physician or a microscopic blood cell traveling through the body.

The use of nanotechnology in the field of medicine could revolutionize the way we detect and treat damage to the human body and disease in future. Nanofibres can stimulate the production of cartilage in damaged joints. Nano particles may be used, when inhaled, to stimulate an immune response to fight respiratory viruses. Quantum Dots (qdots) may be used in the future for locating cancer tumors in patients and in near term for performing diagnostic tests in samples.

CONCLUSIONS

The nanotechnology will help to improve health by enhancing the efficacy and safety of nanosystems and nanodevices. Moreover, early diagnosis, implants with improved properties, cancer treatment and minimum invasive treatments for heart disease, diabetes and other diseases are anticipated. In the coming years, nanotechnology will play a key role in the medicine of tomorrow providing revolutionary opportunities for early disease detection, diagnostic and therapeutic procedures to improving health and enhancing human physical abilities, and enabling precise and effective therapy tailored to the patient. Nanomedicine is in infancy, having the potential to change medical research dramatically in the 21st century. Nanomedical devices can be applied for analytical, imaging, detection, diagnostic and therapeutic purposes and procedures, such as targeting cancer, drug delivery, improving cell-material interactions, scaffolds for tissue engineering, and gene delivery systems, and provide innovative opportunities in the fight against incurable diseases. Many novel nanoparticles and nanodevices are expected to be used, with an enormous positive impact on human health. Over the next ten to twenty years nanotechnology may fundamentally transform science, technology, and society offering a significant opportunity to enhance human health in novel ways, especially by enabling early disease detection and diagnosis, as well as precise and effective therapy tailored to the patient.

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Futuristic Geriatric Hospital

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Abstract: An integration of modified built environment can reinforce the personal environment to support. Strategies must be formulated to cope with differencing health needs, cultures, climates and budgets. Design responses must embrace all parts and aspects of the hospital. Hospital architecture must facilitate technology adoption, implementation and also contribute to the efficiency and transparency of processes. It must provide a seamless integration of clinical requirements with building planning and designing issues. It has been rightly said that healthcare facilities age unpredictably with changing medical technology, and evolving healthcare delivery system rendering some obsolete while relieving others. It has to be acknowledged that what is built for today will not be permanent. Hospital for tomorrow will be places that contribute to the healing process. The hospitals of tomorrow will be green buildings; they will incorporate excellent features that result in environment protection, water conservation, energy efficiency, usage of recycled products and renewable energy. Evidences galore, which have proved that well designed hospital environment, can have a significant impact on patient recovery and welfare.

Key Words: Geriatric Hospital, Futuristic Hospital, Environmental Facilitation, Geriatric Day Hospital, Hospital Architecture, Emerging Trends

INTRODUCTION

Hospitals were first constructed at the commencement of the Christian era to shelter sick/ weary travelers and persons who were poor/ill to be treated at home. The transformation of the role and function of the hospital through the ages has been metamorphic. It has to be accepted that bricks and mortar alone do not make outstanding hospitals. Major transformations are occurring in delivery of healthcare. Advances in basic sciences including molecular biology, evidence based medicine, demographic and epidemiological changes have and are transforming medical care. This has directly impacted and continues to influence the architecture design and planning of future hospitals.

With changing hues of times, healthcare provisioning has assumed the role of one of the most challenging and dynamic services. Patient is the focus of all activities in a healthcare organizations and for redressal of their needs coupled with those of attendants and staff requires the multipronged strategies including those of hospital architecture. Evidences galore, which have proved that well designed hospital environment can have a significant impact on patient recovery and welfare.

Much of the hospital architecture strength comes from the intense regards for the need of patients, staff and visitors. The age old essence of architecture viz respect for function, structural integrity, awareness of time, integration with environment and expression of meaning are still valid. The art and science of hospital architecture calls for the fact that the environment should restore the dignity of patients, offer comfort and safety to visitors, staff and patients.

OBJECTIVE

Set a new vision and direction for both acute and community geriatric medical care and to produce a better model of medical care for these complex older patients.

NATURE OF THE PROBLEM

Over the next 20 years the major diseases will be dementia, delirium, care giver fatigue / collapse, adverse drug reactions, recurrent falls, osteoporotic fractures, malnutrition with complications including recurrent infections, prolonged, expensive and complicated hospital stay¹. The lack of multidisciplinary holistic care in the community has overwhelmed both the GP's and the hospital ED with avoidable geriatric presentations.

The lack of an electronic medical record, inability of the hospital to provide rapid access to old medical records and the fragmentation of medical information, results in a delay in medical treatment and worsens the health outcome.

Experts warned Monday that the United States faces a massive health care shortage that threatens to leave millions of seniors without proper health care within the next three decades. A report issued by the Institute of Medicine says that medical and nursing schools are training far too few doctors and nurses on how to care for the elderly.²

EXTENT OF THE PROBLEM

In this older group any acute illness may cause preventable major geriatric syndromes including delirium, falls, loss of mobility leading to prolonged, complex and costly acute hospital admission requiring prolonged rehabilitation and complex post acute care. These acute hospital admissions could potentially be avoided by better and early appropriate geriatric community care. 50% of geriatric patients greater than 75 years of age presenting to the Gosford Emergency Department are admitted as a direct result of major preventable adverse drug reactions³.

The lack of domiciliary consultation for geriatric patients to support the General Practitioners in the community results in premature functional decline in these patients and potentially preventable public hospital Emergency Department presentations and acute hospital admissions.

FUTURISTIC HOSPITALS: GENERAL CONSIDERATIONS

Emerging Issues

The emerging issues related to hospital architecture are mainly linked to the changing role of the hospitals. The main changes that have occurred in the healthcare delivery system are as follows⁴.

- * Enhanced patients expectations: The patients have become more quality conscious as well as price sensitive. They expect clinical, administrative and supportive services as well as design of facilities to be conducive to their requirements.
- * Epidemiological and demographic changes: There has been a change in the pattern & in the incidence of lifestyle diseases and geriatric related healthcare problems.
- * Emphasis on ambulatory / daycare: Hospital stay is gradually being programmed for high dependency inpatient care and for other cases more emphasis is on shorter stay.
- * Enhanced standards: There has been an up gradation of standards and norms in the delivery of healthcare in almost all aspect.
- * Changing function of hospitals: Hospitals are an evolving system. Hospitals apart from curing the sick have the added functions of maintenance and prevention of health, biomedical research and providing

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community outreach services. Focus has shifted from treating illness to creating wellness.

- * Health Insurance: Health insurance is gradually permeating as an important facet of healthcare delivery system. The providers of insurance and healthcare as well as the recipients view the hospital as an important hub for healthcare delivery.
- * Advancement in Medical Sciences: Advancement in medical sciences dictate/change the paradigm of healthcare delivery. Trends and dimensions in molecular biology, pharmaceuticals and surgical interventions have changed medical management outcomes. New diagnostic and therapeutic modalities require special controlled environment, energy requirements and other engineering services

Strategic Essentials

Hospitals inevitably are a combination of technologies, processes and human resources. Any structure may have many functions and any function may be fulfilled by alternative structure or process. Hospital architecture must facilitate technology adoption, implementation and also contribute to the efficiency and transparency of processes. It must provide a seamless integration of clinical requirements with building planning and designing issues. Strategies must be formulated to cope with differencing health needs, cultures, climates and budgets. Design responses must embrace all parts and aspects of the hospital.

Some of the strategic issues⁵, which must be considered, are:

Design for flexibility and expandability: Due to the complexity of hospital organization and diversity in various factors such as operations, functions and development, alterations and expansion of buildings are varied and frequent. Buildings should be adaptable to changing requirements. Jhon Weeks, the British architect had remarked. "Functions change so rapidly that designers should no longer aim for an optimum fit between building and function. The real requirement is to design a building that will inhibit change of function least and not that will fit specific function best". Some of the futuristic patterns for obtaining flexibility are:

- * Buildings designed to facilitate the docking of mobile and plug in modules. It is likely that specialized major diagnostic and diagnostic surgical equipment will be manufactured in self contained pre-constructed modules intended for docking at strategic points – 'ports' in the building.
- * Heat, ventilation and air conditioning (HVAC) will be modularized and zoned with vertical circulation, mechanical shafts and transport system moved from the core of the building to the perimeter in order to create free fields within the core floor plate that are easily adaptable to different layouts
- * As and when functions/equipment expand it should be possible to extent buildings as well as equipment and installation easily. It has to be acknowledged that building and function life span differs. The golden architectural principle of indeterminacy should be followed which enables a "building to grow with order and change with calm".
- * In order to combat obsolescence in hospital buildings universal space modules, modular design and interchangeable components which may be reinstalled / replaced should be utilized to keep space with changing needs.
- * Anticipate Change in Demand Functions: None of the varied elements are static, for as technology develops, medical understanding progresses and their combined application expired so do social demand and expectations.

NEED TO PLAN FOR THE FUTURE

It has been rightly said that healthcare facilities age unpredictably with changing medical technology, and evolving healthcare delivery system rendering some obsolete while relieving others. It has to be acknowledged that what is built for today will not be permanent. Prediction is very difficult, particularly when it concerns the future. It is a Herculean task to visualize hospitals for tomorrow since the impacting dimensions that are and will evolve the future hospitals are multifactorial and not always

predictable. It has been commented that if hospital architecture is restricted to antiquated specifications and cookbook approaches, artistic freedom will be converted into a bureaucratic rigidity. It is highly desirable to make an attempt to preview the hospitals for tomorrow since only then that hospitals constructed at present will be fulfilling the functions of the future.

CHANGING PARADIGM - FUTURE ARCHITECTURE

It is a known fact that the patient's negative and positive experiences in a medical environment have residual effects on the healing and care processes. In patient focused architecture the parameters which define quality of the healing environment are space, privacy, comfort, variety and communication. A study on the design of hospitals had stated that the ill patient is apprehensive and anxious. Stress stimulates a defence mechanism. The patients long for privacy. Physician patient relationship can blossom in privacy. Privacy should not be confused with isolation. Variety should always be provided in the planning and design of the healing environment since everyone benefits from a breath of fresh air, from a change of scene, from going to the outside world and from seeing beyond the confines of the rooms.



Futuristic Hospital with shuttle bay & helicopter pad

PATIENT WILL BE THE FOCUS

Hospitals for tomorrow will be planned and designed with patient focused philosophies. The patient centered architecture will facilitate their participation as partners in their care. The architecture will be welcoming to the patient and the hospitals design would value human beings over technology. The living spaces for patients will provide them privacy, comfort, safety, security and enable them to be in touch with nature. The architecture would be a humanizing one, which is a friendlier and a responsive place providing customized care based on patients needs and values. The architecture would respond to the functional requirements of providers of care and technology as well as to the emotional, physical and psychological needs of patients. Adoption, adaptation and implementation of technologies would also be patient focused.

LIFE ENHANCING ARCHITECTURE – A SINE-QUA-NON FOR THE FUTURE

It must be appreciated that there is a difference between good architecture and the mere act of building. The hospitals are differential and highly specialized institutions. Hospital for tomorrow will be places that contribute to the healing process. An appropriate design and architecture has the capability of transforming healthcare facilities into welcoming places to get well. The primeval forces of nature, i.e. sun, wind, water and earth have an effect on health and should be utilized for creating a healing environment. The ambience should blend with functionality to provide healthcare in a comfortable, safe and an aesthetically pleasing environment. It has rightly been said that a hospital needs to be the most wonderful place in the world – it needs to heal.

ASSISTED LIVING - A WAY OF LIFE IN THE FUTURE⁶

Hospitals in the future will be utilized mainly for intensive and critical care. The medical care of other ailments would be provided by ambulatory care

facilities, day care centres, healthcare and home care hotels. Transmural care, i.e. patient tailored care provided on the basis of close collaboration and joint responsibilities between hospitals and healthcare home centers will be adopted for convenience, comfort and cost-effectiveness. The assisting living residences will accommodate residents with a range of cognitive and physical abilities and offer facilities which will maximize the quality of life, independence, autonomy, safety, dignity, choice and privacy.

CHANGE – AN ESSENTIAL FEATURE

Hospitals of the future would require to change their functions and roles frequently. This will be necessitated due to patient needs and expectations, technological and medical advancements as well as change in healthcare norms.

The hospital of the future should thus be designed for flexibility and expandability. Universal/multipurpose/modular design would enable the golden architectural principle of indeterminacy to be followed, i.e. enabling buildings to grow with order and change with calm. Hospital buildings will be adaptable to changing requirements and designed so as to inhibit change of function least.

ENVIRONMENT FRIENDLY AND GREEN INSTITUTIONS

The hospitals of the future would be environment friendly. Solar, wind, energy and biogas would be optimally utilized. Waste disposal would be appropriately done. Essence of environment will be an essential ingredient of hospital planning and design. The hospitals of tomorrow will be green buildings, i.e. they will incorporate excellent features that result in environment protection, water conservation, energy efficiency, usage of recycled products and renewable energy.

BARRIER FREE ENVIRONMENT

A barrier free environment to facilitate the disabled or, differently abled, in facility utilization will be an essential component of all the hospitals. The facilities in the hospitals would be accessible and usable by person with disabilities.

BOUNDARYLESS INSTITUTIONS

In the future, the more common hospital functions will move closer to patients and only a few specific, specialized functions will be concentrated at other places. Telemedicine capabilities would be fully utilized. The hospitals would be a hub in a network serving patients in hospitals and homes. Advancements in information and communication technology will enable healthcare to be provided independent of time and place.

EXISTING AND FUTURE NORMS

In future, the existing norms of hospital construction will be changed. Patient focused operational restructuring will be the guiding principle. It has been rightly commented upon that building codes reflect and perpetuate the technology of some earlier period. They restrict the potential use of new ideas and materials. In the hospitals of the future, hospital norms, grids, schedule of accommodation will change keeping in time with the need, expectations and functionality, e.g. the use of laparoscopic surgery, robotic surgery will make the present norms of OT redundant. Public – private partnerships and outsourcing of facilities would also be a norm rather than an exception and will impact on the planning and designing of hospitals.

RELOCATABLE HOSPITALS

There will be a significant number of modular healthcare buildings built from pre-engineered modules. The shorter period of construction and flexibility of design, ease of deconstruction and alteration for alternative use will make these relocatable hospitals a common feature either as stand alone facilities or docked in facility with existing healthcare facilities.

IMPACT OF EMERGING TECHNOLOGIES

It is envisaged that technologies such as nanotechnology will impact on the hospitals of tomorrow in areas such as infrastructure, staffing, and space programming.

AESTHETICS – AN ESSENTIAL REQUISITE

Though patients give the highest priority to obtaining the best treatment, it has to be considered that they are people with eyes, ears and other senses and deserve to receive pleasure from the environment.

Aesthetics is now considered an essential ingredient of hospital design and planning. Aesthetics, which is the quality of the total experience our surroundings give us as, perceived by our senses and intellect, should be planned for all its dimensions as follows:

- * Psychological aesthetics which includes happiness, joy and pleasure.
- * Spiritual aesthetics, which suggests hope, contentment and peace
- * Physical aesthetics implies well being, ease and convenience
- * Intellectual aesthetics inspires humour, interest and contemplative delight

HEALING ARCHITECTURE

A hospital needs to be the most wonderful place in the world. It needs to heal. The hospital must have a humanizing architecture that can positively contribute to the healing process. Studies have linked poor healthcare facility design to elevated blood pressure, anxiety and longer hospital stays. The physical environments of the hospital should fulfil the following two conditions: it should do no harm and it should facilitate the healing process. Exposure to nature through interaction or access to view has a positive healing effect. Hospitals should provide a cheerful and inviting ambience and a caring and healing environment.

FUTURISTIC HOSPITALS: SPECIAL CONSIDERATIONS

Initially, the first wave of geriatricians focused on dependent long stay patients. By applying clinical skills, developing inter-disciplinary teams, assessing patients holistically and comprehensively, improving the environment, providing equipment and improving education, geriatricians were able to optimise function and well-being.

The realisation that many of these patients were not suffering from “old age” but had iatrogenic diseases (e.g. contractures, pressure sores) or conditions that were wrongly thought of as “social problems” (e.g. immobility, incontinence, falls) led to the wish to assess ill old people early in the course of their illness. It took many years to progress to elderly care units in district general hospitals. Geriatricians, often working single-handedly in lack-lustre departments some distance from the main hospital, had previously had inadequate staffing levels and few diagnostic resources. Recruitment was difficult, standards of care were patchy and morale was low.

In recent years, the landscape has altered further. Specialisation within geriatrics has helped improve the standards of care for patients with specific conditions. Stroke units, falls clinics, continence promotion clinics, movement disorder clinics, orthopaedic geriatric wards, delirium units, memory clinics are a few examples. Latterly, more geriatricians have developed an interest and expertise in community geriatrics. Geriatricians have always been willing to change if patient care improved in consequence. In many ways, there has never been a better time to be old and ill or disabled.

ENVIRONMENTAL MODIFICATION

An integration of modified built environment that is barrier free and safe, coupled with social, health and other services can allow the older person to remain independent⁷. In this way, the built environment can reinforce the personal environment to support.

Muscle weakness consequent upon aging and other sensory deficits make elderly highly prone to accidents. The fear of falling or hurting themselves makes them less active, especially in the bathrooms, because of floors that become slippery when they are wet. It would be prudent to recommend slip resistant floorings in the bathrooms. These could be textured ceramic tiles. If the existing floor cannot be changed, then mats may be used to cover at least those spaces where water is likely to wet.

The outside path should be smooth, hard & with levelled surface. Irregular surfaces such as cobblestones, coarsely exposed aggregate concrete and bricks should be avoided.



Anti Slip Bathroom Tiles

Handrails are must on both sides of the corridors, staircase, in bathrooms and toilets. Bars ought to be round, to facilitate comfortable grabbing, as many elderly people may have arthritic fingers. These bars should be fixed at a height of 900 mm. A 300 mm long extension of the handrail should be provided at the start and end of ramps and stairs. Handrails attached to walls should have a clearance no less than 50 mm from wall.



Non Slip Tread Cap in Stairs



Smooth Textured Pathway

Steps or sudden level changes in built environment should be avoided, in order to prevent falls. The tread surfaces should have slip resistant material. The steps should be provided with nosings that have slip resistant strips. Slanted nosings are preferred over projecting nosings so as not to pose difficulty for a person using walking stick or walker as these aids may be stuck in the recessed space or projecting nosing. In addition, open risers should be avoided. The stairs should be constructed with regular sizes of tread and riser. Half steps and triangular steps at turnings are to be avoided. Landing at regular and short intervals must be provided to enable the elderly to rest.



Slanted Nosings for Stairs

The first and last step both tread and riser, on every stair flight, should be marked with a paint that has a colour in contrast to the gray of the steps to make it more defined. This will enable the elderly person to move around without hesitation. Even lighting of those areas having steps or stairs is necessary to prevent falls.

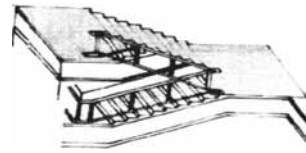
Ramp must have a very gradual slope and must be finished in non-slip material with handrails on both sides. They ought to be accompanied with low riser steps with handrail on both sides for those who prefer to use steps. The built environment in and around should not be cluttered with objects like flower pots, dustbins, etc. in the corridors, passages, pathways in gardens etc. There should be no projecting elements in the passages like pipes, columns etc. It is best to recess all appliances and filling wherever possible. The surface treatments of certain walls where one might come into contact should be as far as possible smooth in finish. This is because the elderly may graze themselves, as their skin is no longer as supple as it used to be when

they were younger. So a slight modification of smoothening the surface will increase the feeling of comfort in elderly people.

The whole idea is to modify the built environment in such a way that access to the movement for elderly becomes barrier free.

LIGHT & VISION

Majority of the elderly persons have diminished vision. Older eyes are less able to change focus quickly and are more likely to experience blurred vision. An 80 year old, for example requires three times as much light as a 20 year old. The elderly also have more difficulty seeing clearly in shadowy spaces and adapting to different brightness levels when moving from room to room. During these intervals, steps or furniture may be hard to spot, making them hazardous.



Landing at Regular and Short Intervals

Carefully planned lighting can help compensate for these limitations. The lights in the entrances should be bright during the day and switch to lower levels during the night to decrease the sharp contrast of light inside and outside of the building. One should plan to have well lit rooms and passages in which the colours of various objects like doors, handles, electrical switches etc. are in contrast to the walls of the house to make them easily visible and identifiable.

If the flooring in passages, long corridors and pathways in the open have defined edges by the use of different colours or textures it will help the short sighted to walk steadily and independently. Similarly, the stairways having contrasting colours at the beginning and end of stairs also help the elderly with weak vision.

COLOURS & CONTRAST

Glare and extensively bright light worsen impaired vision. Hence, the built environment should have adequate and well-distributed lighting. Using net curtains, can cut off glares from windows. It is advisable to minimize the use of shiny floor finishes and highly polished surfaces to reduce reflections which may hurt the eyes. Electrical switches should be large and piano-type with embossing for differentiation of switches for fan, light and bell etc.

SOUND & HEARING

Like vision many elderly people suffer from loss of hearing. It would be highly beneficial if the rooms should be provided with sound absorbing materials which will help reduce the reverberations of sound and make normal speech audible to elderly. Many curtains, mats, carpets or fabric wall coverings in the form of paintings or decorations, can achieve this.

JOINT STIFFNESS & MOBILITY

As many elderly people suffer from arthritic hands causing finger and hand impairments, reduction of strengths and dexterity, it is recommended that all taps, door knobs, hand rails etc. should be of such design that need very little wrist action or finger grip.

Most elderly persons suffer from stiff knee joints. It is ideal to provide western type of water closet which is installed at least 45 cm above ground level. This facilitates minimum bending of knees and the people can get up easily without straining oneself too much.

USER-CENTERED INTERFACE DESIGN AND ELDERLY

At the clinical department of Oncology at the Medical University Hospital in Graz, a pilot system for an interactive patient communications system

(PACOSY) was examined⁸. The patients were able to retrieve and enter information interactively via a touch screen panel PC connected to the Hospital Intranet. The Interface was designed for patients with little or no computer experience. The results were very encouraging and it helped increase the independence of the patients, improve communication and thereby increasing the level of quality and satisfaction.

FUTURISTIC HOSPITALS: CLINICAL CONSIDERATIONS

Clinical Governance

Patients seen as out-patients or day patients by an individual consultant or member of his or her team should have at least one recorded assessment of both their mental and functional states in the care records.

Care Records

Introducing a single process for assessing the health and social care needs of older patients, developing personal care plans and sharing this information as people move through the care system is of paramount importance. The Single Assessment Process (SAP) underpins much of the reforms towards delivering personalised care, joined-up services, timely response to identified needs and the promotion of health and active life.

Geriatric health care provisioning ought to be organised in a continuum as discussed below:

Day Hospitals

Day Hospitals (DH) are out-patient healthcare facilities in which multi-professional assessment, treatment and rehabilitation is available on attendance for a full or part-day basis for older people in the community. GDH is an important component of comprehensive services for older people.

Day Hospitals, where they exist, should play an active and effective role at the interface between primary and secondary care as part of the continuum of specialist health services for older people outside an acute hospital setting. DHs have a particular role to play as part of, and supporting, a seamless intermediate care provision through provision of a comprehensive assessment. DHs have an important role in chronic disease management through their partnership with primary care⁹. By regular review of at risk patients, exacerbations, disability and handicap and inappropriate admissions can be reduced by managing the condition, and avoiding iatrogenic disease.

Future Day Hospitals may become part of a hospital without walls containing day surgery, out patient clinics, radiological and pathological investigations, advice centres, assessment rooms for therapists and integration with social services as well as links with community matrons in the management of chronic disease.

Acute Assessment and General Hospital Care

Older people benefit as much from appropriate investigation and treatment as younger people and they are entitled to receive equivalent, efficient, timely and effective services so far as management of acute problem is concerned. Once acute care has been rendered, it becomes imperative that there should be adequately planned provision for Specialist Services (like for - Stroke, Falls, Pressure Sores, Pain, Orthogeriatrics and Continence . . . etc) thereafter.

Non-acute Care

Intermediate care

Intermediate Care is conceived as a range of service models aimed at "care closer to home". The two underpinning aims are, firstly, to provide a genuine alternative to hospital admission for some carefully selected patients and, secondly, to provide rehabilitation and supported discharge.

An intermediate care service should have a clear function (admission prevention and/or post-acute care), incorporate comprehensive (multi-disciplinary) assessment.

Community based care

Hospitals catering to older people should provide comprehensive services in the community also, to support general practitioners and primary care teams caring for older people.

Mental Health Services

Good mental health underpins the well being of older people. Older people with mental health problems are entitled to have a diagnosis made and

appropriate treatment initiated. Hence, it is a must for any geriatric centre.

Rehabilitation

The WHO defines rehabilitation as a wide range of activities in addition to medical care which includes psycho-social care and occupational therapy. It is a process aimed at enabling people with disabilities to reach and maintain their optimal, physical sensory, intellectual, psychological and or social and functional levels. Adequate provision for this is a must for any geriatric centre.

Palliative Care

All older patients at the end of their life, are entitled to holistic person centred palliative care equivalent to that provided to people suffering from cancer.

Abuse of Older People

Abuse of older people is common, frequently hidden, and insidious in its capacity to deny respect and basic human rights for one of the most vulnerable sectors of society. It is the responsibility of those working in health care of older people to understand risk factors and signs of possible elder abuse, and know the correct way of managing this, when suspected.

Dignity in Care

Older people are more likely than younger people to become seriously ill and to face the prospect of dying. They and their families need to know that they will be treated with respect for their dignity if they become ill and that they will receive good end of life care.

Concerns about lack of respect for the dignity of older people in care settings calls for evolution of a set of standards of care for older people. Standards should be set for mental health care, acute hospital care and for the more general principles of person-centred care.

Preferences for Care at the End of Life

When seriously ill patients are nearing the end of life, they and their families sometimes find it difficult to decide on whether to continue medical treatment and, if so, how much treatment is wanted and for how long. In these instances, patients rely on their physicians or other trusted health professionals for guidance¹⁰. Frequently, however, such discussions are not held. If the patient becomes incapacitated due to illness, the patient's family and physician must make decisions based on what they think the patient would want.

CONCLUSION

Hospitals are matrix organization, an amalgam of cultural, social, architectural, technological and economical factors. To enable them fulfil their role pertinent to the times, it is essential that hospitals should be envisioned for the present and the future. Hospital buildings have to be designed taking into consideration the present and futuristic requirements. Patient focused architecture, technology integration with environment, shape optimization, care givers requirements, structural integrity, harmonious convergence of the clinical, diagnostic, therapeutic, administrative and hospitality dimensions are essentials that would be incorporated in building hospitals of the future. Some of existing healthcare hospitals already have a number of facilities incorporated that are perceived as essentials for tomorrow.

The hospitals of tomorrow will be able to strike a balance between the need of the professionals, the wish of the patients and the community and provide an effective, holistic, ethical, standardized, accessible, affordable, acceptable, safe and secure healthcare institute.

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Detection of Fetal Nucleic Acid in Maternal Plasma: A Novel Noninvasive Prenatal Diagnostic Technique

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Abstract: Prenatal diagnosis is routinely offered to the antenatal women seeking advice regarding genetic abnormalities in the fetus. The routine tests available for prenatal screening and diagnosis are invasive and have risk of miscarriage. The detection of fetal nucleic acid especially the cell free fetal DNA in maternal plasma is a newer non invasive prenatal diagnostic technique. Its analysis is based on distinct and detectable differences between fetal and maternal genomes thus it can be employed in the detection of aneuploidy, single gene disorders, sex linked diseases and pregnancy related disorders like preeclampsia.

INTRODUCTION

Prenatal diagnosis is an established part of modern obstetrics. It is routinely offered to the antenatal women seeking advice regarding genetic abnormalities in the fetus or as such it can be part of routine screening offered to all antenatal women.

The tests available for prenatal screening and diagnosis involve removal of fetal cells directly from the uterus, using either chorionic villous sampling (CVS) at 11-14 weeks or amniocentesis after 15 weeks. Although this approach to the fetal testing is gold standard and gives definitive diagnosis, the chances of miscarriage (around 1%)¹ and invasiveness makes it inconvenient to pregnant women.

Thus the need for the non-invasive methods of detection of fetal cells led to detection of these fetal cells in the cervical mucus^{2,3} and in maternal blood. Research has now mainly focused on strategies for detecting genetic elements from the fetus present in the maternal circulation.

It is popularly thought that placenta forms an impermeable barrier between mother and child, but on the contrary there is bidirectional traffic between the fetus and the mother during pregnancy⁴. Intact fetal cells present in maternal blood present an attractive target for non-invasive prenatal diagnosis (NIPD), particularly for the diagnosis of fetal sex and chromosomal abnormalities. In 1990, Bianchi et al first isolated intact fetal nucleated red blood cells for the purpose of prenatal diagnosis⁵. Since then, the isolation and detection of fetal cells from maternal blood has been extensively investigated by different researchers^{6,7}, and various methods of fetal cell enrichment were developed⁸. However, results to date have been disappointing because of:

- Scarcity of intact fetal cells in the maternal circulation (around one cell/ml of maternal blood)⁹
- Low efficiency of enrichment.
- Difficulties with chromosomal analysis associated with abnormally dense nuclei in some cells¹⁰
- Persistence of fetal cells in the maternal circulation for decades following pregnancy potentially causing false-positive results in subsequent pregnancies.

Therefore the majority of recent research has focused on cell-free fetal DNA (cffDNA) in the maternal blood.

Mandel and Metais were first to discover the presence of small amounts of extracellular DNA in the circulation of both healthy and diseased subjects in 1947. After 50 years the presence of fetal DNA in the maternal circulation was demonstrated by Lo et al. Fetal DNA can be detected from the 4th week of gestation, though only reliably from 7 weeks, and the concentration increases with gestational age from the 16 fetal genomes per ml of maternal blood in the first trimester to 80 fetal genomes per ml in the third trimester, with a sharp peak during the last 8 weeks of pregnancy. Fetal DNA originates trophoblast cells and comprises around 3-6% of the total cell-free DNA in maternal circulation during early and late pregnancy, respectively (the other 94-97% being maternal cell-free DNA). Unlike cellular DNA, circulating cffDNA consists predominantly of short DNA fragments rather than whole chromosomes, of which 80% are <193 base-pairs in length. In contrast to fetal cells, cffDNA is rapidly cleared from the maternal circulation with a half life of 16 minutes and is undetectable after 2 hours of delivery.

METHODS OF DETECTING cff DNA

Isolation of fetally derived cell-free DNA in an overwhelming background of

maternal cell-free DNA is a significant technical challenge. There are a number of general problems associated with detecting cffDNA in the maternal circulation:

- Concentration of all cell-free DNA in blood is relatively low.
- Total amount of cell-free DNA varies between individuals.
- cffDNA molecules are outnumbered 1:20 by maternal cell-free DNA molecules.
- Fetus inherits half its genome from the mother so that cannot be distinguished.

The basic principle in extracting the cffDNA is to take initially maternal plasma, separate cellular matter by centrifugation, followed by isolation and purification of all cell-free DNA, followed by exploiting the small differences between the fetal and maternal DNA sequences in order to make a specific fetal diagnosis.

To date, the majority of studies have focused on the detection of paternally inherited sequences that are entirely absent from the maternal genotype, such as those on the Y chromosome of male fetuses. Variable regions of repeated DNA (short tandem repeats or STRs) can be used to identify paternally inherited sequences. Importantly, all these methods rely upon the fetus inheriting a uniquely paternal sequence that is conveniently located for a particular diagnosis. The most common technique currently used for detection and identification of specific cffDNA sequences are:

Polymerase chain reaction (PCR). Most popular types of PCR used are

- real-time quantitative PCR¹⁸
- Nested PCR¹⁹
- pyrophosphorolysis-activated polymerization PCR²⁰
- digital PCR which allows the exact number of original template DNA molecules to be counted.²¹

*Mass spectrometry*²², in which the precise mass of each DNA fragment is analysed to determine the genetic sequence, and hence detect fetal-specific alleles that differ from the maternal sequence by as little as a single base. *Multiplexed maternal plasma DNA sequencing analysis* to rule out fetal trisomy 21 among high risk pregnancies²³.

The accuracy and reliability of detection can be significantly improved by increasing the proportion of fetal DNA relative to maternal DNA in the sample thus increasing the signal-to-noise ratio. There are two alternative methods specifically aimed at this:

1. **Selective enrichment of fetal DNA:** It is based on a difference in the average physical length of fetal and maternal DNA fragments, which can be exploited to increase the relative amount of cffDNA. Fetal derived DNA fragments are generally smaller than those that are maternally derived (mostly less than 313 base-pairs in length). Therefore, by using standard size fractionation to select only DNA fragments <300 base-pairs, circulating cffDNA can be enriched such that it comprises around 70% of the total cell-free DNA, prior to detection and identification by either PCR or mass spectrometry.
2. **Suppression of maternal DNA by the addition of formaldehyde**²⁴: A chemical that is thought to stabilize intact cells, thereby inhibiting further release of maternal DNA into the sample and increasing the relative proportion of fetal DNA. However, the use of formaldehyde for this purpose is controversial²⁵.

CLINICAL APPLICATIONS OF cff DNA ANALYSIS

cff DNA analysis is based on distinct and detectable differences between

fetal and maternal genomes thus it can be employed in the detection of:

1. Sex determination can be done by detecting cffDNA sequences on the Y chromosome; thus mainly helpful for sex-linked disease, such as haemophilia, Duchenne muscular dystrophy, X-linked mental retardation, adrenoleukodystrophy, Alport's syndrome, X-linked severe immunodeficiency, retinitis pigmentosa, X-linked hydrocephalus, anhidrotic ectodermal dysplasia, Hunter's syndrome, Menke's syndrome and Lesch-Nyhan syndrome. Sex determination is also important in cases where development of external genitalia is ambiguous and in some endocrine disorders, such as congenital adrenal hyperplasia (CAH), where there is masculinization of the female fetus, which is preventable with antenatal treatment. It has recently been shown that some false positives are due to the presence of a vanishing (male) twin. In order to reduce this problem, it has been suggested testing for fetal sex by cffDNA should be accompanied by an ultrasound scan, which could be done early in pregnancy, as loss of the twin usually occurs in the first 7 weeks.
2. Single gene disorders can be detected by identifying a paternally inherited allele in cffDNA; Huntington's disease, achondroplasia, myotonic dystrophy, fetal carrier status in cystic fibrosis, hemoglobinopathy, CAH.
3. Aneuploidy can be identified by detecting an abnormal concentration of a particular chromosome, potentially using cffRNA specific to the fetus and chromosome of interest i.e. Down's syndrome (trisomy 21), Edward syndrome (trisomy 18), Patau syndrome (trisomy 13), Turner syndrome (XO) and triple X syndrome (XXX) in female births, Klinefelter syndrome (XXY) and XYY syndrome in male births.
4. Pregnancy-related disorders can be identified by detecting either the presence of a working copy of the Rhesus gene or an elevation in the absolute concentration of cffDNA in abnormal functioning of placenta (usually measuring Y chromosome DNA of male pregnancies). It is elevated by 2–3 folds before the onset of preeclampsia and 2–14 folds during preeclampsia²⁶. In addition to preeclampsia, a number of other pregnancy-related disorders have been linked to an elevated concentration of cffDNA which include preterm labour, hyperemesis gravidarum, invasive placental, intrauterine growth restriction, foeto-maternal haemorrhage and polyhydramnios.

TECHNICAL DIFFICULTIES

There are a number of technical and clinical obstacles to achieving high diagnostic accuracy:

- It is important to emphasize that complete fetal genotyping is not conceivable using cffDNA in the maternal circulation and that the genetic information derived from cffDNA is entirely restricted to the specific DNA sequence (or chromosome) detected.
- False negatives can be the result of failure to extract or detect sufficient material, due to individual variability in the amount of total cell-free DNA and the small proportion of fetal versus maternal cell-free DNA.
- False positives can be the result of either technical issues, such as contamination, or clinical abnormalities such as the presence of a non-identical vanishing twin.

Therefore, extensive clinical trials will be required for each application to evaluate both the analytical and clinical validity before this technique could be used reliably in a clinical setting.

UNIVERSAL FETAL MARKERS

A major area of current research is aimed at finding universal fetal-specific markers that could be used either as diagnostic tests in their own right or to confirm and quantify the presence of fetal DNA independent of sex or other specific diagnostic tests. These could be used alongside clinically relevant diagnostic tests as a positive control for the presence of cffDNA, in order to highlight false-negative results either caused by low levels of circulating DNA below the detection limit of the test or problems with the DNA extraction process. One of the methods under investigation is the detection of specific DNA sequences located on the autosomal chromosomes that can be shown to be paternally inherited, including:

1. Single nucleotide polymorphisms (SNPs), or point mutations, which differ between the maternal and paternal genomes but may not be directly linked to a specific disease^{27,28}. It relies upon selective enrichment of the cffDNA followed by analysis by a highly sensitive technique such as mass spectrometry.
2. Polymorphic segments of DNA that vary between the maternal and

paternal genomes, such as STR sequences. Because of the highly variable nature of STRs, the paternally inherited fetal STR sequence will differ in the number of repeats from the maternal sequence. Amplification of these STR sequences will therefore result in two major products corresponding to the maternal alleles (and the maternally inherited fetal allele) and one minor product corresponding to the paternally inherited fetal allele. However, the technique has yet to be optimized for clinical diagnostic use and the sensitivity and specificity have not been established.

Fetal nucleic acids other than cffDNA detected in the maternal circulation which can be helpful in the prenatal diagnosis are:

- Detection of cell free fetal RNA (cffRNA): Like cffDNA, cffRNA is detectable within the maternal circulation early in the first trimester and is rapidly cleared following birth, with a half-life of 14 minutes²⁹. Since the expression of certain genes is unique to pregnancy, detection of placental/fetal RNA is an extremely promising avenue for research, as it is relatively easy to isolate completely from background maternal RNA.
- Detection of proteins derived from genes that are uniquely expressed in the placenta or fetus. Placentally expressed genes may result in potentially diagnostic fetal proteins in the maternal bloodstream³⁰.

CONCLUSION

The study of fetal proteomics is currently still in the infancy, with the primary aim being to improve the panel of serum markers used in screening for Down syndrome and Rh D typing. It is expected that over the coming years, technological advances will make it possible to implement it for a number of other clinical conditions.

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Role of Hospital in Pandemic: Our Experience

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Abstract: Background: Flexible guidelines have been laid down by various international and national authorities for pandemic preparedness and response of Health-care Facilities during various phases of the pandemic, which are updated and widely communicated to the nations worldwide. The hospitals are responsible for adopting these guidelines and prepare themselves for any eventuality. Current study presents the role played by a Tertiary Care Hospital (SKIMS) in Northern India in the recent H1N1 flu pandemic.

Methodology: Review of the records pertaining to H1N1 management was performed to assess the preparedness of the hospital in dealing with the pandemics. Further, comparison of the Hospital's Preparedness with the recommended guidelines was performed to identify scope for improvement.

Observations: The hospital started preparations for the pandemic in June 2009, when some states in India were already affected. A multidisciplinary H1N1 committee was framed which participated in the pandemic preparedness plan and laid down recommendations conforming to the national and international guidelines. Nodal office was established for coordination of the pandemic management. An isolation ward with separate access was readied after some requisite engineering modifications and more space identified in anticipation of a surge. Logistic support in the form of durables and consumables were procured from the contingency fund and stockpiled. Communication with external and internal agencies was vital to the effective pandemic management. Awareness and training were imparted across all sections of the Hospital employees. Vaccines were made available and employees vaccinated. Public awareness and education was created at every opportunity. Recording and reporting was a regular feature. A total of 100 suspected patients were admitted till January 2011. Of these 16 were confirmed positive, four patients expired. Gaps between the hospital's preparedness and recommended guidelines were identified for future preparedness and response.

Conclusion: Lesson learnt is that the hospitals should have a Pandemic Plan akin to a Disaster Plan, in view of the viruses lurking at various phase levels in our immediate environment.

Keywords: H1N1 Flu Pandemic, Pandemic preparedness, Interim Guidelines for H1N1.

INTRODUCTION

A pandemic has been defined as "An epidemic usually affecting a large proportion of the population¹, occurring over a wide geographic area such as a section of a nation, the entire nation, a continent or the world. Pandemics of viral influenza occur after every 30-40 years. In the 20th century some devastating pandemics occurred esp.; the 1918 or Spanish flu pandemic which claimed around 20-100 million lives with a case fatality rate of >2.5%. The devastation was worse than world war 1². In the present century the epidemics of SARS (corona virus infection), Avian influenza (H5N1infection) and the latest H1N1 flu infection leading to either local outbreaks, epidemics or pandemics has forced the International and National Health Care Authorities to frame and emphasize pandemic preparedness plans. The preparedness planning becomes all the more necessary in view of the already meager resources available for healthcare in the developing nations. In response to the potential viral threats the WHO, CDC and other health care authorities have laid down flexible and adaptable guidelines on pandemic planning for Health care Facilities which have been adopted by the nations worldwide, including India. Further the healthcare facilities should also check with the national and local health authorities for local guidance in addition to consideration of their unique circumstances and needs that may not be addressed otherwise.

The Ministry of Health & Family Welfare, Government of India has also laid down guidelines for pandemic management in Hospitals and identified public Hospitals in all the states and Union Territories for management of the H1N1 flu pandemic, one such Hospital being Sher-I-Kashmir Institute of Medical Sciences (SKIMS), located in a Northern state of Jammu and Kashmir, India.

The current study presents the preparedness and response of SKIMS Hospital which is a 625 bedded Tertiary Care Hospital, in the management of recent H1N1 Influenza pandemic. It also endeavours to identify the gaps and scope for improvement for future preparedness for pandemics.

OBJECTIVES

Study the preparedness of the Hospital for the management and handling of

H1N1 flu pandemic.

Compare the pandemic preparedness of the SKIMS hospital with recommended International and National guidelines.

MATERIALS AND METHODS

The study was based on retrospective review of the records for the year 2009 -2010, related to the preparedness and response of the hospital for the H1N1 pandemic which included:

- Review of Internal and external correspondences pertaining to H1N1 flu.
- Review of the case management records
- For comparison of the Hospital Pandemic Preparedness and response to H1N1 with reference standards, updated guidelines by International Health authorities, such as World Health organization (WHO), Department of Health and Human Services US (HHS) Centres for Disease Control, US (CDC), Occupational safety & Health Administration (OSHA) and National Health Authorities, like Ministry of Health and family Welfare (MoH&FW) were reviewed. The gaps between the Standard Guidelines and Hospital's Pandemic Preparedness plan were identified so that a practical Pandemic Preparedness plan could be framed for future use.

OBSERVATIONS AND DISCUSSION

SKIMS hospital had a total of 100 suspected H1N1 flu admissions, out of which 16(16%) were confirmed positive. First patient was admitted in August 2009. The cases were clustered around the winter of 2009-2010, although two cases were reported in the summer of 2010. The youngest patient was aged 14 years and the oldest 60 years. Mean age was 34.9 years. Five(31.25%) were females. Four (25%) patients expired and 06 (37.5%) with ARDS needed Intensive care management. Two patients had associated comorbidities, rest were healthy adults. One patient who expired, had multiple co morbidities including hypertension, old MI, COPD and drug addiction (Table 1).

Review of the correspondence pertaining to management of H1N1 flu reveals that preparations for the pandemic began in the month of June

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Table1: Profile of Confirmed H1N1 Inpatients

Date-of Admission	Age	Sex	Travel history	Comorbid conditions	Care	Outcome
20.08.09	40	M	No	Nil	Intermediate	Cured
01.12.09	21	F	No	Nil	Intensive	Expired
18.12.09	55	M	Yes	+	Intensive	Expired
19.12.09	50	M	Yes	Nil	Intermediate	Cured
27.12.09	40	F	No	Nil	Intensive	Cured
29.12.09	50	M	Yes	Nil	Intermediate	Cured
07.01.10	50	F	No	Nil	Intermediate	Cured
16.01.10	60	M	No	+	Intensive	Cured
21.01.10	23	M	No	Nil	Intermediate	Cured
17.02.10	18	F	No	Nil	Intermediate	Cured
20.02.10	32	M	NO	Nil	Intermediate	Cured
11.03.10	31	M	Yes	Nil	Intermediate	Cured
17.07.10	14	M	No	Nil	Intensive	Cured
21.07.10	26	M	No	Nil	Intensive	Expired
27.12.10	25	M	No	Nil	Intermediate	Cured
17.01.11	25	F	No	Nil	Intensive	Expired

2009.

Meetings chaired by the Medical Superintendent were held in which 7-8 members including Head Internal medicine, Head microbiology, consultant Hospital Administration, Senior Resident Hospital Administration, Nursing Superintendent, Hospital Infection Control Nurse and Materials Management Officer participated. A three member team consisting of Head Department of Internal & pulmonary Medicine, Consultant Hospital Administration and Joint Nursing Superintendent was formed to facilitate the management of patients with H1N1 flu. A nodal office with Consultant Hospital Administration as nodal officer assisted by two Residents of Hospital Administration was established to facilitate implementation of the plan.

Facility and facility access: A 16 bedded isolation ward was prepared after some requisite engineering modifications for infection control. Glass partitions were raised in the ward between cubicles. Air Handling units of the ward were sealed and negative pressure was maintained with the help of exhaust fans discharging to an open area, while procurement of negative pressure equipment was initiated. A triage area was identified and made functional for patients of Influenza like illness (ILI) on the emergency side of the Hospital. In order to restrict the spread, the area was connected with the isolation ward through a separate access for admitted flu patients without the need to traverse the main hospital corridor. Visitor restrictions to the triage and ward area were maintained with the help of hospital security. Additional space in the form of a 32 bedded ward was identified in anticipation of a surge. In spite of all these preparations some patients needed admission to the Critical Care Unit of the Hospital for intensive monitoring and mechanical ventilation.

Logistic Support: Durables like ventilator were procured from the contingency fund. Procurement process for negative pressure equipment for the Isolation Ward was also initiated. Consumables like N95 respirators, Personal protective equipment (PPE), hand sanitizers, etc., were also procured and stockpiled. Some material support was extended by the State Nodal Centre in the form of provision of PPE, sample collection kits, N95 masks and antiviral drugs (oseltamivir) etc.

Hospital Surveillance: Surveillance in the emergency department and wards was increased to detect cases of influenza like illness (ILI). Any ILI among the patients and Hospital staff was viewed with suspicion of H1N1 flu. As no testing facility was available in the Hospital, their samples were sent to the National Center for Disease Control (NCDC) lab, New Delhi for confirmation and reporting.

Communication: Information exchange that was accurate and timely was a key to the effective management of the pandemic flu.

External communication: written as well as verbal communication was held with following agencies:

- **MoH & FW:** Written(mail,E-mail,fax) and verbal(telephonic) communication was held between the Hospital and ministry regarding guidelines, feedback on planning and implementation of

preparedness plan, reporting of cases and number of vaccinations performed. MoH&FW also cautioned the hospital against a resurgence/2nd wave of H1N1 pandemic in june-july 2010.

- **NCDC Delhi:** which was the nearest designated testing facility for the hospital for coordination of H1N1 testing and reporting of tests, was communicated with telephonically and through fax.
- **Media:** Public media was used to create awareness among the masses. Senior faculty of the hospital delivered interactive sessions over mass media channels like television, daily newspapers etc. A Public relations officer was designated to answer the queries of the media and state authorities.
- **Public:** Attendants of the patient needed reassurance and were informed and explained about home isolation precautions regarding the patient and themselves.
- **State Nodal Center:** Communication with State Nodal Center was held for provision of logistic aid.
- **Airport Authority:** Airlifting of samples to NCDC required proper information, labeling of carriers and other communication with the airlines and airport authorities.

Internal communication: Internal communication was necessary for the coordination of patient care with various Departments, like Internal& Pulmonary Medicine, Critical Care Unit, Emergency Department, Materials Management Department, Housekeeping Department etc.

Education and Training: Training programs in the form of CME, Table Top Exercises, were held for doctors, nurses and paramedical staff. Awareness programs were held for nursing and other paramedical staff regarding prevention and control of H1N1 flu infection.

A Table Top Exercise for Pandemic preparedness on H1N1 flu was organized in collaboration with the MoH&FW in which the faculty and residents of the hospital participated. Case discussions at grand rounds and mortality meetings were also held.

The Hospital Infection Control Office published pamphlets for circulation among Hospital staff for prevention and control of infection. Posters for public regarding respiratory hygiene and cough etiquette were displayed in waiting areas of Outpatient Department and Emergency Department.

On the Job Trainings were provided by the HICN for use of Personal Protective Equipment, hand washing technique and waste handling and management.

The patients and their attendants were counseled regarding control of spread, treatment and prophylaxis.

However, it was difficult to convince the hospital staff including doctors and nurses to avail vaccination although the H1N1 specific vaccine (panenza) was provided by the Government of India(GOI) free of cost. Utilization of the vaccine was only 50%.

Occupational Health: Healthcare safety of employees was ensured through provision of infection control logistics like hand sanitizers, N95 masks to those working in the isolation ward, PPE when high risk procedures like lifting of nasopharyngeal or throat swabs, endotracheal suction, etc. were anticipated. Vaccination was provided. Few HCW who fell ill were given special permission to stay at home till they recovered. Antiviral medication (oseltamivir) was provided to HCW who had acquired the infection.

STANDARD GUIDELINES VIS-À-VIS PANDEMIC PREPAREDNESS AT SKIMS HOSPITAL

Guidelines for pandemic preparedness existed much before the H1N1 pandemic occurred^{3,4}. Based on the WHO classification system prepared in 1999 and reviewed in 2005 for phasing various stages of the pandemic development/ progress, the MoH & FW developed an Influenza Preparedness and response Plan for the country in which hospital systems received

Interpandemic Period	Assess availability of hospital beds for general treatment /critical care and identify gaps. Develop infrastructure to augment critical care support. Hospitals to evolve/ strengthen hospital disaster plan for managing mass casualties/fatalities. Develop protocols for clinical case management. Evolve infection control policies. Prepare bio safety and Waste Management protocols and ensure its implementation. Training of Laboratory Personnel for handling clinical samples. Increase awareness.
Pandemic Alert Period	Review hospital disaster manuals with special attention to surge capacity for managing critically ill patients; managing fatalities and availability of requisite manpower. Ensure provision of isolation facilities and strict infection control practices. Assess effectiveness of clinical management protocols and review. Conduct CME to all levels of staff for management of cases and infection control practices. Pre test existing arrangements through simulation exercises /mock drills
Phase 3: Human infection/s with a new sub-type but no human to human spread or at most rare instances of spread to a close contact.	Ensure that the cases are reported as per surveillance protocol. Create additional surge capacity to cope large scale morbidities and mortalities in both Govt and Private Sector. Continue assessing effectiveness of clinical management protocols. Review infection control practices and enforce implementation as per protocol
Phase 4 Small cluster/s with limited human to human transmission but spread is highly localized, suggesting that the virus is not well adapted to humans.	Hospital systems to contain and reduce human to human virus transmission to limit morbidity and mortality among the affected population. Ensure that the cases are reported as per surveillance protocol. Create additional surge capacity to cope large scale morbidities and mortalities in both Govt and Private Sector. Continue assessing effectiveness of clinical management protocols. Review infection control practices and enforce implementation as per protocol
Phase 5: Larger cluster/s but human to human spread still localized, suggesting that the virus is becoming increasingly better adapted to humans, but may not yet be full transmissible (Substantial Pandemic risk).	To monitor public health resources for pandemic response to ensure health system in readiness for triage and treatment. Prevent spread of infection through nosocomial route. Create surge capacity within existing hospital systems and generate additional resources by establishing day care centers and temporary hospitals. Establish triage system. Ensure availability of adequate health personnel; if required mobilize from other states. Ensure safety of health care workers by vaccination/ prophylaxis, barrier practices, use of PPEs and skill update training. Ensure correct waste disposal practices, including terminal disinfections. Enforce implementation of recommended infection control practices. Implement guidelines for management of mass fatalities.
Phase 6: Increased and sustained transmission in general population	To monitor public health resources for pandemic response. to ensure health system in readiness for triage and treatment. Prevent spread of infection through nosocomial route. Create surge capacity within existing hospital systems and generate additional resources by establishing day care centres and temporary hospitals. Establish triage system. Ensure availability of adequate health personnel; if required mobilize from other states. Ensure safety of health care workers by vaccination/ prophylaxis, barrier practices, use of PPEs and skill update training. Ensure correct waste disposal practices, including terminal disinfections. Enforce implementation of recommended infection control practices. Implement guidelines for management of mass fatalities
Post Pandemic Period	Hospital systems Strengthen hospitals for next pandemic wave Review effectiveness of treatment and counter measures identify deficiencies and fill gaps. Replenish stock of anti virals and other essential drugs/ consumables. Ensure that overworked staff has opportunities for rest.

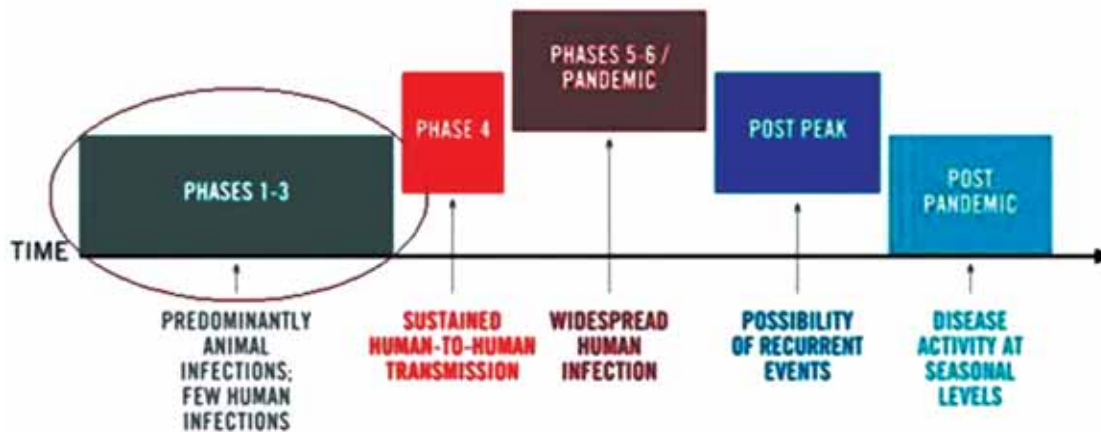


Fig1: Pandemic flu Phases(Source:WHO Global Alert and Response)

specific guidelines for capacity building and infrastructure upgradation as per pandemic phase as under:⁵ The U.S. Department of Health & Human Services (HHS) has recommended planning according to the phase (Fig1) of the pandemic⁶. Healthcare facility responsibilities in the interpandemic and pandemic alert periods as per HHS guidelines include:

- Develop planning and decision making structures for responding to pandemic influenza.
- Develop written plans that address (a) disease surveillance in the hospital (b) hospital communications (c) education and training (d) triage, clinical evaluation, admission procedures (e) facility access (f) occupational health (g) use and administration of vaccines and antiviral drugs (h) surge capacity (i) Supply chain and access to critical inventory needs (j) mortuary issues.

According to the CDC facilities should review, and if not already in place, develop *written pandemic preparedness plans* anticipating widespread transmission of 2009 H1N1 influenza in communities⁷.

Checklists have been developed by the WHO⁸, CDC⁹ etc for quick review of pandemic preparedness of a Healthcare facility including hospitals. OSHA (Occupational safety and health Administration) has also developed guidance for healthcare settings for occupational safety of the HCW¹⁰.

For Prevention and Control of Infection Standard Guidelines have been laid down by all the authorities including CDC, which have been updated from time to time.

Recommendations¹¹ of CDC for prevention and control of infection include:

- Promote and administer seasonal influenza vaccine
- Take Steps to Minimize Potential Exposures
- Monitor and Manage Ill Healthcare Person
- Adhere to Standard Precautions
- Adhere to Droplet Precautions
- Use Caution when Performing Aerosol-Generating Procedures
- Manage Visitor Access and Movement within the Facility
- Monitor Influenza Activity
- Implement Environmental Infection Control
- Implement Engineering Controls
- Train and Educate Healthcare Personnel
- Administer Antiviral Treatment and Chemoprophylaxis of Patients and Healthcare Personnel when Appropriate
- Considerations for Healthcare Personnel at Higher Risk for Complications of Influenza

SKIMS hospital began preparations for the H1N1 pandemic in June 2009 only after receiving a letter from Ministry of Health regarding the preparedness status of the hospital. WHO declared H1N1 a pandemic in June 2009.

All the above mentioned responsibilities such as steps to minimize potential

exposure, isolation facility, triage (engineering controls), surveillance, infection control practices (administrative controls), concern for occupational health, communication etc, were carried out well during the pandemic by SKIMS hospital but a written pre-pandemic plan was lacking. Biosafe lab facility was not developed and mortuary issues were not anticipated. Although training and awareness to all the categories of HCW was provided but they needed counseling and education regarding the foremost protective and preventive measure i.e., vaccination. Checklists should also have been adopted or laid down by SKIMS to assess its state of preparedness. However an incident Command Centre in the form of a nodal office was established as recommended in a WHO checklist⁸, which facilitated excellent coordination during the pandemic peak.

CONCLUSION

WHO Director General declared the end of H1N1 pandemic on 10th August 2010. But at the same time she cautioned the world about the unpredictability of the pandemics. Avian flu which is presently at phase 3 is a lurking global threat. The study which presents the role played by a Hospital in Northern India is probably a model of other such hospitals in the developing world, constrained by lack of resources, meager health budget allocations and lack of scientific planning. A Pandemic Preparedness plan is expected to go a long way in preparing these resource crunched hospitals to deliver an efficient response. Pre-existing guidelines await adoption and implementation with / without modifications to suit the needs of these hospitals for future pandemic preparedness.

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Management of Oral Lichen Plannus: A Clinical Study

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Abstract: Lichen planus, a chronic autoimmune disease, affects the skin and mucous membrane. It is characterized by alternating periods of symptomatic remission and exacerbation. Different treatment modalities have been tried with limited success. Presently, treatment of lichen planus aimed at alleviating symptoms during periods of exacerbation and to prolonge the duration of remission. A regular follow-up of patients is required as there is high risk of malignant transformation in few types of oral lichen planus.

Key words: Lichen planus, mucocutaneous, local drug delivery

INTRODUCTION

Lichen planus is a chronic autoimmune, mucocutaneous disease. It can affect the oral mucosa, skin, genital mucosa, scalp and nails. In the majority of patients with oral lichen planus (OLP) there is no associated cutaneous lichen planus or lichen planus at other mucosal sites. This may be called "isolated" OLP¹. It commonly affects the middle-aged patients² and has a female predilection. OLP is also seen in children, although it is rare^{3,4}. The disease affects 0.5-2% of the population. The clinical history confirms the relationship between OLP and oral cancer, although the degree of the risk involved is controversial. Therefore, OLP should be considered a precancerous lesion, emphasizing the importance of periodic follow-ups in all the patients⁵. Various treatment modalities for lichen planus have been tried including topical and systemic steroids, retinoids, immunosuppressive drugs, surgery, lasers and photochemotherapy.

ETIOLOGY

The etiology of lichen planus still remains unknown. Lichen planus is believed to result from an abnormal T-cell-mediated immune response in which basal epithelial cells are recognized as foreign because of changes in the antigenicity of their cell surface⁶. Current data suggest that oral lichen planus is a T-cell-mediated autoimmune disease in which autolytotoxic CD8⁺ T cells trigger the apoptosis of oral epithelial cells⁷. The CD8⁺ cytotoxic T cells may trigger keratinocyte apoptosis through activation of the cells by an antigen associated with major histocompatibility (MCH) class I on basal keratinocytes⁷.

Oral lichen planus has been found to be associated with diseases and agents, such as viral and bacterial infections, autoimmune diseases, medications, vaccinations and dental restorative materials. Carrozzo et al⁸ have demonstrated a strong association between hepatitis C viral infection and OLP. However, the association of OLP with HCV infection appears to be dependent on geographical heterogeneity⁸. Moravvejet al⁹ in 2007 found statistically significant differences in *H. Pylori* infection between patients with lichen planus and a control group. However, an etiologic role for *H. pylori* in lichen planus is not yet properly established. Various studies have investigated the association of candida infection and oral lichen planus but failed to establish as an etiologic factor.

CLINICAL FEATURES

OLP was first described clinically by Wilson in 1869 as a chronic mucocutaneous disorder¹⁰. Cutaneous lichen planus is recurrent, itchy^{11,12} and not contagious¹³. In most of the patients, OLP is asymptomatic while some patients may report of a roughness of the lining of the mouth, sensitivity of the oral mucosa to hot or spicy foods, painful oral mucosa, red or white patches on the oral mucosa, or oral ulcerations. The clinical history

includes phases of remission and exacerbation¹⁴.

Six clinical forms of OLP have been described which are white forms namely reticular, papular, plaque-like and red forms namely the erosive (ulcerated), atrophic (erythematous) and bullous^{15,16}. Among the types, reticular and erosive are the main types¹⁷. It is not uncommon for the same patient to present with multiple forms of OLP. Mucosal lesions, which are multiple, generally have a symmetrical distribution, particularly on the mucosa of the cheeks, adjacent to molars, and on the mucosa of the tongue, less frequently on the mucosa of the lips (lichenouscheilitis) and on the gums (the atrophic and erosive forms localized on the gums manifest as a desquamative gingivitis), more rarely on the palate and floor of the mouth^{13,18}. However, this clinical appearance of desquamative gingivitis is not pathognomonic of erosive OLP and may represent the gingival manifestation of many other diseases such as cicatricial pemphigoid, pemphigus vulgaris, epidermolysis bullosa acquisita, and linear IgA disease^{19,20}. The most common type of OLP is reticular form with the characteristic feature of slender white lines (Wickham's striae) radiating from the papules. Patients with reticular lesions are often asymptomatic, but atrophic (erythematous) or erosive (ulcerative) OLP is often associated with a burning sensation and pain²¹.

A greater malignant potential has been recognized for atrophic, erosive form of OLP and the plaques form on the back of the tongue^{5,22}. A regular follow-up of patients with OLP should be performed and in suspected cases, biopsy should be provided.

CLINICAL STUDY

Cases reported to Department of Oral Medicine and Radiology, Tamil Nadu Government Dental College, Chennai with oral lichen planus from March 2010 to April 2011. A total number of 79 patients were diagnosed oral lichen palnus.

THERAPEUTIC OPTIONS

Currently, treatment for OPL is focused mainly to eliminate mucosal erythema, ulcerations and alleviate symptoms disease during periods of activity and, if possible, increase the periods of disease quiescence. Excellent oral hygiene maintenance is believed to reduce the degree of severity of the

Table 1: Age wise grouping of the patients with oral lichen planus (n=79)

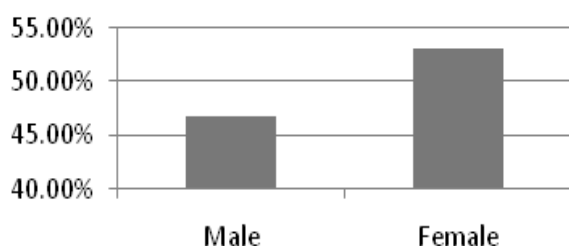
AGE GROUP	MALE PATIENTS	FEMALE PATIENTS	TOTAL
< 10 years	0(0%)	0(0%)	0(0%)
10-20 years	0(0%)	3(3.79%)	3(3.79%)
21-30 years	5(6.32%)	6(7.59%)	11(13.92%)
31-40 years	8(10.12%)	9(11.39%)	17(21.51%)
41-50 years	10(12.65%)	11(13.92%)	21(26.58%)
51-60 years	7(8.86%)	9(11.39%)	16(20.25%)
>60 years	7(8.86%)	4(5.06%)	11(13.92%)
TOTAL	37(46.83%)	42(53.16%)	

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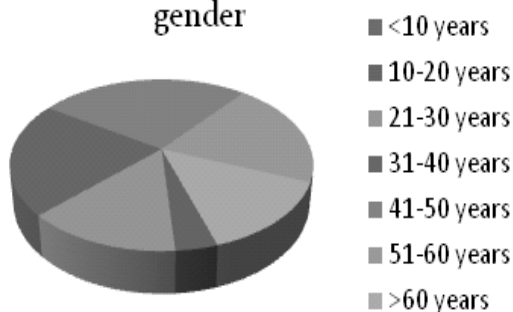
Male:Female ratio



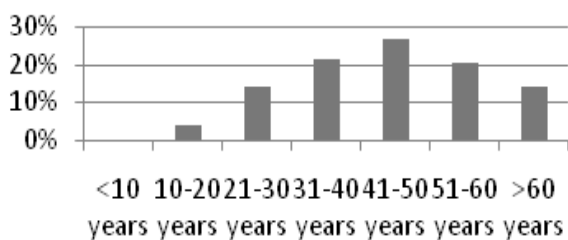
Male:female ratio



Age wise distribution for both gender



Age wise distribution for both gender

**Table 2:** Frequency of occurrence of types of oral lichen planus

Reticular	Papular	Plaque-like	Erosive	Atrophic	Bullous
55(69.62%)	2(2.53%)	3(3.79%)	10(12.65%)	7(8.86%)	2(2.53%)

symptoms and duration associated with OLP. Reticular type is often asymptomatic and seldom requires treatment.

CORTICOSTEROIDS

Currently, corticosteroids are the drug of choice for the treatment of OLP. It may be employed in the form of topical superficial application or intralesional injection; or systemic or combination of topical and systemic. Topical corticosteroids are the mainstay in treating mild to moderately symptomatic lesions. Options (presented in terms of decreasing potency) include 0.05% clobetasol propionate gel²³, 0.1% or 0.05% betamethasone valerate gel²⁴, 0.05% fluocinonide gel, 27 0.05% clobetasol butyrate ointment or cream, and 0.1% triamcinolone acetonide ointment²⁵.

Patients can apply the prescribed topical corticosteroids upto 4 times a day because topical agents adhere poorly to the moist mucous membranes. In patients with widespread symptomatic lesions, in whom direct mucosal application of topical medication would be too uncomfortable, options include 1.0 mg/mL aqueous triamcinolone acetonide or 0.1 mg/mL dexamethasone elixir²⁶.

Intralesional injection of corticosteroid²⁵ for recalcitrant or extensive lesions involves the subcutaneous injection of 0.2-0.4 mL of a 10 mg/mL solution of triamcinolone acetonide by means of a 1.0-mL 23- or 25-gauge tuberculin syringe.

The advantage of topical steroid application is that side effects are fewer than with systemic administration.

Systemic corticosteroids are probably the most effective treatment modality for patients with diffuse erosive OLP or multi-site disease, but the literature on their use is limited to non-randomized clinical trials. Both methylprednisolone and prednisone have been employed for recalcitrant severe erosive OLP²⁷. Systemic prednisone can be used to control the ulcers and erythema in OLP but it is not better than treatment with topical triamcinolone acetonide alone²⁸. Systemic corticosteroids may be indicated in patients whose condition is unresponsive to topical steroids or in patients with mucocutaneous disease and in high doses (1.5-2 mg/kg/daily), but adverse effects are possible even with short courses^{29,30}.

IMMUNOSUPPRESSANTS

Tacrolimus is a macrolide immunosuppressant with a mechanism of action similar to that of cyclosporine, but is 10 to 100 times more potent and is better able to penetrate the mucosal surface.³¹ Treatment with topical tacrolimus 0.1% ointment four times daily induced a better initial therapeutic response than triamcinolone acetonide 0.1% ointment in patients with symptomatic OLP. However, relapses occurred frequently in both groups within several weeks after the cessation of both the treatments³².

RETINOIDS

Retinoids are metabolites of vitamin A. They have been noted to have antikeratinizing and immunomodulating effects^{33,34,35}. Retinaldehyde 0.1%³⁶, isotretinoin gel 0.1%³⁷ have been tried in OLP and they showed good clinical efficacy. OLP has been treated with fenretinide and tazarotene gel 0.1% successfully^{38,39}. These studies suggested that topical retinoid might be a suitable therapeutic agent in the treatment of hyperkeratotic OLP.

LASERS

Excimer 308 nm lasers could be an effective choice in treating symptomatic OLP⁴⁰⁻⁴². Treatments with these lasers are painless and well tolerated.

SURGERY

Surgical excision, cryotherapy, CO2 laser, and ND:YAG laser have all been used in the treatment of OLP. In general, surgery is reserved to remove high-risk dysplastic areas⁴³.

PHOTOCHEMOTHERAPY

In this method, clinician uses ultraviolet A (UVA) with wavelengths ranging from the 320-400 nm, after the injection of psoralen. It was first used in the treatment of recalcitrant OLP⁴⁴. One potential drawback of PUVA therapy is the risk of the squamous cell carcinoma (SCC) development in a condition with premalignant potential, and until more extensive studies have been performed, it must be considered as an experimental method^{45,46}.

LOCAL DRUG DELIVERY

The oral cavity has been proposed as a potential topical delivery site for local and systemic delivery of therapeutic agents. Drug delivery via the oral mucosa has several advantages and disadvantages and is summarized in table below⁴⁷.

Advantages	Disadvantages
• Accessible • Self-administrable • Oral mucosa repairs rapidly after damage or injury • Different areas of oral cavity have different permeability characteristics • Highly hydrated environment to dissolve drug • Sustained delivery possible • Potential reduction of systemic side effect	• Permeability barrier of the oral mucosa • Saliva washes away drug • Mastication and speech may dislodge delivery device • Taste important consideration • Highly enzymatic environment • Relatively small surface area • Risk of choking or swallowing on delivery device

CASES PRESENTATIONS

CASE 1: A clinically and histopathologically diagnosed erosive lichen planus in a 52 years male patient (Figure 1a,1b) treated with topical application of 0.1% triamcinolone acetonide followed by intralesional injection. Two weeks of treatment completely heals the lesion (Figure 1c,1d).



Figure 1a
(Pre-treatment)

Figure 1b



Figure 1c
(Post-treatment)

Figure 1d

CASE 2: Lichen planus of gingiva (Figure 2a) manifesting as desquamative gingivitis in a 38 years male patient treated with local drug delivery system(costume tray made from polyethylene sheets) with 0.1% triamcinolone acetonide. Costume tray (Figure 2b) is loaded with 0.1% triamcinolone acetonide (Figure 2c) and then inserted in the mouth (Figure 2d). Review of patient after 1 week (Figure 2e) and 2 weeks (Figure 2f) shows marked reduction in symptoms and erythema.



Figure2a

Figure2b



Figure2c

Figure2d

(Pre-treatment)



Figure2e(1 week)

Figure2f(2 weeks)

(Post-treatment)

CASE 3:Clinically diagnosed reticular type lichen planus (Figure 3a) in a 32 years female patient treated with topical application of clobetasolpropionate 0.05%.Review of patient after 1week (Figure 3b), 2 weeks (Figure 3c) and 3 weeks (Figure 3d) shows resolution of erythema and Wickham's striae. There is some evidence of post-treatment melanosis.

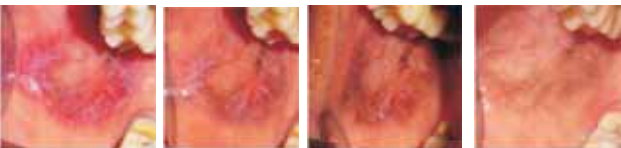


Figure3a

Figure3b

Figure3c

Figure3d

(Pre-treatment)

(Post-treatment)

CASE 4: An erosive lichen planus (Figure 4a,4b) in a 72 years male patient treated with 0.1% triamcinolone acetonideintralesional injection shows resolution of the lesion after 1 week review (Figure 4c,4d).



Figure4a

Figure4b

Figure4c

Figure4d

(Pre-treatment)

(Post-treatment)

DISCUSSION

Our short study is in acceptance with the previous dataof prevalence of oral lichen planus which shows highest in middle age female patients. Reticular type OLP is most commonly found. No patient below 10 years is affected by oral lichen planus. The low prevalence of OLP in younger age groups may be attributed to lower stress level, lack of much permanent dental restorations, simplicity in food habits and overall well-being of general health.

Although steroid therapy remains the backbone of treatment of OLP, its use must be justified. Steroid therapy either topical or systemic can cause adrenal suppression if used for prolonged periods. A thorough medical history should be taken before the commencement of the steroid therapy to avoid medical complications. The lowest-potency

steroid that proves effective should be used.

Patients with oral lichen planus should be counseled about the causes, nature and course of the condition and response to different treatment modalities. Causative agents like dental restorations or drugs must be identified and proper corrective approaches should be followed. Patients experience high rates of recurrences after the cessations of treatment and this should not discourage them for getting further treatment. Regular follow-ups allow the clinicians to examine and evaluate the patients thoroughly. Any suspicious lesions must be sent for biopsy for histopathological examination as there is high chances of transformation, in few forms of lichen planus, into squamous cell carcinoma.

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Obesity-Prevent rather than cure: Histopathological and clinical Perspectives

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Abstract: Obesity is a modern pandemic. It has turned into a common, serious and costly disorder. Obesity is not just a cosmetic consideration. It is a dire health dilemma directly harmful to one's health. Obesity is a chronic disease affecting increasing numbers of children and adolescents as well as adults. The longer a person is obese, the more significant obesity-related risk factors become. Obesity is increasing in an epidemic manner in most countries and constitutes a public health problem by enhancing the risk for Coronary heart disease, Type 2 diabetes, Cancers (endometrial, breast, and colon), Hypertension, Dyslipidemia, Stroke, Liver and Gallbladder disease, Sleep apnea and respiratory problems, Osteoarthritis, Gynecological problems (abnormal menses, infertility)

INTRODUCTION

The adipocyte number is a major determinant for the fat mass in adults. However, the number of fat cells stays constant in adulthood in lean and obese individuals, even after marked weight loss.

Adipose tissue is a complex, essential, and highly active metabolic and endocrine organ. Adipose tissue not only responds to afferent signals from traditional hormone systems and the central nervous system but also expresses and secretes factors with important endocrine functions. These factors include leptin, other cytokines, adiponectin, complement components, plasminogen activator inhibitor-1, proteins of the renin-angiotensin system, and resistin.

Altered adipocyte function changes production and secretion of adipokines, such as leptin, adiponectin, angiotensinogen, plasminogen activator inhibitor-1, resistin, and several inflammatory molecules.

Fat cells are chemical factories and body fat is potent stuff: a highly active tissue that secretes hormones and other substances with profound and sometimes harmful effects on metabolism, weight and overall health.

DISCUSSION

If a person keeps overeating, fat cells grow rapidly. When they reach the limit, they don't divide; they send out a signal to nearby immature cells to start dividing to produce more fat cells. Thus this starts a cascade of events leading to unlimited proliferation of adipocytes and the more the fat accumulation, more the number of fat cells accumulating fat and more the active division of cells. Thus an exponential growth of fat cells occurs. This can be exemplified by the fact that a typical overweight adult has around 75 billion fat cells. But in the case of severe obesity, this number can be as high as 250 to 300 billion.

Fat cells tend to increase in number most readily when excessive weight is gained due to overeating and or inactivity during the following periods:

- During late childhood and early puberty
- During pregnancy
- Most commonly, during adulthood when extreme amounts of weight are gained

Fat expands in 2 ways

A. Fat Cell Number

- Fat cell number does not decrease with weight loss
- Increases 5 fold until age 22 years
- Increase continues with nutritional excess
- Non-obese person has 25-30 billion fat cells
- Obese person has 260 billion cells

B. Fat Cell Size

- Fat cell size reduces with weight loss

- Adults fill existing fat cells when they over eat

EMBRYOLOGICAL PERSPECTIVE

Infants begin to develop fat cells during the third trimester of pregnancy. Fat cells divide and multiply in the body. When the fat cell is full, it goes through active mitosis, divides in half and becomes two. When both of those two cells become full of fat, they, too, divide. It goes on and on and on. Fat cells do not have the capability of dissolving and leaving the body. Once fat cells develop in the body, they remain there for life. The early rudiments of obesity may hence be laid in early life.

GENETIC PERSPECTIVE: OUR GENES WOULD NOT ALLOW US TO BE NON OBESE

Normally, a gene known as PPAR controls the amount of fat cells that are made and the size of those cells. A mutation in this gene causes switching of the gene to 'on' position causing more fat cells to form and these cells get fatter faster than normal fat cells.

The other gene regulates production of a hormone called "leptin," which suppresses appetite when fat cells become too full. Like PPAR, mutation of this gene occurs in only a small number of people. A subset of obese humans have normal or relatively low leptin levels (H²5-10% of subjects)^{1,2} In well-known animal models such as the ob/ob mouse and the fa/fa Zucker rat, obesity is entirely genetic in origin and is inherited in a classical Mendelian recessive fashion. Exceedingly rare, humans also have obesity attributable to defined mutations in the genes such as those encoding leptin, its receptor and the melanocortin-4 receptor. However, this does not apply to the common type of obesity which is a fine example of a multifactorial disease determined by the interaction between genes and the environment. The very rare human mutations provide important proof of concept that these gene products play a role in normal energy homeostasis, but they do not necessarily tell us much about their role in common human obesity.

Rare but crucial mutations are:

- Leptin Produced by adipose tissue, leptin reduces food intake in rats if centrally injected. Mutation on chromosome 7 found in some obese families
- Leptin receptor CNS receptor for leptin, Mutation on chromosome 1 associated with three cases of human obesity
- Melanocortin 4 receptor involved in the suppression of appetite Mutations on chromosome 18 associated with several cases of obesity
- Prohormone convertase 2 Converts proinsulin to insulin and C-peptide. Polymorphisms on Chromosome 20 are associated with a higher relative risk of NIDDM and obesity

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- Differences in leptin sensitivity and/or leptin production have been suggested to play a role in the pathogenesis of obesity. The majority of human and rodent obesity is associated with hyperleptinemia, suggesting that in these cases leptin resistance is responsible for this condition^{3,4,5}

Microscopic alterations in adipose tissue of obese persons:

Consistently, obesity is associated with Histological changes of the type:

- Increase in numbers of adipocytes,
- Increase in size of adipocytes,
- Infiltration of adipose depots by mononuclear cells
- Relative rarefaction of blood vessels,
- Relative rarefaction of neural structures.

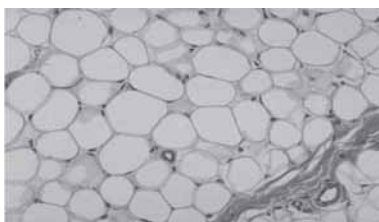


Figure 1: Histological appearance of fat cells. There is a thin cell membrane that bounds the cytoplasmic lipid, which appears clear in this section because normal tissue processing removes lipids. The cell nucleus is pushed to one side by the lipid. Connective tissue septae divide lobules of fat and carry the vascular supply.

Fat cells in obese people are “sick” compared to those in lean people. It has been found that significant differences exist in the fat cells of the obese participants compared with the lean participants.”The fat cells found in obese patients are deficient in several areas.

- The obese people’s fat cells showed stress on the endoplasmic reticulum (ER), which helps cells synthesize proteins and monitor how they are folded. When the ER is stressed, it produces several proteins that ultimately lead to insulin resistance. Insulin resistance, in turn, plays a major role in the development of obesity-related conditions. The differences in the fat cells between obese and lean people may help explain the link between obesity and a higher risk of diabetes, heart disease, and stroke.⁶
- Obese individuals have a relatively large amount of hypertrophic adipocytes compared to lean subjects
- The specific activity of the lipogenic marker enzyme G3PDH was 50% lower in total adipocytes of obese as compared to that of non obese subjects.
- Omental adipocytes from obese subjects also had lower basal lipolytic levels, and a lower lipolytic response to p-adrenergic stimulus. It is possible that the impaired lipolytic response contributes in time to the enlargement of the triglyceride depot. The reduced ability to store additional triglycerides, would result in an increased amount of circulating lipids, elevating the risks associated with the metabolic syndrome.

FAT CELL NUMBERS ARE ‘SET FOR LIFE’

The total number of fat cells per person remained relatively constant over time. Even extreme weight-loss strategies, such as bariatric surgery, do not reduce the number of fat cells. No amount of dieting will alter the number of fat-hoarding cells in our bodies.

An individual is born with a predetermined number of fat cells, with women generally inheriting more than men. The number of fat cells then grows through late childhood and early puberty, after which it is pretty much set. Fat cell number increases more rapidly in obese children than in lean children. The amount of fat someone has is a reflection of both the number and the

size of the fat cells.

QUANTITY VERSUS SIZE OF FAT CELLS

Fat cell numbers are different between two people yet it is possible for both to have a similar fat percentage. For example if someone had 500 million fat cells and a second person only had 300 million fat cells, these two people could both have a similar fat percentage if the second person has a sedentary lifestyle causing more fat to be stored in his/her cells. That is, the fat cells have become fuller and contain a greater volume within each cell. In this case it would result in a fat percentage higher than normal for this person but around the same as the first person with a higher number of fat cells.

FAT CELLS ONCE GAINED ARE NEVER LOST.

Even if an individual loses weight the size of fat cells is reduced not the number which remains constant. A fat cell is 95% fat. If it dies, it leaves behind insoluble fat, in obese people; the fat tissue often produces too many bad hormones and too few good ones.

It can be safely assumed that once the obesity is set it is difficult if not impossible to reverse the nature of this phenomenon.

THE NUMBER OF FAT CELLS IS GENETICALLY PREDETERMINED

In an individual the number of fat cells present is genetically predetermined as a result of which an individual who has a larger number of fat cells early in life is more prone to get obese as compared to an individual whose is non obese. Accumulation of various characters such as sedentary life style, aggressive eating, too much high calorie diet would complement the genetic trait.

The longer the course of obesity, the more difficult it is to have it treated. The more obese the person more difficult it is to have an effective control. Two of the Healthy People 2010 national health objectives⁷ are:

- to reduce the prevalence of overweight and obesity among adults to less than 15% and
- to reduce the prevalence of obesity among children and adolescents to less than 5%. This site provides a variety of information designed to help people understand the severity of obesity, the efforts being made to address it, and how to maintain a healthy weight.

RESULT

Given the serious nature of chronic diseases and conditions associated with obesity and the fact that obesity is difficult to treat, prevention is extremely important. The fact that both medical and surgical treatments for curing obesity have not proven to be effective in most cases and the associated adverse effects of these therapies prompts one to realize the need of effective prevention at an early stage with concurrent reduction in the occurrence of other associated diseases.

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Hydronephrosis Secondary to Uterovaginal Prolapse and Mixed Malignant Mullerian Tumor-An Interesting Case Report

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Abstract: This is a patient's convoluted presentation with Mixed Malignant Mullerian Tumor (MMT) who came to us as a case of hydronephrosis and a detailed clinical workup of her renal condition led us to diagnosing her as suffering from uterovaginal prolapse with Mixed Malignant Mullerian Tumor side by side. In the real sense, her actual malady was masked by her kidney condition and after surgery, which is the primary treatment¹, she was found to have Malignant Mixed Mullerian Tumour in its early stage. The patient was operated and followed up and post operatively she did well.

Key words: Hydronephrosis, uterovaginal prolapse, Malignant mixed Mullerian tumour (MMT)

CASE PRESENTATION

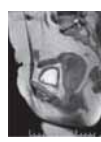
A 60 year old para 4 Kashmiri woman, presented to an Urologist with complaints of a recurring bilateral flank pain of few months duration. This was associated with a feeling of being unwell. All her deliveries were normal vaginal births with postpartum period being uneventful. She was post menopausal for the past 8 years with no history of postmenopausal bleeds. Physical examination revealed a moderately ill looking woman who was not wasted and mildly pale. The abdomen was soft and non-tender with no palpable mass. She was evaluated with an Ultrasound KUB, X ray KUB region and Urine examination. Ultrasound showed bilateral grade 11 hydronephrosis and hydroureter with bulky uterus, X ray KUB did not pick up any radio opaque shadow in KUB region and urine examination revealed full field pus cells.

In her diagnostic work up, her haemoglobin was 10.5 and the rest of her haemogram was within normal limits. Her renal function tests and liver function tests were within normal limits. Her urine for culture and sensitivity was sterile. IVU done showed a grade 3 hydronephrotic left kidney with hydroureter with delayed contrast excretion plus grossly dilated calyceal system of right kidney.. No calculus seen. RENAL SCINTIGRAPHY displayed grossly dilated PCS of Rt. kidney, enlarged left kidney with decreased perfusion. Gfr =63.3. Urologists initial impression was high pressure bladder. Meanwhile patient was referred to us for bulky uterus. A speculum vaginal examination revealed a grade 3 uterovaginal prolapse with a congested cervix. She had a mixed consistency discharge from the vagina which was non-foul smelling. A bimanual examination revealed a non tender bulky uterus with mildly restricted mobility and free fornices. We decided to go for MRI pelvis and diagnostic D & C.

MRI pelvis with GAD study showed heterogeneously enhancing mass lesion within endometrial cavity extending into cervical canal as described likely malignant.

The patient was counseled about treatment and further management and consented to a diagnostic D&C, the histopathology of which revealed Mixed Malignant Mullerian pathology. She subsequently underwent laparotomy and a radical hysterectomy was performed along with repair of prolapse. Intraoperatively it was confirmed that uterovaginal prolapse was the cause of hydronephrosis. There was no parametrial infiltration per op and no ascites either. Vaginal cuff was not involved.

HPE of the specimen revealed carcinosarcoma (*Malignant mixed mullerian tumour*). Myometrial invasion less than 50 percent, cervix not involved, margins uninvolved, no regional lymph node metastasis. Primary tumor –



T1aN0M0.

Postoperatively, the patient fared excellently. On follow up repeat ultrasounds showed improvement in hydronephrosis.

DISCUSSION

The incidence of hydronephrosis and hydroureter is variable. Recent literature varies prevalence at 25/323 (7.7%) and 31/189 (17.4%)^[2, 3]. The hydronephrosis can be unilateral also. The prevalence of hydronephrosis is higher in older patients and increases with increasing severity of prolapsed⁴. Malignant mixed Mullerian tumours are commonly found in post menopausal women with utero-cervical cancer but what sets this patient's situation apart is her oblique presentation as a kidney patient and her evaluation and diagnosis went all around to the end point of genital cancer. Histopathology of her cancer revealed an epithelial and sarcomatous component and these tumours are aggressive, but in her case was caught early. The hydronephrosis was a result of the drag of the genital organ prolapse which lead to stretching of the ureters and obstructive nephropathy.

Managing of this category of malignancy is challenging, especially in low resource settings, due to the relative rarity of this disease.^{5,6} Due to this, clearly defined guidelines for management are not defined and thereby the lack of evidence of treatment protocol outcomes. Imaging techniques and modalities are a potent tool in the diagnostic armamentarium. Early diagnosis and timely surgery followed by radiotherapy as an effective back up, is the key⁷.

CONCLUSION

This case clearly gives us an example that when a postmenopausal women comes with vague urological & gynaecological complaints of immediate or near recent onset and has other apparent systemic manifestations that can mislead or be misinterpreted, it is wise to be extra vigilant and be aware of the human body's subtle masquerades to hide the primary root of the main problem.

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