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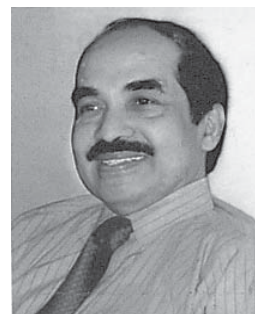
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PRESIDENT WRITES

Dear Fellows and Members,

I am so happy to write to you on this page of our Journal. This volume of the JIMSA contains a focus on lifestyle modification and its benefits in coronary heart disease; infact lifestyle modification from a young age is a very rewarding preventive health measure, which we do not stress adequately and obtain compliance for. In the interest of our communities we must do it and set up examples.



The range of other articles in our journal gives a measure of the vision of IMSA. We are to meet at the Manipal University for the IMSACON During November 2nd, 3rd & 4th. I look forward to meeting all of you at meet.

*Wishing all fellows & members of the Academy
a happy and fruitfull year 2008.*

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 CME;s 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 not 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'.*

Dr. Pinnamaneni Narasimha Rao International Award

Appeal by Vice-President IMSA



Dr. P. Narasimha Rao
Ex. President, IMSA World H.Q.



Dr. R.R. Thukral
Vice President IMSA World H.Q.

Dear Fellows and Members

You are aware late Dr. P. Narasimha Rao, an international figure both in the academic and teaching had been the President of this prestigious organization for more than a decade from 1990 to 2002. He was President of Medical Council of India and Vice Chancellor of various universities. He had to his credit several outstanding contributions to the medical fraternity till his death. He had been in close association with IMSA since its very inception in 1981. The Academy has flourished tremendously during his tenure as President. Keeping in view his status, services rendered to the mankind and on the insistence of senior Fellows, the Academy has established an **International Award** in his honour named '**Dr. Pinnamaneni Narasimha Rao International Award**', on the lines of Dr. B.C. Roy National Award. Substantial funds are needed for this prestigious award. Initially, the family of Dr. P. Narasimha Rao has contributed a fair amount of money and has also assured to contribute more.

I appeal to all our Fellows and Members to contribute generously for this noble cause in the memory of this dedicated acadamecian - Dr. P. Narasimha Rao. A separate open fund is open for this Award.

Wishing you all a happy and prosperous year 2008

R.R. Thukral

IMSA Member Directory 2007

Dear Fellows and Members

International Medical Sciences Academy has published Directory of IMSA Fellows and Members containing information about their mailing addresses, telephone Nos. email addresses, wherever available. The Directory was released at the inaugural function of **IMSACON 2007** held at Manipal, Karnataka in November, 2007. I shall request you to send a demand draft of Rs. 300 to enable us to send to you a copy of the Directory by post. You can also collect in person if you so wish.

H.K. Chopra

IMSA Chapter Activities

CME Delhi Chapter

- 7.11.2007 Dr. H.K. Chopra: "Sepsis an Overview"
Dr. Alka Gujral: Gynecological disorders and Sepsis
Dr. Kapil Kochar: Surgical disorders and Sepsis
Dr. Manoj Kumar: Bone and Joint Infections
Dr. Rajeev Malik: Neonatal Septicemia
Dr. Sanjeev Verma: Antibioqram in sepsis
15.12.2007 Dr. Vanita Pathak Ray: Glaucoma Management- New Dimensions
Dr. Chandrima Paul: Glaucoma Imaging-Recent Advances
Dr. Amit Vikram Datta: An Overview of Glaucoma Surgery

CME Tamil Nadu Chapter

- 14.10.2007: Dr. M. Jayakumar, "Chronic Kidney Disease Epidemic: Sitting back and looking forward"
22.10.2007: Dr. T. Rajendran, "Etiology and epidemiology of Chikungunya and Dengue Fever"
(Mid Term CME : Dr. V. Ramasubramanian : "Tackling Chikungunya and Dengue Fever"
(Jointly organized with K.J. Hospital)
11.11.2007 : Prof. Raviramalingam : "Cochlear Implants and Overview"
09.12.2007: Dr. Saradha Suresh : "Problem of Anaemia in Children"

RCME Tamil Nadu Chapter

- 19.8.2007: Dr. M. Raj Kumar : Common Vascular Problems
Dr. Bhuwaneswari: Ophthalmological Conditions in General Practice
28.9.2007: Dr. G. Sivakumar : The current management of diabetic foot diseases; Role of Preventive Strategy
Dr. Gnana Sundaram : Mouth is the mirror of the diseases
28.10.2007 : Dr. V. Kannan : Hypothyroidism
Dr. C.D. Natarajan : The Management of Chronic Diarrheal Diseases in Children
Dr. R. Kandiah: Treatment of Myopia
Dr. M. Ashok : Use of Laser in Ophthalmology

Honour

Dr. S. Ramesh, Professor and Head, Department of Pediatrics, Raja Mathiah Medical College Hospital, Annamalai University received the **Prof. Ebrahim Award for the Tropical Paediatrics**, at the 12th APCP, the award carries a citation a cash prize of Rs. 5000/- .

Dr. Udana Rathnapala
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Election of Fellows/Members Oct.- Dec. 07

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FROM EDITOR'S DESK

In the present issue, subject of "Life style and coronary artery disease" has been brilliantly discussed by **Prof. S.C. Manchanda** in an editorial; I would like to express my gratitude to him for agreeing to write for JIMSA at a very short notice. The paper is quite relevant in the present scenario of increasing prevalence of life style related diseases; it supplements the observations made by original article, specially in relation to hypertension and coronary artery disease. There are several interesting original articles and case reports, appearing in this issue which will be of great interest to the readers of JIMSA. An update article by **Prof. N.S. Neki** presents an exhaustive review on "Oxygen Therapy - State of Art" and gives practical information about this commonly practised life saving treatment.

The issue also contain a *symposium* on **prevention of chronic kidney disease (CKD) in India** under the guest editorship of **Professor Sanjay K. Agarwal**, Department of Nephrology, AIIMS, New Delhi, India. The articles are suitably selected and have been contributed by experts in the field from different parts of the country. CKD is one of the major health problems of the country. Because of the devastating consequence of End Stage Kidney Failure (ESKF), requiring expensive renal replacement therapy; CKD is causing tremendous impact - both physical and financial - on the health of the population. The problem is further compounded by the increasing prevalence of Diabetes Mellitus - an important cause of CKD. The symposium amply highlights the preventive strategies for containing this problem. I am extremely grateful to Prof. Sanjay K. Agarwal and several other authors for their contributions to the symposium.

I take this opportunity to thank the members of the Editorial and Advisory Board for their help and guidance in editing this issue and also to the several advertisers without whose help, this publication would not have been possible.

I wish to extend my greetings, to all readers of JIMSA for a very happy, prosperous and healthy year 2008

P. D. Gulati

JIMSA BEST PUBLISHED ARTICLE AWARDS

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 three years.
- (2) Age Limit for the principal author/main researcher should be 45 years and below.
- (3) Number of awards: Three (3) annually, carrying a gold plated medal, citation and cash prize (1st Rs. 3000/-, 2nd Rs. 2000/-, 3rd Rs. 1000/-)
- (4) 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.
- (5) Awardees should preferably plan to receive the award at the annual IMSA conference - IMSACON.

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LIFESTYLE AND CORONARY ARTERY DISEASE

The modern age of rapid industrialization, urbanization and globalization has brought about a drastic change in life styles of people all over the world. Life style related diseases especially coronary artery disease, have become the major cause of death and disability all over the world apart from causing a huge economic burden to the society.

What is lifestyle? Lifestyle may be defined as physical, psychological and social ways of living patterns which should promote health (physical, mental, social and spiritual), happiness and well being. There are *four major components* of lifestyle which are linked with coronary artery disease. These components are : 1. Diet ; 2. Physical Exercise; 3. Mental Stress; 4. Tobacco use.

Diet : Several epidemiological studies have shown that diet and nutrition are linked to coronary artery disease (CAD). Saturated fats, trans fatty acids and dietary cholesterol increase the LDLc levels which are directly related to CAD. Mono saturated fats and polyunsaturated fatty acids (especially Omega-3 fatty acids) are protective and may decrease lipid levels. Use of plant sterols/stanols and soluble fibre can achieve further lowering of LDLc levels. Antioxidants present in fruits and vegetables, nuts, tea and red wine may also be helpful in reducing oxidative stress. A healthy cooking oil which is low in saturated fats, high in mono saturated and omega-3 fatty acids (such as mustard oil) should be used. Excess of salt, refined high glycemic carbohydrates and fast foods should be avoided to prevent hypertension diabetes mellitus and obesity.

Physical Exercise : Regular physical exercise (like brisk walking, jogging, cycling swimming or playing games etc.) for about 30 min. daily lowers cholesterol levels, blood pressure, obesity, blood sugar levels and prevents inflammation. Regular exercise also increases the HDL cholesterol. People who maintain an active lifestyle have a 45% lower risk of developing coronary heart disease than sedentary people. Physical exercise is also beneficial in patients with congestive heart failure.

Tobacco Consumption : Any type of tobacco (smoking cigarettes, bidis, hookah, cigar or chewing tobacco) is a leading risk factor for development of coronary artery disease (especially at a young age), stroke and peripheral artery disease. The effects of tobacco on the cardiovascular system are multiple including platelet activation, endothelial dysfunction, inflammation, altered lipid levels and metabolism and hemodynamic effects. Compared to non smokers, smokers have higher risk of sudden death. Even passive smoking increases the risk of heart disease by about 30%. Cessation to exposure to tobacco leads to fast decline in the risk, half of excess risk of acute myocardial infarction is gone in 1 year, most is gone in 3 years.

Mental Stress : There is growing literature suggesting that psychological factors are linked with development of coronary artery

disease and with prognosis in patients following acute coronary events. Following *components of psychological stress* have been linked with development of CAD : a) *depression, anxiety, panic disorder ; b) social isolation and lack of social support; c) acute and chronic life events; and d) type A behaviour, hostility, anger.*

Managing stress by relaxation techniques (especially yoga) have been shown, in several studies, to decrease the risk of morbidity and mortality in patients with CAD.

Modification of lifestyle : Several studies have demonstrated that modification of each life style component (diet, exercise, tobacco and stress) has beneficial effect for secondary and primary prevention of CAD. However, adherence to lifestyle modification has been unsatisfactory.

Role of Yoga – a lifestyle Polypill : Yoga is not merely a few postures or exercises but a holistic intensive life style modification which involves diet control (satvik diet, high fiber vegetarian diet, tobacco avoidance, physical exercise and stress control). Hence, yoga can be considered a life style polypill with no side effects. A few studies have demonstrated that yoga is helpful in controlling risk factors for coronary artery disease like hypertension, diabetes mellitus, obesity, dyslipidemia and mental stress. Three randomized studies using coronary angiography have demonstrated that yoga life style is able to retard the progression of advanced coronary atherosclerosis and even cause slight regression. The compliance with this holistic lifestyle modification has been reported to be excellent. There is need for further and larger studies with yogic lifestyle modifications.

RECOMMENDED READING

- Rosengren A et al for INTERHEART investigators : Association of psychosocial risk factors with risk of acute MI. In 11119 cases and 13648 controls from 52 countries. *Lancet* 364: 953, 2004.
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- Bensen H : The physiology of Meditation, *Sc. Arm* 226:84, 1972.
- Alternative Medicine – Expanding Horizons. A report to NIH on alternative medical systems and practices in the USA, 1992.

Dr. S.C. Manchanda

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ETHICAL GUIDELINES FOR BIOMEDICAL RESEARCH

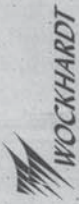
The need for uniform ethical guidelines for research on human subjects is universally recognised. It has acquired a new sense of urgency as the critical issues in the area of biogenetic research involving human subjects have become acute. Apart from the mandatory *clinical trials on new drugs, a number of diagnostic procedures, therapeutic interventions and prevention measures* including the use of vaccines, are being introduced which involve human subjects. Further the advent of *new medical devices and radio-active materials* and therapeutic benefits of *recombinant DNA products* have added a new dimension to the ethical issues that need to be considered before evaluating these for their efficacy, utility and safety.

Any research using the human beings as subjects shall bear in

mind the following principles of : i) **essentiality**, (ii) **voluntariness**, **informed consent**, (iii) **non exploitation**, (iv) **privacy and confidentiality**, (v) **precaution and risk minimisation**, (vi) **professional competence**, (vii) **accountability & transparency**, (viii) **maximisation of public interest and distributive justice** (ix) **institutional arrangements** (x) **public domain** (xi) **totality of responsibility** and (xii) **compliance**.

Recent advances in the field of **Assisted Reproductive technologies, organ transplantation, Human genome analysis, and gene therapy** promise unquestionable benefits to mankind. At the same time, they raise many questions of law and ethics, stimulating public interest and concern.

(Source : ICMR Publication 2000)



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THE ROLE OF LIFESTYLE INTERVENTION ON BLOOD PRESSURE REDUCTION: ITS IMPACT ON CORONARY HEART DISEASE

J. Shahamfar*, V.K. Gupta**, M.K. Daga***, S. Dastgiri*, S.H. Hakim*, Khaki. P*

*Departments of Community Medicine & Cardiology, School of Medicine, Tabriz University of Medical Sciences, Iran

**Department of Community Medicine, Maulana Azad Medical College (MAMC) New Delhi, India

***Department of Medicine, MAMC & Lok Naik Hospital, New Delhi, India

Department of Epidemiology, Faculty of Health & Nutrition, Tabriz, Iran

Abstract : Epidemiological studies indicate that the risk of Coronary Heart Disease (CHD) increases continuously with increasing blood pressure. Several factors have been identified, not as independent cardiovascular risk factors, but as factors, which have been shown to increase blood pressure; such as excess weight, alcohol and sodium intake and smoking. A total of 100 patients aged less than 65 years were interrogated. Statistical analysis: Data was entered in SPSS software version 12 to get blood pressure recordings associated with the CHD patients at 95% confidence interval of the difference and paired t-test. All severely ill patients, patients aged more than 65 years were excluded. Lifestyle modification interventions included exercises, weight reduction decreased, alcohol consumption, and dietary modification. Smoking cessation, stress management were assessed; intake of antioxidants and fish oil supplements, was also noted. Patients in lifestyle intervention group significantly reduced the intake of saturated fat, sugar and cholesterol ($p < 0.001$), increased their exercises ($p < 0.01$) and stopped smoking ($p < 0.05$) when compared with the usual care group. This study demonstrated that modification of lifestyle in CHD patients can reduce risk factors of CHD and blood pressure, and prevent second heart attack.

Key words: Lifestyle, coronary heart disease, and modification

INTRODUCTION

Coronary heart disease (CHD) is the single most important cause of death and, more importantly, the single biggest cause of premature death in modern, industrialized countries. In addition, it is an increasing cause of death in developing countries. The CHD mortality rates in 1994 for men and women in 32 countries were studied; there is clearly a wide variation in these rates, the highest being found in Eastern Europe, Northern Ireland and Scotland and the lowest rate in Spain, France and Japan; mortality rates are generally much higher for men; this distinction is present at all ages but is less after the menopause in women¹. Epidemiological surveys indicate that the risk of coronary heart disease increases continuously with increasing blood pressure, the higher the individual's blood pressure, highest the risk, the lower the blood pressure the lower the risk². Blood pressure levels vary in different populations and by social class. There are racial differences in the occurrence of hypertension; for sample, Black Africans who live in westernized societies have higher blood pressure and more strokes than their caucain counterparts. An example of the cultural differences that occur is seen in Africa with Black Africans who have moved to westernized cities having higher blood pressure than Black Africans who continue to live in a rural setting. Blood pressure rises, as people grow old in westernized societies, but again not in rural, undeveloped ones. Finally, there is genetic component - hypertensive families³. A systematic review identifying 30 trials found that in people over the age of 44, reduction of 100 m mol sodium reduced systolic blood pressure by 6 mmHg. Although this magnitude of change requires a substantial alteration in diet with intensive intervention⁴. A recent trial of the dietary approach to stop confirms that intensive multiple lifestyle interventions can reduce blood pressure by 5 mmHg⁵. Systematic reviews support increasing dietary potassium⁵, reducing weight⁶⁻⁷ and increasing exercise⁸. A large cohort study found that eating fruits and vegetables reduces the risk of ischemic stroke⁹. There is mixed evidence that increasing the intake of fiber, fruit and vegetables lowers blood pressure⁴. However,

most of the studies addressing the efficacy of intervention have been carried out either in hypertensive patients in life style tightly controlled secondary care settings, or in general population groups^{11, 12}.

MATERIAL AND METHODS

The study was carried out in Shahid Madani Heart Hospital in CCU ward, Cardiology department in Tabriz University of Medical Sciences during 2003-2004. Objective of this study was to assess effectiveness of lifestyle modification in reducing of blood pressure in coronary heart disease patients. The patients were divided into two groups, 50 patients in intervention group and 50 patients in control group; and assessed by questionnaire prepared for assessment of lifestyle and risk factors of CHD patients as per guidelines laid down by the center for disease control¹⁴. The behavioral risk factor survey questionnaire concentrates on behavior and addresses risk factors for CHD patients; cardiologist determined the validity of questionnaire. A test-retest reliability study (n=100) using the instrument in 20 patients, showed reliability coefficients of 0.06 or greater for all risk factor variables reported here.

Exclusion Criteria: All the severely ill patients, patients aged more than 65 years, all patients from out side of Tabriz Sampling: formula for calculation of sample size for studies commonly pursued in Medical Research as follow:

Statistical Analysis: Studies using the student t-test randomized controlled trials with one experimental group and one control group) and considering alpha error only.

$$N = \frac{(Z\alpha)^2 \times 2 \times (S)^2}{(d)^2}$$

$Z\alpha$ = value for alpha error, S^2 = Variance, d = difference to be detected
 N = sample size

The sample size on the basis of blood pressure recording was chosen. Thus by rounding of number a total of 100 patients was included in this study. To collect the information on various aspects, focusing the objectives of the study, were analysed. The data collected through the questionnaire, clinical assessment and investigation were entered in the computer before and after education in both intervention and control groups, using SPSS software version 12 carried out analysis.

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e-mail: jafar_shaham@yahoo.com

First frequency distributions of patients according to socio-demographic, history of present illness, past history and general physical examination, lifestyle assessment, were tabulated.

RESULTS

The analysis showed that fruit and vegetable consumption was slightly higher than expected, better-educated patients were more likely to have better knowledge regarding both blood pressure and cholesterol and knowledge level was generally higher after intervention for blood pressure than cholesterol, level of education was associated with risk factors after adjusting for age, sex. The college graduates were able to state their own blood pressure and to know that 140/90 mmHg or less is a good blood pressure thus were more than three times knowledge able than patients who had not completed high school; college graduates also had higher odds of engaging in regular aerobic exercise and lower odds of being obese; educational level also affected the body mass index(BMI), the interaction between sex and education was significant ($p < 0.01$); those with BMI 25.9 kgr/m² in lifestyle intervention group reduced the intake of saturated fat, sugar and high diet cholesterol ($p 0.001$), increased their exercise level after education ($p=0.01$) and stopped smoking ($p < 0.05$) when compared with control group; 95% confidence interval was significant.

DISCUSSION

The main finding of this study was that education and modification of lifestyle of patients with intervention package were independently associated with behavioral risk factors for cardio vascular disease and reducing of blood pressure; smoking; lack of regular exercise, and obesity, as well as knowledge about blood pressure, were significant. In order to study the effect of risk factor modification by means of NIL pharmacological interventions in patients suffering from CHD, we scrutinized every risk factor separately. Each factor was amenable to modification through interventions, aimed at behavior change. Behavior oriented interventions, incorporating cognitive and behavioral factor smoking cessation techniques, showed positive results in reducing smoking rates in MI patients¹⁵. Elevated serum cholesterol concentrations were reduced by intensive dietary modification. Thus, major changes on dietary habits can be achieved in CHD patients, and this may even lead to stabilization or regression of coronary atherosclerosis. Several studies indicated that physical exercise may prevent progression of atherosclerosis as well. Secondary prevention programs aimed at increasing physical exercise can bring about reduced cardiovascular mortality and morbidity, although unambiguous evidence concerning these effects is still lacking. Thus, to be maximally effective, risk management should focus on selection of patients most likely to benefit from particular program, or even better, patients should be referred to the treatment that is most appropriate for their needs. This is in accordance with recent general guidelines for cardiac rehabilitation as formulated by WHO and later Great Britain, the Netherlands and other European

countries; these emphasize determination of the patients needs and individual sub goals for rehabilitation in theory, the most suitable type of cardiac rehabilitation, should be chosen, but in actual practice the needs of individual patients are still barely taken into account. To optimize the effects of cardiac rehabilitation, every patients should be screened to determine which risk factors contribute to his or her condition, after which the most suitable cardiac rehabilitation program should be applied. Very likely this approach will improve the patients motivation, which could have a favorable influence on the effects of the intervention. It was shown that exceptionally motivated patients make comprehensive lifestyle changes that lead to improved cardiovascular status. To reach the majority of patients better applicable, although effective behavioral interventions should be developed. In particular the motivation to sustain favorable effects, should be enforced, with more intensive changes; whatever the patient decides, the cardiologist should support this decision and explain the relative risks, benefits, costs, and side effect of each secondary prevention approach, be it invasive or noninvasive, pharmacological, or non pharmacological.

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DEPRESSION IN ELDERLY: A CROSS-SECTIONAL STUDY IN RURAL SOUTH INDIA

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Abstract : The objectives of the study were to determine the prevalence of depression in elderly rural population and also study the socio-demographic correlates of the depressive disorders among the elderly in this community. It was cross sectional study performed on the elderly subjects of rural area of Udipi taluk Karnataka in South India over 8 months period. A total of 627 elderly individuals of age group of 60 years and above, were interrogated : results were subjected to statistical analysis i.e proportions and their 95% confidence intervals, Chi-square test, multiple logistic regression and its 95% confidence interval. The prevalence of depression in elderly population was determined to be 21.7%. The prevalence in the age group of 80 years and above and those individuals who had a history of death in the family within the last six months were found to be 34.4% and 52.4%, respectively. Multiple logistic regression analysis revealed that these two correlates were independently associated with depressive disorders in elderly population.

Key words: Depression, Prevalence, Correlates, Elderly, Multiple Logistic Regression

INTRODUCTION

The Indian aged population is currently the second largest in the world. The proportion of those who would be aged 60 years and above is estimated to be 7.7% for the year 2000, and this proportion is expected to reach 12.6% in 2025. A high prevalence of mental disorders is seen in old age. Predominant among these is *depression*¹. The future projections of global DALY's in the year 2020 show that mental disorders are projected to increase to 15% of the global disease burden and unipolar major depression could become the second leading cause disease burden after ischemic heart disease² especially in high-income countries. The community-based mental health studies have revealed that the point prevalence of depressive disorders among the geriatric population in India varies between 13 and 25 percent According to the observations made by the World Health Organization, the *correlates* = *disorders in old age* are reported as genetic susceptibility chronic disease and disability, pain,, frustration with limitations in activities of daily living - events (widowhood, separation, divorce, bereavement, poverty, social, isolation) and lack of adequate social support. Though depression is the commonest mental health problem in old age, very few community-based studies had been conducted in India, to understand the problem. No such study had been conducted in the past in Udipi taluk of Karnataka. Considering this background, a community-based mental health study was conducted in the rural area of Udipi taluk to determine the disease burden of depressive disorders and to study the correlates of depression among the elderly in the community.

MATERIAL AND METHODS

The rural field practice area of the Department of Community Medicine, Kasturba Medical College, Manipal is located in the coastal area of Udipi taluk in Udipi District of the state of Karnataka in South India. The total geriatric population (≥ 60 yrs) in the field practice area is approximately 10.5% of the total population covered by the rural field practice area.

Study period: 8 months (March to October 2002).

Setting: Three villages i.e.—Udayavara, Kadekar, and Katapady.

Study Design : Cross-sectional study.

The sample size was estimated for finite population with the help of EPI-info version 5.0 statistical package. The total geriatric population ($>=60$ yrs.) covered by the 3 RMCW homes was estimated to be of 2259. Here, the confidence level was taken as 95%, 11.2% prevalence rate of depression, required relative precision of the estimate was set at 20% and

a non-response rate of 10% was included; hence, the final sample size was determined as 627.

Sample size : 627 people in the age group of 60 yrs and above, who were permanent members of their respective households, were selected for the study.

Sampling method : Simple Random Sampling 'without replacement method using the Probability proportionate to size (PPS) technique was used.

Sampling Procedure - Exclusion criteria: If a designated house was found locked during the first visit and the eligible residents could not be contacted and even after 2 successive revisits then they were all excluded from this study. **Criteria For Defining A Non-Respondent:** If a designated respondent was non-cooperative or had severe behavioural problems or cognitive impairment, had severe hearing impairment or articulation disorder, had any terminal illness or if he could not be contacted during two separate revisits after the first, then he was considered a non-respondent

Selection Procedure: Due to some on-going projects in some of the field practice areas, only 3 centres out of the total 6 RMCW (Rural Maternity And Child Welfare) Homes were chosen for our project As all the villages in the field practice area are culturally and socio-demographically identical, this selection bias had minimal effect on the results, Using PPS (probability proportionate to size) method, the required number of participants from each village was decided. Then the households and participants were randomly selected from updated family folders in RMCW homes using the random number table. All the eligible candidates of the selected households were interviewed as it was presumed that the effect of genetic susceptibility would be minimal because only 4% of our study population had either 1st degree or 2nd degree relatives residing together in the same household.

Study Instruments: A fact sheet consisting of information regarding the household of the respondent was used for data collection. A semi-structured proforma containing information regarding the socio-economic status of the individual that was later estimated by the modified Udai Pareek Scale⁸ was also used, Presence of depressive disorders was determined using the instrument **Mastering Depression In Primary Care Version 2.2:** It had two components: (a) WHO (five) Well-being Index (1998 version), (b) Major (ICD-b) Depression Inventory. Cognitive impairment was estimated by the 6CIT Dementia Test. Mastering Depression In Primary Care Version 2.2 and the 6CIT Dementia Test were translated into Kannada and Hindi by the researchers and back-translated into English by another expert, not acquainted with the original versions. The back-translation was subsequently compared with the original version by a psychiatrist for conceptual equivalence of the items.

Organization Of Field Work And Data Collection

The investigator, along with three field ANMs (auxiliary nurse mid-wives),

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were trained by the psychiatrists on how to administer the questionnaires. All our study instruments were pre-tested to determine whether they optimally suited our field conditions. At the beginning, officials of the local panchayat office, village leaders, Anganwadi workers and the ANMs were contacted and their help was sought to understand the geography of the sites and to trace the households. After informed verbal consent was obtained, the designated respondent(s) of a particular household was administered the selected sets of questionnaires by the investigator along with the help of the field ANMs. Care was taken to ensure privacy and confidentiality of the interview as part of the study. A brief general health check-up of the respondent was conducted at the beginning to establish a good rapport with him and also to gain his confidence. All the questionnaires administered in the field were evaluated and rated on the spot, and if a respondent became positive in any of our screening or diagnostic instruments he was immediately handed over a referral slip and sincerely requested to visit the psychiatry OPD of Kasturba Hospital, Manipal at the earliest for a free consultancy. The participants having obvious medical disorders were referred to the nearest RMCW homes for a free health check-up. The diagnoses generated by the instruments in our study were strictly kept confidential and were reconfirmed by consulting a senior faculty member of the department of psychiatry of KMC Hospital, Manipal before arriving at a final ICD-b diagnosis for data analysis.

Data Analysis

The collected data was tabulated and analysed by using the statistical package SPSS (Statistical Package For Social Sciences) version 10.0 for Windows. Findings were described in terms of proportions and their 95% confidence intervals. chi-square test was applied to study the relationship between different variables and depression. To determine the independent effect of various factors on depressive disorders, multiple logistic regression was performed and their significance was estimated in terms of adjusted OR and its 95% confidence interval. *P* value less than 0.05 was considered as significant.

RESULTS AND DISCUSSION

During our field survey, 487 households were visited and 627 individuals in the geriatric age group of 60 years and above were contacted. Among these 627 elderly people, we could interview only 609 individuals for the assessment of depressive disorders (97.1%). The 18 individuals, whom we could not interview due to various reasons, were categorized as *non-respondents* (2.9%). The baseline characteristics of the population surveyed revealed that 36.0% were males while 64.0% were females. Majority (52.6%) belonged to the age group of (60-69) years. Only 58.7% of the elderly were literates. Majority (61.2%) belonged to the middle socio-economic status and 56.3% of the individuals were married.

The overall prevalence of depressive disorders among the elderly of 60 years and above was found to be 21.7% (95% CI 18.4-24.9). Our study findings were consistent with the observations made by Nandi et al⁴, West Bengal, Ramachandran V. et al⁵ Madras and Tiwari S.C. Lucknow,³ who had determined the prevalence of depressive disorders in the geriatric population to be 22.0%, 24.1% and 13.5% respectively. However, a high prevalence of depressive disorders of 52.2% among the elderly 60 years was observed in the study conducted by Nandi et al⁹ in the rural areas of West Bengal. In contrast to these observations, Rao Venkoba A. et al¹⁰ Madurai had recorded the prevalence of depression to be as low as 6.0%. Studies conducted by Newman at Canada, and Kennedy et al⁶, USA reported prevalence of depression among the elderly to be 11.2% and 16.9%; respectively. We had also assessed the status of positive well-being by using the WHO (Five) Well-Being index (version 1998). We had observed that the prevalence of depressive disorders was high among individuals whose status of positive well-being was poor (75.9%) as compared to those who were satisfactory (5.3%). Table 1 Shows the prevalence of depressive disorders according to various socio-demographic correlates.

In this study, the prevalence of depressive disorders was higher among

Table 1: Prevalence of Depressive Disorders according to the Socio Demographic Correlates

Socio Demographic Correlates	Number Of Subjects Interviewed (N)	Individuals With Depressive Disorders (N)	Prevalence Of Depressive Disorders (%)	χ^2 , df, p
1. Sex				
Male	216	43	19.9	$\chi^2 = 0.6$, $df=1$, $p = 0.433$
Female	393	89	22.6	
2. Age Group (Years)				
60-69	320	56	17.5	χ^2 for linear trend = 36.0, $p < 0.001^*$
70-79	228	55	24.1	
80	61	21	34.4	
3. Religion				
Hindu	488	110	22.5	$\chi^2 = 1.2$, $df=2$, $p = 0.548$
Christian	81	14	17.3	
Muslim	40	8	20.0	
4. Socio-Economic Status				
Low	210	53	25.2	$\chi^2 = 2.9$, $df=2$, $p = 0.232$
Middle	377	76	20.2	
High	22	3	13.6	
5. Marital Status				
Married	342	70	20.5	$\chi^2 = 0.7$, $df=1$, $p = 0.413$
Unmarried/ Widowed/ Separated	267	62	23.2	
6. Type Of Family				
Nuclear	165	34	20.6	$\chi^2 = 0.2$, $df=1$, $p = 0.674$
Joint / Extended	428	95	22.2	
7. Living Arrangement In The Household				
Living With Spouse	318	66	20.8	$\chi^2 = 0.5$, $df=2$, $p = 0.784$
Living Only With Children/Relatives	275	63	22.9	
Living Alone	16	3	18.8	
8. Literacy Status				
Illiterate	252	64	25.4	$\chi^2 = 3.5$, $df=1$, $p = 0.061$
Literate	357	68	19.0	
9. Previous Occupation				
Unskilled	212	49	23.1	$\chi^2 = 4.3$, $df=3$, $p = 0.230$
Skilled	159	39	24.5	
Professional	39	4	10.3	
Housewife	199	40	20.1	
10. Habits				
Smoking	92	19	20.7	$\chi^2 = 0.1$, $df=1$, $p = 0.798$
Alcohol Consumption	103	30	29.1	
Tobacco Chewing	241	63	26.1	
Pan Chewing	303	78	25.7	
11. Family History Of Psychiatric Illness				
Present	41	8	19.5	$\chi^2 = 0.1$, $df=1$, $p = 0.728$
Absent	568	124	21.8	
12. History Of Death In The Family Within Last 6 Months				
Present	21	11	52.4	$\chi^2 = 12.1$, $df=1$, $p = 0.001^*$
Absent	588	121	20.6	

* *p* value < 0.05 is considered as significant

females (22.6%) than males (19.9%), but this difference was not found to be statistically significant ($\chi^2 = 0.616$, $df=1$, $p = 0.433$). Our study findings are consistent with the study by Blazer¹² (1979, North Carolina), where the prevalence of depression was similar in both sexes. However, the studies conducted by previous workers^{5,6,11,13} had documented a high prevalence of depression among the elderly females. Higher standards of living, matriarchal family system and a high female literacy rate (94.6%) could explain a lower prevalence of depression among females in our study.

The age of the respondents ranged between 60 to 93 years, while the mean age was found to be 69.0 years (SD 6.8). The prevalence of depressive disorders was highest (34.4%) in the age group of 80 years and above. The difference in prevalence of depression between different age groups was found to be statistically significant ($\chi^2 = 9.932$, $df=2$, $p = 0.007$). The prevalence of depressive disorders showed a positive linear trend of increase with the progression of age, which was also found to be statistically significant. Majority of the population were Hindus (80.1%). The prevalence of depressive disorders did not vary widely among the Hindus (22.5%), Christians (17.3%) and Muslims (20.0%) and the difference was not found to be statistically significant. Similar findings were reported from a study conducted by Tiwari³. The prevalence of depressive disorders was high among the individuals belonging to the low economic status (SES) group (25.2%) and high socio-economic status (13.6%) groups. But the difference between these groups was not found to be statistically significant. Studies conducted by several workers^{5,6,13} had observed the prevalence of depressive disorders to be significantly higher among the elderly belonging to the low SES group. The prevalence of depressive disorders was similar among the unmarried widowed or separated individuals (23.2%) as compared to their married counterparts (20.5%). Our study findings were not consistent with the previous studies^{5,6} who had documented a significantly high prevalence of depressive disorders among the widowed individuals, in this study, we had observed that majority of the unmarried, widowed or separated individuals were women (92.1%) with only a few staying alone (5.6%) and deprived of any living child (5.2%). Better

standards of living, a satisfactory level of family support systems network, high female literacy rate (94.6%) and matriarchal family system could explain a lower prevalence of depression among these individuals in our study.

In this study we found that the prevalence of depressive disorders remained similar in case of both nuclear (20.6%) and print/extended families (22.2%). The respondents, staying alone 16 (2.6%), were not included under nuclear family. - In this study, only 16 (2.6%) of the individuals were living alone. The prevalence of depression among those who were staying alone, living only with their children or relatives or living with their spouse was found to be 18.8%, 22.9% and 20.8% respectively. But the difference between these groups was not found to be statistically significant. These findings were in contrast with the studies conducted by Ramachandran⁵.

Blazer Dan¹² and Kennedy Gary J.⁶ who had observed a significantly high prevalence of depression among those living alone.

The prevalence of depressive disorders among illiterates was higher (25.4%) as compared to literates (19.0%). The difference between the two groups was however, not found to be statistically significant. Ramachandran V.¹⁵ Madrasad also reported similar observations. Studies conducted by Kennedy et al¹⁶ and Penninx et al also reported a significantly higher prevalence of depression among individuals with lower level of education. None of the respondents were unemployed in the past. The proportion of housewives affected with depressive disorders was 20.1%. The prevalence of depressive disorders was almost similar among the unskilled (23.1%) and skilled (24.5) labourers. Some of the previous^{5,6} had reported a higher prevalence of depression among the unemployed individuals.

As compared to smoking and alcohol consumption (17.2%), tobacco chewing (39.2%) and pan chewing (49.9%) habits were common among the geriatric population in Udupi Taluk. In this study, the prevalence of depression was found to be significantly high among the having pan chewing individuals (25.7%), tobacco chewing (26.1%) and alcohol consumption (29.1%) habits. In a study conducted by Hämäläinen J. et al¹⁴ from Finland, it was found that cigarette smoking and alcohol consumption were important risk factors for major depressive episode.

The prevalence of depression was similar among those who gave a history of psychiatric illness (19.5%) as compared to those without family history of psychiatric illness (21.8%) and the difference between the groups was not found to be statistically significant. These findings are in contrast with the observations by Ojen Van¹⁵ who reported a significantly high prevalence of depression among those with a positive family history of mental disorders. This difference from our study might be due to social stigma resulting in considerable number of under-reported and undiagnosed cases of mental illness.

The prevalence of depression was high among the individuals who had a history of death in their family within the last 6 months. The difference between the two groups was found to be statistically significant. Similar observations were also noted by Kennedy Gary⁶.

Table 2 describes the association between correlates of depressive disorders according to the univariate as well as the multivariate analysis.

It was observed by univariate analysis age group of 80 years and above and a history of death in the family within last 6 months had strong and significant association with depressive disorders. However, Multiple Logistic Regression analysis revealed that age group of eighty years and above and a history of death in the family within last six months had independent significant association with depressive disorders in the geriatric population. These findings are consistent with the observations from the study conducted by Kennedy Gary⁶.

CONCLUSIONS

In this study, the prevalence of depressive disorders among the geriatric population was determined to be 21.7%. The prevalence rates of depression among the males and females were 19.9% and 22.6%, respectively. Multiple logistic regression analysis revealed that age group of 80 years and above and a history of death in the family within the last six months were independently associated with depressive disorders in the geriatric population.

LIMITATIONS

Due to feasibility constraints, we could not interview the people who lived in the open and were homeless. Due to the lack of practical skills in communication, we could not interview the non-respondents who were having severe hearing impairment and aphasia. Since the proportion of non-respondents and the individuals who were homeless was very small in our study population, we expect only a minimal effect on our prevalence estimate.

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Table 2: Correlates Of Depressive Disorders:

Correlates Of Depressive Disorders	Category	OR (Unadjusted)	95% C.I.	OR (Adjusted)	95% C.I.	p value
Gender	Male	1.00	-	-	-	-
	Female	1.18	0.78-1.77	1.27	0.71-2.26	0.419
Age Group (yrs)	(60-69) yrs	1.00	-	-	-	-
	(70-79) yrs	1.50	0.99-2.28	1.36	0.84-2.18	0.211
	≥80yrs	2.48	1.36-4.52	2.03	1.02-4.05	0.045*
Socio-economic Status	High	1.00	-	-	-	-
	Middle	1.60	0.46-5.55	1.52	0.41-5.71	0.536
	Low	2.14	0.61-7.51	2.58	0.66-10.00	0.171
Marital Status	Married	1.00	-	-	-	-
	Unmarried/ Widowed/ Separated	1.18	0.80-1.73	0.98	0.30-3.22	0.976
Living arrangement in the household	Living with spouse	1.00	-	-	-	-
	Living only with Children/ Relatives	1.14	0.77-1.68	0.64	0.19-2.12	0.462
	Living Alone	0.88	0.24-3.18	0.58	0.10-3.42	0.548
Literacy Status	Literate	1.00	-	-	-	-
	Illiterate	1.45	0.98-2.13	1.07	0.67-1.71	0.784
Habits	Absent	1.00	-	-	-	-
	Present	1.30	0.82-2.06	1.004	0.59-1.70	0.988
History of death in family in last 6 months	Absent	1.00	-	-	-	-
	Present	4.25	1.76-10.23	5.17	2.03-13.18	<0.001*

* p value <0.05 is considered as significant



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ROLE OF CARDIAC MRI IN ACQUIRED DISEASES OF THE HEART

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Abstract : Even though Magnetic Resonance Imaging (MRI) has been in the forefront of imaging for the past two decades; it has only recently been perfected to a point where it can effectively capture the image of a beating heart. This has been possible with the recent development of high speed and high strength magnets, which are capable of providing detailed images of the heart. Cardiac MRI provides an accurate, safe, fast and non-invasive means of evaluation of the heart in congenital as well as acquired diseases; it can assess pericardial, myocardial and endocardial lesions and at the same time offer information about the functional status of the heart. Cardiac MRI was performed in 32 patients of age group ranging from 25 to 78 yrs. The procedure was carried out on a 1.5 Tesla (Siemens Magnetom Symphony) MR system using available protocols for cardiac imaging at a tertiary care centre. The study provided a new approach to the analysis of acquired diseases of the heart. Pericardial disease, damaged myocardium as a result of ischaemic heart disease and cardiomyopathies could be easily identified using this imaging modality. Therapeutic planning whether surgical or medical was to a great extent aided by the anatomic and functional information available from these images.

Conclusion: Cardiac MRI is a rapid, non-invasive and accurate technique for the diagnosis, pre-operative evaluation as well as post-operative assessment of a large number of cardiac diseases. Cardiac MRI has come to stay and with continued improvement in technology it will soon become an integral part of imaging studies of the heart.

INTRODUCTION

Magnetic Resonance Imaging (MRI) is becoming the gold standard for non-invasive assessment of cardiac morphology and function. High contrast between moving blood and myocardium, increased spatial resolution and lack of ionizing radiation make it an outstanding modality for assessment of myocardial anatomy and function. Complex congenital cardiac anomalies can be evaluated and morphological details of various chambers, septum, defects and anomalous connections are depicted accurately. Cardiac MR imaging has further utility in follow up of patients after corrective surgery. Assessment of cardiac function is another field where MRI scores over other available imaging modalities; quantification of ventricular volumes, ejection fractions and assessment of ventricular wall motion for dyskinesia are all possible using wall motion cine images¹. Cardiac MRI scores over conventional non-invasive imaging modalities in evaluation of cardiomyopathies also. It accurately assesses the myocardium, septal thickness and chamber volume during systole as well as in diastole². Perhaps the greatest advancement in cardiac MRI is its ability to evaluate myocardial viability following myocardial infarction as well to assess the effects of revascularization procedure on myocardial function. MRI is superior to echocardiography in evaluating various types of cardiac tumours with reasonable level of accuracy and it has a particular advantage of differentiating thrombus from tumor³. Pericardial disease has been evaluated using echocardiography ever since this modality has been available to clinicians; however its evaluation with echocardiography is limited if no effusion exists or if the effusion is complex. MRI does not have these limitations; instead it has high sensitivity in the diagnosis of pericardial effusion, thickening and most importantly constrictive pericarditis⁴.

This article presents our experience with state-of-the-art applications of cardiac MRI in a variety of diseases of the heart and also reviews the current status and future prospects of this relatively new modality of imaging.

MATERIAL AND METHODS

Patient population

A total of 32 patients (20 males and 12 females) with age ranging from 25 to 78 yrs were included in this study, which was undertaken from July 2004 to June 2005 at the MRI centre of a tertiary care centre. The various indications for cardiac MRI included pericardial disease (10 cases); cardiomyopathy (9 cases) myocardial viability studies (8 cases); evaluation of arrhythmias (5 cases).

Patient preparation

A detailed history was elicited from each patient including principal symptoms and signs, echocardiographic and cardiac catheterization data and operative status. MR-compatible electrocardiographic leads were placed on the anterior chest wall before imaging and attached to the MR imaging unit to provide electrocardiographic gating. The patient was positioned head-first in supine position with an integrated body array coil attached to the chest and MR imaging performed using breath holding as well as non-breath holding techniques. Detailed instructions regarding breath holding was given to the patients prior to commencement of the MR examination.

Cardiac MRI protocol

MR imaging was performed using 1.5 Tesla Siemens Magnetom Symphony MR equipment using standard protocols for MR imaging. To evaluate myocardial viability post contrast studies were performed using Gadolinium diethylene-triamine-pentaacetic acid (Gd-DTPA) in the dose of 0.2mmol/kg body weight administered intravenously. Initial image acquisition was done immediately after giving the contrast agent and subsequently delayed images were acquired after 12 and 16 minutes.

RESULTS

Data collection and image analysis

Cardiac MRI was performed in 32 patients and the MR images were reviewed by a panel of two radiologists both trained in MRI. The images obtained were evaluated for anatomical details, functional information about flow across valves and defects were assessed. Cine acquisitions provided information in real time regarding myocardial wall thickness and wall motion. The various abnormalities detected

on cardiac MRI in these patients are summarized in Table 1.

Table 1. Various abnormalities detected on cardiac MRI (N=32)

Abnormalities	Number of cases
<i>Pericardial Disease</i>	
· Pericardial effusion	4
· Pericardial thickening	3
· Constrictive pericarditis	1
· Normal study	2
<i>Cardiomyopathy</i>	
· Hypertrophic cardiomyopathy	3
· Dilated cardiomyopathy	2
· Normal study	3
<i>Myocardial viability studies</i>	
· Viable myocardium	3
· Irreversible myocardial damage	5
<i>Evaluation of arrhythmias</i>	
· Dysrhythmogenic Rt ventricular Dysplasia	3
· Normal study	3

DISCUSSION

The concept of using MRI as a modality to image the heart was considered a huge challenge till a few years ago; however with the recent development of modern technology and better software this has been overcome and the current state of the art MR machines allow us to image the beating heart non-invasively.

Apart from evaluation of congenital heart disease there are a number of acquired conditions of the heart, which can be accurately assessed using MRI. The pericardium, which has been traditionally, imaged using echocardiography; has now been increasingly imaged using MRI. The visceral pericardium, which consists of a single layer of cells and is not imaged on MRI in normal subjects; the parietal pericardium, which consists of fibrous tissue shows low signal on both T1 and T2, weighted images⁵. In normal patients the pericardium measures 2mm in thickness and is better visualized in systole, due to an increased pericardial space during cardiac ejection. On MRI thickened pericardium appears as a widened pericardial line of low signal on both T1 and T2 weighted images. On cine images a thickened pericardium has a constant width through out the cardiac cycle, whereas the pericardium in pericardial effusion has cyclical changes in width. Pericardial effusions complicated by adhesions or loculations are clearly shown on MRI; transudative effusion appears as low signal intensity on spin echo images and can be differentiated from an exudative or hemorrhagic effusion that has high signal intensity⁶. In addition, cine images can depict diastolic collapse of the chambers, which indicates tamponade. MRI has high sensitivity in the diagnosis of constrictive pericarditis; the presence of pericardial thickening in constrictive pericarditis differentiates it from restrictive cardiomyopathy. In such patients proper diagnosis is vital because although their presentations can be similar, their treatments differ markedly. Constrictive pericarditis requires pericardiectomy; restrictive cardiomyopathy necessitates medical management. In the present study there were four patients who had pericardial effusion, 3 had pericardial thickening (Fig 1) and 1 patient had constrictive pericarditis. In all these patients MRI proved to be extremely useful in establishing the diagnosis and helping the clinician in instituting definitive therapy without wasting valuable time.

The cardiomyopathies, which represent muscular disorders of the heart; are subdivided into hypertrophic, dilated and restrictive types, each with unique pathological and physiological characteristics. MRI has been used as an investigative tool that aids in the understanding the anatomy as well as the physiological changes associated with this disorder. In hypertrophic cardiomyopathy MRI identifies the site and extent of hypertrophy. Additional findings that can be demonstrated include increased end-diastolic and decreased systolic thickening of the septal wall and systolic

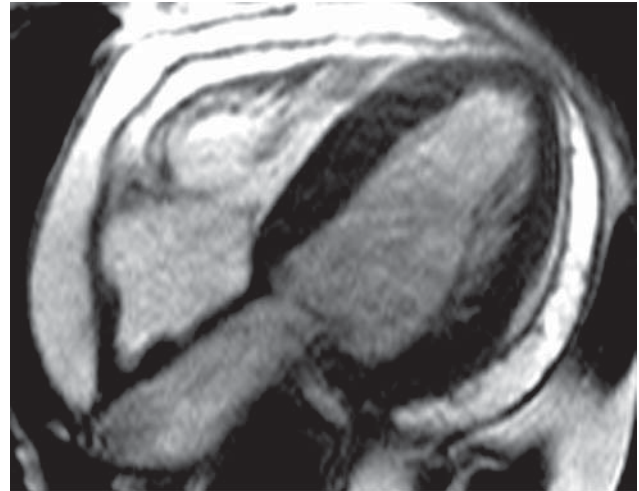


Figure 1. Pericardial thickening.
T2 weighted left ventricular outlet view (LVOT) showing pericardial thickening on the left side with significant pericardial effusion.

anterior motion of the mitral valve⁷. In the present study 3 patients had MR evidence of hypertrophic Cardiomyopathy in the form of apical and septal hypertrophy with increased end-diastolic and decreased systolic thickening of the septal wall. Dilated cardiomyopathy, which is the common end point of a variety of factors like alcohol, toxins, ischemia and viral disease leading to morphological changes of a grossly dilated heart. Pathologically, there is underlying myocardial fibrosis, accounting for the reduced contractility despite the increased muscle mass. MR imaging reveals a dilated heart with reduced ejection fractions. In the present study there were 3 patients who were detected to be having dilated cardiomyopathy (Fig 2). Restrictive cardiomyopathy is uncommon and results from infiltrative conditions leading to myocardial stiffness and restriction. Clinically, this disorder may have a presentation similar to that of constrictive pericarditis and based on hemodynamic studies it may be difficult to differentiate constrictive pericarditis from restrictive cardiomyopathy. MRI can help solve this problem by identifying increased pericardial thickness, which is seen in constrictive pericarditis, thus differentiating it from restrictive cardiomyopathy⁸.

Cardiac MRI has been used increasingly in the evaluation of ischaemic heart disease; perhaps the greatest advancement of cardiac MRI is its ability to evaluate myocardial viability following infarction. Interpretation of myocardial viability is based on results from two different techniques; wall-motion using cine acquisitions and contrast enhancement imaging. Wall-motion cine images identify myocardial wall thinning and abnormal wall contraction whereas the presence of delayed myocardial enhancement after administration of gadolinium-based contrast agents accurately delineates irreversibly damaged myocardium and hence predicts areas that will not recover functionally even after revascularization⁹. In the



Figure 2. Dilated Cardiomyopathy
T2 weighted four-chambered view of a diastolic frame from cine acquisition showing dilated left ventricle with thinning of the myocardial wall.

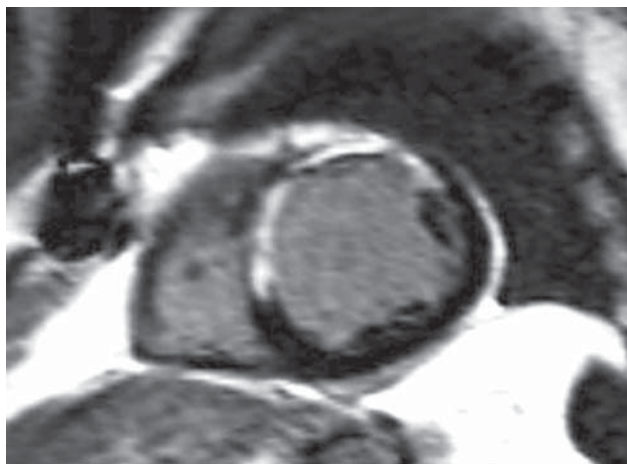


Figure 3. Non-viable myocardium
Delayed post contrast short axis MR image showing transmural enhancement of the anterior wall of the left ventricle consistent with non-viable myocardium.

present study 8 patients with documented coronary artery disease on coronary angiography were subjected to cardiac MRI with the aim to evaluate viability of the myocardium. The results based on post contrast delayed studies revealed presence of viable myocardium in 3 patients whereas in 5 patients there was evidence of irreversible myocardial damage (Fig 3).

Initially described in 1977, arrhythmogenic right ventricular dysplasia (ARVD) is a rare and familial disease characterized pathologically by fibrous and fatty replacement of the right ventricular myocardium. Patients generally present with arrhythmias of Rt ventricular origin, which may lead to sudden death. MRI has shown good results in diagnosing ARVD by providing information about regional wall motion, fatty infiltration of the Rt ventricular free wall and myocardial thinning¹⁰. On T1-weighted images focal areas of increased signal is observed in the Rt ventricular myocardium because of fatty infiltration. In the present study 6 patients were evaluated for suspected dysrhythmic Rt ventricular dysplasia by MRI and the same was confirmed in 3 patients whereas 3 were normal.

Latest research has opened up newer horizons in the field of cardiac

imaging with a view to image the coronary arteries, which have been known to be one of the most difficult arterial circulations to image. The challenges for MRI in imaging coronary arteries are their inherent complex geometry and tortuosity, their small caliber and their continual displacement by respiratory and cardiac motion. With improvement in technology and continued research into the various techniques of 2 and 3-dimensional MR imaging, it will soon be possible to image the coronary circulation using MRI. Since 20–40% of all diagnostic catheter coronary angiograms reveal no clinically significant stenosis, the development of an accurate and non-invasive technique to image the coronaries using MRI would represent a significant improvement in management of patients with suspected coronary artery disease.

In conclusion it is reiterated that cardiac MRI has already emerged as a useful technique in the evaluation of congenital and acquired heart diseases. It has a specific role in myocardial viability studies and is being increasingly used as a “one-stop” comprehensive imaging modality in the morphologic and functional evaluation of the heart. With the continuing shift towards non-invasive diagnostic procedures the applications of cardiac MRI will continue to expand and with the ongoing advancements in equipment and scanning techniques it is not far when MRI will be the leading imaging modality for all types of cardiovascular diseases and in particular ischaemic heart disease.

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CORRIGENDUM

Corrected versions of few spelling mistakes in the abstract of the article: Human Campylobacteriosis - an underdiagnosed etiology of Bacterial Diarrhea in India (April-June 2007 Issue) Vol. 20, No. 2 Page 147 are as under:

Dearrioea	to be spelled as	Diarrhoea
Immunocomprised	to be spelled as	immunocompromised
Hort	to be spelled as	Host
Culture	to be read as	Cultural

Inconvenience caused is highly regretted.

Editor

Next Issue Highlights

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- Burden of Diabetes in the Developing World
- Young Onset Diabetes Mellitus
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- Gestational Diabetes Mellitus in India
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A STUDY ON IMPACT ASSESSMENT OF HEALTH EDUCATION INTERVENTION ON ROAD SAFETY AND ACCIDENT PREVENTION AMONG PRIMARY SCHOOL CHILDREN OF TADONG GOVERNMENT SCHOOL, EAST SIKKIM

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Abstract : The health education materials for Road Traffic Accident (RTA) prevention were developed on the basis of information on "road safety and accident prevention" provided in the WHO brochure for 2004. Content validity was assessed by the experts in the field of community medicine and college of nursing and instruments were modified according to their recommendations. Conducting a pre-test in five children of 5th Mile Tadong for feasibility, acceptability, time management and expenses, assessed reliability; the data collected were used as a guide to modify the instruments accordingly. Proportions were used to derive information on baseline characteristics. Paired-t-test was used to compare the pre-test and post-test results of KAP on RTA prevention among the experimental and the control groups, separately. Chi-square test was applied to the pre-test and post-test results between both the groups to assess the impact of health education intervention on RTA prevention. Significant improvement in the knowledge between both the groups was observed in the following aspects: (a) RTA could be prevented by minimal presence on roads. (b) RTA could be prevented by avoiding playing on roads. (c) RTA could be prevented by respecting traffic signals. Significant improvement in positive attitude was observed by are : (a) Waiting for the elders to accompany them even when they are late for school. Significant improvement in practice regarding RTA prevention showed improvement in the following aspects: (a) Use of helmets even by a pillion rider. (b) Always following traffic rules. This indicates the effectiveness of the health education intervention on road safety and accident prevention measures among the primary school children.

Key Words: Road Traffic Accident, School Children, Health Education, Paired t-test, Chi-square test

INTRODUCTION

A significant number of children in developed and developing countries are subjected to Road Traffic Accident (RTA) which is currently placed at 9th position in the list of global burden of disease. It has been projected to become the 3rd most leading contributor to the global burden of disease by 2020. The World Health Organization, in its effort to control the alarming increase of RTA and road fatalities, recognized World Health Day on 7th April 2004, to provide and opportunity to focus the world's attention on the problem of RTA.^{1,2,3}

A study conducted by Jha N. et al^{4,5} from South India revealed that among 726 RTA victims, 83% among them were males while only 17% females. Among various injuries limb and the face were commonly affected areas to suffer external injuries head injuries were the commonest form of internal injuries seen in the victims (34.1%) These injuries were common among bicycle riders, pedestrians and riders of motorized two wheelers.^{4,5}

Vakilli R. et al,⁶ in their study showed that the age most prone for accident was between 12-16 years, followed by age group 4-8 years; 20.7% of all accidents were motor vehicle accidents. They suggested that preventive measures are needed to be taken for children regarding strict and definite traffic rules to prevent RTA in children,⁶ There is a need for road safety education directed towards students. Pre-school children may be introduced to elementary concepts of road safety through stories. Primary school children may be given practice guidance on the use of side walls and road crossing technique.⁷

Due to hilly terrain locations and lack of facilities of playgrounds, the children of Sikkim often make roads as their playground. Since most of children dwell from family of illiterate parents, they are unaware of basic road-traffic rules. With increase in road fatalities every year, many children either die or get disabled for rest of their lives due to RTA. Thus, a structured health education intervention is necessary for primary school going children, to reduce the rate of road fatalities in the state.

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MATERIALS AND METHODS

Tadong, Government Senior Secondary School of East Sikkim, Gangtok has a total capacity of 2000 students from different parts of Gangtok, East Sikkim. The study group was constituted by students from 5th standard of the age group of 9 to 16 years. Most of them resided in nearby localities and traveled to school on foot. Majority belonged to middle-class families. The school is located along the national highway NH 31 A.

Study Design: An experimental study (Randomised Control Trial) of health education intervention. **Setting:** Tadong, Government Senior Secondary School, Gangtok East Sikkim. **Study Population:** 102 students of primary level of class V from Section "A" and "B". **Sample Size(N):** Total sample size was 102. Out of which Experimental group comprised of 51, control comprised of 51 students. **Sampling Technique:** Randomisation Technique was applied to select the experiment and control groups after study obtaining informed verbal consent from participants of this study.

Inclusion Criteria: (i) All students of selected class and sections, (i.e. sections A and B of fifth standard). (ii) Students who were present at the time of pre-test & gave informed verbal consent to participate in the study.

(b) **Exclusion Criteria:** Students who were absent during the pre-test were excluded from this study.

Study Instruments (i) A 22- item structured pre-test questionnaire, with four parts: (a) PART-I of the questionnaire items were for the assessment of the socio-demographic profile of the students. (b) PART-II was for assessing the knowledge of primary school children regarding Road Safety and Accident Prevention. (c) PART-III for assessing attitude of primary school children towards Road Safety and Accident Prevention. (d) PART-IV for assessing the practice of primary school children regarding Road Safety and Accident Prevention (ii) A 15- item structured health education module of "Road Safety and Accident Prevention". The instrument was developed on the basis of the information on "Road Safety and Accident Prevention" provided in the WHO brochure for 2004. Experts in the

field of Nursing, Community Medicine, Pediatrics, Medicine & Surgery assessed the content validity and its appropriateness to be applied for primary school children. The tool was modified according to their suggestions and recommendation. Nepali Version of health education material was developed in consultation with literate expert in the language. Pre- testing was done in five students and data discarded to assess the feasibility, acceptability, time management and expenses.

Data collection Procedure After procuring permission from the principal of the school, the students of class five were approached for data collection. After obtaining informed verbal consent from students, the study & control groups were chosen through Randomization method by picking up lots. Section B was chosen for the study group and section A for the control group by lottery method. Students from both the section from both groups were interviewed using the structured pre-Test questionnaire and data collected regarding their existing knowledge, Attitude and Practice on Road Safety and Accident Prevention Measures. A second visit was made the following day and a structured health education intervention was implemented only to the experiment group. A third visit was made a week later and Post-Test was administered to both the experiment and the control groups. The responses were recorded for analysis. The teachers of this school were provided with copies of WHO brochure, 2004 and the children were provided with a calendar depicting 'ROAD SAFETY TECHNIQUES'. Finally, health education regarding RTA prevention was administered to all participants in this study which also reinforced the existing knowledge of study group.

Data Analysis Data collected was tabulated and analyzed with respect to the Pre-Test scores of study and control groups by using the Statistical Package for Social Sciences (SPSS) version 10.0. The results were expressed in terms of means & their standard deviations. Paired t-test and Chi-square tests were applied wherever applicable. A p-value <0.05 was considered as statistically significant.

RESULTS

Baseline Characteristics

Majority (58%) of the subjects belong to the age group of 9-12 years. Proportions of males were more in this age group (53%). Proportions of females were more in the age group of 13-16 years, accounting for 51% of the parents were literate among them, 75% fathers and 46% mothers were literates.

Table-1 shows significant improvement in knowledge after health education intervention regarding following issues; Prevention of RTA by following (a) traffic rules and respecting traffic signals, (b) being careful on road, (c) avoiding playing on road, (d) following proper precautions while crossing road in the plains and in hilly terrains and (e) stating the

Table 1: Pre – Test and Post- Test results of Study group on Knowledge regarding RTA prevention

SI. NO.	KNOWLEDGE	PRE – TEST (n=51) Mean ± SD	POST – TEST (n=51) Mean ± SD	P – value
1.	If proper precaution taken, RTA could be prevented	10.5 ± 0.5	2.0 ± 0.00001	0.0001*
2.	Following traffic rules could prevent RTA	1.4 ± 0.5	1.9 ± 0.3	0.0001*
3.	Being careful on the road could prevent RTA	1.3 ± 0.4	1.0 ± 0.2	0.0001*
4.	RTA could be prevented by avoiding playing on road	1.4 ± 0.5	1.1 ± 0.2	0.0001*
5.	Negligence, Ignorance and Drunken Driving are risk factors for RTA	1.4 ± 0.5	1.9 ± 0.3	0.0001*
6.	Correct responses for traffic light signals & their indicators	1.1 ± 0.3	2.0 ± 0.00001	0.0001*
7.	Precautions need to be taken while crossing road in plains	1.6 ± 0.5	2.0 ± 0.00001	0.0001*
8.	Precaution need to be taken while crossing road in hilly terrain	1.9 ± 0.3	2.0 ± 0.00001	0.0001*

* p value ,0.05 is considered as significant

risk factors of RTA as negligence, ignorance regarding traffic rules and drunken driving (f) correct responses for traffic light signals and their indicators. However, knowledge regarding prevention of RTA by avoiding playing on the road and by being careful on the road. Needs suggests further reinforcement.

Table 2: Pre – Test and Post- Test results of Study group on attitude regarding RTA prevention

SI. NO.	ATTITUDE	PRE – TEST (n=51) Mean ± SD	POST – TEST (n=51) Mean ± SD	P – value
1.	Willing to practice road safety measures in daily life	1.4 ± 0.4	2.0 ± 0.00001	0.0001*
2.	Paying attention to traffic rules even in hurry.	1.5 ± 0.5	2.0 ± 0.00001	0.0001*
3.	Waiting for elders to accompany when late for school.	1.2 ± 0.4	2.0 ± 0.00001	0.0001*

* p value ,0.05 is considered as significant

Table-2 shows significant improvement in positive attitude of the subjects towards RTA prevention after effective health education intervention.

Table 3: Pre – Test and Post- Test results of Study group on practice regarding RTA prevention

SI. NO.	PRACTICE	PRE – TEST (n=51) Mean ± SD	POST – TEST (n=51) Mean ± SD	P – value
1.	Always looking to both sides before crossing roads.	1.2 ± 0.3	2.0 ± 0.00001	0.0001*
2.	Always used seat belts while traveling in car	1.1 ± 0.3	1.9 ± 0.3	0.0001*
3.	Always used helmets even as a pillion rider	1.3 ± 0.5	2.0 ± 0.1	0.0001*
4.	Always following traffic rules	1.4 ± 0.5	2.0 ± 0.00001	0.0001*

* p value ,0.05 is considered as significant

Table-3 reveals that after health educational intervention, the subjects showed significant improvement in their practices regarding RTA prevention as depicted by multiple responses to the questions put for assessing the practice. This finding suggested that the health education intervention was effective in reinforcing road safety practices among the subjects.

Table 4: Pre – Test and Post- Test results of control group on knowledge regarding RTA prevention

SI. NO.	KNOWLEDGE	PRE – TEST (n=51) Mean ± SD	POST – TEST (n=51) Mean ± SD	P – value
1.	If proper precautions taken, RTA could be prevented	1.5 ± 0.5	1.7 ± 0.4	0.007*
2.	RTA could be prevented by following traffic rules	1.4 ± 0.5	1.6 ± 0.5	0.0001*
3.	Being careful on the road could prevent RTA	1.7 ± 0.5	1.2 ± 0.4	0.001*
4.	RTA could be prevented by avoiding playing on road	1.2 ± 0.4	1.1 ± 0.2	0.013*
5.	Negligence, ignorance and Drunken Driving are risk factors for RTA	1.5 ± 0.5	1.9 ± 0.3	0.0001*
6.	Correct responses for traffic light signals & their indicators	1.5 ± 2.8	1.2 ± 0.4	0.348
7.	Precautions need to be taken while crossing road in plains	1.6 ± 0.4	1.7 ± 0.5	0.103
8.	Precaution need to be taken while crossing road in hilly terrain	1.8 ± 0.4	1.8 ± 0.4	0.709

* p value ,0.05 is considered as significant

Table-4 shows that there is significant improvement in the knowledge of the subjects regarding RTA prevention is issues related to its prevention by following proper precaution and by following traffic rules and also stating of risk factors RTA as negligence, ignorance and drunken driving. This improvement in the knowledge of the control group could be due to the reason that diffusion of knowledge might have occurred from the study group to the control group. Also the control group, might have acquired knowledge from there teachers, parents, near-relatives and elders, after the pre-test was conducted.

Table 5 shows that there was no significant improvement of attitude in control group regarding RTA prevention as majority already had positive attitude towards practicing road safety measures and paying attention to traffic rules during Pre-Test.

Table 5: Pre – Test and Post- Test results of control group on attitude regarding RTA prevention

SI. NO.	ATTITUDE	PRE – TEST (n=51) Mean ± SD	POST – TEST (n=51) Mean ± SD	P – value
1.	Willing to practice road safety measures in daily life	1.8 ± 0.4	1.7 ± 0.4	0.569
2.	Paying attention to traffic rules even in hurry.	1.5 ± 0.5	1.5 ± 0.5	0.322
3.	Waiting for elders to accompany when late for school.	1.1 ± 0.3	1.2 ± 0.4	0.322

* p value ,0.05 is considered as significant

Table 6 reveals significant Improvement in practice regarding RTA prevention in the following aspects: (a) Always looking to both sides before crossing the road, (b) using seat belts and (c) always following the traffic rules. This improvement may be attributed to the fact that subjects,

Table 6: Pre – Test and Post- Test results of controll group on practice regarding RTA prevention

SI. NO.	PRACTICE	PRE – TEST (n=51) Mean ± SD	POST – TEST (n=51) Mean ± SD	P – value
1.	Always looking to both sides before crossing roads.	1.2 ± 0.4	1.3 ± 0.4	0.024*
2.	Always used seat belts while traveling in car	1.0 ± 0.2	1.1 ± 0.3	0.044*
3.	Always used helmets even as a pillion rider	1.4 ± 0.5	1.4 ± 0.5	0.322
4.	Always following traffic rules	1.6 ± 0.5	1.7 ± 0.5	0.013*

out of curiosity and interest to learn more, might have consulted their parents, elders, teachers and even their friends in the experimental group after the Pre-Test was conducted. This clearly shows that the Pre-Test questions were successful in arousing enough curiosity and interest among control group to learn more about RTA prevention.

Table 7 shows the comparison between both experimental and control group on proportion of appropriate/correct responses in pre-test and post-test on knowledge of Attitude & Practice (KAP) regarding RTA.

- (1) Improvement in knowledge of study group was observed to be higher in post-Test as compared to the control group. This difference could be attributed to effective health education intervention. The difference in correct responses of study and control group was found to be statistically significant regarding the following aspects ; (a) RTA could be prevented by being careful on roads, (b) RTA could be prevented by avoiding playing on road and (c) Correct responses for traffic light signal and their indicators.
- (2) Improvement in positive attitude of study group was also found to be significantly higher in Post-Test as compared to the control group regarding (a) willingness to pay attention to traffic rules even when in a hurry and (b) willingness to wait for elders to accompany even when getting late for school.
- (3) Change in practice RTA preventive norms of study group was observed to be significantly higher in post-test as compared to the control group regarding the following aspects: (a) always looked to both sides before crossing road and, (b) always used seat belts while traveling in car. But the difference in practice of study and control group was found to be statistically significant regarding (a) always used helmets even as a pillion rider and (b) always followed traffic rules. The above findings confirm that improvement in knowledge, Attitude & Practice of the study group regarding RTA prevention in significantly higher in Post-Test as compared to control group due to

Table 7 : Comparison between both study and control groups on proportion of appropriate/correct responses in pre-test & post-test on kap regarding RTA

SL NO.	KNOWLEDGE	GROUP	(Post-Test) (%)	(Post-Test) (%)	X2 (Yates corrected wherever applicable), p value
1.	RTA could be prevented by following traffic rules	Experimental	41	90	2.79, p= 0.095
		Control	35	59	
2.	RTA could be prevented by being careful on roads	Experimental	26	4	15.62 p= 0.00007*
		Control	65	24	
3.	RTA could be prevented by avoiding playing on road	Experimental	37	6	4.82 P= 0.028*
		Control	18	24	
4.	Major risk factors of RTA are negligence, ignorance & drunken driving	Experimental	41	88	0.15, p= 0.615
		Control	47	88	
5.	Correct responses for traffic light signals & their indicators	Experimental	10	100	22.8 p= 0.000002*
		Control	16	18	

SL NO.	ATTITUDE	GROUP	(Post-Test) (%)	(Post-Test) (%)	X2 (Yates corrected wherever applicable), p value
6.	Willing o pay attention to traffic rules even when in a hurry	Experimental	55	100	3.66, p= 0.056
		Control	51	55	
7.	Willing to wait for elders to accompany even when getting late for school	Experimental	24	100	8.08, P= 0.004*
		Control	65	24	

SL NO.	ATTITUDE	GROUP	(Post-Test) (%)	(Post-Test) (%)	X2 (Yates corrected wherever applicable), p value
8.	Always looking to both sides before crossing roads.	Experimental	8	100	0.01, P= 0.941
		Control	24	33	
9.	Always used seat belts while traveling in car	Experimental	12	88	2.98, P= 0.078
		Control	6	14	
10.	Always used helmets even as a pillion rider	Experimental	28	98	12.45, P=0.0004*
		Control	35	39	
11.	Always following traffic rules	Experimental	35	100	10.1, P=0.001*
		Control	59	71	

* p value ,0.05 is considered as significant

effective health education intervention.

SUMMARY AND CONCLUSIONS

An study was conducted among 102 primary school children of Tadong, Government Senior Secondary School, Gangtok on Impact of structured health education intervention on knowledge, attitude and practice regarding Road Safety and Accident Prevention. 51 students from fifth standard constituted the study group and 51 constituted control group. Among the study and control group, significant improvement in knowledge was observed in the following aspects: (a) RTA could be prevented by being careful on road, (b) RTA could be prevented by avoiding playing on road, (c) RTA could be prevented by respecting traffic light signals. Improvement in attitude was observed in both the groups regarding waiting for elder to accompany them to school even when they are late. Practice regarding RTA prevention showed improvement in the following aspects : (a) Use of helmets even as a pillion-rider & (b) All time following traffic rules. This indicates the efficacy of the health education intervention regarding RTA prevention among the primary school children.

LIMITATION

The study was limited to the students who were available during the study period & informed verbal consent to participate in the study. Since the proportion of non-cooperative students and those who were absent during pre-test interview days was very small we expect only a minimal effect on the results.

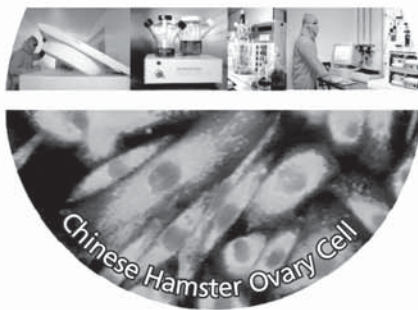
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ROLE OF ULTRASONOGRAPHY IN PREDICTING TECHNICAL DIFFICULTIES DURING LAPAROSCOPIC CHOLECYSTECTOMY

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Abstract: This prospective study was conducted on 75 patients undergoing laparoscopic cholecystectomy in JNMC Hospital, Aligarh between Nov 2002 and Apr 2004. Patients with choledocholithiasis were excluded. Findings at time of surgery, level of difficulty faced by the operating surgeons and outcome of surgery were recorded. Ultrasonographic and per-operative findings were compared with respect to the level of difficulty (Easy or Difficult) encountered in laparoscopic surgery and requirement of conversion point of 75 cases: 34 (44%) had easy and 41 (56%) had difficult laparoscopic surgery. 9 (12%) cases required conversion. Common causes of difficulty during laparoscopic dissection were intra-peritoneal adhesions and hepatomegaly. Common causes of conversion were intra-abdominal adhesions and presence of multiple calculi in gall bladder. Preoperative ultrasonography identified multiple gallstones and hepatomegaly in all (100%) cases. However ultrasonography was not much helpful in identifying Intra-abdominal adhesions (34.78% accuracy of detection). Hence, a difficult laparoscopic cholecystectomy can be predicted based on preoperative ultrasonography findings.

Keywords: Laparoscopic cholecystectomy, Ultrasonography, Gall stones.

INTRODUCTION

Laparoscopic cholecystectomy is the gold standard treatment for symptomatic cholelithiasis. However, in many patients conversion is required, either because of technical difficulties or intra-operative complications; usually resulting from dense adhesions, inflammation and abnormal anatomy. Some preoperative variables may help to predict the risk of conversion or a difficult operation.

Ultrasonography is the most widely available, affordable, non-invasive and reliable radiological investigation for evaluation of patients prior to surgery. It can tell about the anatomy of common bile duct, anatomy of Calot's triangle, about the presence of adhesions in peritoneal cavity, about the no. and size of stones in gall bladder, and about the presence of stones in common bile duct, if any. It can also tell about the gall bladder wall thickness, and any peri-cholecystic edema.

METHODS

This prospective study has been conducted on 75 patients with the diagnosis of cholelithiasis admitted in the surgical wards of JNMC Hospital, Aligarh between Nov.2002 and Apr.2004 who were subjected to laparoscopic cholecystectomy as a treatment for the same. Patients with choledocholithiasis were excluded from the study. In all patients, findings at the time of surgery, the level of difficulties faced by the operating surgeons and the outcome of surgery were recorded. The ultrasonographic findings, per-operative findings & complications of all patients were tabulated and then the entire data was evaluated with respect to the level of difficulty (easy or difficult) encountered in laparoscopic dissection and the requirement of conversion (required or not), using 'Stepwise Binary Logistic Regression Model using SPSS 10 Software system'. The model was tested by 'Hosmer & Lane Shaw Test' and was found to fulfill the criteria of 'Goodness of Fit'. This means that the model predicted the outcome variables accurately.

RESULTS

1. In 34 (44%) patients laparoscopic dissections was easy, and in 41 (56%) patients some form of difficulties were encountered while doing laparoscopic dissection.
2. The common causes of difficulty encountered during laparoscopic dissection in our study were intra-peritoneal adhesions and hepatomegaly.
3. In 9 (12%) cases, conversion to open procedure was required.

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Common causes of conversion identified in this study are intra-abdominal adhesions and presence of multiple calculi in gall bladder, in that order. Other factors found to be significantly affecting the risk of conversion are poorly visualized Calot's triangle, presence of accessory Rt. hepatic artery and hepatomegaly in that order.

4. Per operatively, in 26 (34%) patients adhesions were found, of which pre-operative USG could detect the adhesions in 8 (10.7%) patients only. That constitutes 30.76% of the patients, which actually had adhesions. Thus the diagnostic significance of USG for detection of intra-operative adhesions is not much.
5. Multiple gallstones were found to be significantly responsible for conversion. Preoperative USG gives a good account of no. of gallstones. Out of 9 patients requiring conversion, 6 (66.66%) were having multiple gallstones and preoperative USG could detect that in all these patients. Similarly the other significant predictor of conversion i.e. hepatomegaly was correctly diagnosed by preoperative ultrasonography in all 12 (100%) cases. As we can interpret from table 1, ultrasound could detect with very high accuracy the size of the gall bladder (88%), gall bladder wall thickness (86.67%), no. of gall stones (100%) and common bile duct diameter (94.45%). However ultrasonography was not much helpful in identifying intra-abdominal adhesions (34.78% accuracy of detection). Also the findings of long cystic duct, presence of accessory right hepatic artery and of aberrant branch of Right hepatic duct could not be suspected on the basis of ultrasonography.

Table 1 Comparison of per operative and deagnortie ultrasound findings in gall bladder dision

Feature	Per-operative Finding	Finding on USG	Diagnostic accuracy of USG	
GB Size	Normal	46	45	88%
	Contracted	20	24	
	Distended	9	6	
GB Wall Thickness	Normal/ Thin Walled (<4 mm)	55	50	86.67%
	Thick Walled (>4 mm)	20	25	
No of stones in GB	Single	21	21	100%
	Multiple	54	54	
CBD diameter	Normal (<7mm)	71	67	94.45%
	Dilated (>7mm)	4	8	
Adhesions around Calot's Δ	Detected	23	8	34.78%
	Not Detected	52	67	
Accessory Rt Hepatic Artery	Detected	1	0	0%
Long Cystic Duct	Detected	1	0	0%
Aberrant branch of Rt Hepatic Artery	Detected	1	0	0%

DISCUSSION

We found a conversion rate of 12% in our study, whereas the conversion rates reported in previous studies vary from 1.2% to 35%. This conversion rate is comparable to that reported by McLoughlin et al¹ and Liu et al², who reported conversion rates of 10.41% and 9% respectively. But this conversion rate of ours is higher than that reported by Southern Surgeons Club³ and Cuschieri et al⁴, who published very low conversion rates of 4% and 5.3% respectively. On the other hand Zucker et al⁵ and Kiviluoto et al⁶ have reported comparatively higher conversion rates of 27% and 16.5, respectively. We noted an overall complication rate of 16% in our study with major complications requiring conversion occurring in 4 (5.33%) cases Table 2. Our major complication rate was very similar to that of Koo et al⁷ and of Southern Surgeons Club³, who reported major complication rates of 5.5% and 5.1%.

Table 2: Complications encountered during laparoscopic dissection

Complication	No. of patients	Outcome
Lost stones and Bile leak in peritoneal cavity	8	Improved on Conservative treatment
Superficial Wound Infection	2	Improved on Conservative treatment
Prolonged bile leak in post-operative period	2	Controlled by itself
Excessive Bleeding from the Liver bed	2	Conversion done and managed on table
Injury to Acc. Rt Hepatic artery	1	Conversion done and managed on table
Injury to aberrant branch of Rt hepatic Duct	1	Conversion done and managed on table

In our study no CBD injury was noted. Zucker et al⁵ also did not report any CBD injury from their case series. Many other workers have reported low rates of CBD injury. Cuschieri et al⁴ reported CBD injury in only 0.32% of their cases. Koo et al⁷ found that the overall complication rate and incidence of CBD injury was 5.5% and 0.2% respectively. Overall complication rate in our study is higher than those reported by other workers. The reason for that is that the surgeons in our institution are still in the learning phase of for laparoscopic surgery.

Our study revealed that presence of intra-abdominal adhesions was the most significant reason for conversion of surgery. Kama et al⁸ also made similar observations. In our study pre-operative USG could detect the adhesions in 34.78% cases only. Rattner et al⁹ also concluded that value of ultrasonography in detecting intraabdominal adhesions was not much. We found multiple gallstones to be an important reason for conversion. Small stones can often cause obstruction in Hartman's pouch, hence proper retraction is not maintained. Around 70% of our entire study population had multiple Gallstones and they were identified correctly by the pre-operative USG. It has previously been observed that single large stones tend to pose difficulty in grasping the gall bladder, thus causing difficulty in surgery but Sakuramoto et al¹⁰ observed that number of gallstones does not correlate with technical difficulty during surgery.

In our study patients with hepatomegaly posed problems in laparoscopic dissection. This is because it is difficult to put the epigastric port in correct place and because of the limited mobility of the dissecting forceps, put in,

through the epigastric port. This confirms the findings noted by Dararkah¹¹. Increased gall bladder wall thickness (>4 mm) has been reported to be a significant predictor of difficult laparoscopic surgery by Kama et al⁷. Thickness of gall bladder wall on pre-operative USG represents the present inflammation or fibrosis due to repeated previous attacks of acute illness. Such inflamed tissue is difficult to handle and dissect and thus surgery becomes difficult. However our analysis did not find this factor to be important, an observation is in agreement with that of Chen et al¹², who found that although thickness of gall bladder wall can be demonstrated very well on pre-op USG, its not very significant predictor of conversion. Abnormal and aberrant anatomy of Calot's D is always associated with problems in dissection. In our study, presence of accessory right hepatic artery was found to be having significant association with conversion. Carmody et al¹³ also made the same observation.

We found USG to be very good in detecting hepatomegaly and no. of calculi in gall bladder but its efficacy in detecting intra-abdominal adhesions was not good (only 35%). USG can find out with very high degree of accuracy the thickness of gall bladder wall, diameter of CBD, presence of any stone impacted in Hartman's pouch, peri-cholecystic edema and mobility of gallstones. Also, high resolution USG can detect intra-abdominal adhesions in up to 50% cases. Chen et al¹² have found USG findings to be of help in detecting potentially difficult cases. On the other hand, Carmody et al¹³ reported that pre-operative evaluation of gall bladder using USG had little value in screening for technical difficulties.

CONCLUSIONS

1. Presence of intra-abdominal adhesions, hepatomegaly and multiple gallstones on pre-operative USG are reliably significant preoperative predictors of difficult surgery and conversion.
2. Chances of difficult laparoscopic dissection and conversion can be reliably predicted by proper pre-operative abdominal ultrasonography of the patients.

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CORRIGENDUM

Article - 'Darusentan : A promising drug for resistant hypertension' published in July –September, 2007 Issue (Vol. 20. No. 3) at page - 245, under **Drug Profile** Names of the authors may be read as 1) Dr. Bhupinder Singh Kalra and 2) Dr. Vandana Tayal, Deptt. of Pharmacology, Maulana Azad Medical College, New Delhi, India.

Omission is highly regretted.

Editor

PATTERN OF CONGENITAL HEART DISEASES IN CHILDREN AT RURAL HOSPITAL OF CENTRAL INDIA

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Abstract: It was hospital based study conducted over a period of two year from July 2004 to June 2006. Methods: 129 children up to twelve year of age with clinical suspicion of congenital heart disease were subjected to chest X-ray and electrocardiography while the final diagnosis was confirmed by echocardiography. 72(56%) were male and 57(44%) female children. 82% of children with congenital heart disease presented at age less than 5 years and only 18% at age above 5 years. Among the acyanotic congenital heart disease group, ventricular septal defect was the commonest lesion found in 29% of cases, followed by atrial septal defect 18%. Perimembranous ventricular septal defect and ostium secundum atrial septal defect were the commonest type detected on echocardiography. Tetralogy of Fallot was the commonest cyanotic lesion found in 8.52% followed by complex congenital heart disease in 5.42% and transposition of great arteries in 3.10% of cases. In order to avoid complications, early detection of congenital heart disease is of utmost importance for proper management.

Keywords: Congenital heart disease, Acyanotic, Cyanotic, Echocardiography.

INTRODUCTION

Congenital heart disease (CHD) is defined as the structural, functional or positional abnormality of the heart, in isolation or in combination present from birth, but may manifest any time after birth or may not manifest at all. A study on 11,000 consecutive live births in a tertiary care hospital in Delhi gave as incidence of CHD as 3.9/1000 live birth, whereas in an autopsy study from Chandigarh, the incidence was as high as 7.5/1000 births¹. In our country majority of child births still takes place at home and routine neonatal screening is not common, so it's very difficult to calculate true birth prevalence of congenital heart disease. Until 1930 it was believed that rheumatic heart disease was the most common form of heart disease in children. Within recent years, the statistics in most cardiac centres have shown that CHD is the more common of the two². Congenital heart diseases may present in any age group from neonatal age to adolescent age group and it may present with or without cyanosis, rapid breathing, perspiration, some with congestive cardiac failure, cyanotic spells, while some children may be asymptomatic but with a cardiac murmur detected during examination for any other illness³. This study was conducted to determine the profile of individual congenital heart lesions in cyanotic as well as acyanotic patients at rural hospital.

MATERIAL AND METHODS

This study was conducted in Department of Pediatrics, Mahatma Gandhi Institute of Medical College, Sewagram over a period of two year from July 2004 to June 2006. All the children with clinical suspicion of Congenital Heart Disease were evaluated with detailed history and clinical examination. They were initially investigated by performing complete blood cell count, chest X-ray and electrocardiography and final diagnosis was confirmed by echocardiography. **Inclusion criteria:** 1. Children up to 12 years of age; 2. Suspicion of congenital heart disease. **Exclusion criteria:** 1. Age more than 12 years.; 2. Children with acquired heart disease.

RESULTS

Total of 129 children were included in this study. Age group ranged from newborn to 12 years. 82% of children with congenital heart disease presented at age less than 5 years and 18% in age group of 6 to 12 years (Table 1). 72(56%) children were males and 57(44%) were females. Male to female ratio was 1.26:1 (Table 2). Two-thirds of children were having acyanotic congenital heart lesions. The response of mother of the children with CHD to antenatal history eg. H/O irradiation or drug or hormonal ingestion, exanthematous fever, six months prior to conception was

Table - I: Age distribution of CHD children

Age distribution of CHD children		
Age group	No. of Cases	Percentage
0-1month	18	13.95
1month - 1 year	41	31.78
1year - 5year	49	37.98
5year- 10year	14	10.85
10year-12year	7	5.42

Table2: Relative distribution of congenital heart diseases lesion in children

CHD Lesions	Total Number (n=129)	Male (n=72)	Female(n=57)	Ratio (M:F) (1.26:1)
1. Acyanotic CHD				
ASD	24	13	11	1.18:1
VSD	38	24	14	1.71:1
PDA	7	1	6	0.16:1
ECD	5	3	2	1.5:1
Mixed	6	4	2	2:1
2. Obstructive CHD				
PS	5	3	2	1.5:1
AS	2	1	1	1:1
COA	1	1		
3. Cyanotic CHD				
TGA	4	3	1	3:1
TOF	11	4	7	0.57:1
Ebstein's anomaly	2	2	0	-
TA	3	2	1	2:1
PAPVC	2	2	0	-
TAPVC	2	1	1	1:1
Single Ventricle	2	1	1	1:1
4. Complex CHD				
	7	4	3	1.33:1
5. Miscellaneous Condition				
	8	3	5	0.6:1

VSD: Ventricular septal defect, ASD: Atrial Septal Defect, PDA: Patent ductus arteriosus, ECD: Endocardial cushion defect, COA: coarctation of aorta AS: Aortic stenosis, PS: Pulmonary stenosis, TOF: Tetralogy of Fallot, TGA: Transposition of great vessels, TA: Tricuspid Atresia, EA: Ebstein's anomaly, TAPVC: Total anomalous of pulmonary venous connection, LCAPA: left coronary artery arise from pulmonary artery

unreliable to establish possible causative factor. Family history was positive in 8(6.20%) cases with CHD. Family studies indicate a 2 to 10 fold increase in the incidence of CHD in sibling of affected parents or in the offspring of the affected parents⁴. Therefore, it's recommended that family members of patients with CHD should also be screened for early detection and treatment.

Symptoms started in infancy in 92% of patients. The commonest symptoms were breathlessness, palpitation, failure to thrive, repeated chest infection and cyanosis; 9 (6.97%) patients had extracardiac malformation

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in which more than one system was involved. 92(71.31%) patients were anemic. 63 (48.83%) patients fall in PEM grade III and 33 (25.58%) in PEM grade II. Among the acyanotic CHD group, ventricular septal defect (VSD) was the commonest lesion found in 29% of cases, followed by atrial septal defect 18%. Perimembranous VSD and ostium secundum ASD were the commonest type of lesion detected on echocardiography. Tetralogy of Fallot (TOF) was the commonest cyanotic lesion found in 8.52% followed by transposition of great arteries in 3.1% and Tricuspid atresia in 2.32% of cases. Complex congenital heart disease was found in 5.42% of cases (Table 3).

Table 3: Relative distribution of congenital heart diseases lesion in children:

CHD	Total Number(n=129)	Percentage (%)
1. Acyanotic CHD		
ASD	24	18
Ostium Primum	4	
Ostium Secundum	19	
Sinus Venosus	1	
VSD	38	29
Perimembranous	25	
Muscular	10	
Inlet	2	
Swiss-Chiese	1	
PDA	7	5.42
ECD	5	3.87
Mixed		
PDA+VSD	1	0.77
PDA+ASD	1	0.77
ASD+VSD	4	3.1
2.Obstructive CHD		
PS	5	3.87
AS	2	1.5
COA	1	0.77
3. Cyanotic CHD		
TGA	4	3.1
TOF	11	8.52
Ebstein's anomaly	2	1.55
TA	3	2.32
PAPVC	2	1.55
TAPVC	2	1.55
Single Ventricle	2	1.55
4. Complex CHD	7	5.42
5. Misce. Condition		
Cor-triartium	1	0.77
Congenital MS	1	0.77
Bicuspid Aortic valve	2	1.55
LCAFA	1	0.77
Dextroposition of heart	3	2.32

Note:Abbreviations as in Tables 2

DISCUSSION

Congenital heart diseases (CHD) represent one of the major groups of birth defects and make up approximately 1% of human malformations⁵⁻⁷. CHD contribute significantly to infant mortality because 10% of infant deaths are due to congenital malformations, and 50% of the latter are cardiovascular malformations⁸. This study does not give a true incidence or prevalence of congenital heart disease in total population because this study was confined to hospital only. In this study more than two-third of CHD were acyanotic.

Maximum number of children with CHD was observed up to 5 years of age same finding was observed in the study done by Al-EHAG⁹. Number of males was 72 and females were 57 with a ratio of 1.26:1. Bassili A et al¹⁰ reported that there was a male predominance in case of pulmonary stenosis and single ventricle, while in case of PDA, mitral valve prolapse, and partial atrioventricular canal defect female predominance. In this study, the female dominance of patent ductus arteriosus and male dominance of ventricular septal defects was observed in acyanotic CHD. In cyanotic CHD the female dominance of TOF and male dominance of TGA was observed

In acyanotic CHD patients, 38(29%) had ventricular septal defect, majority with perimembranous type. 38 patients had isolated ventricular septal defect while 5 children had other cardiac lesions along with ventricular septal defect (VSD). One case had evidence of pulmonary hypertension, who had Eisenmenger with cyanosis. VSD was the commonest CHD in a study performed by Jaiyesimi F et al¹¹ and Grech-V¹². Studies by Vashishtha et al¹³ and Srivastava et al¹⁴ in India also reported VSD as the

commonest CHD. ASD and PDA was reported as 23% and 11% by Shreshta et al¹⁵, 7.5% and 22% by Jaiyesimi F et al¹¹, 18% and 14% by Chadha SL et al¹² and 11.4% and 4.81% by Samanek M et al¹⁶ while the corresponding figures in our study were 18% and 5.42%.

Among the cyanotic lesions, TOF 11(8.92%) was the commonest congenital heart lesion followed by TGA 4(3.10%). This result is comparable with the studies done by Hag AL⁹, Jaiyesimi F et al¹¹ Tefuarani N et al¹⁷ and Van der Horst RL¹⁸. TOF was reported in 13.6% cases by Vashishtha et al¹³; while in our study it was 8.92%. Pulmonary stenosis was found in 3.87% of the cases, which was comparable with the study done in Sudan⁹. Complex cardiac lesion was found in 5.42% in our study, while Jacobs EG reported 3.9% cases of intracardiac mixing¹⁹. In the latest decades of the 20th century, considerable progress has been made in recognizing congenital malformations, including heart defects, with high-resolution fetal echocardiography. Therefore, there was a significant decrease in the number of newborns with CHD. In most cardiac centers, fetal echocardiography is performed in all cases with extracardiac anomalies (20). Furthermore, a proper identification and treatment of CHD early in the prenatal period will protect the family from the economic and emotional burden caused by having such a child with CHD. According to my knowledge, this is the first study carried out in rural hospital for assessing the profile of congenital heart disease children in rural area of Maharashtra state. 2-D echocardiography and Color Doppler examination of all neonates, infants and children suspected of CHD is essential for correct diagnosis and proper management.

CONCLUSIONS

The children who present with repeated chest infections, respiratory distress, cyanotic appearance, poor feeding and failure to thrive should be specifically examined for congenital heart disease and if required referred for tertiary care to ensure timely treatment by surgical intervention after necessary confirmatory investigations. Our study performed over a period of two years shows that non-cyanotic congenital heart disease is more common than cyanotic heart disease.

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BILATERAL ACCESSORY BICEPS : A CASE REPORT

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Abstract: Presence of supernumerary head of biceps brachii muscle are common, with variable frequency in different populations. However presence of bilateral accessory biceps muscles has been rarely reported. During routine anatomical study of an adult female cadaver, bilateral accessory biceps was observed with dissimilar attachment of the lower ends. The right side tendon was attached to the radial tuberosity beneath the main tendon while the muscle on the left side was attached on the medial border of the radius just above the interosseous membrane, 2.5 cm below the radial tuberosity.

INTRODUCTION

The biceps brachii is a large fusiform muscle having two proximal attachments. The long head is attached to the supraglenoid tubercle of the scapula and the short head to the coracoid apex in common with the coracobrachialis. The two parts blend into a common belly in the lower third of the arm and its tendon gets attached to the dorsal aspect of the radial tuberosity. The tendon shows a medial expansion (bicipital aponeurosis) that merges with the deep fascia of the forearm. Unilateral presence of supernumerary head of biceps brachii has been variously quoted as 12% in African blacks, 18% in Japanese and 10% in European whites^{1,2,3}. The shaft of humerus, medial intermuscular septum, capsule of the shoulder joint, tendon of pectoralis major and terminal part of the deltoid or coracobrachialis are the anomalous sites of the supernumerary head². Bilateral three headed biceps was reported by Swieter and Carmichael³ with each third head having a proximal humeral attachment and these heads distally join the conjoint tendon. Ozan et al⁴ had observed an unusual accessory biceps brachii muscle originating from the tendon of deltoid and this then gave three tendinous slips on approaching the cubital fossa. Two of these join the bicipital aponeurosis whereas the third tendon was attached to the ulnar head of pronator teres. In our case study, an accessory muscle in relation to biceps brachii showing unusual distal attachment was bilaterally observed and in being reported.

CASE REPORT

In the course of gross anatomical examination of the flexor compartment of the arm of an adult female cadaver, an accessory muscle was seen bilaterally. The right biceps brachii (fig.) had its long and short heads arising from the supraglenoid tubercle and the coracoid process of scapula respectively and these two fused with each other 5 cm above the lateral epicondyle of humerus. The conjoint tendon so formed got attached to the radial tuberosity and the bicipital aponeurosis turned medially to merge with the deep fascia of forearm. The accessory muscle arose from the humeral shaft just superomedial to brachialis and lateral to the insertion of coracobrachialis. It formed a 14 cm long strap belly ending in a cord like tendon. This passed under cover of the main tendon, gave slip to the bicipital aponeurosis and then got attached to the radial tuberosity dorsal to the conjoint tendon. This accessory muscle received innervation from the musculocutaneous nerve.

The left side biceps brachii had similar attachments and the conjoint tendon was formed 3.5 cm superior to the lateral epicondyle of humerus with similar lower attachment as the right muscle. The accessory muscle showed similar proximal attachment as seen on the right side. However, a 3 cm long tendinous cord was seen to connect it to the tendon of pectoralis major in the inferior part of bicipital sulcus. It formed a long muscle belly and bial 5 cm long tendon lying dorsal to the biceps tendon. It then turned anteromedially to be inserted on the medial border of radius 2.5 cm below the tuberosity and just above the interosseous membrane and it also had few fibres inserting in to the bicipital aponeurosis.

DISCUSSION

Common sites of attachment of the supernumerary head of biceps are usually from various regions of the shaft of humerus to the fascia covering the

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Left biceps brachii with Accessory third head. -L-long head, S-short head, A-accessory head T-main tendon, t-accessory tendon.

short head. However, this head always joined the main muscle or tendon distally. In a bilateral four headed biceps of an old Japanese woman, the third head had origin from the shaft of humerus and insertion into the main tendon. The fourth head with a fibrous origin from the intertubercular sulcus joined the confluence of the main tendon and the third head. In addition, the left third head gave a slip to the posterior fascia of pronator teres forming a tunnel for the median nerve and brachial artery where it was compressed. The accessory biceps reported by Ozan et al⁴ arose from the tendon of deltoid and it gave three slips in the cubital fossa, two of these joined the bicipital aponeurosis and the third the ulnar head of pronator teres. Median nerve compression could be felt during supination of the forearm⁵.

In our case the accessory biceps was present bilaterally with similar proximal attachments from the shaft of humerus just superomedial to brachialis and lateral to the lower end of coracobrachialis. The left and right muscle then formed independent bellies and tendon which ran alongside the main belly. The left muscle⁶ inserted to the medial border of radius 2.5 cm below the radial tuberosity while the right muscle was attached to the radial tuberosity with the main tendon of its respective side. Both muscles gave fibrous slips which joined the bicipital aponeurosis of the respective sides. The muscles received innervation from branches of musculocutaneous nerve. The bilaterality as well as its mode of insertion is rare. This muscle⁶ can enhance the power of elbow flexion and supination of the forearm. The knowledge of such entities can be helpful to the surgeons as this region is prone to fractures and the accessory muscle can be used in free muscle transplantation for the elbow flexion.

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KIKUCHI-FUJIMOTO DISEASE IN YOUNG MALE : A CASE REPORT

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Abstract: A 23-year-old male presented with fever, cough and lymphadenopathy of one months' duration. Lymph node biopsy revealed a diagnosis of Kikuchi's disease. Although the disease has been recognized worldwide, to our knowledge no cases have been reported previously from Vidharbha region.

Keywords: Kikuchi-Fujimoto disease, Histiocytic necrotizing lymphadenitis.

INTRODUCTION

Kikuchi-Fujimoto disease- KD (histiocytic necrotizing lymphadenitis) was first described in Japan in 1972 and is now recognized worldwide¹ with a higher prevalence in the east Asian population there have been sporadic case reports from Europe and America and by late 1994 there had been some 120 cases described in the world literature²⁻³. It is a benign disorder, predominantly affecting young women with a predilection for cervical lymphadenopathy. It is a distinct clinicopathological entity of unknown etiology. About 16.6% to 40% of patients with KD are reported to have cutaneous involvement⁴. No diagnostic laboratory tests are available for KD. The definite diagnosis of KD can be made reliably only via histopathologic study from an open biopsy of the affected lymph nodes. The intermingling of distinctive crescentic histiocytes, karyorrhectic debris, and plasmacytoid monocytes in the form of nodules and the paucity of neutrophils are consistent findings that should permit a confident histopathologic diagnosis of KD⁵.

CASE REPORT

A 23-year-old male presented to us with fever, cough and lymphadenopathy of one month duration. Firm, discrete, non-tender lymphadenopathy involving bilateral deep cervical and left axillary groups was present. Vitals was stable. Systemic examination did not reveal unusual findings. His hematological investigations showed anemia (Hb, 8 g%), leucopenia (total leucocyte count, 3,200/cmm) and mild thrombocytopenia (platelet count, 1,10,000/cmm); the ESR was 95 mm/h and direct coombs test was negative. Urine analysis showed traces of proteins and the 24-hour urine protein was 164mg. The blood glucose, liver function tests, blood urea, serum creatinine, and ECG were normal. A chest X-ray and ultrasonography of abdomen were normal. Blood VDRL, HIV(ELISA), Mantoux test and rheumatoid factor were negative. FNAC of the axillary lymph node was suggestive of Kikuchi's disease. Hence excision biopsy was performed which revealed a dense inflammatory infiltrate and fibrosis. The infiltrate was characterized by lymphoid tissues with germinal centers and numerous eosinophils with eosinophilic microabscess formation. A proliferation of small venule-sized vessels was noted. There was no evidence of malignancy and no organisms were noted. The patient was started on antibiotics. After a follow up period of one month patient was symptomatically better. On clinical examination all the cervical and axillary glands disappeared; the antibiotics were then stopped.

DISCUSSION

Kikuchi-Fujimoto disease (KD) is now a well-known, benign, self-limiting disease. The youngest patient described to date was 8 years, 8 month old⁶. KD predominantly affects females (male:female ratio 1:4), with a mean age of 30 years. The disease commonly presents with cervical lymphadenopathy, which may be painless and isolated, or accompanied by diffuse lymphadenopathy, fever, chills, myalgia and non-specific skin

lesions. Systemic symptoms are severe when extra-nodal involvement is present. Although recurrences are possible, it clears spontaneously in 1-4 month⁷. This disease usually involves cervical lymph nodes; however, involvement of axillary, mesenteric, mediastinal, inguinal, intraparotid, iliac, celiac, and peripancreatic lymph nodes has been reported as well^{3,8,9}. The cause of this rare, self-limiting disease remains unknown. It may be due to a hyperimmune reaction to an infectious agent. Several infectious agents, including Epstein-Barr virus, HHV-6, HIV, Parvovirus b19, Yersinia, and Toxoplasma have been suggested⁷.

Clinically, tuberculous lymphadenitis remains a major differential diagnosis, especially in developing countries like India. Patients may be empirically started on antituberculous therapy (ATT), with no significant response. Biopsy of the lymph node reveals the actual diagnosis¹⁰. The clinical manifestations include lymphadenopathy, fever, cutaneous erythema, diarrhea, vomiting chest pain, arthralgia, and hepatosplenomegaly³⁻⁵. Patients with Kikuchi-Fujimoto disease may develop anemia, leukopenia, atypical lymphocytosis and raised erythrocyte sedimentation rate¹¹. Histologically, KD has to be differentiated from India and¹². KD is self-limiting, as spontaneous improvement and disappearance of symptoms frequently occur within 1 to 6 months of initial onset. However, recurrence of lymphadenopathy; and fatal cases have been reported¹³. Corticosteroids are suggested as an appropriate treatment¹². Recent therapeutic options for KD include ciprofloxacin¹⁴, chloroquine and hydroxychloroquine¹⁵. Response to antimicrobials suggests a possible microbial etiology^{14,15}; KD should be considered in the differential diagnosis of cervical lymphadenopathy.

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OXYGEN THERAPY : STATE OF ART

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Abstract: The primary goal of oxygen therapy is to correct alveolar and or tissue hypoxia. Oxygen is a drug. Unlike most pharmaceutical agents, oxygen either has been taken for granted or ignored as a therapeutic drug. It should be prescribed in a dose and therapy has to be continuously monitored and dose adjusted to ensure adequate oxygenation and to save precious oxygen from wastage. The oxygen therapy should be evaluated clinically and by the help of pulse oximeter. At the same time, oxygen toxicity, although, uncommon occurring in many forms, must be kept in mind.

INTRODUCTION

Oxygen (O₂) therapy has played a vital role in health care since the early nineteenth century. After the introduction of oxygen as the therapeutic agent by Alvin Barach¹, it has been widely available and frequently used. The delivery of O₂ to the tissues depends upon adequate function of cardiovascular (cardiac output and flow), hematological (Hb and its affinity for O₂) and the respiratory (arterial O₂ pressure) systems. Thus tissue hypoxia is not only relieved by O₂ therapy but it needs functioning of all three oxygen systems². Though the advances in respiratory therapy have made it possible to administer O₂ properly and assess its effectiveness through invasive and non-invasive means, yet very few physicians, nurses and allied health professionals understand O₂ therapy³. Very few prescriptions in hospital practice specify the correct dosages and methods of administration of oxygen. Many workers^{4,5,6,7} have reviewed the role of oxygen therapy and its toxicity in various clinical situations in the past. Through this article, an attempt has been made to further review in great details the physiology of tissue oxygenation, current indications and guidelines of O₂ therapy, role of short term/long term O₂ therapy, administration devices and pathophysiological basis of O₂ toxicity with its overuse.

PHYSIOLOGY OF O₂ DELIVERY AND UPTAKE

Oxygen is the second most common gas forming the normal external air (20.93%), preceded only by nitrogen (78.10%). O₂ is vital to sustain life. The partial pressure of O₂ in inspired air at sea level is about 160 mmHg. Total body O₂ uptake (VO₂) is the difference between total O₂ delivery and the amount of oxygen that returns in the mixed venous blood and is given by $VO_2 = Q_t X (CaO_2 - CVO_2)$, where Q_t is the cardiac output and CaO₂ and CVO₂ are O₂ contents of arterial and venous blood respectively. The O₂ uptake is determined by cellular O₂ demand. When total O₂ delivery falls to a certain level, which differs from organ to organ, it results in decreased O₂ uptake (VO₂) and tissue hypoxia. The cellular O₂ tension at which tissue hypoxia begins to develop is known as critical O₂ tension and is usually less than 5 mmHg⁸. The main consequence of hypoxaemia is tissue hypoxia, which usually manifests as organ dysfunction and/or metabolic acidosis. Acute hypoxaemia leads to series of physiological responses which increase the O₂ delivery to tissues⁹. The dissociation and the binding of oxygen by haemoglobin are not directly proportional to the pO₂ of its environment but instead exhibit a sigmoid-curve relationship, i.e. the haemoglobin-oxygen dissociation curve.

The shape of this curve is very important physiologically, as it permits a considerable amount of oxygen to be delivered to the tissues with a small drop in oxygen tension. For example, in the environment of lungs, where the partial pressure of oxygen (oxygen tension), measured in millimeters

of mercury (Hg), is nearly 100 mmHg, the haemoglobin molecule is almost 100% saturated with oxygen (point A, as shown in Figure I). As the RBC travels to tissues where the partial pressure of oxygen drops to an average 40 mmHg (mean venous oxygen tension), the haemoglobin saturation drops to about 75% saturation, releasing about 25% of oxygen to tissues (point B). In situations such as hypoxia, a compensatory "shift to the right" of haemoglobin-oxygen dissociation curve occurs to alleviate a tissue oxygen deficit (Figure 2).

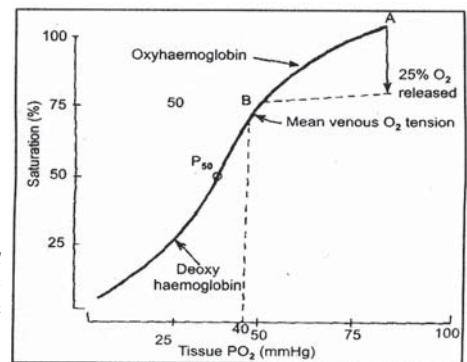


Fig. I
Showing normal
haemoglobin-
oxygen
dissociation curve

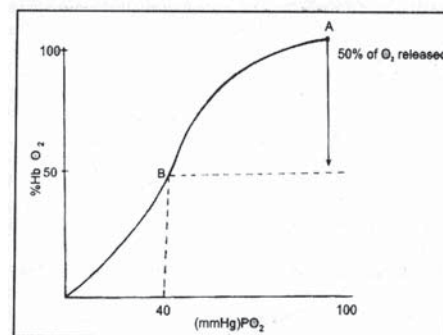


Fig. 2 Showing
right-shifted
haemoglobin-
oxygen
dissociation
curve

This rightward shift of the curve, mediated by increased levels of 2,3-DPG results in a decrease in haemoglobin's affinity for the oxygen molecule and an increase in oxygen delivery to tissues. Note that the oxygen saturation of haemoglobin in the environment of the tissues [40 mm Hg pO₂ (see point in the Figure II)] is now only 50%; the other 50% of the oxygen is being released to the tissues. The RBCs thus have become more efficient in terms of oxygen delivery. Thus, a patient who is suffering from anaemia due to loss of RBCs may be able to compensate by shifting the oxygen dissociation curve to the right, making the RBCs, while few in number, more efficient. Some patients may be able to tolerate anaemia better than others because of the compensatory mechanism. A shift to the right may also occur in response to acidosis or a rise in body temperature. This shift to the right of the haemoglobin-oxygen dissociation curve is

only one way in which patients may compensate for various types of hypoxia. Other ways include an increase in total cardiac output and increase in erythropoiesis.

A "shift to the left" of the haemoglobin-oxygen dissociation curve leads to an increase in haemoglobin-oxygen affinity and decrease in oxygen delivery to tissues (Figure 3).

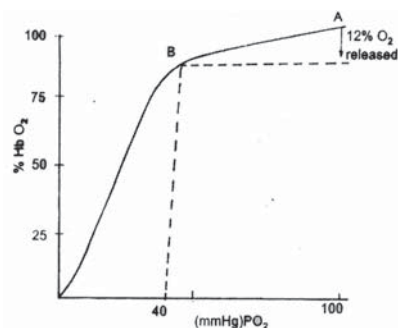


Fig. 3 Showing left shifted haemoglobin-oxygen dissociation curve

With such a dissociation curve RBCs are much less efficient since only 12% of oxygen can be released to the tissues (point B). Various conditions associated with this left shift include alkalosis, increased quantities of abnormal haemoglobins; such as methaemoglobin and carboxy haemoglobin; increased quantities of HbF; or multiple transfusions of 2,3-DPG-depleted stored blood.

TYPES OF HYPOXIA

Clinically hypoxia is of 4 types:-

A) HYPOXAEMIC HYPOXIA: Hypoxia is lack of O_2 at the tissue level while hypoxaemia means a low arterial O_2 tension below normal expected value (85-100 mmHg). A precise PaO_2 which will result in hypoxia can not be identified because various other factors (like Hb, oxyhaemoglobin affinity, cardiac output) interact in a complex manner to deliver O_2 to the tissues. In most of the clinical situations, the direct determination of PaO_2 and arterial O_2 saturation are the only parameters available to the clinician¹⁰. Hypoxaemia may be mild, moderate or severe. Mild hypoxaemia i.e. $PaO_2 = 60-79$ mmHg is generally not associated with hypoxia but O_2 therapy may be useful in reducing the strain on cardiopulmonary system. Moderate hypoxaemia (i.e. $PaO_2 = 45-59$ mmHg) may be associated with tissue hypoxia if cardiovascular system is unable to provide increased cardiac output to meet the tissue O_2 demands. Thus the presence of hypoxaemia does not necessarily indicate the presence of hypoxia. In other situations, hypoxia may be present in the absence of hypoxaemia such as in severe anaemia. Severe hypoxaemia (i.e. $PaO_2 = 45$ mmHg) is always associated with hypoxia and needs correction without delay.

Various causes of hypoxaemia:

- 1. Relative shunting:** In this the amount of O_2 available in alveolar capillary units is insufficient (i.e. low PaO_2) to oxygenate the normal volume of blood perfusing alveoli resulting in low ventilation perfusion ratio. Hypoxaemia due to relative shunting in obstructive airway diseases is usually corrected by O_2 therapy, increased O_2 supply and partial pressure in units with relative shunting.
- 2. Defective ventilation (hypoventilation):** Various causes are:-
 - a) Respiratory centre depression e.g. (i) drugs such as narcotics, anaesthetics and sedatives (ii) cerebral infarction (iii) cerebral trauma.
 - b) Neuromuscular disorders i.e. (i) myasthenia gravis (ii) Guillain-Barre syndrome (iii) brain or spinal injuries; (iv) polio, porphyria, botulism etc.
 - c) Airways obstruction: (a) COPD (b) acute severe asthma
 - d) Restrictive defects; (i) interstitial lung disease; (ii) kyphoscoliosis,

ankylosing spondylitis (iii) severe obesity; (iv) bilateral diaphragmatic palsy.

O_2 therapy corrects hypoxaemia associated with hypoventilation but does not correct hypercarbia and acidosis associated with hypoventilation.

3. Diffusion defects (impaired diffusion and gas exchange):

Various causes are: (a) pulmonary oedema (b) acute respiratory distress syndrome (ARDS) (c) pulmonary thromboembolism (PTE) (d) pulmonary fibrosis

O_2 therapy in such conditions increases PaO_2 thereby increasing the driving pressure of O_2 across the alveolar capillary membrane.

4. Ventilation perfusion abnormalities: Various causes are (i) COPD (ii) pulmonary fibrosis (iii) ARDS (iv) PTE.

5. Absolute shunting: O_2 therapy is usually ineffective to correct hypoxaemia due to absolute shunting because O_2 never reaches blood which is perfusing collapsed or consolidated alveoli as seen in pulmonary edema. However O_2 therapy is given in cases of absolute shunting because probably there is some relative shunt component in all hypoxaemia¹⁰.

B) ANAEMIC HYPOXIA: It is due to decreased O_2 carrying capacity of blood due to low Hb or decreased ability of Hb to carry O_2 in conditions like carbon monoxide poisoning and methemoglobinemia. O_2 therapy in anemic hypoxia produces little benefit by increasing O_2 content through small increase in dissolved O_2 at higher PaO_2 ¹¹.

C) CIRCULATORY HYPOXIA: It is due to arterial - venous shunting as in sepsis or capillary stagnation of blood on account of low cardiac output. It is rarely associated with hypoxaemia. O_2 therapy produces only marginal benefit.

D) HISTOTOXIC HYPOXIA: It is due to inability of the tissues to utilize available O_2 , as seen in cyanide poisoning.

EFFECTS OF HYPOXIA

The general features attributable to mild to moderate hypoxaemia are restlessness palpitation, sweating, altered consciousness, headache, confusion, tachypnoea and tachycardia, occurring as a result of vasoconstriction of vascular beds supplying skin, muscles and abdominal viscera as well as vasoconstriction of pulmonary vascular beds. Severe hypoxia may result in cyanosis, bradycardia, hypertension and or hypotension, somnolence and confusion. Hypercapnia accompanies hypoxaemia in conditions responsible for defective ventilation or hypoventilation as listed above.

INDICATIONS FOR OXYGEN THERAPY

Oxygen can be administered either as high or low concentration in all the conditions associated with hypoxaemia. In conditions like COPD in which there is a risk for hypercarbia, low concentration should be used. In acute lung conditions (without underlying chronic lung disease) like pulmonary embolism, pneumonia, tension pneumothorax, acute severe asthma, pulmonary edema or myocardial infarction, a higher concentration of O_2 can be given. Similarly in fibrosing alveolitis, there is no retention of CO_2 , so high concentration can be given as in such conditions, there is no risk of induction of hypoventilation. Maintaining PaO_2 above 60 mmHg gives O_2 saturation of 90%. During acute exacerbation of COPD, chemoreceptor drive for ventilation is eliminated which leads to reduced alveolar ventilation. Hypoxaemia should be reduced immediately by giving O_2 generally in a concentration of 24% to improve oxygenation without losing the respiratory stimulant effect. O_2 can be given as short term or long term therapy.

INDICATIONS OF SHORT TERM OXYGEN THERAPY

a) Hypoxia: As explained earlier, hypoxemia is the major indication for O_2 therapy. Severe hypoxaemia (PaO_2 45 mmHg) is almost always associated with tissue hypoxia and needs correction without delay. In mild and moderate hypoxaemia, tissue hypoxia may be prevented by appropriate response of cardiopulmonary system. O_2 therapy in such cases decreases the "excessive work of breathing and excessive myocardial work". Hypoxaemia due to relative shunting responds

best to O₂ therapy followed by hypoxemia due to impaired diffusion as explained earlier.

- b) **Acute myocardial infarction:** Therapeutic or prophylactic use of low flow oxygen 2 lits/min should be used routinely. However there is lack of data to suggest that acute O₂ therapy alters the mortality in acute uncomplicated MI.
- c) **Co-poisoning and carboxyhemoglobinaemia:** In Co-poisoning, the O₂ transportation is reduced by formation of carboxyhemoglobin and also release of O₂ to the tissues is reduced by shifting of O₂ dissociation curve to the left. The administration of high concentration (100%) O₂ decreases the half life of carboxyhemoglobin from 320 minutes to 60 minutes and increases the total arterial O₂ content by increasing the dissolved O₂ and also increased PaO₂ helps in dissociation of Hb Co. By using hyperbaric oxygen, the results achieved are faster¹².
- d) **Methemoglobinaemia:** 100% oxygen is the treatment of choice while reversing the cause of methemoglobinaemia.
- e) **Sickle cell crisis:** Although the clinical response to supplemental O₂ is variable, initial therapy with 100% O₂ is advisable.
- f) **Spontaneous pneumothorax and pneumomediastinum:** In pneumothorax less than 15% of hemithorax, the rate of pleural air absorption can be increased using 100% of oxygen. It increases ten times the gradient for movement of gas from capillaries in parietal and visceral pleura to air in pleural cavity by replacing nitrogen with oxygen in capillaries¹³. Such a modality should not be used beyond 12-16 hours to avoid oxygen toxicity.
- g) **Gas gangrene:** If available hyperbaric O₂ is life saving in treating patients seriously infected with clostridium perfringes. Increased O₂ tension in tissues can inhibit the growth of organisms and toxin production¹⁴.
- h) **Severe pneumonia:** In severe acute bacterial or viral pneumonias, there may be hypoxaemia and respiratory failure. O₂ is given at a flow rate of 4-6 L/min to achieve PaO₂ above 60 mmHg. Bronchial hygiene and treatment with antibiotics and other drugs is further continued.
- i) **Interstitial lung disease:** Patients may have respiratory failure due to fulminant onset or because of intercurrent infection. The lungs are stiff and have low compliance. As these patients need oxygen for prolonged periods, one should wean oxygen to FiO₂ of about 40% as early as possible. Some patients may become dyspnoeic even after mild exertion and such cases benefit from O₂ administration before and after physical activity.
- j) **Acute severe bronchial asthma (status asthmaticus):** These patients have severe airways obstruction and inflammation. They are usually having hypoxaemia which is corrected by giving O₂ at a flow rate of 4-6 L/min to achieve FiO₂ of 35-40%. Flow rate may be adjusted to maintain PaO₂ of about 80 mmHg or more. The risk of hypercarbia and Co₂ narcosis is more in COPD rather than acute severe asthma and such cases need assisted ventilation. Sedatives and tranquilizers should never be given since they may precipitate Co₂ retention in patients of COPD and bronchial asthma.
- k) **ARDS:** In such cases to correct hypoxaemia, ventilator controlled administration of O₂ often with PEEP (positive end expiratory pressure) is required. The desirable PaO₂ of about 60 mmHg with lowest possible FiO₂ is achieved with PEEP of about 10-15 cm H₂O. After the initial 24 hours, FiO₂ should not exceed 60% (to reduce the risk of O₂ toxicity).
- l) **Pulmonary thromboembolism:** Hypoxaemia in the presence of pulmonary thromboembolism is common but not essential. O₂ is required when there is breathlessness and hypoxaemia which depends upon the amount of pulmonary circulation occluded. Pulmonary infarction is prevented by alveolar oxygen and systemic bronchial vascular anastomosis which can be enriched with O₂ therapy.

Goals of Oxygen therapy : The goal is to relieve hypoxaemia by increasing

alveolar tension, to reduce the work of breathing and to decrease the work of myocardium. Oxygen should be used like a drug and its dose should be individualized. Arterial blood gases should be measured repeatedly in patients with acute respiratory failure on O₂ therapy. The goal is to maintain PaO₂ above 60 mmHg. O₂ should be given in low dose continuously since small increase in FiO₂ causes increase in PaO₂ as most patients of COPD lie on the steep part of haemoglobin dissociation curve¹⁵.

INDICATIONS OF LONG TERM OXYGEN THERAPY (LTOT)

This should only be prescribed for patients who have been on maximal medical therapy for atleast 30 days prior to ordering oxygen¹⁶. LTOT may be *continuous, nocturnal or exercise*. **Indications for continuous LTOT** :- (i) PaO₂ ≤55 mmHg measured at rest during non-recumbent position. (ii) PaO₂ 56-59 mmHg with evidence of organ dysfunction (secondary pulmonary hypertension, corpulmonale, secondary erythrocytosis, CNS dysfunction) attributable to hypoxia.

Indications for nocturnal LTOT¹⁸: PaO₂ ≤55 mmHg (or SaO₂ ≤88%) during sleep associated with organ dysfunction attributable to hypoxia.

Indications for exercise LTOT¹⁸: PaO₂ ≤55 mmHg (or SaO₂ ≤ 88%) during exercise. Thus the indications of LTOT are broadly summarized as :- 1) Common pulmonary conditions which require LTOT: (a) COPD (b) Diffuse interstitial lung disease (c) Cystic fibrosis (d) Bronchiectasis. 2) Non-pulmonary conditions which may require LTOT includes: (a) Pulmonary hypertension (b) Recurrent CHF due to cor-pulmonale (c) Erythrocytosis.

O₂ dosage in LTOT: COPD patients are given O₂ at the rate of 1-2 L/min. Some of the patients with chronic respiratory diseases may require high flow rates. PaO₂ should be maintained at 60 mmHg or so. During sleep or exercise or other activities, flow rate may be increased by 1-2 L/min.

Benefits of LTOT: Its benefits are documented in patients with COPD and other chronic pulmonary disease with hypoxaemia as it increases their survival and quality of life. Patients of interstitial lung disease become comfortable and there occurs improvement in pulmonary hypertension and right heart failure.

OXYGEN DELIVERY SYSTEMS: The oxygen therapy can be administered from an O₂ concentrator in the form of compressed gas or liquid O₂ enricher. The advantages and disadvantages of various oxygen sources are summarized in the following Table.

Table : O₂ delivery systems

System	Advantages	Disadvantages
Cylinders	O ₂ can be stored indefinitely. Can be used with O ₂ conserving canulas and diamond valves. O ₂ concentration constant, useful for bed ridden patients and have low cost.	Heavy, non portable, must be stored securely
Concentrators	Less expensive, some models are small enough to use for travel; they are useful for bed ridden patients	Require electricity, filter changes and regular maintenance; noisy; cost may be high. O ₂ concentration declines as flow rate increases. limited flow rates available.
Liquid	Extremely portable; useful for ambulatory patients including those who have to remain away from home for work; require little maintenance. O ₂ concentration constant and provides O ₂ at the rate of 2 L/min for about 6-9 hours; O ₂ delivered from a stationary source.	Costly; excess venting may pose a fire hazard; potential for skin burns from extreme cold temperature; requires regularly scheduled deliveries.
Enrichers	Because of lower concentration, no risk of fire; does not require regular deliveries	Because of the lower concentration, must use higher flow rates to provide sufficient oxygenation; these higher flow rates may be incompatible for some patients, require electricity, may be costly in high energy cost areas, require regular services.

Usually there are 2 types of O₂ delivery systems i.e. **high flow systems and low flow systems**. High flow systems provide higher and more reliable FiO₂ levels so as to completely satisfy the patient's inspiratory demand¹⁹. The low flow system entrain or uses room air and provides low flow from an exogenous O₂ source and thus is insufficient to meet all inspiratory requirement⁷.

High Flow Oxygen Systems

In this delivery system, the patient is breathing only the gas which is supplied by the apparatus. Both high and low O₂ concentration can be administered by this system. Most high flow systems use a **Venturi device** or **Venturi mask**. It fits lightly over the nose and mouth. It is based on the Bernoulli principle which states that lateral pressure of a gas decreases as its velocity of flow increases. Thus O₂ flowing at a high velocity in the form of a jet through a narrow orifice to the base of the mask creates negative pressure, entraining atmospheric air through the perforation in the face piece. They are available in different forms and can deliver low fixed concentrations of oxygen at 24%, 28%, 35%, 40% and 60%. It is essential for the success of these masks that the total flow is in excess of the peak inspiratory flow throughout the respiratory cycle²⁰. FiO₂ can be calculated by the formula $20+4 \times O_2 \text{ flow (L/min)}^{21}$.

Low Flow Oxygen Systems

As described earlier, this system does not fulfil total inspiratory requirement and part of tidal volume must be supplied by breathing room air. The factors controlling the oxygen concentration in this system include (a) capacity of available reservoir (b) oxygen flow rate (L/min) (c) patient's ventilatory pattern. Thus FiO₂ in this system varies considerably with changes in tidal volume and ventilatory pattern. The longer the tidal volume, the lower the FiO₂ or the smaller the tidal volume, the higher the FiO₂. Various devices used in this system are:-

- 1. Nasal canulae:** They are the simplest of all low flow system devices. They are cheaper, comfortable and patient is able to eat or speak. With nasal canulae, flow rate varying from 1-6 L/min, O₂ concentration varying from 24-44% is delivered depending upon patient's ventilatory system. These can be easily used for domiciliary O₂ therapy. In hospitalized patients, these canulae with soft pronged plastic tubes are inserted about 1 cm in each naris. O₂ has to be humidified while using these canulae²². The disadvantages are nasal irritation, otic lesions and contact dermatitis.
- 2. Nasal catheter:** The light rubber nasal catheter is inserted after lubricating its tip with liquid paraffin until the tip is visible behind the uvula in the oropharynx.
- 3. Simple O₂ masks:** A nasal canula with more than 6 L/min flow does little to increase inspired O₂ concentration, mainly because the anatomic reservoir is filled². To provide higher FiO₂ with flow system, the size of O₂ reservoir can be increased by placing a mask over nose and mouth. The flow rate with mask should never be less than 5L/min in order to prevent rebreathing. Above 5 L/min, most of exhaled air will be flushed from the mask. With simple O₂ masks, flow rate varying from 6-8 L/min, O₂ concentration varying from 40-60% is delivered.
- 4. Partial rebreathing masks:** To deliver more than 60% of O₂ by a low flow system, the capacity of O₂ reservoir needs to be increased. This is possible by attaching a reservoir bag to the mask. There is no one-way valve between the bag and mask in partial rebreathing mask. The O₂ flow rate should be between 6-10 L/min and bag must never be collapsed during inspiration to prevent CO₂ build up in system. With this flow rate, the very early exhaled air (the first one third of expiration) will go back into the bag and remaining two thirds of tidal volume (alveolar gas) will escape into the atmosphere via expiratory parts of the mask²³. This theoretically decreases the amount of O₂ required by one

third.

- 5. Non-breathing masks:** They prevent retrograde flow of expired gas into the reservoir bag. The flow of O₂ should be sufficient to maintain an inflated reservoir bag. Depending on patient's ventilatory pattern, a near FiO₂ of 1.0 is delivered to the patient.
- 6. Oxygen conserving canulas:** They are capable of delivering high flow oxygen, require less O₂ and portable systems last longer. But disadvantages include heavy weight and cosmetically apparent due to larger construction.
- 7. O₂ demand devices:** They share same advantages as with O₂ conserving canulas and are used with a nasal canula. But disadvantages include different flow patterns and create big noise.
- 8. Transtracheal oxygen:** It does not cause nasal irritation, otic lesions and contact dermatitis. It conserves oxygen, improves exercise tolerance. Patient's appearance is improved. But disadvantages include high cost, increased chances of infection at the site and mucous balls causing sudden choking and death.
- 9. Oxygen to tracheostomy via aerosol device:** It supplies humidified oxygen but drawback is non-portable and requires frequent analysis of FiO₂.

Despite the fact that high flow systems are accurate and their use is advocated by some clinicians²⁴, yet low flow systems are widely used since they are simple to use and provide more comfort to the patient.

PERSPECTIVES OF DOMICILIARY OXYGEN USE IN INDIA

The aim of O₂ therapy at home is to make the patient active and encourage exercise and other activities outside home. The use of domiciliary O₂ use in India is mainly limited to cities and thus more people are using this facility with increased compliance. At present there is no organized supply of O₂ and the cost is high. Supply is difficult in rural areas. Patients of COPD with hypoxaemia at rest, having arterial PaO₂ <55 mmHg or patients with cor pulmonale or secondary polycythemia having PaO₂ between 55-59 mmHg in a stable clinical state need home oxygen. O₂ systems available for use at home include gas cylinders, concentrators, liquid system and enrichers. The patients have to be selected carefully taking into account their education, income and social status. But there is definite improvement in the quality of life and life span of the patients despite the fact there is still irregular and inadequate treatment. Other limitations include difficulty in procurement of O₂, lack of medical expertise and no clear cut policy on reimbursement to employees.

DANGERS OF OXYGEN THERAPY (OXYGEN TOXICITY)

O₂ therapy is a hazard especially in intensive care units, where O₂ therapy may be administered over a period of days. O₂ toxicity usually manifests in one of several forms including CNS, pulmonary and ocular manifestations especially in premature neonates. The major factors affecting the onset and severity of toxicity are the concentrations of the gas used, duration of exposure and the susceptibility of the individual person. Clinically O₂ toxicity can be divided into 2 groups; firstly in which the patient is exposed to very high concentrations of O₂ for short duration like in hyperbaric O₂ therapy and secondly where lower concentrations of the gas are used but for longer periods. These two can result in acute and chronic O₂ toxicity respectively. The acute toxicity has predominant CNS effects while chronic toxicity has predominant pulmonary effects^{25,26,27}.

- I. CNS toxicity "BERT effect":** Bert originally described that CNS toxicity occurred at O₂ pressure of >3 ATA, but it may even occur at lower pressures if exposure is prolonged. Early manifestations include twitching of perioral and small muscles of hand²⁸. Intense peripheral

vasoconstriction due to hyperoxia and diaphragmatic twitching can result in facial pallor²⁷ and "cogwheel breathing"²⁹ respectively. Continued exposure can result in nausea and vertigo followed by altered behaviour, clumsiness and finally tonic-clonic convulsions and the patient has no memory of the crisis^{27,30}. A neurogenic pulmonary edema associated with convulsions has also been reported³¹. The factors responsible for CNS toxicity include increased PaO₂, stress, fatigue, cold and dietary deficiency of trace elements like selenium, zinc and magnesium^{25,27,32}. CNS toxicity is mainly due to oxidation and polymerization of SH groups of enzymes leading to their inactivation, which further leads to cellular damage.

II. Pulmonary toxicity "Smith effect": It occurs after prolonged exposure to oxygen >0.5 ATA i.e. usually after 10 hours of oxygen at IATA²⁸. Prolonged and/or high concentrations of oxygen may damage the pulmonary epithelium, and inactivate the surfactant, form intra-alveolar oedema and interstitial thickening and later fibrosis, leading to pulmonary atelectasis³³. The lung lesions resemble those of paraquat poisoning³⁴. Clinically pulmonary toxicity is characterized by features of tracheobronchitis, ARDS and pulmonary interstitial fibrosis²⁸. In majority of patients, the symptoms of carinal irritation, uncontrolled coughing, chest pain and dyspnoea usually subside 4 hours after cessation of exposure³⁵.

III. Eye toxicity: It can occur in the form of myopia, reversible constriction of peripheral field of vision and delayed cataract formation. Patient can develop retrolental fibroplasia. Ocular effects may be more when the whole eye is exposed to high ambient oxygen concentration and pressure, as in an oxygen tent, rather than when hyperoxia occurs via arterial circulation, e.g. following oxygen administration via a facemask²⁷.

Retrolental fibroplasia: It is characterized by the presence of opaque membrane behind the lens. It is a major cause of blindness in infants, usually developing within 6 months. It is due to liberal administration of high oxygen concentration >40% for a prolonged period (1-2 days) following birth. Premature infants of less than 30 weeks of gestation or 1500 gms birth weight are more susceptible³⁶. They are also likely to develop chronic lung disease and intraventricular haemorrhage.

Pathophysiology of retrolental fibroplasia : Normally, retinal vascularization continues shortly after birth. High concentration of O₂ and/or prolonged exposure cause vasoconstriction especially in the temporal part of the retina, which is the last to be vascularized, and there is obliteration of the lumen due to anoxic endothelial damage. After withdrawal of O₂ therapy, regeneration of the vessels in the area occurs with extension into the vitreous beyond the retina. Dilatation and rupture of these vessels can result in vitreous or retinal haemorrhage, fibrosis and adhesions leading to retinal detachment and blindness.

IV. Toxic effects on other tissues: Hyperbaric O₂ therapy may cause abnormal RBC morphology with or without a reduction in circulation mass of RBC's²⁵. Rarely serous otitis media and dysbaric osteonecrosis may occur in astronauts²⁵.

V. Carbon dioxide narcosis: In patients with COPD, status asthmaticus, weakness of respiratory muscles (e.g. from polyneuritis, poliomyelitis or myasthenia gravis) and in those with central respiratory depression from narcotic poisoning, head injury or raised intracranial tension, the alveolar ventilation is inadequate to prevent a rise in the arterial carbon dioxide tension (PaCO₂). With increasing hypercapnia (usually V/Q mismatch), the respiratory centre becomes progressively more tolerant of CO₂ and its activity is maintained by the hypoxaemic drive reflexly through carotid and aortic bodies. A removal of this stimulus by O₂ administration reduces this ventilation still further with a consequent rise in PaCO₂. This produces syndrome of CO₂ narcosis with raised intracranial tension, characterized clinically by sweating, twitching, drowsiness, convulsions, papilloedema and coma. It is a serious complication³⁷.

Pathophysiology of oxygen toxicity It is due to free radicals production

such as superoxide anions, hydrogen peroxide and hydroxyl radicals formed when FiO₂ is high^{31,32}. These free radicals cause lipid peroxidation especially in cell membranes, inhibit nucleic acid and protein synthesis and inactivate cellular enzymes. Normally various antioxidant enzymes e.g. glutathione peroxidase, catalase and superoxide dismutase protect the body from these free radicals, but in hyperoxic situations, there is increased production of free radicals, leading to swamping of enzyme systems and ultimately free radicals escape inactivation²⁸. Oxygen toxicity can also be caused by non-radical mediated injury by cellular metabolic alteration or by enzyme inhibition. Glutamic acid decarboxylase enzyme is inhibited in CNS while low level of enzyme gamma aminobutyric acid (GABA) leads to seizures^{25,31}.

Other dangers of oxygen therapy 1. Physical risks: Oxygen being combustible, fire hazard and tank explosion is always there. It is more with high concentration of oxygen, use of pressure chambers and in smokers. The patient should be advised not to smoke in the presence of O₂. 2. Nasal irritation and painful ulcers of the nares: These are seen with catheters and masks and can be prevented by lubricating the nasal catheter with jelly.

MONITORING OXYGEN THERAPY

Oxygen therapy should be given continuously and should not be stopped suddenly until the patient has recovered, since abrupt discontinuation can wash out small body stores of O₂ resulting in fall of alveolar O₂ tension. The oxygen apparatus should have a flow meter to adjust the dose and the doctors should specify the dose (e.g. 2-3 L/min) by nasal cannula or face mask. Unfortunately most of flow meters are broken and O₂ flow is assessed by bubbling the cannula in a container containing water. This practice should be avoided. The oxygen apparatus should contain a humidifier bottle. The oxygen should bubble through the water in the humidifier bottle. The water in the humidifier bottle should be changed daily to prevent growth of bacteria. The dose of O₂ should be calculated carefully. Partial pressure of O₂ can be measured in the arterial blood. Complete saturation of hemoglobin in arterial blood should not be attempted. Arterial PO₂ of 60 mmHg can provide 90% saturation of arterial blood, but if acidosis is present, PaO₂ more than 80 mmHg is required. In a patient with respiratory failure, anaemia should be corrected for proper oxygen transport to the tissues. A small increment in arterial O₂ tension results in a significant rise in the saturation of haemoglobin. Under normal situations, no additional benefit is achieved by raising PaO₂ level to more than 60-80 mmHg. An increase of 1% oxygen concentration increases O₂ tension by 7 mmHg. Measurement of arterial blood gases repeatedly is difficult. So a simple and non invasive technique to assess O₂ therapy is the use of pulse-oximeter. Start with nasal cannula. Increase the flow rate till O₂ saturation is more than 90% or there is clinical improvement. If O₂ requirement is more than 8 L/min with face mask, start ventilation. Pulse-oximeter should not be the sole criteria for adjusting dose. Even if O₂ saturation is more than 90%, O₂ has to be given if the patient is breathless³⁸.

(a) Arterial blood gases (ABG): The most commonly used measures of gas exchange are partial pressures of O₂ and CO₂ in arterial blood i.e. PaO₂ and PaCO₂ respectively. These partial pressures do not directly measure O₂ or CO₂ content but rather measure driving pressure for gas in blood. The actual content also depends on stability of gas in plasma and the ability of any component of blood to bind with gas. The O₂ content can be calculated by the following formula in normal blood (at 37° C, pH 7.4) i.e. O₂ content = 1.34 x [Hemoglobin] x saturation + 0.0031 x Po₂. Since 1 gram of hemoglobin (Hb) carries 1.34 ml O₂ when fully saturated and amount of O₂ that can be dissolved in plasma is proportional to Po₂ with 0.0031 ml O₂ dissolved per deciliter of blood per mm Hg O₂. The measurement of O₂ saturation is also important for the determination of O₂ content.

(b) Alveolar Gas Equation: The assessment of oxygenation is the alveolar - arterial O₂ difference (P_A O₂ - P_a O₂) commonly called alveolar arterial O₂ gradient (or A - a gradient). For determination of (A - a) gradient, the

alveolar P_{O_2} (PA_{O_2}) is calculated by following formula called alveolar gas equation: $PA_{O_2} = FI_{O_2} \times (P_B - PH_2O) - Pa_{CO_2}/R$ where FI_{O_2} is fractional concentration of inspired O_2 ($=0.21$), P_B is Barometric pressure (about 760 mm Hg at sea level), PH_2O is water vapour (47 mm Hg when fully saturated at 37° C) and R is respiratory quotient (ratio of CO_2 production to O_2 consumption i.e. $N = 0.8$). After substituting values with patient breathing at sea level, equation becomes $PA_{O_2} = 150 - 1.25 \times Pa_{CO_2}$. The alveolar – arterial O_2 difference is then calculated by subtracting measured Pa_{O_2} from calculated PA_{O_2} . In healthy young person breathing room air the (A-a) gradient normally is less than 15 mm Hg (this value increases with age and goes up to 30 mm Hg in elderly).

PREVENTION AND MONITORING OF OXYGEN TOXICITY

Because the treatment is purely symptomatic, prevention and monitoring for early recognition of toxicity is of prime importance. The point of importance is that sudden stoppage of O_2 at the onset of toxicity, may sometimes aggravate the symptoms – “the oxygen off effect”²⁷. Monitoring of pulmonary toxicity is based on reduction (usually 10%) in the vital capacity of the patient^{27,35}. Other indicators of monitoring include reduced lung compliance and diffusing capacity for carbon monoxide. To predict pulmonary damage after prolonged O_2 therapy, unit of pulmonary toxicity dosage (UPTD) is calculated. One minute of 100% oxygen at 1 atmosphere is taken to produce 1 UPTD. A UPTD of 1425 will produce a 100% reduction in vital capacity²⁵. Electroencephalogram has no value in the monitoring of CNS toxicity²⁷. Exogenous antioxidants especially vitamin C and E may be used prophylactically in high risk infants. The recommended dose of vitamin E is 100 mg/kg/day for 4-6 weeks³⁷. Adrenalectomy, hypophysectomy and the hypothyroid state are associated with reduced severity of toxicity as is the use of alpha adrenergic blockers²⁷. Supplementation of dietary trace elements may be helpful in deficient states.

CONCLUSION

The beneficial effects of oxygen therapy have been extensively investigated in patients with COPD with hypoxaemia^{39,40}. The ability to provide supplemental oxygen is a powerful tool in the management of critically ill patients with many disorders. Its injudicious use may lead to toxicity of CNS, lungs, eyes and other tissues. But hypoxia must not be left untreated in view of toxicity since hypoxia is common and damage caused is severe and rapid in comparison to oxygen toxicity which is uncommon. The patient education is also an important aspect. The patient should clearly understand the oxygen prescription, the safety precautions to follow when using oxygen and expected benefit of oxygen therapy.

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HEPARIN IN THE TREATMENT OF ULCERATIVE COLITIS, DOES IT HAVE ANY ROLE?

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Abstract : Ulcerative colitis is an idiopathic, chronic inflammatory condition with increased prevalence in the western countries as compared to India. At present a number of drugs are available for the treatment of ulcerative colitis but still 15-20% patients require colostomy. Recently extensive experimental studies showed efficacy of heparin in this condition, but clinical trials in humans showed variable response as such there is a need of large randomized controlled trial to establish its efficacy.

Key words: Heparin, ulcerative colitis, inflammation

INTRODUCTION

Ulcerative colitis is an inflammatory disease, primarily involving the colonic mucosa; the extent and severity of colon involvement are variable. The incidence of ulcerative colitis in western countries is 6-8 cases per 1,00,000 populations approximately. Ulcerative colitis seems to be rare among South Asians residing in the Indian subcontinent but is common amongst migrants to developed countries. The reported incidence of ulcerative colitis from north India is 6.02 per 100,000. Despite intensive research, pathogenesis remains unclear, but certain features of the disease have suggested several possible areas of aetiological importance. Most emphasis has been given to the inflammatory hypothesis, suggested by heavy mucosal infiltration by inflammatory cells, inflammatory cytokines and increased mucosal permeability.

Drugs like 5-aminosalicylic acid (sulfasalazine), different antibiotics, corticosteroid, immunomodulatory drugs, and IgG anti-TNF α antibody infliximab (restricted use) have shown variable effectiveness, none of these induce complete remission; 15% patients need colostomy as a consequence of failed medical therapy. Apart from the anticoagulant action/anti-inflammatory property of heparin has been proved in several studies. Heparin is a member of a family of polysaccharides known as glycosaminoglycans. It is synthesized exclusively in the mast cells of lung, intestine and liver, the effects are mediated by its physicochemical properties of the compound rather than the specified pharmacological properties which depend upon the 3-D-sulfated group on glucosamine. Since this proteoglycan is present in varying structures and are capable of binding chemokines, various ligands, growth factor proteins, ECM, causing cell adhesion and can modulate a variety of biological events beyond simply serving as a non-thrombogenic surface. Leukocyte recruitment from the vasculature to the site of inflammation is one of the initial events in inflammation. Heparin has been shown to interfere with the key first step in leukocyte recruitment by inhibiting binding of P-selection and L-selection to rCAM-1 in vascular endothelial cells¹.

Heparin has been extensively studied in the experimental model. Russian scientists were the first to use unfractionated heparin in this drug as early as 1980 of unfractionated heparin in moderately severe non-specific ulcerative colitis; 8 mg produced rapid relief of rectal bleeding and colostomy rates decreased from 16% to 6%². Since then there have been several open uncontrolled studies employing both fractionated and unfractionated heparin^{3,4}. The study by Gaffney et al, showed positive clinical response in 9 of 10 patients with prolonged remission; steroids and/or sulfasalazine were continued. The only reported side effect was injection site haematoma in one patient and rectal bleeding increased in two patients in the first week of therapy. Similar protocol was followed in another open label study by Bazier et al. showed significant clinical improvement but one of them required surgery for major haemorrhagic complication LMWH has less effect on coagulation profile and bone mineralization compared to UFH and it is easy to use⁵.

The first randomized, multicentric, comparative trial was designed by Panes et al⁶. Comparison was made between intravenous methyl-prednisolone and heparin infusion in 25 patients. This study reported that monotherapy of heparin is not having any significant improvement over methyl prednisolone besides it increases bleeding complications. But the open label study by Bazier et al, had shown significant clinical improvement with UFH monotherapy though this study was conducted in small number of patients.

Vri et al⁶, enrolled active severe ulcerative colitis patients refractory to steroid

therapy daily. 20 out of 25 patients showed good improvement endoscopically and histologic features of inflammation improved but there was no significant reduction in the number of mucosal *micro* thrombi. No serious adverse events were noted and tolerability was excellent. The largest trial reported so far in 100 patients of mild to moderate ulcerative colitis who were treated with LMW heparin for six weeks showed no benefit of low molecular weight heparin over placebo in mild to moderately active ulcerative colitis⁸. (Table)

Table Clinical trials of heparin in ulcerative colitis patients

Authors	Study design	Patient Selection	Heparin and other treatment	Duration of Treatment	Result
1. Gaffney et al, 1995	Open label	10, poorly controlled UC	UFH, IV to SC along with sulfasalazine and prednisolone	6 months or more	Remission in 9 patients
2. Bazier et al, 1996	Open label	6, moderate to severe UC refractory to steroid	UFH, IV to SC. No other drugs allowed	4 weeks	Significant clinical improvement in 4 patients
3. Evans et al, 1997	Open label	16, active UC (relapse cases) unresponsive to high dose corticosteroid	UFH, IV to SC	12 weeks	Remission in 14 patients
4. Folwaczny et al, 1999	Open label	13, severely active UC, CD 12, mild to moderately active UC, refractory to steroid	UFH, IV then SC	8 weeks	Remission in 7, Remission in none
5. Torkvist et al, 1999	Open label	17 of UC, 3 of CD	LMWH, SC	12 weeks	Complete remission in 6 Symptomatic improvement in 5 patients
6. Ang et al, 2000	Randomized Controlled trial	25, moderate to severe UC	Heparin IV & SC, hydrocortisone And oral prednisolone	5 weeks	Equal efficacy with steroid
7. Panes et al, 2000	Multicentric Randomized comparative trial with blinding	25, moderate to severe UC	LMWH, IV infusion Vs Placebo IV infusion in addition to methyl prednisolone infusion	8 weeks	No significant benefit
8. Botan et al, 2001	Open label	12, UC patients with flare ups	LMWH, SC weekly all patients were taking high dose mesalazine	12 weeks	Clinical remission in 8 patients
9. Vrij et al, 2001	Open label	26, moderate to severe active steroid refractory UC	LMWH, SC BD	8 weeks	Improved clinical symptoms in all Patients
10. Bloom S et al, 2004	Randomized trial	100 patients of UC	LMWH Vs placebo	6 weeks	No benefit over placebo

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COMBATING DRUG ABUSE : ROLE OF COMMUNITY AND MEDICO-LEGAL PERSONNEL

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Abstract : *The problem of drug abuse is growing at an explosive rate world-over. Drug abuse refers to self-administration of a drug for reasons other than medical in an amount, strength, frequency or manner that damages the physical and or mental functioning. Substance dependence requires three or more of the symptoms are present. It mostly affects adolescents and young population in particular students community harming them both physically and mentally thus disrupting their peace and harmony. This calls for crucial role of the family, community, social organizations and medico-legal personnel apart from law enforcing agencies, doctors, psychologists, and psychiatrists. The marijuana group of drugs predominantly cause psychological dependence and can well be controlled by exercising strong will power and active co-operation of family members and community. The opioid group of drugs causes physical dependence and mainly requires prompt medical attention, close surveillance from the family and rehabilitation programmes for ex-drug takers under guidance of social or government organizations. The long-term goals of combating drug abuse include prevention, treatment and rehabilitation of drug abuser. Community, social organizations and Ministry of welfare are basically concerned with prevention and rehabilitation aspects of drug abusers. Preventive strategies should evolve programmes for creating drug awareness and about overall adverse consequences of drugs of abuse; identifying and motivating drug abusers to accept counseling and detoxification programmes; undertaking prolonged follow up for maintaining drug free life; and chalking out rehabilitation programmes in ex-drug takers for their social integration. The Ministry of welfare should establish more counseling and de-addiction centers along with rehabilitation programmes for the addicts. It is commonly observed that male drug abusers are more often rehabilitated by social organizations but female addicts are ignored despite the fact drug addiction stamps a greater stigma on them. The medico-legal personnel play a pivotal role to find out prevalence and involvement of various drugs of abuse amongst drug abusers, to identify toxicological features of drugs of abuse, to develop awareness programmes particularly about Narcotics and Psychotropic Substances Act and Prevention of Illicit Traffic in Narcotic Drugs and Psychotropic Substances Act for the general masses towards containing menace of drug abuse and finally advising the authorities e.g. State Police Administration, Narcotic Control Bureau, Central Police Organization etc.*

Drug abuse, a multidimensional and multifaceted social scourge is defined as the use, usually by self administration, of any drug in a manner that deviates from the approved medical or social patterns within a given culture. The term relates to taking a drug for reasons other than medical, in an amount, strength, frequency or manner that damages the physical and/or mental functioning.^{1,2}

The term addiction refers to compulsive drug use. The American Psychiatric Association (APA) defines substance dependence (addiction) as a cluster of symptoms indicating that the individual continues use of the substance despite significant substance related problems. Dependence (addiction) requires three or more of the symptoms whereas abuse can be diagnosed when only one or two symptoms are present.³

The problem of drug abuse is growing at an explosive rate and of late it has spread its malevolent tentacles to almost every part of the globe surmounting almost all barriers of race, caste, creed, religion, age, sex, educational status, economic strata etc. with astounding ease to the extent that no population is spared off this social evil. Surprisingly a large percentage of young individuals particularly students are being hooked on dependence producing drugs.^{4,5} Apart from oral and intravenous drugs of abuse, inhalant abuse, which elicits psychoactive effects and mostly affects adolescent and young population, is being visualized as an important drug abuse problem in our country.⁷

Drug abuse not only ruins both the addict and the family physiologically, socially and economically to the extent of causing disruption of peace, harmony and happiness, but also it creates major apprehension in the mind of peace loving citizens too.^{8,9}

Viewed in these perspective, one can easily visualize the crucial role of the family, community and social organizations, law enforcing agencies and medico-legal personnel apart from doctors, psychiatrists and psychologists.

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ROLE OF COMMUNITY IN COMBATING DRUG ABUSE

The community plays a precise and pivotal role in the management of drug abuse. The marijuana group of drugs like ganja, bhang, hashish, charas etc. are the most widely abused drugs.² These predominantly cause psychological dependence which can be eliminated by exercising strong will power together with the cooperation of the family members and community.⁸ The opioid group of drugs like opium, morphine, heroin, brown sugar etc. cause metabolic or physical dependence and it is extremely difficult to control this addiction on its own.^{1,2} This explains why parent's appeal, persuasion, pressure, coaxing, cajoling and even punishment failed to work. These cases require prompt medical attention along with constant surveillance and cooperation from the family and society at large.^{9,10}

The long term goals of combating drug abuse comprise of integrated measures for prevention, treatment and rehabilitation of drug abuser and finally to help the addict for reintegration into the society. Community, social organizations and Ministry of Welfare are basically concerned with prevention and rehabilitation aspects of drug abusers.¹¹

COMMUNITY VIS-À-VIS PREVENTIVE ASPECTS

The overall strategy for prevention involves an active cooperation of the family members and the community; an attention to aspects of social environments in which drugs are abused and developing preventive policies at community level. Social organizations should chalk out programmes for creating drug awareness in masses, identifying and motivating drugs abusers to accept counselling and detoxification programmes, formulating strategies to change life style of abusers, and to supervise a prolonged follow up for maintaining a

drug free life. Besides, evolving rehabilitation programmes for ex-drug takers.¹¹

A multitude of factors are responsible for drug abuse such as familial discord, social ostracism, stresses and strains of modern life, emotional insecurity, erosion in social and moral values, professional rivalry, apart from curiosity of floating high, dreamy and pleasurable sensations. Controlling these factors is an important facet of the preventive aspect of drug abuse.¹¹ A majority of these factors can tactfully be tackled by family members, social organizations and community as a whole.

Young girl abusers specially require proper attention for they are more complicated to deal with since they are drawn into 'drug-net' by their boy friends and usually afford drugs by indulging in prostitution or smuggling activities. In case of married ones, the husbands of some are joint parties to their addiction. They too require a community support.

Nevertheless, the Ministry of Welfare is the nodal agency for drug abuse prevention, it should establish more counselling and de-addiction centres along with rehabilitational programmes for addicts.¹¹ Community plays only a supportive role regarding prevention of drug trafficking or supply of illicit drugs. It should be tackled and controlled through strict legal actions, by adopting stringent measures for illegal cultivation of drugs of abuse and slapping penal actions against drug peddlers/drug launderers. Social workers and neighbours residing in the vicinity of illegal cultivation of drugs manufacture of drugs or drug peddlers can help a great deal by informing law enforcing agencies for their containment.¹¹

PSYCHOLOGICAL DEPENDENCE AND ROLE OF COMMUNITY

Although, strong psychological craving, disturbed emotional states, depressive or anxiety disorders require psychologist and psychiatrist help, yet family and voluntary social organizations definitely play a pivotal role on one or more of the following counts :

- (i) To create drug awareness and to convince those who use drugs, to quit.
- (ii) To warn drug addicts for the overall adverse consequences of drug abuse and its reflection on their quality of life and that they may lose their jobs too owing to drug abuse.
- (iii) To create awareness about transmission of HIV in intravenous drug abusers presumably owing to needle sharing behaviour.
- (iv) To dissociate the addicts from their social environment so as to prevent access to the drugs through friends or drug peddlers.
- (v) To boost drug addicts psychologically and to instill a feeling of security, confidence, mental and social well being.
- (vi) To dispel fear about poor self-image, feeling of despair, depression and anxiety.
- (vii) To create strong motivation for drug therapy/de-addiction.
- (viii) To cordon off ex-drug takers to prevent relapse.
- (ix) To protect especially female addicts from pressure tactics of drug peddlers / peers who thrust upon them prostitution or smuggling.
- (x) To promote yoga, meditation, religious conversations and socio-economic welfare programmes for the addicts/ex-drugs abusers.

PHYSICAL DEPENDENCE AND ROLE OF COMMUNITY

Since addiction to opiates develops very quickly, is very severe and dangerous, hence these cases initially require a comprehensive medical and neuropsychologist help and are best treated at specialized de-addiction centres.^{1,2} The family and social organizations step in as soon as the addict is detoxified or weaned away from the offending

drug, to impart integrated preventive measures so that addict is able to lead a healthy drug free life.

Besides, social workers and social organizations should adopt strict vigilance over hospitals and de-addicting clinics since these may be potential sources for the development of drug sub-culture owing to assembly of a large number of addicts with diverse addiction profiles. Lastly, the enlightened citizens should also actively contribute to prevention of drug abuse by keeping himself and his family away from 'drugs', by remaining alert to any request / suggestion to keep or carry 'drugs' to help others remain drug free and by informing law enforcing agencies for an effective elimination of this menace.¹¹

ROLE OF COMMUNITY IN REHABILITATION

A proper rehabilitation of addict is the crying need of hour. Since ex-drug abusers are often inadequately prepared for social integration owing to poor self esteem and /or vocational skills hence social acceptance and affection should be extended to drug abuser within a framework of discipline. Equally important is the attitude towards ex-drug abuser of his family members, neighbours, working colleagues, friends and society as a whole. Ex-drug abusers should be allowed to readjust to group living in the family/society and to reevaluate their goals and aims.¹¹

Although male drug addicts are more commonly rehabilitated by social organizations but the female addicts are ignored despite the fact that drug addiction stamps an even greater stigma on them. Rehabilitation of female addicts is a tedious and risky affair as during recovery their strong sexual urge come to the fore and the addict is driven to satisfy the same, therefore most rehabilitating centres have expressed their helplessness in handling the volatile consequences of this aspect.

In brief, not only an active participation of community through voluntary welfare organizations, social workers and family is desired for rehabilitation of addicts but also they should chart out a cohesive, concerted plan for an effective containment of drug abuse.¹¹

ROLE OF MEDICO-LEGAL PERSONNEL IN CONTROLLING DRUG ABUSE

In wake of dependence liability and other toxicological features of drugs of abuse along with self destructive behaviour of drug abuser culminate into a steep rise in suicide rates together with an escalating criminal violence have seized our attention to propound the crucial role of medico-legal personnel in containing menace of drug abuse.

It is exhilarating that our country has enacted very powerful, strict, deterrent laws pertaining to narcotics and related drugs i.e. Narcotics and Psychotropic Substances Act, 1985 with amendment in 1989 and Prevention of Illicit Traffic in Narcotic Drugs and Psychotropic Substances Act, 1988, to upset the appellation of 'Narco Power'. The law provides rigorous imprisonment ranging 10-20 years and a fine of Rs. 1-2 lacs or more. The maximum penalty provided for in the law includes death penalty without remission in respect to certain specified second offences. In light of the above, one prime sphere where medico-legal experts can actively and usefully contribute is to advise the authorities - State Police Administration, Narcotics Control Bureau, Narcotics Commissioner of India, Directorate of Revenue Intelligence, Central Economic Intelligence Bureau, Collectorate of Customs and Central Excise, Central Police Organization etc. who are empowered to take action under various provisions of the law.

An allround rising trend in drug abuse and its changing patterns owing to various responsible factors has also brought into limelight the prime role of medico-legal experts to explore prevalence and involvement of various

drugs of abuse like opium, morphine, heroin, cocaine, smack or brown sugar etc. amongst drug abusers together with inhalant drug abuse which usually does not draw legal actions.

Yet another responsibility of medico-legal personnel is that they should report to various toxicological features noticed once a drug abuser is using bizarre mixture/cocktail of 'drugs'. This will reflect to changing patterns of drug abuse and adverse effects in different groups of individuals.

Another sphere where medico-legal specialist play pivotal role is in creating awareness about deleterious and fatal effects of drugs of abuse in the society by furnishing detailed data on their toxicological adverse effects profile. Besides they can play an anchoring role by motivating addicts against induced disability by 'drugs'.

The medico legal experts are responsible for determining the cause of death particularly where cause of death cannot be pinpointed or where the cause is due to drug of abuse. Besides, they have to give their opinion about estimation of time since death which is important in all medico-legal cases. Every effort should be made to track down these cases to curtail under-reporting. Moreover, all poisoning death cases should be thoroughly probed for the involvement of 'drugs' so as to quantify their exact prevalence.

Obviously, the experts in the medico-legal field are the men of the crisis, their valuable services in the field of drug abuse are not only going to cast far reaching repercussions in the medical realm but also to carve out a niche in respect to social welfare and containment of drug abuse. It may be admitted that many precious lives that would otherwise be lost, can be saved by effectively combating the pernicious onslaught on the society by drug abuse. We hope that medico-legal personnel will live up to these expectations and their line of action in this direction will be worth noting.

CONCLUSIONS

Not only the gigantic problem of drug abuse is tearing the basic fabric of our culture and moral values but also the adoption of ostrich like approach by Ministry of Welfare and medical personnel in general to quell this social scourge is quite disheartening. Ruminating over this challenging subject, we suggest an active participation of community, social organizations and family as well as a predominant specific role of medico-legal specialist for an effective containment of menace of drug abuse.

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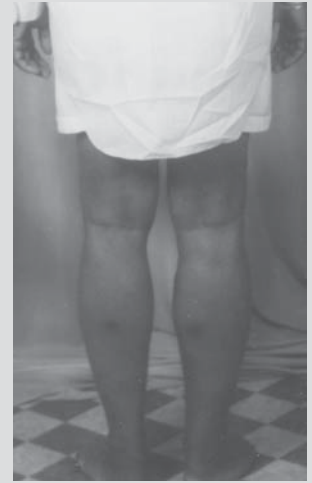
UNUSUAL PRESENTATION OF ABNORMAL THYROID STATE

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CASE I

A 38 years old male with history of delayed onset of puberty presented with features suggestive of myxedema which included generalized swelling, hoarseness of voice, constipation and cold intolerance. He also had muscle complaints in the form of muscle pain, cramps, stiffness and weakness (especially proximal muscle type). On examination, he had bilateral calf muscle hypertrophy (see photograph) with percussion myoedema, wasting as well as slowness of both contraction and relaxation phases of deep tendon reflexes. His thyroid profile revealed T3-42 ng/dl, T4-2.1 ug/dl, TSH-41.9µU/mL and CPK was 510 u/L. In this patient with features of myxedema and bilateral calf muscle hypertrophy, a diagnosis of **Hoffman syndrome** was made. In hypothyroid state, abnormalities of skeletal muscle include diffuse myalgia, stiffness, increased volume and slowness of contraction and relaxation. Cretinism in association with these abnormalities is known as **Kocher-Debre Semelaigne syndrome**. Thyroxine administration is known to correct these muscle disturbances.



Photograph of patient of myxedema showing bilateral calf muscle hypertrophy

CASE II



A 62 year old male patient, non smoker, non diabetic and vegetarian from Himachal Pradesh, presented with progressive swelling of legs for five years. He also complained of heat intolerance, palpitation increased appetite and loss weight seven years back. In view of the above history, a diagnosis of **thyrotoxicosis** was made. He was put on Tab. Carbimazole in adequate dosage and his symptoms subsided with the treatment beyond 6 months. He was subjected to subtotal thyroidectomy in the year 2000 with complete amelioration of symptoms. Four months following surgery, he complained of swelling and thickening of the skin on skin of tibia on the both legs. The swelling progressively increased to the present size. On examination, he was clinically euthyroid with a scar mark on the neck and prominent eyes. But he had no obvious exophthalmos. There was bilateral diffuse swelling of the legs in the anterior aspect (see photograph), which was non-pitting, coarse, dry, thick and was associated with peau-de-orange appearance. His Laboratory profile including T3, T4 and TSH levels were normal. The thyroid scan showed residual thyroid tissue. The skin biopsy showed diffuse fibro-connective tissue. This skin condition was **diagnosed as pretibial myxedema**. It is uncommon in Indian subjects and has no definite treatment except local application of corticosteroids. The patient was put on local corticosteroids but was unfortunately lost on subsequent follow up.

SYMPOSIUM : PREVENTION OF CHRONIC KIDNEY DISEASES IN INDIA

OUR GUEST EDITOR



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Dr. Sanjay K. Agarwal is currently working as additional professor in the department of nephrology at All India Institute of Medical Sciences, New Delhi. He did his graduation and post graduation in medicine from K.G's Medical College Lucknow. After doing his nephrology training from AIIMS, he is presently working as faculty member since 1989. He obtained many scholarships during his undergraduate and postgraduate training. He has many awards to his credit like National Merit Scholarship during schooling, Commonwealth Medical fellowship, SENIOR HOECHST LECTURESHIP ON DIABETES" by API, BC Bansal Oration and Khullar Oration by Indian Society of Nephrology, Membership of National Academy of Medical sciences, Fellowship of Indian College of Physician and International Medical science Academy. He is member of Project Review Committee of ICMR, CKD Collaborative Group" for making management guidelines for chronic kidney disease in India, Member of "CKD Registry group" in India, Ethics committee for Central Council for Research in Homeopathy.

He is regular reviewer for many national and international journals and is in editorial committee of many national journals. He has served as executive committee of many national nephrology societies. He has pursued 16 funded projects as principal investigator and has 134 publications to his credit, along with 14 chapters in books and guided 36 postgraduate theses. He is regular speaker in national and international conferences.

Other than interest in hepatitis and renal medicine, renal transplantation, his main area of interest is chronic kidney disease and its related issues. He has been invited to deliver "Key Note Address" on Diabetic Nephropathy in Type 2 : Current Status" at ICMR-WHO workshop on Guidelines for Management of Type 2 Diabetes held at Chennai. He has also been invited to represent India and deliver two guest lectures in the conference on " PREVENTION OF RENAL DISEASES IN THE EMERGING WORLD: TOWARDS GLOBAL HEALTH EQUITY" jointly organised by Rockefeller Foundation and International Society of Nephrology, to be held at Italy in 2004. He was recently invited to represent India for KDIGO (Kidney Disease Improving Global Outcome) controversy conference held at Amsterdam in 2006.

EDITORIAL

India, like many other developing countries has seen a rapid increase in the risk of chronic diseases and death during the past few decades. This increasing burden of chronic diseases along with existing burden of communicable diseases is straining already stretched health services of the country. This is leading to increase in economic burden; the increase that is best documented in relation to diabetes, stroke, cardiovascular disease and chronic kidney disease. In this regard, though diabetes, cardiovascular diseases and strokes are well recognized by the public, physicians and the government, *chronic kidney disease (CKD)* is still unrecognized as a major chronic disease responsible for economic load to the government. In 1998, World Health Organization mentioned the ten common causes of death in India and CKD never figured in that document. However, when one looks into the absolute number of death due to CKD, it is likely to be one of the common 5 causes of death in India. Similarly, if one look the medical curriculum of the undergraduates prescribed by the Medical Council of India, there is no mention of CKD as one of the topics to be covered.

Of the approximately 1 million people in the world with severe CKD who are being treated with some form of renal replacement therapy, 90% live in developed countries. As against this, only 5-10% of patients of end stage renal disease (ESRD) of the world getting some form of renal replacement therapy (RRT) live in developing countries. In India, of the approximately 1.5 Lakh new ESRD patients every year, only 5-10% get some form of RRT. Outcome of the rest of the patients of ESRD can easily be interpreted. Thus, it is obvious that country like India cannot afford to manage all patients of ESRD. Thus, prevention of CKD is a crucial issue not only for the medical fraternity but the government also. Of all the causes of CKD, diabetes and hypertension constitute approximately 60% cases of CKD. Both the diseases are also easy to diagnose, follow and treat, provided there is commitment to do so at every step i.e. at the level of physicians, policy makers, government and patients. It is necessary to disseminate this information at every forum we have at our hand.

Keeping this in mind, the symposium on "**Prevention of Chronic Kidney Disease in India**" is being brought out in this issue of the journal. This is another attempt to briefly highlight the problem of CKD, its magnitude, causes and prevention. It is important to know that all the authors are experts in the field of kidney diseases and the chapters written have nicely brought out all the issues related to the topic, more so in the context of our own country. At last, I personally feel that the symposium will be very useful for all the stakeholders in relation to CKD to have a concise review on all the issues related to the problem and will ultimately help in patient care.

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MAGNITUDE AND EPIDEMIOLOGY OF CKD IN INDIA

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Abstract : Chronic kidney disease (CKD) is an important public health problem all over world including India. Prevalence of CKD is revealingly high and is also increasing. Further, even milder degree of CKD is an important cause of increased mortality. Treatment of CKD and its advanced stage, that is end stage renal disease (ESRD) is consuming a huge proportion of health resources in most other countries and in India it is beyond the reach of an average Indian. Thus assessment of magnitude is important for the prevention of CKD. Magnitude of CKD can be judged by the acceptance of patients on renal replacement therapy (RRT), incidence of CKD and/or ESRD or prevalence of CKD / ESRD. Due to various reasons, prevalence of CKD is the most viable way to assess magnitude of problem. Other criteria can only be extrapolated from this data. Further, prevalence of CKD can be hospital based or community based. Due to obvious advantages, community based data is most appropriate though difficult to study. In hospital-based data, there are variable reports about etiology of CKD. But, chronic glomerulonephritis, diabetic nephropathy, tubulointerstitial diseases were the three common causes of CKD. In one center, diabetes as cause of CKD has shown to be increased with time. In two community-based studies, prevalence of CKD was 0.16% and 0.78%, respectively, though the methodology was different in two studies.

Chronic kidney disease (CKD) is an important public health problem all over world including India¹. The word chronic renal failure (CRF) is changed to CKD by National Kidney Foundation (NKF), U.S.A as CKD is more acceptable name for understanding by the common man and also because at some stage person may have chronic kidney disease but kidneys are still functioning normally and NOT failed. Thus, now CKD is much more accepted terminology than CRF. NKF, USA has classified CKD into five stages (Table-1)².

Table-1 Stages of Chronic Kidney Disease

Stages	Description	GFR (ml/min/1.73m ²)
Stage-1	Kidney damage with normal or high GFR	> 90
Stage-2	Mild ↓ GFR	60-89
Stage-3	Moderate ↓ GFR	30-59
Stage-4	Severe ↓ GFR	15-29
Stage-5	Kidney Failure	< 15 or Dialysis

Recently, this staging has been modified by KDIGO (Kidney Disease: Improving Global Outcome) in its meeting held recently³. Firstly, the treatment also needs to be included in staging. It means if patient is on dialysis, the word 'D' should be added after the stage. Like if patient with stage 4 is on dialysis, it should be labeled stage 4D. Secondly, all transplant patients have been included as a patient of CKD and word 'T' should be added with stage. Like a renal transplant patient in stage 2 should be labeled stage 2T.

Prevalence of CKD is revealingly high and is also increasing. While the annual population of United States is 1.3%, annual growth of end stage renal disease (ESRD) in same population is approximately 8%. Not only it is common, but it is also utilizing huge cost for its management. It can be estimated from the fact that 8% of US budget is being utilized for only 0.7% of ESRD population. Further, even milder degree of CKD is an important cause for increasing the mortality. Even increase in creatinine from 1 mg% to 1.5 to 2.0 mg% increases all causes mortality from 19% to 37%. Thus it is clear that CKD has become one of the important chronic non-communicable disease epidemics all over the world. It is also clear that treatment of CKD and its advanced stage, that is end stage renal disease (ESRD) is consuming a huge proportion of health resources in most of the country and in India it is beyond the reach of an average Indian.

Thus, it is crucial that assessment of magnitude and prevention of CKD should become an important goal of the medical fraternity, government and public at large in any country, including India.

MAGNITUDE OF CKD

Magnitude of CKD in any population can be judged in following ways

1. Acceptance rate of renal replacement therapy

One of the ways of assessing the magnitude of CKD is acceptance rate of ESRD on renal replacement therapy (RRT); maintenance dialysis and renal transplant. However, this method of assessing CKD may be more applicable in the countries where treatment is government funded. Otherwise, in the country like India, where treatment of CKD is not government funded in most of the cases, assessing the magnitude on the basis of acceptance rate for RRT will be underestimating the magnitude of CKD. This is because more than 80% patients of ESRD practically never get any form of RRT due to various reasons, of which at least one is cost involved in the therapy.

2. Incidence of CKD / ESRD

Second way of assessing magnitude of CKD is by way of assessing incidence of CKD/ESRD in the population. This method of assessing CKD is again possible in smaller countries where all the people's health status is known, not only once but also on a regular basis and data is approachable. In a country like India, where there is no general practitioner (GP) system and every one is free to choose his doctor, this type of information is not possible at present and may be difficult in future also.

3. Prevalence of CKD / ESRD

Another way of knowing the magnitude is by knowing prevalence of CKD/ESRD. This is the only way of knowing the disease magnitude related to CKD in India. Information regarding prevalence can be obtained in three ways; from the *whole community*, from a *sample representing the community* and from the *hospital based data*.

There are some studies from India regarding *hospital-based data* in relation to CKD. From our own hospital, between 87-98, out of 14796 new patients seen in nephrology outpatients, CRF was found in 47.8% cases⁴. Here it is important to note that this was CRF and not CKD. Many of the patients might be having CKD and in term of CKD prevalence, this will be underestimation. Further, from our own hospital, when we tried to compare the data from 87-98 and 98-2004, the prevalence of CRF increased from 47.8% to 58%

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(Unpublished data). In another study done by us involving 48 hospitals representing all over India, prevalence of CRF was found to be approximately ~0.8%⁵. In another study from India, MK Mani⁶ from Chennai in south India, while initiating a screening program in general and more so for diabetes and hypertension at community level in rural area (total population 25,000), reported a prevalence of chronic renal failure (CRF) of 0.16% and other renal diseases (short of CRF) in 0.7% cases. In this study, a preventive and social health worker (PSHW) travelled from house to house and a brief questionnaire related to renal illness were asked from each member of family. Urine was examined for albumin and reducing substance by using sulphosalicylic acid and benedict solution respectively. However, it is important to note that all subjects were not evaluated with blood tests for urea/creatinine and only those who had some abnormality in urine test/blood pressure and/or positive response to a questionnaire were subjected to blood test for urea/creatinine. Ideally speaking, this will not give true picture of CKD, though it may be practical solution in a community based screening program, where blood sample from every individual may not be a viable option.

The most definitive study so far from India is one done by our group in a *community setting*⁷. Four thousand nine hundred and seventy two (4972) subjects in community in urban area in city of Delhi were screened for urine examination, blood urea and creatinine estimation with a specific aim to find out prevalence of CRF. In addition, other information related to kidney disease, diabetes and hypertension was also collected, though it was not the primary aim of the study. Indian Council of Medical Research, New Delhi, funded this study. A thorough history and a detail physical examination including blood pressure measurement as per our questionnaire were done in each subject of the family of the age of 16 years and above. After this a fresh mid stream urine sample was examined for albumin and sugar using dipstick. Of the 4972 subjects evaluated, prevalence of CRF, defined as serum creatinine more than 1.8 mg% (Upper limit of our laboratory) persistent for more than three months in absence of any reversible factor, was found to be 0.79% or 7852 per million population (pmp). This figure is much higher than the figure in the study of Mani⁶ because author had not screened the subject with serum creatinine estimation while we took blood sample in each subject for finding our prevalence of CRF. A 1998 report from the third cycle of the National Health and Nutrition Examination Survey (NHANES III), conducted from 1988 to 1994 in USA estimated that if we take serum creatinine > 1.7 mg% as cutoff for CRF (a value close to 1.8 mg%, what we had taken as cutoff for defining CRF in present study), then during the same period, CRF cases were 12 times more than ESRD cases². Extrapolating this information, if we take ESRD patients to be 10% of CKD patients, from our own study, prevalence of ESRD comes out to be 785/pmp in India. There are many screening program on smaller scale are being conducted by physicians and nephrologist in different parts of India, however, there are no other peer reviewed data on the magnitude of problem of CKD in our country.

ETIOLOGY OF CKD/ESRD

The next issue related to CKD is cause of CKD. Again causes of CKD can be found out either in hospital or in community based studies. As discussed previously, there is only two community-based data on CRF in India. Dr. Mani's study has not published in detail the etiology of CRF in his 0.16% of CRF patients in the community. Our own study was although not planned to study etiology of CRF, of the 0.79% patients of CRF, 41% were due to diabetes, 22% due to hypertension and 16% due to chronic glomerulonephritis (CGN).

Thus, if we combine diabetes and hypertension, they constituted 63% of all cases of CRF in our study⁷. One may argue that etiology of hypertension as cause of CRF is controversial and many of other diseases causing CRF may be attributed to hypertension, as hypertension is a common early manifestation in many other diseases causing CRF. We classified hypertension as cause of CRF only if patient had long history of hypertension with evidence of other target organ damage in absence of other cause of CKD. As compared to community-based studies, if we compare hospital-based studies from India for the etiology of CRF/ESRD⁸⁻¹⁰, the data is variable (Fig 1). This figure also compares these studies with the data from USRDS

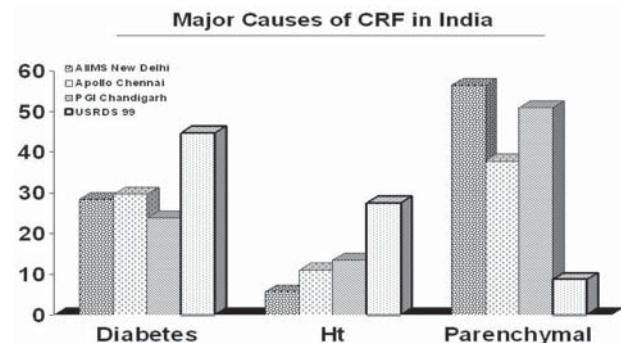


Fig.1 Causes of CRF in India.

(United State Renal data System) of 1999. Nearly 25% of all cases of ESRD in all these studies were due to diabetes and 6-13% were due to hypertension. However, we must realize that these studies are based on the data of tertiary care hospitals and do not represent community. For example in all these studies, mean age of patients was in early forties while in our community based study, mean age of patients of CRF was 59 years. There may be a bias in favour of younger persons attending hospitals. This can cause differences in etiology of patients of CRF attending hospitals as compared to patients in community. Further, if we see the CRF cases due to diabetes and hypertension only in one of these studies¹⁰, the mean age of cases was nearly 50 years. Also, in the same study, in patients over 40 years of age, diabetes and hypertension comprised more than 55% of cases of CRF, the pattern nearly similar to as seen in our community based study. All this suggests that even in India, diabetes and hypertension are responsible for at least nearly 60% of all cases of CRF. With increasing problem of diabetes in India, the absolute number of diabetic CKD/ESRD is likely to be enormous in time to come.

If we compare our own two studies, one hospital based and one community based study (Table-2), there are few striking differences. Mean age of patients of CRF in community is much higher than in

Table-2 Comparison of two studies of AIIMS

	Out Patient Study	Community Study	P value
No of Cases of CRF	7165	37	
Mean age (Yrs)	37	59	<0.001
Males %	72%	48.6%	0.001
Diabetes %	28.4%	41%	0.09

hospital-based study and males are more common in hospital-based study. This may be due to bias of younger and male patients seeking/getting treatment in hospital setting. Further, diabetes is much more common as cause of CRF in community based study than hospital based study. In fact, we expect that community based study, though restricted to city of Delhi, is more representative than hospital based

study as bias will be much less in community based study, though in our study, generalization to other community of India may not be possible. This may leads to the presumption that even in India, diabetes is the commonest cause of CRF /CKD as against chronic glomerulonephritis, which was being considered a commonest cause few years back. Even while comparing our own data from outpatients between two time period, (1987-98 and 1999-2004) it was found that there was increase in diabetes as cause of CRF from 28.4% to 33.6% (Unpublished data) Fig.2.

Another source of information about etiology of CKD is the pilot

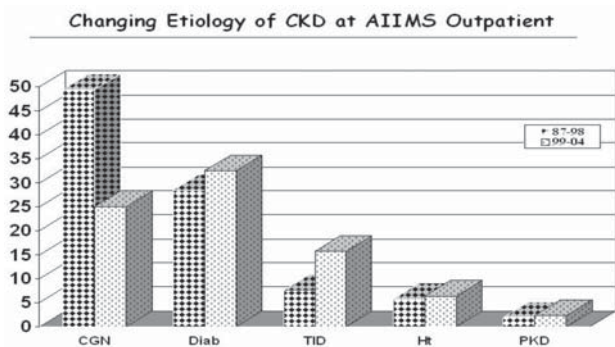


Fig.2 Changing Pattern of Etiology in Outpatient at AIIMS.

project started by Indian Society of Nephrology since June 2005, of which AIIMS was one of the member centers. This project was aimed at finding out many issues related to CKD in India, including spectrum of diseases causing CKD. It is to recall that it is also a hospital based data, though being done all over country at many centers. Till the data of 840 subjects being enrolled in this project from our center, males constituted 71% of these subjects and mean age was 47.3 years. Majority of patients were in stage CKD 3-5 groups. Diabetes mellitus as cause of CKD was seen most commonly in 29.7% patients followed by chronic glomerulonephritis and tubulointerstitial disease in 17.5%

and 11.8% respectively. Thus, in this prospective hospital-based data from our center, diabetes was commonest cause of CKD. Similar are the results of pooled data of this registry from all over the centers (Unpublished), though at present it cannot be published.

In addition to these studies, there are many more centers who are doing screening program regarding CKD in India and a multicentric study is also being conducted for CKD in collaboration with Boston medical school on the lines of 'KEEP' but the details of these ongoing studies are not yet known.

To conclude, CKD and its late stage that is end stage renal disease is a major problem for India and with increasing diabetes burden, it is going to increase further. Managing whole population of these patients will be impossible for India, where many other issues demand more priority than CKD. However, the money invested at this time in establishing prevention program for CKD in India is definitely going to give results in years to come and ultimately on long-run will still be cost effective; the saved money can be utilized for other health care programs. But, in my opinion, it is going to be difficult to convey this idea and to impress upon the current policy makers/political system of the country.

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Drug Profile

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Therapeutic indications - Deflazacort is indicated in wide range of indications, similar to corticosteroids such as, asthma & allergic disorders, rheumatoid arthritis, juvenile chronic arthritis, polymyalgia rheumatica, nephrotic syndrome, renal transplantation, neurological disorders.

Dosage & Administration: Deflazacort is a glucocorticoid derived from prednisolone, 6 mg of Deflazacort has approximately the same anti-inflammatory potency as 5 mg prednisolone or prednisone. For acute disorders, up to 120 mg/day Deflazacort may be needed; maintenance dose is - 3-18 mg/day.

In hepatic impairment, the dose should be adjusted to the minimum effective dose. *Renally impaired patients*, no special precautions are necessary. In *children*, the indications are the same as for adults; alternate day administration may be appropriate; dose of Deflazacort usually lies in the range 0.25-1.5 mg/kg/day. **Deflazacort withdrawal:** Deflazacort shows less HPA axis suppression; hence the only can be easily withdrawn with less risk of withdrawal symptoms. Once, a daily dose equivalent to 9 mg Deflazacort is reached, dose reduction should be slower to allow the HPA-axis to recover, particularly if more than 73 week therapy is given.

Contraindications : *Systemic infection* unless specific anti-infective therapy is employed; *hypersensitivity* to deflazacort or any of the ingredients; patients receiving *live virus immunization*.

Special warnings : (a) **Adrenal suppression** : Withdrawal must always be gradual to avoid acute

adrenal insufficiency, being tapered off over weeks or months.

(b) **Anti-inflammatory/immunosuppressive effects and infection** : Suppression of the inflammatory response and immune function increases the susceptibility to infections and their severity. The clinical presentation may often be atypical and serious infections such as septicaemia and tuberculosis may be masked and may reach advanced stage before being recognized.

Special precautions : The following clinical conditions require special caution and frequent patient monitoring is necessary: (a) *Cardiac disease* or congestive heart failure (except in the presence of active rheumatic carditis), hypertension, thromboembolic disorders. Glucocorticoids can cause salt, water retention and increased excretion of potassium; dietary salt restriction and potassium supplementation may be necessary; (b) *Gastritis or oesophagitis, diverticulitis, ulcerative colitis* if there is probability of impending perforation, abscess or pyogenic infections, fresh intestinal anastomosis, active or latent peptic ulcer; (c) *Emotional instability* or psychotic tendency and epilepsy; (d) Previous *corticosteroid-induced* myopathy; (e) *Liver failure*; (f) *Hypothyroidism and cirrhosis*, which may increase glucocorticoid effect; (g) *Ocular herpes simplex* because of possible corneal perforation.

Pregnancy : Deflazacort does cross the placenta; caution should be exercised **Lactation**: Corticosteroids are excreted in breast milk, no data are available for Deflazacort.

Fluid and electrolyte disturbance: Sodium and water retention with hypertension, oedema and heart failure, potassium loss, hypokalaemic alkalosis, are less with the drug.

Drug interactions: The same precautions should be exercised as for other glucocorticoids; it is recommended to increase the maintenance dose of Deflazacort when liver enzyme inducers, are co-administered, e.g. rifampicin, rifabutin, carbamazepine, phenobarbitone, phenytoin, primidone and aminoglutethimide. For ketoconazole which inhibit liver enzymes, reduction in dose is required; in patients taking estrogens, corticosteroid requirements may be reduced. The efficacy of coumarin anticoagulants may be enhanced by concurrent corticosteroid therapy. The renal clearance of salicylates is increased by corticosteroids and steroid withdrawal may result in salicylate intoxication. Antacids may reduce bioavailability; leave at least 2 hrs between administration of deflazacort and antacids.

HYPERTENSIVE NEPHROSCLEROSIS AND ITS PREVENTION

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Abstract : With increasing life expectancy, hypertension has emerged as an important worldwide public health problem. It has become a leading cause of chronic kidney disease and increases risk of CKD progression and cardiovascular disease risk. JNC VII Report defines normal blood pressure as systolic and diastolic readings of <120 AND <80 mm of Hg respectively. The kidneys play a key role in the regulation of fluid volume and vascular tone. The histological lesions of hypertension-induced kidney damage are non-specific, the earliest and most frequent lesion in longstanding hypertensives is segmental hyalinization of interlobular arteries and afferent arterioles, glomerular and tubular compartments are affected secondarily. Therapeutic interventions aimed at reducing kidney damage in hypertension are aimed at reduction of systemic blood pressure, reduction of pressure transmission to the renal microvasculature and modification of local molecular pathways to attenuate tissue injury. Management starts with lifestyle modification and then to drug therapy. The choice of drug is influenced by the presence of concomitant medical conditions. Diuretics and drugs acting at the renin-angiotensin pathway are the preferred agents. The latter are especially useful in proteinuric individuals. Statins are important adjuncts in those with high cholesterol. In future, strategies that either directly halt the molecular processes leading to hypertensive renal damage or allow reversal of established renal damage may become available.

INTRODUCTION

In this era of chronic diseases, hypertension has emerged as an important worldwide public health problem. As the life expectancy increases, an increasing proportion of the ageing population is developing hypertension; an individual who is normotensive even at the age of 55, carries a 90% lifetime risk of developing hypertension.¹ Hypertension prevalence depends on the racial and ethnic population mix in different geographic areas as well as the criteria used to define it. This condition is traditionally classified into 'essential' and 'secondary' categories. The term 'essential' was coined with the understanding that an increase in blood pressure is a necessary phenomenon required to maintain normal organ perfusion as the arteries stiffen with age, but has largely been discarded in favor of 'primary' or 'idiopathic' hypertension. The frequency of secondary forms of hypertension depends on the nature of population studied and extensiveness of the evaluation, and varies from 6% in general population to 35% in referral centers.²

EPIDEMIOLOGY

BP readings in the general population fall in a Gaussian distribution, but are skewed towards the higher end, making it difficult to choose a single value that would denote the cut off between normotension and hypertension. The definition and grading of hypertension has evolved over the last 25 years; the latest criteria have been proposed in the Seventh Report of Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure (JNC 7)³. According to this report, normal blood pressure is defined by systolic and diastolic readings of <120 AND <80 mm of Hg respectively. Stage I and II hypertension are defined as SBP of 140-159 and/or DBP 90-99 and SBP e'' 160 and/or DBP e'' 100 respectively. A new category of "prehypertension", defined as a SBP of 120-139 OR DBP 80-89 mm of Hg, was introduced in this report.

The third National Health and Nutrition Examination Survey carried out in the United States between 1988 and 1991 used the JNC V criteria, and categorized 24% of the adult population as having hypertension⁴. The prevalence was 4% amongst the 18-34 year olds, but increased to 58.5% in the age group 65-74 years⁵. African-Americans exhibit a 50-75% higher prevalence and have the highest incidence of hypertension-related ESRD⁶. The 1998 Health Survey in England defined high BP as SBP e''140 and DBP e''90, or antihypertensive drug use, and found the prevalence to be

40.8% for men and 32.9% for women⁷. Indian urban population studies of the mid-1980s used older WHO guidelines for diagnosis (BP e''160 and/or 95 mmHg) and reported hypertension prevalence of 1.2-4.0%⁸. Subsequent studies have reported a steady increase in prevalence: from 5% to 12-15%⁹. Prevalence is lower in the rural Indian population, although there has been a steady increase over time here as well. The most recent studies using revised criteria (BP e''140 and/or 90 mmHg) have shown a prevalence of 15-40% among urban adults¹⁰.

Hypertension is a leading cause of end-stage kidney disease (ESRD) in the west. Hypertension was listed as the cause in 27% of incident ESRD patients in the United States in 2000, second only to diabetes mellitus¹¹. However, the basis for making this diagnosis is not uniform in all reports. In a prospective study of 56 Caucasian patients, the clinical diagnosis of hypertensive nephrosclerosis could be confirmed on renal biopsy in only 48%, whereas 35% showed atherosclerotic disease¹². Hypertension was listed as the primary cause of chronic kidney disease (CKD) in 14.5% of cases in the Indian CKD Registry (Rajapurkar M, for Indian CKD Registry Group).

On the other hand, a major contribution of hypertension in the progression of all types of chronic kidney diseases is not doubted. Both SBP and DBP were shown to be strong independent predictors of ESRD in the cohort of 332,544 men followed up for 16 years for the Multiple Risk Factor Intervention Trial. In comparison to the normotensive (BP d''120/80), those with a SBP e'' 210 mm Hg or DBP e''120 mm Hg exhibited a 22-fold increased risk of developing ESRD¹³. Hypertension is also an important cardiovascular disease risk predictor. Starting at 115/75 mm Hg, the CVD risk doubles with each increment of 20/10 mm Hg³.

KIDNEYS AND BLOOD PRESSURE

The kidneys play a key role in the regulation of fluid volume and vascular tone. The intravascular volume control involves regulation of water and sodium excretion and vessel tone depends upon secretion of vasoactive substances by the kidneys. An elevation in renal perfusion pressure results in an increased excretion of sodium and water, the so called "pressure natriuresis/diuresis". According to Guyton, pressure natriuresis promotes the excretion of sodium and water until blood volume is diminished sufficiently to return blood pressure back to normal range¹⁴. Many compounds, including rennin, vasopressin, atrial natriuretic peptide and angiotensin II play an important role in this pressure natriuresis. The renin-angiotensin system is a powerful regulator of arterial pressure, sodium balance and intraglomerular pressure¹⁵.

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EFFECTS OF HYPERTENSION ON KIDNEYS

The adverse effects of hypertension on kidneys are determined by the level of systemic blood pressure as well as the abruptness with which this pressure load is transmitted to the renal vascular bed. Increase in systemic blood pressure is normally followed by proportionate autoregulatory vasoconstriction of preglomerular arterioles so that the high pressure is not transmitted to the renal microvasculature, and the renal blood flow and glomerular hydrostatic pressure are maintained at a constant level^{16,17}. The histological lesions of hypertension-induced kidney damage are non-specific, and do not allow differentiation between the different causes of high blood pressure. The earliest and most frequent light microscopic lesion in longstanding hypertensives is segmental hyalinization of interlobular arteries and afferent arterioles. Media is affected preferentially, and exhibits a diminished number of smooth muscle cell nuclei¹⁸. Immunofluorescence and electron microscopy reveal deposits of plasma constituents such as IgM and complement components (C1q, C3) within the hyalinized areas¹⁹. Similar lesions are noted in animal models of chronic hypertension. The glomerular and tubular compartments are affected secondarily. Some patients, especially those with pronounced narrowing of the interlobular arteries and afferent arterioles, may exhibit prominent ischemic collapse of the glomerular tuft. These lesions have been described under the rubric of "benign nephrosclerosis". The lack of a specific phenotype makes it difficult to quantitate the contribution of hypertension to progressive renal diseases of other etiologies, as the classical vascular pathology of hypertension is usually obscured by lesions of underlying disease. An accelerated glomerulosclerosis superimposed on the intrinsic phenotype is often the only finding^{20,21}.

A different histological picture dominates patients in whom the blood pressure rise is sudden and exceeds the autoregulatory limits. Dubbed "malignant nephrosclerosis", these lesions predominantly affect the intimal space of small sized blood vessels, particularly the interlobular arteries and afferent arterioles²². The subendothelial compartment gets filled up with plasma and cellular blood constituents. This is often accompanied by fibrinoid necrosis of the media. The intimal process dominates, however, and leads to severe narrowing of the vascular lumen. Over time, myointimal cells make their appearance, followed by collagen deposition. Hyperplasia of the juxta-glomerular epithelioid cells, ischemic collapse of the glomerular tufts, tubular atrophy, and interstitial fibrosis usually follow²³. At one time, it was believed that decline in glomerular filtration rate occurred only in those with malignant nephrosclerosis, but this view is now largely discounted.

PATIENT EVALUATION

The main objectives³ of evaluation of patients with hypertension are: 1. lifestyle assessment and identification of other cardio-vascular risk factors; 2. investigation for the presence of secondary causes of hypertension; and 3. evaluation of target-organ damage (Table 1). This requires a proper medical history, physical examination, laboratory tests, and specific diagnostic procedures.

Ambulatory BP Monitoring

In contrast to office measurements, which are intermittent and taken at fixed time points, twenty-four-hour ambulatory blood pressure monitoring allows periodic (half hourly or hourly) documentation of blood pressure during normal daily activity and provides an idea of "blood pressure load"²⁴. Ambulatory monitoring is useful for evaluation of 'white-coat' and drug resistant hypertension, and in those developing hypotensive symptoms with medications, episodic hypertension, or autonomic dysfunction. Ambulatory BP values are usually lower than clinic readings. Hypertensive individuals have a mean BP >135/85 and >120/75 mm Hg during daytime and sleep respectively²⁵. There is some suggestion that ambulatory BP records correlate better with target-organ injury than office measurements^{26,28}. Another utility of ambulatory BP monitoring is

evaluation of the extent of diurnal variations in BP. Normally, BP decreases by 10% to 20% during sleep; individuals who do not show this decrease (non-dippers) are at increased risk for cardiovascular events²⁷. The proportion of non-dippers increases as renal function deteriorates²⁴.

Table 1: Evaluation of a patient with hypertension*

Major Risk Factors:
Cigarette smoking
Obesity (BMI ≥ 30)
Physical inactivity
Dyslipidemia
Diabetes mellitus
Microalbuminuria or estimated GFR <60 mL/min
Family history of premature cardiovascular disease (men <55 years or women <65 years)
Identifiable Causes of Hypertension:
Chronic kidney disease
Primary aldosteronism
Renovascular disease
Chronic steroid therapy and Cushing syndrome
Pheochromocytoma/Coarctation of the aorta
Thyroid or parathyroid disease
Target-Organ Damage:
Left ventricular hypertrophy/angina or prior myocardial infarction, heart failure, stroke or transient ischemic attack, chronic kidney disease, peripheral arterial disease/retinopathy *modified from JNC 7 recommendations (reference 3)

MICROALBUMINURIA AND HYPERTENSION

Excretion of increased amounts of albumin in urine, yet below the threshold value for positivity by routine dipstick testing, is a feature of many diseases including hypertension. Antibody-based assays (radioimmunoassay, enzyme immunoassay and nephelometry or turbidimetry) are required to detect such small amounts of albumin. Termed microalbuminuria, this corresponds to an albumin excretion rate of approximately 20-200 μ g/min or 30-300 mg/day. Commercial test strips allow quick semi-quantitative screening²⁹. Use of a timed 24-h urine sample is considered as 'gold standard' but the urine albumin-creatinine ratio on random urine samples is an acceptable alternative; a ratio of 30-300 μ g albumin/mg creatinine indicates microalbuminuria³⁰. Several studies have shown a strong influence of microalbuminuria in predicting cardiovascular risk in diabetic and non-diabetic hypertensive subjects^{31,32}. It has been interpreted as an indicator of generalized inflammatory process or endothelial dysfunction in several conditions including diabetes, essential hypertension, obesity and metabolic syndrome. Some recent studies, most notable of which is the PREVEND trial conducted in the Dutch city of Groningen, have shown that presence of even smaller quantities (<30 mg/day) of albumin or albumin fragments may indicate increased cardiovascular risk³³. Such small quantities can be detected only by HPLC. This finding needs confirmation in prospective studies.

PREVENTION OF HYPERTENSIVE RENAL DISEASE

Therapeutic interventions aimed at reducing kidney damage in hypertension can be tailored to fulfill one or more of the following three broad strategies: 1) reduction of systemic blood pressure load; 2) reduction of pressure transmission to the renal microvasculature; and 3) modification of local molecular pathways that mediate eventual tissue injury.

Out of these three approaches, the most successful one is the reduction of systemic blood pressure by non-pharmacological and pharmacological means. According to current standards, the acceptable blood pressure goal for target organ protection is <140/90 mmHg; reduced further to <125-130/75-80 mmHg in those with diabetes or chronic kidney disease³. The algorithm for the treatment of hypertension as proposed by JNC 7 is shown in Figure 1. The first step in mild-to-moderate hypertension should always be *life-style modification*; *drug therapy* should be considered only if these fail or when the hypertension is severe.

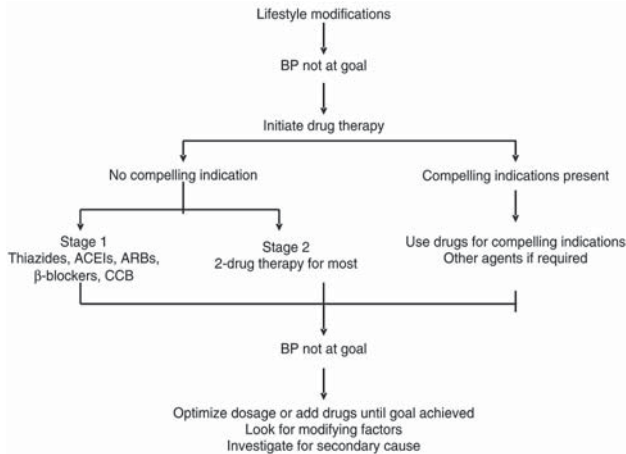


Figure 1: Algorithm for treatment of hypertension (modified from JNC 7³)

LIFESTYLE MODIFICATIONS (TABLE 2)

Healthy lifestyle is critical for the prevention management of hypertension. Major lifestyle modifications shown to lower BP include weight reduction in the overweight^{34,35}, increased physical activity³⁶, cessation of smoking and moderation of alcohol consumption³⁷. JNC 7 also recommends adoption of diet rich in potassium and calcium and low in sodium, as described in the Dietary Approaches to Stop Hypertension (DASH) study³⁸. Lifestyle modifications not only decrease blood pressure by itself but also enhances efficacy of antihypertensive drugs.

Prehypertension has not been considered a disease in JNC 7, but identifies individuals at high risk of developing hypertension. All prehypertensives should be strongly advised to practice lifestyle modification. Those with diabetes or CKD are candidates for appropriate drug therapy if a trial of lifestyle modification fails to reduce their BP to 130/80 mmHg or less.

Table 2: Life-style modifications in hypertension

Modification	Recommendation
Weight reduction	Maintain Body mass Index between 18.5-24.9 mg/m ²
Diet	1. Adopt a diet rich in fruits, vegetables and low-fat dairy products with reduced content of saturated and total fat. 2. Reduce dietary sodium intake to ≤ 100 mEq/L (6 gm of sodium chloride or 2.4 gm of sodium)
Physical activity	Regular aerobic physical activity such as brisk walking (at least 30 min per day, most days of the week)
Alcohol consumption	Limit consumption to no more than 2 drinks per day in men and no more than 1 drink in women and lighter-weighted persons
Smoking	Stop smoking completely

DRUG THERAPY

Life-style modifications alone are sufficient to bring the BP down to goal only in a minority of individuals, and most require drug therapy for adequate control. Given below is the list of drugs which are used for blood pressure reduction. Multiple drugs are frequently required to achieve the target.

1. Diuretics (thiazides and loop diuretics)
2. Angiotensin converting enzyme inhibitors (ACEI)
3. Angiotensin receptor blockers (ARB)
4. b-adrenergic blockers
5. a-adrenergic blockers
6. Calcium-channel blockers (CCB), especially dihydropyridines
7. Centrally acting drugs (e.g. clonidine, methyldopa)
8. Vasodilators (e.g. minoxidil, hydralazine)

In this era of evidence-based medicine, there is little data on the differential renoprotective effects of antihypertensive agents in management of uncomplicated hypertension. The primary outcome measures in most antihypertensive clinical trials have been heart failure, ischemic heart disease or stroke. Most of the available data on renoprotection has come from studies on patients with pre-existing chronic kidney disease of diabetic and nondiabetic etiologies.

Table 3: Considerations for individualization of anti-hypertensive therapy

Indication	Initial Therapy	Second line therapy	Notes/Cautions
DM with nephropathy	ACEI/ARB	Add thiazide, β-blockers, LA-CCB, ACE/ARB combo	Cardioselective β-blockers
DM without nephropathy	ACEI/ARB or thiazide	Combo 1st line Rx or β-blockers, LA-CCB	If serum creat > 1.8 mg/dL, use loop diuretic for volume control
Angina	β-blockers + strongly consider ACEI	LA-CCB	Avoid short acting nifedipine
Prior MI	β-blockers + ACEI	Combine additional Rx	
CHF	β-blockers + ACEI + spironolactone (ARB if ACEI intolerant)	Hydralazine /nitrates thiazide or loop diuretics as additive therapy	Avoid non DHP-CCB (diltiazem, verapamil)
Prior CVA or TIA	ACEI/diuretic combination		BP reduction ↓ recurrent events
Renal Disease	ACEI/diuretic as additive Rx	ARB if ACEI intolerant Combo other agents	Avoid ACEI if bilateral Renal artery stenosis
LVH	ACEI, ARBs, DHP-CCB, thiazide, β-blockers < 55 yr		Avoid hydralazine and minoxidil

Several guidelines on managing hypertension have been published, four in 2003 alone. While containing large measures of agreement, these guidelines are not unanimous in their recommendation of the initial antihypertensive drug and the method of subsequent management; whether drugs should be added (stepped-care) or exchanged (sequential design). JNC 7, chiefly on the basis of the results of the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT)³⁹, recommends use of diuretics, particularly thiazides, as the first line agent. This trial compared chlorthalidone, lisinopril, amlodipin and doxazosin in about 45,000 individuals (32% African-Americans), all above the age of 55 years. Compared to diuretic-treated individuals, those treated with doxazosin⁴⁰ and amlodipin had higher rates of heart failure, and lisinopril-treated individuals showed increased frequency of heart failure as well as stroke³⁹. Other smaller trials like Perindopril Protection against Recurrent Stroke Study (PROGRESS)⁴¹ have shown similar findings. The lower cost of thiazides makes them particularly attractive as the initial agents. Diuretics also enhance the antihypertensive efficacy of multi-drug regimens; and help achieve BP control in cases of resistant hypertension. According to JNC 7, hypertension can only be defined as drug-resistant when diuretics have been tried and found ineffective as a part of combination therapy³.

The ALLHAT trial, however, has been criticized on several counts,

specifically the generalizability of findings in a selected patient population, and the assumption that drugs added later (in the second or third step) are not important in outcome analysis. The Second Australian National Blood Pressure Trial⁴² reported better outcomes in white elderly men with a regimen that began with an ACE inhibitor compared with one starting with a diuretic. Most studies that have shown favorable effects of ACE-inhibitors have used them in larger dosage than those used in clinical practice (e⁺ 10 mg/d of ramipril, 20-40 mg/d of benazepril or e⁺ 8 mg/d of perindopril). It has been suggested that different treatment approaches may be required for managing blood pressure in different population groups. In a study of single-drug therapy, it was found that young white individuals responded better on ACE inhibitors and b-blockers, but poorly to diuretics whereas the BP in older whites responded best to CCBs. Blacks of all ages responded poorly to ACE inhibitors⁴³.

Many studies, including Study of Left Ventricular Dysfunction (SOLVD)⁴⁴, Survival and Ventricular Enlargement (SAVE)⁴⁵ and Heart Outcomes Prevention Evaluation (HOPE)⁴⁶ have demonstrated that ACEIs reduce cardiovascular and stroke-related morbidity and mortality. Several trials, like ACE Inhibition in Progressive Renal Insufficiency (AIPRI)⁴⁷, ACE Inhibitors in Diabetic Nephropathy⁴⁸, RENAAL⁴⁹ and IDNT⁵⁰ have confirmed the renoprotective effect of ACEIs and/or ARBs in those with CKD of both diabetic and non-diabetic etiologies. The African American Study of kidney disease and hypertension (AASK)⁵¹ showed ACEI to be more effective than b-blockers or dihydropyridine CCBs in slowing the decline in GFR in patients with non-diabetic kidney disease, even in patients who did not have significant proteinuria. JNC 7 and Kidney Disease Quality Outcome Initiative (K-DOQI)⁵² recommend using these drugs preferentially in those with heart failure, diabetes or chronic kidney disease (Table 3), especially in those with significant proteinuria (> 1g/d). Because of their physiological differential effects on the afferent and efferent arterioles, a moderate acute decline in glomerular filtration rate (GFR), reflected by up to 30-35% increase in serum creatinine above baseline is expected after initiating treatment with ACEIs or ARBs. This should not be a reason to withhold or stop treatment. A watch must be kept for the first-dose effect and later development of hyperkalemia, especially in those receiving potassium-sparing diuretics or substantially reduced GFR.

Centrally acting drugs and vasodilators are usually used in combination with other drugs in cases of refractory or resistant hypertension and seldom on their own as first line agents. A notable exception has been the Kidney Help Rural Trust project⁵³, in which cheap drugs like reserpine have been successfully used for bringing down the blood pressure. However, their efficacy in target organ protection has not been examined.

In many individuals, complete normalization of systemic blood pressure is not sufficient in halting progression of kidney disease completely. Whether other renoprotective approaches would be useful in adding to the effect of conventional antihypertensive therapy remains to be seen. Mitigating renal damage by reducing intrarenal transmission of systemic blood pressure can be theoretically achieved by protein restriction, but benefit of this approach is only modest and discernible in only those with more advanced renal disease⁵⁴. Similarly it may become possible in future to independently modulate the downstream molecular mediators of tissue injury.

The place of drugs that do not reduce the blood pressure in target organ protection due to hypertension is being explored. Anglo-Scandinavian Cardiac Outcomes Trial-Lipid Lowering Arm study (ASCOT-LLA)⁵⁵ showed that a group of hypertensive patients that received 10 mg/day of atorvastatin had a 36% relative risk reduction in the primary study end point of combined nonfatal myocardial infarction plus fatal coronary heart disease. In addition, the secondary end points of nonfatal and fatal stroke (27% relative risk reduction), total coronary events (29%), and total cardiovascular events and related procedures (21%) were also significantly affected. There was a 13% reduction in all-cause mortality, which was not significant. The ALLHAT-LLT⁵⁶ however showed that addition of pravastatin does not have any added benefit then the usual care in moderately hypercholesterolemic hypertensive patients. There is some

evidence that high doses of atorvastatin may, by itself, reduce BP levels, especially systolic BP.

CONCLUSIONS

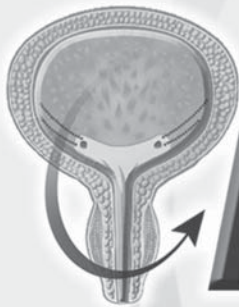
Hypertension is a common clinical and public health problem. It is an important cause of ESRD, and plays a major role in worsening the progression of chronic kidney disease due to other causes. There is insufficient data to determine optimum renoprotective strategies for those with uncomplicated hypertension. The current recommendations include adequate BP control by combination of life-style modifications and one or more drugs, especially diuretics and drugs acting on renin-angiotensin axis. Statins are important adjuncts in those with high cholesterol. In future, strategies that either directly halt the molecular processes leading to hypertensive renal damage or allow reversal of established renal damage may become available.

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DIABETIC NEPHROPATHY AND ITS PREVENTION IN INDIA

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Abstract: The prevalence of type 2 diabetes has shown an alarming increase over the past few decades. This increase has been most marked in the poorer countries of the world, which are ill equipped to tackle the challenges posed by this epidemic. Thus we have a large population at risk for developing diabetic complications, including nephropathy. Diabetic nephropathy accounts for the majority of individuals entering renal replacement therapy in the developed world and increasingly in developing countries as well. Diabetic nephropathy can be prevented or reversed if detected early enough. However, it is well known that not everyone with diabetes develops nephropathy. There are wide variations in the prevalence of nephropathy among diabetic individuals from country to country and even among different regions and ethnic groups in a country. These variations might be due to different definitions and methodologies used by different authors or might reflect true genetic variation in susceptibility. A recent population based study from south India showed that the prevalence of overt nephropathy was 2.2% and that of microalbuminuria was 26.9%. Duration of diabetes, HA1C, and systolic blood pressure were the common risk factors for overt nephropathy and microalbuminuria. There is also familial aggregation of kidney disease in Type 2 diabetes. This has led to the concept of genetic susceptibility in the pathogenesis of diabetic nephropathy. Diabetic nephropathy, once established, is usually irreversible and the curative options are expensive and not easily available. Hence, stress is increasingly being laid on the prevention of kidney disease in persons with diabetes. The stage of microalbuminuria offers great scope for institution of preventive measures. It has been recommended that all Type 2 diabetic patients be screened for microalbuminuria at the time of diagnosis of diabetes. It should be remembered that diabetic patients with kidney disease have multiple cardiovascular risk factors and that most of them die from cardiovascular events rather than the kidney disease. Hence a multifactorial intervention program should be adopted in these patients, targeting all these risk factors.

INTRODUCTION

Diabetes, the most common metabolic disorder, is among the leading causes of end-stage renal disease worldwide¹. Diabetic nephropathy or diabetic kidney disease accounts for the majority of individuals entering renal replacement therapy in the developed world and increasingly in developing countries as well. The emotional and financial repercussions to the affected individuals and families are considerable. Nevertheless, diabetic nephropathy can be prevented and early kidney disease can be reversed if detected early enough. However, the most cost-effective modality for preventing diabetic nephropathy, however, is the prevention of diabetes per se.

MAGNITUDE OF THE PROBLEM

It has been estimated that there are around 170 million diabetic patients in the world². Most of these are Type 2 diabetic patients. Type 1 diabetes accounts for only a miniscule proportion of diabetic individuals in most parts of the world, including India. The prevalence of Type 2 diabetes has shown an alarming increase over the past few decades. This increase has been most marked in the poorer countries of the world, which are ill equipped to tackle the challenges posed by this epidemic. Factors such as increasing urbanization, changes in diet and adoption of sedentary lifestyle have been put forward to explain the epidemic of Type 2 diabetes. As of the year 2000, there were 171 million diabetic patients in the world; this number is projected to rise to 366 million by the year 2030. India has the dubious distinction of being the Diabetes Capital of the world; in 2000, more than 30 million of its citizens had diabetes, and the number is expected to rise to 80 million by 2030. China and the U.S. are in second and third place, respectively².

Thus we have a large population at risk for developing diabetic complications, including nephropathy. However, it is well known that not everyone with diabetes develops nephropathy. There are wide variations in the prevalence of nephropathy among diabetic individuals from country to country and even among different regions

and ethnic groups in a country. The prevalence of microalbuminuria varies from 7 to 9% in White U.K. populations³ to 26% in Pima Indians⁴ and 42% in Nauruans⁵. These variations might derive from differing definitions and methodologies used by different authors or might reflect true genetic variation in susceptibility.

Evidence from immigrant studies seems to support the premise that persons of Asian Indian ethnic origin are more susceptible to develop certain complications of diabetes, including nephropathy. This observation was made initially by Allawi et al in the U.K.⁶ and later confirmed by Feehally and colleagues⁷. Essentially similar conclusions were drawn by Chandie Shaw et al⁸ and Stewart et al⁹ in their studies on multiethnic populations in the Netherlands and Australia, respectively. However, studies on another multiethnic population in Singapore failed to show increased susceptibility of South Asians to diabetic nephropathy¹⁰.

There is little information on the prevalence of diabetic nephropathy from India, which is home to the largest number of diabetic subjects in the world. Moreover, all the data mentioned below are derived from clinic-based studies, which do not portray the full picture. Viswanathan et al in 1991, reported the prevalence rate of microalbuminuria to be 28.5% in a cohort of 316 Type 2 diabetes patients¹¹. In the same year, Gupta et al noted microalbuminuria to be present in 26.6% of Type 2 diabetes patients studied by him in a clinic in North India¹². John et al, working in a teaching hospital in South India noted prevalence rates of 8.9% and 19.7% for diabetic nephropathy and microalbuminuria, respectively¹³. Mohan et al, working in a diabetes centre in South India, observed a prevalence rate of 36.3% for microalbuminuria¹⁴ and 6.9% for macroproteinuria¹⁵ among Type 2 diabetic subjects.

A recent population based study on the prevalence of diabetic nephropathy in urban south Indian was published by us¹⁶. This study showed that the prevalence of overt nephropathy was 2.2% and microalbuminuria was 26.9%¹⁶.

DEFINITIONS AND STAGES

Diabetic nephropathy has conventionally been described as proteinuria of 500 mg or more per day, in association with an elevated

blood pressure and relentless fall in glomerular filtration rate (GFR), usually in the presence of coexisting diabetic retinopathy. It has long been known that diabetic nephropathy in Type 1 diabetes passes through a series of well-defined stages (Table 1). To an extent, the same stages hold good for Type 2 diabetes also. However, in Type 2 diabetes, renal disease is often well-established at diagnosis of diabetes and the progression to end-stage renal disease occurs faster.

The stage of microalbuminuria deserves special mention. Microalbuminuria refers to that level of urinary albumin excretion which cannot be detected using conventional dipsticks and which requires specialized techniques for detection. Persistent microalbuminuria is the earliest sign of diabetic kidney disease. Aggressive intervention at this stage can retard or even reverse the progression of kidney disease. Moreover, microalbuminuria has also been found to be an independent predictor of cardiovascular morbidity and mortality¹⁷.

Table 1. Stages Of Diabetic Nephropathy

Stages	Designation	Structural Changes	GFR	UAE (µg/min)	BP
Stage I	Hyperfiltration or hypertrophy	Glomerular hypertrophy	= 150	May be ↑	N
Stage II	Normoalbuminuria	↑ BM thickness	↑ 20-30%	N	N
Stage III	Microalbuminuria	Further ↑ BM thickness	↑ GFR	20-200 µg/min	↑ or N
Stage IV	Overt proteinuria	Clear abnormalities Mesangial matrix ↑ and cells ↓	↓	>200 µg/min dipstick positive	Hypertension present
Stage V	End stage renal disease	Glomerular closure	↓	>200 µg/min	Hypertension present

Risk Factors for Diabetic Nephropathy

The most important modifiable risk factors for developing nephropathy are sustained hyperglycemia¹⁸⁻²¹ and systemic hypertension²²⁻²³. Loss of the usual nocturnal drop in BP may be the first abnormality noted in essential hypertension. Such "non-dippers" have increased risk at developing albuminuria and are found to have higher mortality from cardiovascular disease. Dyslipidemia, cigarette smoking, proteinuria levels and dietary factors are other postulated risk factors. Some studies have identified male sex, duration of diabetes and pre-existing retinopathy as risk factors for microalbuminuria²⁴⁻²⁵. There is also a close link between cardiovascular disease and nephropathy. In the landmark United Kingdom Prospective Diabetes Study (UKPDS) trial, annual rates of death from cardiovascular disease were 0.7% in normoalbuminuric individuals, 2% in those with microalbuminuria, 3.5% in those with macroalbuminuria and 12.1% in those with elevated serum creatinine or on renal replacement therapy²⁶. A recent clinic-based study conducted by us in Chennai found age, duration of diabetes, diastolic blood pressure, HbA1c and fasting plasma glucose levels to be risk factors for microalbuminuria¹⁴.

Even after we exclude the influence of all the known risk factors, there remains a subset of patients who have an increased susceptibility to diabetic nephropathy. It has been well-established that there is strong familial component in the development of diabetic nephropathy. Vijay et al have shown that there is familial aggregation of kidney disease in Type 2 diabetes in South India, which is independent of the familial clustering of Type 2 diabetes²⁷. This has led to the concept of genetic susceptibility in the pathogenesis of diabetic nephropathy. There is no consensus as to whether there is one major gene effect or several minor ones; current evidence favours

the latter²⁸. Small effects of several polymorphisms in various genes have been identified. Considering the central role of the renin-angiotensin-aldosterone system (RAAS) in the pathogenesis of diabetic nephropathy, most of the studies so far have looked at the genes representing the proteins involved in this cascade. Several studies have noted that the D allele of the angiotensin converting enzyme (ACE) gene is associated with faster loss of renal function²⁹⁻³¹.

PATHOGENESIS AND PATHOLOGY

Diabetic nephropathy is characterized by alterations to various elements of the glomerular ultrastructure, including the mesangial cell, endothelial cell, podocyte and basement membrane. Increased intraglomerular pressure, loss of negatively charged glycosaminoglycans and increased basement membrane pore size all contribute to albuminuria. Microscopy reveals basement membrane thickening, expansion of mesangial matrix and proliferation of mesangial cells, which all contribute to the decline in GFR. There also occurs effacement of the podocyte foot processes and loss of the podocytes themselves, which contribute to proteinuria and ultimately to glomerulosclerosis.

Many postulates have been put forth to explain the pathogenesis of diabetic nephropathy. Most of these focus on the direct effects of hyperglycemia and formation of advanced glycation end-products (AGEs). Increased flux through the hexosamine and polyol pathway has also been implicated. It is suggested that oxidative stress might be the central process linking all these pathways³². Several growth factors like insulin-like growth factor-I, transforming growth factor α and connective tissue growth factor are known to be involved in glomerular hyperfiltration and hypertrophy³³.

The role of intraglomerular hypertension and the renin-angiotensin system in the pathogenesis of diabetic nephropathy has been well documented. Elevated intraglomerular pressure can lead to glomerular damage by direct pressure effects or indirectly by increasing proteinuria. It is well known that patients with diabetes have elevated intraglomerular pressures, which can be present even in the face of a normal systemic arterial blood pressure and even before signs of kidney disease appear. Activation of the renin-angiotensin system plays an important role in producing and maintaining elevated levels of intraglomerular pressure in these patients. Angiotensin II, the active product of this system, produces selective vasoconstriction of the glomerular efferent arteriole, thereby raising the intraglomerular pressure. It also promotes proliferation of mesangial cells and accumulation of mesangial matrix, both of which promote protein leak. It follows that interventions aimed at blocking the renin-angiotensin cascade will have a beneficial effect in preventing and retarding the progress of diabetic nephropathy.

Diabetes produces characteristic changes in renal structure. The most specific lesion of diabetic glomerular disease is nodular glomerulosclerosis or Kimmelstiel-Wilson lesion; however this is only found in 40 to 50% of proteinuric patients³³. Other changes, which are more commonly seen include diffuse glomerulosclerosis, fibrin caps, capsular drops, increased basement membrane thickness, microaneurysms and Armani-Ebstein lesions (glycogen-containing inclusions in tubular epithelial cells)³⁵.

SCREENING FOR NEPHROPATHY AND MONITORING OF RENAL FUNCTION

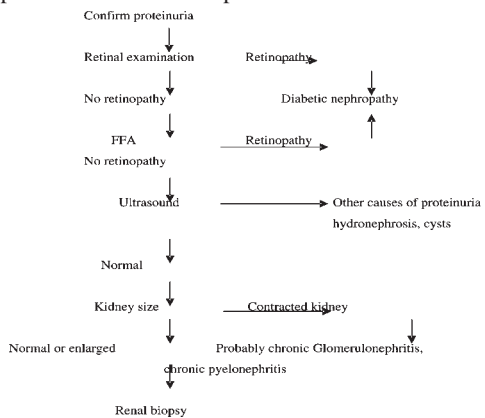
Diabetic nephropathy, once established, is usually irreversible. The curative options are expensive and not easily available. Hence, stress is being laid on the prevention of kidney disease in persons with diabetes.

Estimation of urine albumin excretion provides an easy method of screening for kidney disease in diabetic individuals. The stage of microalbuminuria offers great scope for institution of preventive measures. It has been recommended that all Type 2 diabetic patients be screened for microalbuminuria at the time of diagnosis of diabetes³⁶. In Type 1 diabetes, the initial screening is to be performed 5 years after diagnosis of diabetes³⁷, although certain authorities recommend earlier screening. A positive result should be confirmed by repeat testing as soon as possible. For all practical purposes, estimation of albumin-creatinine ratio in a spot urine sample will suffice for estimation of microalbuminuria³⁶. An early morning sample is preferred. The test should be performed when the patient is in stable glycemic control and free from acute infections including urinary tract infection.

Once persistent microalbuminuria is confirmed, urine should be tested at each visit, and renal function monitored using serum creatinine measurements and estimation of GFR. The latter can be calculated using the Cockcroft- Gault formula or the Modification of Diet in Renal Disease (MDRD) equation³⁷, although recent data indicate that both these formulae tend to underestimate GFR in diabetic patients³⁸.

Proteinuria in the absence of diabetic retinopathy, renal disease in diabetes of short duration, renal insufficiency in the absence of proteinuria and presence of active urinary sediment or hematuria should alert the clinician to the possibility of **non-diabetic renal disease** (*see aligrothm*). Such patients warrant further detailed investigation to find out other potentially reversible causes of nephropathy. An algorithm for the evaluation of such patients is given below. However, a significant proportion of these patients will turn out to have diabetic nephropathy on renal biopsy. In a series of 16 clinically diagnosed non-diabetic renal disease patients studied by us, eight (50%) were found to have diabetic nephropathy on biopsy³⁹.

Workup Of A Patient With Suspected Non-Diabetic Renal Disease



PREVENTION OF DIABETIC NEPHROPATHY

The most cost-effective method to prevent any diabetic complication would be to prevent the development of diabetes in a population. Several studies have shown that Type 2 diabetes is indeed preventable, using lifestyle modifications alone or in combination with pharmacotherapy⁴⁰⁻⁴⁴. However, once a person is found to have diabetes, the focus shifts to the ways in which the development of nephropathy can be prevented in him. There are two important aspects to this primary prevention of nephropathy viz. control of blood sugar and control of blood pressure.

Several large studies have shown that strict glycemic control, maintaining an HbA1c level of less than 7%, leads to decreased risk of developing clinical and structural abnormalities of diabetic nephropathy. Both the Diabetes Control and Complications Trial (DCCT) in Type 1 diabetic patients⁴⁵ and the UKPDS in Type 2 patients⁴⁶ showed significant reduction in the risk of development of microalbuminuria in the intensive treatment group compared to conventional treatment. The Kumamoto study also demonstrated a reduction in the development of macroalbuminuria as well as microalbuminuria in patients subjected to intensive glycemic control⁴⁷. The benefits of tight glycemic control may extend beyond the actual period of tight control, as has been shown in the Epidemiology of Diabetes Interventions and Complications (EDIC) study⁴⁸.

Hypertension is common in diabetic patients, even in the absence of nephropathy⁴⁹. Treatment of hypertension significantly reduces the risk of microvascular and macrovascular complications in Type 2 diabetes. Target levels of blood pressure for the diabetic patient have been set at <130/80 mmHg, which is lower than that recommended for the general population⁵⁰. However, there is no threshold of blood pressure below which further lowering does not produce further risk reduction²³. Considering the proven cardio and renoprotective benefits of ACE inhibitors, it would seem logical to initiate antihypertensive treatment in diabetic subjects using this class of agents, adding other drugs as and when necessary. Regardless of the class of drug used, what really matters is that the blood pressure targets are met in a given patient.

Other strategies in the primary prevention of diabetic nephropathy include cessation of smoking and treatment of dyslipidemia. However, there is no firm evidence supporting the benefits of such interventions in this setting.

MANAGEMENT OF DIABETIC NEPHROPATHY

Once persistent micro or macroalbuminuria is established, it may not be possible to completely reverse the process of kidney damage. However, the progress of the disease can be delayed substantially. The goals of treatment would be to prevent the development of macroalbuminuria in microalbuminuric patients, and to prevent or delay the decline in renal function in macroalbuminuric patients. The same principles outlined in the section on primary prevention hold good here as well. However, there are certain subtle differences. The role of tight glycemic control in the management of established microalbuminuria and nephropathy remains controversial. Nevertheless, glycemic control should be optimised in all patients. The choice of antidiabetic agent depends on the stage of nephropathy. Once renal insufficiency sets in, metformin, thiazolidinediones, alpha-glucosidase inhibitors and sulfonylureas (except glimepiride, to an extent) are contraindicated. Non- sulfonylurea insulin secretagogues like repaglinide can be safely used⁵¹. However, the mainstay of glycemic management in patients with nephropathy remains insulin. Insulin regimes in nephropathy make use of more frequent injections of small doses of short or rapid acting insulins, restricting the use of longer acting preparations.

Several studies have shown that intensive control of blood pressure has a beneficial effect on albuminuria, irrespective of the antihypertensive agent used⁵¹. This effect is seen in both Type 1 and Type 2 diabetes patient. ACE inhibitors and Angiotensin II Receptor Blocker (ARB) confer additional renoprotective effect on account of their effect of RAS blockade. This beneficial effect is independent of their blood pressure- lowering effect^{52,53}. These drugs inhibit the progression of microalbuminuria to more severe stages of diabetic

nephropathy. Hence ACE inhibitors or ARBs are recommended as first-line therapy for diabetes patients with microalbuminuria, even if they are normotensive³⁵. There is no long-term study comparing the effects of ACE inhibitors and ARBs on progression of albuminuria. Recently, the concept of dual blockade of the RAS using a combination of ACE inhibitors and ARBs has gained acceptance⁵⁴. Several small, short-term studies have shown that the use of such a combination has an additive renoprotective effect^{55,56}. There is no long-term study analyzing the benefits of this combination in diabetic nephropathy.

Inhibition of the RAS can lead to elevation of potassium levels. Use of ACE inhibitors is also associated with a mild initial rise in serum creatinine, which plateaus off after around 2 months. This acute increase rarely exceeds 30 to 35%; higher increases should alert the clinician to the possibility of renal artery stenosis.

Large number of patients with diabetic nephropathy will require three or even four antihypertensive agents to attain target blood pressure levels⁵⁷. Due to their proven renoprotective effects, ACE inhibitors and ARBs remain the first choice drugs. They may be supplemented as and when necessary, with diuretics, beta-blockers, alpha-blockers and calcium channel blockers. Rather than the class of drug used, it is the attainment of blood pressure targets that is more important.

Adoption of a low-protein diet has been associated with delayed progression of diabetic nephropathy in Type 1 diabetes⁵⁸. Replacement of red meat with chicken was also found to be associated with a decline in urinary albumin excretion⁵⁹. Protein restriction might play its beneficial role by improving glomerular hemodynamics. However, extreme protein restriction is not advisable as it raises concerns of malnutrition, particularly in Indian setting.

Till date, there have been no large studies showing whether treatment of dyslipidemia has beneficial effects on the progression of diabetic nephropathy. However, in view of the increased susceptibility of these patients to cardiovascular events, aggressive lipid lowering is indicated.

It should be remembered that diabetic patients with kidney disease have multiple cardiovascular risk factors and that most of them die from cardiovascular events rather than the kidney disease. Hence a multifactorial intervention program should be adopted in these patients, targeting all these risk factors. This involves strategies such as modification of diet, institution of a regular exercise program, cessation of smoking, and pharmacotherapy including aspirin, statins and ACE inhibitors or ARBs. Such an approach will not only help to prevent progression of the renal lesion, but will also reduce the risk of other vascular complications.

END-STAGE RENAL DISEASE

Timely referral to a nephrologist is the cornerstone of general medical management of renal insufficiency in diabetic nephropathy. It is advisable that the patient be referred once the serum creatinine is in the range of 1.5 to 2 mg/dl. Early referral allows better management regarding progression of renal failure and for physical and emotional preparation for renal replacement therapy. It also provides for proper management of renal bone disease and anemia.

NEWER THERAPEUTIC STRATEGIES

The advent of ACE inhibitors and ARBs has revolutionized the treatment of diabetic nephropathy. However there remains a subset of patients who are resistant to the antiproteinuric and renoprotective effects of these drugs. This has prompted the search for newer therapeutic modalities for diabetic nephropathy. Avenues explored include the use of thiamine and its derivative benfotiamine⁶⁰, protein kinase C α inhibitors⁶¹ and inhibitors of advanced glycation end

products⁶². To date, there have been only small studies in humans evaluating the efficacy and safety of these strategies. One novel therapy that holds promise is aldosterone blockade; a few small studies have shown beneficial effects of the aldosterone antagonists spironolactone and eplerenone in reducing albuminuria^{63,64}.

CONCLUSION

Diabetic nephropathy accounts for a large share of the burden of ESRD in developed countries and increasingly in developing countries as well. Established diabetic nephropathy is largely irreversible. However, diabetes patients can be protected from developing nephropathy by strict control of blood sugar and blood pressure. The presence of a well-defined preclinical stage (microalbuminuria) and the availability of effective therapeutic modalities (ACE inhibitors and ARBs) imply that the initial stages of diabetic kidney disease can to an extent be reversed. Treatment of established nephropathy involves control of blood pressure and blood sugar, avoidance of nephrotoxic agents, dietary modifications and early referral to a nephrologist. In the final analysis, though, the prevention of diabetic nephropathy is intricately linked to the prevention of diabetes, which is one of the most challenging tasks facing health workers in this century.

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Conference News

13th ANNUAL INTERNATIONAL CONFERENCE of INDIAN ACADEMY OF ECHOCARDIOGRAPHY will be on **February 8 -10 , 2008 at Ashoka Hotel, New Delhi (India)**

SCIENTIFIC HIGHLIGHTS OF CONFERENCE

Stress on clinical echocardiography with emphasis on role in management issues; Lectures to cater to all levels of echocardiographers & cardiologists; Meet the expert sessions with active interaction with faculty; Interesting live workshops; Daily sessions on interesting case studies; Young Investigator award session; Orations of general interest for participants; **Natesa G Pandian Gold Medal For Best Case Presenter:** (a) The award is applicable to members of IAE (b) age of the presenter must be below 45 years (c) presentation time will be 8 mins (d) the relevant CD containing brief history, relevant investigations, well edited echo images and final diagnosis must be sent to HQ, IAE by 30 November, 2007. (e) 10 best cases will be selected and the presenters will be informed by 31st December, 2007; Free paper sessions will be encouraged; An excellent scientific program of practical importance will be presented;

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Conference News

South Zonal Conference of Medical Microbiologists, SOZOCON - MICRO : 2008 will be held on 20th January, 2008 at Puducherry organized by Sri Manakula Vinayagar Medical College and Hospital, Madagadipet, Puducherry and Indian Association of Medical Microbiologists, Tamil Nadu - Puducherry IAMM Chapter .

Dr. J. Shanmugam
Chairman, SOZOCON - Micro: 2008

CONTRAST INDUCED NEPHROPATHY AND ITS PREVENTION

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Abstract: Contrast medium-induced nephropathy (CIN) is an impairment of renal function occurring within 3 days following the intravascular administration of contrast media (CM), in the absence of an alternative etiology. A widely used marker for the occurrence of CIN is an increase in serum creatinine by >25% or 0.5 mg/100 ml (44 mmol/l) within 48–72 h of contrast administration. The serum creatinine concentration typically peaks on the second or third day after exposure to CM and usually returns to the baseline value within 2 weeks. The assessment of risk factors including dehydration, heart failure, age greater than 70 years, and concurrent use of nephrotoxic drugs, along with measurement of serum creatinine levels in those at risk for impaired kidney function is mandatory. In the presence of risk factors, consideration of alternative imaging techniques, discontinuation of nephrotoxic drugs, and use of low-osmolar or iso-osmolar contrast mediums in reduced doses are recommended. Maintaining adequate hydration and administration of acetylcysteine or other potential prophylactic therapies may be of help in some of these patients.

INCIDENCE AND PREVALENCE

The nephrotoxicity of the radio contrast agent was first described in the 1960s¹. Since then the incidence of contrast medium induced nephropathy (CIN) has increased with increasing use of contrast agent in patients who are sicker, older, and have other co morbidities like diabetes, renal failure, cardiac failure, and volume depletion². CIN is the third most important cause of hospital acquired ARF and accounts for approximately 11% cases³. The prevalence of CIN ranges from 1 to 45% and depends largely upon the comorbidities of the study population and the parameters used to define CIN⁴. CIN occurs in approximately 13% of non-diabetics and 20% of diabetics who undergo contrast procedure⁵. Only 0.5 to 2% of patients who develop CIN will receive dialysis. The need of dialysis heralds a poor prognosis, 36% in hospital mortality and a 2 year survival of only 19%⁵.

DEFINITION

Contrast medium-induced nephropathy (CIN) is defined as an impairment of renal function occurring within 3 days following the intravascular administration of contrast media (CM), in the absence of an alternative etiology^{2,6}. A widely used marker for the occurrence of CIN is an increase in serum creatinine by >25% or 0.5 mg/dl within 48–72 hours of contrast administration^{7–10}. The serum creatinine concentration typically peaks on the second or third day after exposure to CM and usually returns to the baseline value within 2 weeks^{11,12}. Generally, CIN follows a benign course and only rarely necessitates dialysis. Nevertheless, use of CM has been associated with increased in-hospital morbidity, mortality, cost of medical care and long admissions, especially in patients requiring dialysis.

RISK FACTORS

The risk factors for CIN are listed in table 1. However, it is uncertain to what extent these factors independently worsen renal function, as opposed to serving as markers for coexisting conditions. Diabetes is an important risk factor for deterioration in renal function after angiography^{5,13,14}. Other factors variably associated with increased rates of acute renal failure after the administration of contrast medium include age over 75 years, periprocedural volume depletion, heart failure, cirrhosis, renal disease (or dysfunction), hypertension, proteinuria, concomitant use of nonsteroidal anti-inflammatory drugs, and intra-arterial injection. In the setting of acute myocardial infarction or percutaneous coronary intervention, hypotension or use of an aortic balloon pump has been associated with a higher rate of acute renal failure after exposure to a contrast medium^{13,14}. High doses of contrast medium also increases the likelihood of renal dysfunction. The tolerable dose of contrast medium depends on the kidney function^{5,15,16}.

Table 1 : Risk factors (5, 13-18) for contrast induced nephropathy

Non-modifiable risk factors

1. Older age
2. Diabetes mellitus
3. Pre existing renal failure (Estimated GFR of up to 60 ml/min/1.73 m²)
4. Advance congestive heart failure
5. Low left ventricular ejection fraction
6. Acute myocardial infarction
7. Cardiogenic shock
8. Renal transplant

Modifiable risk factors

1. Volume of contrast media
2. Hypotension
3. Anemia and blood loss
4. Pre or post procedural volume depletion
5. Low serum albumin level (<35g/dl)
6. ACE inhibitors
7. Diuretics
8. Non steroidal anti inflammatory drugs
9. Nephrotoxic antibiotics
10. History of structural kidney disease or damage
11. Intra – aortic balloon pump
12. Cholesterol emboli syndrome

PATHOPHYSIOLOGY

The Pathophysiology of CIN is still controversial despite the advances and research related to nephrotoxicity of contrast agents. The mechanisms are probably multifactorial. The important factors in the pathophysiology of CIN are the reduction in renal perfusion by contrast media (CM) combined with the toxic effects on the tubular cells. In vitro studies and studies in animals suggest a combination of toxic injury to the renal tubules and ischemic injury partly mediated by reactive oxygen species^{19,20}. Low blood flow in the medulla, which has a high demand for oxygen, might result from increased perivascular hydrostatic pressure, high viscosity, or changes in vasoactive substances such as endothelin, nitric oxide, and adenosine^{21,22}. Factors impairing medullary vasodilation, such as nonsteroidal anti-inflammatory drugs, may worsen contrast-medium-induced nephropathy. The pathophysiological mechanism of CIN depends on the following factors.

ANATOMICAL FACTORS

The most vulnerable region is the deeper portion of the outer medulla. The relatively high oxygen requirements due to ATP dependent

activity of NaK ATPase pump and saltreabsorption, offer an explanation for the vulnerability. Kidney perfusion is very high for the cortex, but the medullary portions are maintained on the verge of hypoxia where pO₂ levels can be as low as 20mmHg²³. This is a deleterious result for upholding the countercurrent mechanism for controlling urine concentration. Contrast media by increasing vascular resistance intensifies hypoxic injury in this region²⁴. The thick ascending limbs of the loop of Henle exhibit further hypoxic damage, when the kidney is perfused with erythrocyte-free medium²⁵.

ADVERSE EFFECTS OF DIFFERENT CM CLASSES

The physicochemical properties of contrast agents are different. They are classified according to their osmolality and ionicity. High osmolar CM have osmolalities approximately six times higher than plasma, low osmolar CM have osmolality twice as high as plasma and iso osmolar has osmolality almost similar to plasma. It has become clear that many of the side effects were caused by the electric charge. Today it seems that this physicochemical subdivision may actually require reconsideration: iso-osmolar CMs are dimers, and consequently have greater viscosities than the monomeric low osmolar CMs. This can have important implications for renal medullary perfusion and oxygenation²⁶. Iothalamate, a high osmolar agent, strikingly reduces medullary pO₂ to about a third of control levels²⁷. Remarkably, the iso-osmolar CM *iotrolan* impairs local pO₂ to a greater extent than the low osmolar CM *iopromide*²⁷. The decrease in pO₂ by the CM iopromide failed to reach statistical significance. It has also been shown that the iso-osmolar CM, *iodixanol*, reduces blood flow to all regions of the kidney to a greater extent than low osmolar and even high osmolar CM²⁶. Although this decrease in perfusion was more likely to be due to the profound systemic effects of iodixanol considerable fall in blood pressure. Studies have shown that iso-osmolar CM has adverse effects in terms of renal tissue oxygenation, when compared with low osmolar CM^{27,28}. Thus, experimental and animal studies suggest greater nephrotoxicity of iso osmolar contrast compared to low osmolar contrast. The lower nephrotoxicity of low osmolar contrast may be due to lesser viscosity than iso osmolar contrast²⁸. However, a few clinical trials have shown beneficial effect of low osmolar contrast over high osmolar contrast agents²⁹ and iso osmolar contrast agents over low osmolar contrast agents^{6,30}. In contradistinction, other trials have revealed no significant differences between iso and low-osmolar agents in the rates of renal failure requiring intervention or prolonging hospitalization³¹ and mean change in serum creatinine³². More data are needed to confirm the superiority of one contrast agents over others.

CM AND TUBULOGLOMERULAR FEEDBACK (TGF)

CM cause diuresis and activates TGF, which is a key regulator of kidney hemodynamics. Activation of TGF causes vasoconstriction of the glomerular afferent arterioles, and results in a decrease in the glomerular filtration rate (GFR) and an increase in renal vascular resistance. TGF may be responsible for almost 50% of the increase in renal vascular resistance induced by high osmolar ionic CMs. High osmolar CMs are thought to have a greater effect on TGF³³. However, experimental studies^{34,35} with retrograde perfusions of the tubule have already shown that osmolality has no effect on TGF. With orthograde perfusion, quite a lot of transport occurs between tubular fluid and interstitium, and even non-ionic fluids occasionally may be able to elicit the TGF response. Further experiments using mannitol, an osmotic diuretic, do not support that the osmotic diuresis

theory. Increases in osmolality, such as after mannitol infusion or after CM application, decreases NaCl concentration at the macula densa. However, this increase in osmolality also simultaneously increases tubular flow. Therefore, the resulting net change in the amount of NaCl passing the macula densa is negligible³⁶. Finally, blocking the TGF by furosemide does not decrease serum creatinine after administration of CM, which is usually the parameter taken to indicate CIN². Consequently, combining these factors, the theory that the osmolality of a CM causes CIN via the TGF does not appear likely.

ATHEROEMBOLISATION

In addition two other factors involved in the pathophysiology of CIN are micro showers of atheroemboli and atheroemboli induced intrarenal vasoconstriction.

CLINICAL FEATURES

CIN usually manifests as non-oliguric acute renal failure. Patients who have mild renal dysfunction or normal renal function before receiving contrast agents usually have oliguria that lasts for 2-5 days, with recovery to baseline function by day 7. Dialysis requirement is infrequent^{7,8}. Some degree of residual renal impairment has been reported in as many as 30% of those who are affected by CIN⁸. The occurrence of CIN and other co morbid factors like hypotension, sepsis, cardiac disease, atheroembolic disease and use of nephrotoxic medications may contribute to CIN in ICU settings and prolong hospital stay³⁷ and mortality. Levy et al³⁸ have shown a significantly high mortality in 34% in hospitalized patients compared to 7% in control group (p<0.001, odds ratio 5.5). even when severity of co morbid illness was controlled by matching patients by acute physiological and chronic health evaluation scoring. Contrast agents may precipitate *metformin induced lactic acidosis* when CIN occurs specially in patients with impaired renal function³⁹.

DIAGNOSIS

CIN usually develops within 24 to 72 hours following a radiocontrast study. Oliguria is a rare manifestation. The oliguric CIN is characterized by low fractional excretion of sodium during the initial stage, despite no clinical evidence of volume depletion³⁹. The urine analysis reveals renal tubular epithelial cells casts, coarsely granular brown casts, but occasionally may be negative⁴¹⁻⁴². Radio contrast agents may alter urinary sediments even before the rise in serum creatinine. A persistent nephrogram 24 to 48 hours after the contrast study was reported to be sensitive marker of presence of ARF. The positive nephrogram is seen in 83% of patients who develop renal failure while 93 % of patients who do not develop CIN lack its specificity for diagnosis⁴³. Recently, it has been shown that urinary liver type fatty acid binding protein (L-FABP) level can serve clinically as a *predictive marker* for contrast medium-induced nephropathy⁴⁴.

PREVENTION

There is no definite treatment of CIN. CIN preventive strategies should be used in patients who have evidence of chronic kidney disease (CKD). The preventive strategies include risk evaluation and preventive steps.

The basic concepts in prevention of CIN are *hydration, choice and quantity of contrast*, pre, para and post procedural *end organ protection* with pharmacotherapy and post procedural monitoring and care.

RISK EVALUATION

The risk of a decline in kidney function after the administration of

contrast medium rises exponentially with the number of risk factors present⁴⁵⁻⁴⁷. Validated risk-prediction models have been developed for patients undergoing percutaneous coronary intervention (Table 2)^{14,17}. Most risk factors can be detected by history taking and physical examination.

It is not necessary to measure the serum creatinine levels of every patient before exposure to a contrast medium, but measurements should be made before intraarterial use of the medium and in patients with a history of kidney disease, proteinuria, kidney surgery, diabetes, hypertension, or gout⁴⁸. The creatinine clearance rate or the glomerular filtration rate should be estimated from the serum creatinine level, according to either the Cockcroft–Gault⁴⁹ or the Modification of Diet in Renal Disease⁵⁰ formula to identify more accurately patients with values below 50 ml per minute per 1.73 m², who are at increased risk for nephropathy⁴⁵.

Alternative imaging methods not requiring contrast medium should be considered for use in patients with any risk factors. Serum creatinine levels should be measured 24 to 48 hours after administration of the contrast medium. Because of the risk of lactic acidosis when contrast-medium-induced nephropathy occurs in a patient with diabetes who is receiving metformin, it is prudent to withhold this agent until the glomerular filtration rate is greater than

Table 2: Predicting the risk of acute renal failure after per cutaneous coronary intervention

Risk factors	Score
Hypotension Systolic blood pressure <90 mmHg>1 hour or patients need ionotropic support, intra aortic balloon pump within 24 hr of procedure	5
Use of Intra-aortic balloon pump	5
Heart failure class III or IV, or history of pulmonary edema	5
Age >75 yrs	4
Hematocrit <39 for men or <36 for women	3
Diabetes	3
Volume of contrast	1 for each 100 cc
Serum creatinine >1.5 mg/dl or GFR <60ml/min/1.73m ²	42=40-<60=20-39=, <20
Total score	Risk of CIN Risk of Dialysis
≤5	7.5 % 0.04%
6-10	14 % 0.12%
11-15	26.1 % 1.09%
≥16	57.3 % 12.6%

40 ml per minute per 1.73 m² and for the 48 hours before exposure of the patient to the contrast medium⁵¹. In general, the expected rate of CIN is 30 to 40 % and need of dialysis occurs in 2 to 8 % in patients who have a GFR of 30 ml/min/1.73m²⁵².

PREVENTIVE STEPS

Protocols for Administration of Fluids

The majority of studies have recommended administration of fluids as first line therapy to reduce the risk of contrast-medium induced nephropathy. However, the optimal regimes for fluid administration remain unknown.

Trivedi et al have shown that serum creatinine levels increases by more than 0.5 mg per deciliter in 34.6 % patients given water orally

as compared to 3.7% given intravenous saline for 24 hours beginning 12 hours before administration of the contrast medium⁵³. Another study comparing the use of intravenous fluids for 12 hours before and after the procedure with oral fluids plus a single intravenous bolus of fluid showed a lesser mean decline in the glomerular filtration rate 18.3 compared to 34.6 ml/ min/1.73 m² at 48 hours, in the group receiving intravenous fluids after administration of the contrast medium⁵⁴. However, this finding was not confirmed in the other trial⁵⁵.

Mueller et al have compared isotonic saline with 0.45 percent saline, and found that CIN was less likely in patients who were given isotonic saline (0.7%) compared to 2% in 0.45% normal saline group (p=0.04)⁵⁶. The fluid was given at 1 ml per kg/hr for 24 hours starting in the morning of the procedure involving the contrast medium.

Alkalinization of Urine:

Studies have shown that infusion of sodium bicarbonate has a beneficial effect in prevention of CIN. Alkalinization of tubular fluid causes reduction in the levels of pH-dependent free radicals and decreases the extent of injury. Merten et al⁵⁷ have shown that, CIN was less likely within two days after the administration of contrast medium in patients who were given an infusion of isotonic sodium bicarbonate than in those given a saline infusion.

In conclusion, it is reasonable to start volume supplementation with intravenous normal saline or sodium bicarbonate solution 3 to 12 hours before procedure at a rate of 1-2 ml/kg/hour^{2,56,58}. A urine output of 150ml/h should be the target of hydration after procedure. When adequate urine flow rates were achieved in clinical trial setting, there was a 50% reduction in rate of observed CIN⁵⁸.

N-acetylcysteine (NAC)

More data is needed before N-acetylcysteine can be strongly recommended for the prevention of contrast-medium induced nephropathy. Recent meta-analyses⁵⁹⁻⁶² suggest some benefit to N-acetylcysteine (pooled odds ratio, 0.54 to 0.73).

N-acetylcysteine reduces the nephrotoxicity of CMs through its antioxidant and vasodilatory effects⁶³. Tepel et al studied that CIN occurs in 2 percent of patients of N-acetylcysteine group as compared to 21 percent of patients in the control group (P<0.01)⁶⁴. However, the event rate in the control group was unexpectedly high for patients who received low-dose intravenous low-osmolality contrast medium in this study. In the Rapid Protocol for the Prevention of contrast Induced renal Dysfunction (RAPPID) trial⁶⁵, CIN occurred in 5% in patients with NAC plus hydration compared to 21% in patients who had only hydration. Brigouri et al⁶⁶ in study of two dosage regime of NAC 600mg versus 1200mg, have shown less incidence of CIN 3.5% in 1200 mg regime compared to 11% in patients with 600mg regime. It was also observed that benefit of double dose NAC was greater in patients who have received a volume of at least 140 ml of radicontrast (5.4% versus 18.9%, p=0.039) than in those who had less than 140 ml of contrast. This study supports the hypothesis of dose dependent protective effect of CIN. For the most part, subsequent trials have involved patients with reduced kidney function who underwent coronary angiography. Some have shown a benefit and others have shown a lack of effect; many are limited by low power and a lack of blinding⁵⁹⁻⁶². However, this estimate must be interpreted with caution, given the heterogeneous results of the individual trials, the possibility of publication bias, and the under representation of small negative studies. Also, the effect of N-acetylcysteine on outcomes other than minor changes in serum creatinine levels is unknown. However, another metaanalysis of group data of both blinded and non-blinded randomized trials, the overall risk ratio was 0.41(95% confidence interval 0.22-0.79;p=0.007)

on random effects model. Kshirsagar et al⁵⁹ have not supported the routine use of NAC for prevention of CIN in their review since they feel that the beneficial effect of NAC may be because of chance variation.

Theophylline

Theophylline and aminophylline have also been proposed as agents that may reduce the risk of contrast-medium induced nephropathy. In a study from authors center, theophylline has shown beneficial effect on prevention of CIN⁶⁷. A recent meta-analysis found that the mean rise in serum creatinine levels was significantly lower (by 0.17 mg per deciliter [15 μmol per liter]) at 48 hours after administration of the contrast medium among patients receiving either of these medications than among those receiving placebo⁶⁸. However, the clinical importance of this finding is questionable. Since, there was heterogeneity among studies with regard to changes in serum creatinine levels. Overall, no prophylactic agent has been shown conclusively to prevent clinically important contrast-medium induced nephropathy.

Other Approaches to Prophylaxis

Several other interventions have been proposed to reduce the risk of contrast-medium induced nephropathy with limited data support. *Forced diuresis* with furosemide, mannitol, dopamine, or a combination of these given at the time of exposure to the contrast medium has been associated with similar or higher rates of contrast-medium induced nephropathy when compared with prophylactic fluids alone^{2,58-70}. Deleterious effects may be explained by negative fluid balance in some instances.

In general, small randomized trials, have failed to show the beneficial effect of the use of various *vasodilators*, including dopamine, fenoldopam, atrial natriuretic peptides, calcium blockers, prostaglandin E₁, or a nonselective endothelin-receptor antagonist, in reducing the risk of contrast-medium-induced nephropathy in comparison to fluid therapy⁷⁰⁻⁷⁵. A small randomized trial⁷⁶ showed a lower frequency of an increase of more than 0.5 mg per deciliter in serum creatinine levels in patients given captopril for three days as compared with those given placebo, but confirmatory trials are required.

In another small trial, serum creatinine levels were significantly less likely to increase (by >25 percent or >0.5 mg per deciliter) within two to five days of administration of the contrast medium in patients who received ascorbic acid as an antioxidant than in those who received placebo⁷⁷. The baseline serum creatinine level was lower in the placebo group, and both groups reached a similar level after exposure to the contrast medium.

HEMODIALYSIS OR HEMOFILTRATION

The role of hemodialysis in patients at high risk for contrast-medium induced nephropathy remains uncertain. Vogt et al⁷⁸ evaluated prophylactic hemodialysis soon after the contrast procedure and continued for 3 hrs with the aim to remove contrast medium effectively through dialysis. However, this strategy did not show any significant benefit as compared to normal saline alone. Patients who were treated with hemodialysis were more likely to have a decline in renal function and further need of hemodialysis.

Among patients with advanced kidney disease (mean creatinine clearance, 26 ml per minute), an increase in serum creatinine levels of at least 25 percent was significantly less common in patients randomly assigned to prophylactic hemofiltration before and after the administration of contrast medium than in those assigned to receive fluid alone (5 percent vs. 50 percent, P<0.001)⁷⁹. In-hospital death was also significantly less frequent in the hemofiltration group⁸⁰.

However, the serum creatinine level is directly altered by the intervention, and the relationship between the intervention and the reduced mortality rate is unclear. Thus, the results require confirmation. Given the resources to deliver the intervention, this approach would apply only to the most ill.

PERITONEAL DIALYSIS

Intermittent automated peritoneal dialysis removes 43-72% of contrast volume over 16-18 hour. Continuous ambulatory peritoneal dialysis has also been shown to remove 54% (range 36-80%) of administered dose of contrast medium in patients with end stage renal failure^{81,82}.

CHOICE OF CONTRAST MEDIUMS

Iodinated contrast mediums can be classified by osmolality (e.g., high-osmolar contrast mediums, such as sodium diatrizoate; low-osmolar mediums, such as iohexol; and iso-osmolar mediums, such as iodixanol). In a meta-analysis of comparative trials, an increase in serum creatinine levels of more than 0.50 mg per deciliter after administration of the contrast medium in patients with reduced kidney function was less frequent with low-osmolar than with high-osmolar mediums (odds ratio, 0.50; 95 percent confidence interval, 0.36 to 0.68)⁸³. Because of the small number of events, no conclusion could be reached about the effects of osmolality on the need for dialysis.

Iso-osmolar contrast mediums have been proposed as an alternative. One randomized trial involving patients with diabetes who have renal impairment showed a significantly lower frequency of increases in creatinine levels of at least 0.5 mg per deciliter with the iso-osmolar agent iodixanol, than with a low-osmolar agent⁶. However, the rate of renal deterioration in the group receiving a low-osmolar contrast medium was higher than expected. Similarly, in an open-label trial, a maximal increase in serum creatinine levels of greater than 25 percent within a week after the administration of contrast medium was less common with iodixanol than with iohexol (3.7 percent vs. 10 percent), but a lack of consistent timing for measuring creatinine levels in the two groups may have biased the results³⁰. In contrast, other trials have revealed no significant differences between iodixanol and low-osmolar agents in the rates of renal failure requiring intervention or prolonging hospitalization³¹ or in mean changes in creatinine levels

Table 3: Recommendations of interventions commonly used to reduce the risk of Contrast medium induced nephropathy

Intervention	
Intravenous saline therapy	Rate 0.9% normal saline at 1ml/kg/hr, beginning 2-12 hr before administration of contrast medium
Contrast medium of choice	<ul style="list-style-type: none"> • Low or Iso osmolar contrast agents • Evidences support lower nephrotoxicity of low and Iso-osmolar contrast media over high osmolar contrast media. Further data are needed to show relative nephrotoxicity of iso osmolar contrast agents over low osmolar contrast agents. Experimental studies does not support it • Dose; lowest dose is preferred, dose of 5 ml x kg of body weight÷ serum creatinine (mg/dl) is associated with higher risk
Sodium bicarbonate solution	154mmol/l 3ml/kg/hr before administration of contrast agents followed by 1ml/kg/hr for 6 hours after administration. Evidence is based on randomized trial but further data are needed.
N acetyl cysteine	Dose 600 mg BID -4 doses starting before contrast administration. Evidences are based on multiple randomized trials and metanalysis but further data are needed.

after administration of contrast medium³². Further studies are needed before iso-osmolar contrast mediums can be recommended in place of low-osmolar mediums. Experimental studies also did not support the use of iso osmolar contrast as compared to low osmolar contrast agent.

Exceeding a volume of contrast medium of 5 ml per kilogram of body weight divided by the serum creatinine level in milligrams per deciliter strongly predicts nephropathy requiring dialysis¹⁵. Table 3 summarizes recommendations regarding interventions commonly used to prevent contrast-medium-induced nephropathy.

RECOMMENDATIONS

The risk evaluation should be done in every patient as per suggestion in table 2. The assessment of risk factors including dehydration, heart failure, age greater than 70 years, and concurrent use of nephrotoxic drugs, along with measurement of serum creatinine levels in those at risk for reduced kidney function are mandatory.

In the presence of risk factors, consideration of alternative imaging techniques, discontinuation of nephrotoxic drugs, and use of low-osmolar or iso-osmolar contrast mediums in limited doses are recommended. Maintaining adequate hydration and the administration of additional fluids are also recommended. Multiple infusions of contrast medium within a short period of time and the use of mannitol or diuretics are to be avoided. *N*-acetylcysteine or other potential prophylactic drug therapies may be of help in some of these patients.

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LITERATURE REVIEW

VASCULAR ERECTILE DYSFUNCTION IN CHRONIC RENAL FAILURE

Guido, Vincenzo and Domemico

Semin Nephrol 26:42-45

The prevalence of erectile dysfunction (ED) has increased dramatically worldwide in parallel with the aging of the population. In 1995, ED was estimated to be present in more than 150 million men. Considering population aging in Western Countries, estimates predict that more than 300 million men will be affected by ED by the year 2025. ED is a common and often distressing side effect of renal failure. It is present 30% of patients with chronic renal failure and in 50% of patients undergoing dialysis treatment. Uremic men of different ages report a high variety of sexual problems including sexual hormonal pattern alterations, reduced or loss of libido, infertility, and impotence, thereby influencing their well-being. The release of sildenafil citrate, the relationship between ED and the presence of cardiovascular disease (CVD) has been evaluated in several studies. Many of the risk factors for ED are the same as those for cardiac disease. CVD and ED are closely interrelated disease processes. Indeed, ED can be considered a symptom of vascular endothelial damage. Therefore, it can be expected that impotence will appear along with CVD, and the presence of ED suggests the existence of CVD. An accurate evaluation of sexual histories of all men who present to internists, cardiologists, and also nephrologists for early detection of ED may allow for early diagnosis and management of CVD.

LITERATURE REVIEW

Diuretic Use, Residual Renal Function, and Mortality Among Hemodialysis Patients in the Dialysis Outcomes and Practice Pattern Study (DOPPS)

Jennifer L. Bragg-Gresham, Rachel B. Fissell, Nancy A. Mason et al. *Am J Kidney Dis* 49:426-431, 2007.

The role of diuretics in the management of hemodialysis (HD) patients has not been clearly defined, and guidelines for their use in patients with end-stage renal disease (ESRD) do not exist. Use of diuretics was shown to increase urine volume and sodium and potassium excretion in patients on continuous ambulatory peritoneal dialysis therapy. Management of volume status with may reduce the risk of fluid overload and minimize episodes of hypotension during dialysis. In addition, improved overall fluid balance could slow the development of cardiovascular disease and minimize complications of existing cardiovascular disease. The larger urine volume that accompanies diuretic use in both continuous ambulatory peritoneal dialysis and HD patients may allow for a more liberal fluid intake and perhaps allow for a more liberal diet, thus facilitating improved nutrition.

Diuretic use was investigated in 16,420 hemodialysis patients from the Dialysis Outcomes and Practice Patterns Study, a prospective observation of hemodialysis patients selected from nationally representative facilities on 3 continents. Logistic regressions were used to investigate associations between diuretic use and patient characteristics. Outcomes of interdialytic weight gain, increased serum potassium and phosphorus levels, and odds of RRF after 1 year were investigated. Cox regression was used to analyze the association between mortality and diuretic use. Facility diuretic use varied substantially from 0% to 83.9% of patients. Diuretic use decreased sharply after the start of dialysis therapy. Loop diuretic use ranged from 9.2% in the United States to 21.3% in Europe. Where use within 90 days of starting dialysis therapy ranged from 25.0% in the United States to 47.6% in Japan. Diuretic use was associated with lower interdialytic weight gain and lower odds of hyperkalemia (potassium > 6.0 mmol/L). Patients with RRF on diuretic therapy had almost twice the odds of retaining RRF after 1 year in the study versus patients not on diuretic therapy. Patients administered diuretic had a 7% lower all-cause mortality risk (p=0.12) and 14% lower cardiac-specific risk (p=0.03) versus patients not administered diuretics.

Variation exists in facility practices of diuretic use. In patients with RRF, there may be benefit associated with continuing diuretic use rather than automatically discounting diuretic therapy at dialysis initiation.

CHRONIC KIDNEY DISEASE PREVENTION IN INDIA: WHERE ARE WE NOW AND WHERE DO WE GO FROM HERE?

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Abstract: Chronic kidney disease has emerged as a worldwide public health problem in recent years. Data from advanced countries suggest that 10-15% of general population suffers from CKD, and population on RRT represents but the tip of an iceberg of CKD population. Even early stages of CKD increase cardiovascular disease risk and reduce quality of life. The CVD risk in non-ESRD CKD patients is 10-30 times that of people without kidney disease. The annual crude and age-adjusted ESRD incidence rates in India have been estimated at 151 and 232 per million population respectively. ESRD patients belonging to the disadvantaged strata of the society often present for the first time with advanced renal failure, over two-thirds have not had prior medical care, and 75% present with complications that necessitate dialysis within 48 hours of arrival. Early detection of CKD entails screening high risk population such as those with diabetes, hypertension, cardiovascular disease and a family history of CKD by urinalysis and estimation of GFR using any prediction equation. Appropriate preventive strategies include a good blood pressure control to values lower than previously recommended (<120/75-80) and reduction of proteinuria to the lowest possible values (preferably <1 g/day). Drugs that block the rennin-angiotensin-aldosterone axis are preferred antihypertensive and antiproteinuric agents both for prevention of CKD progression and minimizing CVD risk. Additional measures include maintaining careful glycemic control in individuals with diabetes, treating dyslipidemia, losing weight, quitting smoking, and managing anemia. There is also evidence that outcomes can be improved by providing these individuals with specialist nephrology care early in disease. CKD incidence would continue to rise in the foreseeable future unless public health policies are altered to deal with this increasing menace.

INTRODUCTION

The last few decades have been characterized by significant demographic changes in India. The life expectancy has risen from 41.2 years in 1951-1961 to 64.7 years in 2006, and the population growth rate has declined to 1.38%. About 65% Indians are in the age range of 15-65 years (<https://cia.gov/cia/publications/factbook/geos/in.html>). This has been the result of advances in medical practice and technology, eradication of communicable diseases, reduction of nutritional deficiency states and maternal and infant mortality, urbanization and economic improvement. As in the rest of the world, the increasing longevity has led to an increase in the risk of non-communicable chronic diseases related to adoption of an urban lifestyle, unhealthy diet, lack of physical activity and tobacco and alcohol abuse¹. The list encompasses entities such as diabetes, hypertension, obesity, cardiovascular disease (CVD) and cancer. Chronic kidney disease (CKD), neglected until recently by medical professionals, is now recognized as central player in the network of major chronic diseases. The initial realization came from registry data from industrialized nations where dramatic and unexpected increases in the incident and prevalent end-stage renal disease (ESRD) cases entering dialysis programs were observed. In 1984, Eggers et al² estimated that 117,200 patients would be receiving renal replacement therapy (RRT) in USA by 2000. However, these projections were overtaken by reality: the United States Renal Data System recorded a total of 378,862, with a point prevalence rate of 1367 patients per million population in 2000³. More recently, it has been recognized that RRT represents the tip of an iceberg of CKD population, with the number of those with CKD not yet requiring RRT being much greater. According to the Third National Health and Nutrition Evaluation Survey of the USA (NHANES III), the prevalence of CKD in the US adult population was estimated as 10.8%. A total of 4.98% of the male population and 1.55% of the female population had serum creatinine values above 1.5 mg/dl; and 0.64 and 0.33% respectively, had creatinine > 2.0

mg/dl. Older age and male sex were associated with higher creatinine levels⁴.

MAGNITUDE OF CKD IN INDIA

Until recently, no data existed on the incidence or prevalence of CKD in India. Recently, however, some figures have become available. In a population-based study from Bhopal where over 5.7 lakh people are served by a hospital set up to take care of individuals potentially exposed to the methyl-isocyanate gas in the Union Carbide Tragedy of 1984, Modi and Jha⁵ determined the annual crude and age-adjusted ESRD incidence rates at 151 and 232 per million populations respectively. The rate was consistent over a 4-year period. If these figures are validated in other parts of the country, it will place India in one of the top 10 nations in the world in terms of ESRD incidence, and mean that every year over 150,000 new patients would need RRT.

A couple of studies have reported on the CKD prevalence in different Indian communities. Mani⁶ reported a prevalence of chronic renal failure of 0.16% and other renal diseases (short of CRF) in 0.7% amongst a rural population of 25,000 near Chennai who are served by the a prevention program. Agarwal et al⁷ screened over 4900 individuals in urban communities of Delhi, and found a 0.79% point prevalence of individuals with serum creatinine over 1.8 mg/dl. These figures are substantially less than the NHANES data, but because of the sheer population base, represent a staggering load for the Indian medical community.

CKS IMPOSES A HIGH MEDICAL AND ECONOMIC BURDEN

Yearly death rates of ESRD patients are approximately 20%. However, only about 10% of all CKD patients end up on RRT. What about the rest? It is now increasingly recognized that besides its implication on demands for RRT, CKD has major impact on overall population health by substantially increasing the risk for CVD. Large population based-studies have shown that progressive decreases in the glomerular filtration rate (GFR) are associated with increased risks of death, cardiovascular events, and hospitalization⁸⁻¹¹. CKD lowers quality of life, and is expensive to treat. In approximately 4 lakh Medicare patients with diabetes and CKD in the USA, the risk

of death for cardiovascular diseases was 32% over two years, about 6-fold higher than that for development of ESRD. [12] The CVD risk in non-ESRD CKD patients is 10-30 times that of people without kidney disease¹¹. These findings suggest that CKD patients who are advancing toward ESRD carry the heaviest burden of cardiovascular disease (CVD) and that this frequently leads to death before ESRD is reached.

ESRD treatment consumes a disproportionate piece of the healthcare budget pie. Constituting < 1% of the US Medicare population, their care consumes 6.4% of the health care expenditures¹³. This economic burden of ESRD care is even more stark in India. It bears to keep in mind that the minimum annual expenditure for a patient on regular dialysis is Rs 1 lakh, a figure that stands out in sharp contrast to the national annual per capita income of approx Rs 2,000, and where only 3% of the population earns over Rs 50,000/year. The national per capita expenditure on health is Rs 40 per year.

THE SUBOPTIMAL CKD CARE IN INDIA

Data from around the world suggests an epidemic of CKD among certain ethnic groups. These populations include Aborigines in Australia's Northern Territory, and some native Indian communities in the USA, who carry upto 20-fold higher risk than local Caucasians¹³. Especially important are data from certain hospitals and dialysis units from areas in UK where ethnic south Asians form over 50% of the local population. Lightstone and colleagues¹⁴ documented a 4-fold higher ESRD take-on rates amongst south Asians compared to Caucasians. Data from within India is scarce, but in our own center, a major public sector tertiary care hospital, ESRD patients belonging to the disadvantaged strata of the society are over-represented; these individuals often present for the first time with advanced renal failure, over two-thirds have not had prior medical care, and 75% present with complications that necessitate dialysis within 48 hours of arrival. We found a clear impact of patients' socioeconomic status on the access to nephrological care and late presentation with advanced renal failure. Children in Pakistan, which has a population similar to that in India in terms of ethnicity and socio-economic development, have higher blood pressure levels adjusted for body-mass index, than their seen in white children in the United States¹⁵, and childhood levels have been shown to predict levels in adulthood.

CKD patients continue to receive suboptimal care around the world^{13, 16-21}, including developing countries like India. The reasons for this suboptimal care are likely complex, but people at risk because of diabetes or hypertension are often unaware that CKD can be caused by these conditions. In addition, quantitation of albuminuria with sensitive methods is inadequately performed in patients with diabetes. The reasons behind high CKD risk in poorer populations and certain ethnic groups have been under investigation recently. In addition to possible contribution of genes, the role of intrauterine origin of chronic disease in adult age, particularly systemic arterial hypertension and CKD, has come to the fore. It is suggested that lower nephron numbers acquired *in utero* can increase susceptibility to kidney damage from diseases such as hypertension and diabetes, and also cause *de novo* hypertension and renal damage.²² Whether nephrogenesis is influenced by intrauterine malnutrition and/or any adverse intrauterine environment is a matter of speculation. A link between low birth weight and early malnutrition followed by over nutrition in adult life and ultimate development of metabolic syndrome, diabetes and diabetic nephropathy has been suggested and could emerge as a central theme.²³

CKD CAN BE PREVENTED

The debate regarding the issue of upstream preventive strategies has

largely been settled. Other than treatment of the primary disease, it is now generally accepted that a good blood pressure control to values lower than previously recommended (<120/75-80) and reduction of proteinuria to the lowest possible values (preferably <1 g/day), are the most effective preventive strategies²⁴. Initial data came from diabetics with micro- and normoalbuminuria. The Irbesartan in patients with type 2 diabetes and microalbuminuria (IRMA) trial showed that the angiotensin II receptor blocker could prevent the progression from micro- to macroalbuminuria²⁵ and the Bergamo Nephrologic Diabetes Complication Trial (BENEDICT) study showed that an ACE inhibitor may prevent the progression from normo- to microalbuminuria.²⁶

Would a similar approach work in nondiabetics? The African American Study of Kidney Disease and Hypertension Study Group (AASK) trial compared amlodipine, metoprolol and ramipril in 1094 African-Americans aged 18-70 years with hypertensive renal disease (GFR 20-65 ml/1.73 m²); and showed a 22% reduction in the composite end points of GFR slope change, e⁺ 50% reduction in GFR and ESRD in the group treated with ramipril²⁷ over other agents. In a meta-analysis of almost 2000 non-diabetic patients, Jafar et al.²⁸ found a systolic blood pressure goal of 110-129 mmHg to be beneficial in patients with proteinuria exceeding 1 g/day. With an aggressive blood pressure and proteinuria control in high-risk patients with hypertension, microalbuminuria or overt albuminuria, Hoy et al.¹⁶ were able to cut down the renal and non-renal deaths in half with a goal blood pressure of 125/75 mmHg. In the Prevention of Renal and Vascular End Stage Disease Intervention Trial (PREVEND-IT), an ACE inhibitor lowered the number of cardiovascular events by 44% in microalbuminuric nondiabetics²⁹. On the basis of trials conducted in the developed world, it is by and large accepted that drugs that block the rennin-angiotensin-aldosterone axis are preferred antihypertensive and antiproteinuric agents both for prevention of CKD progression and minimizing CVD risk²⁴. Doses higher than those used in current-day practice are advocated. Subgroup analysis of the Heart Outcomes Prevention Evaluation (HOPE) study showed that in subjects with higher baseline levels of albuminuria, intervention with an ACE inhibitor is of particular value³⁰. A similar observation has been made in the Losartan Intervention for Endpoint Reduction (LIFE) study, which included subjects with hypertension and left ventricular hypertrophy¹⁰. REIN-2 study showed no additional benefit from intensive blood pressure control when patients were already on an ACEI³¹. Additional measures include maintaining careful glycemic control in individuals with diabetes, treating dyslipidemia, losing weight, quitting smoking, and managing anemia. Some of these recommendations have been based on studies with relatively small number of patients, and should be accepted cautiously^{32,33}.

To be acceptable, such programs must also be cost-effective. A health economic analysis of the IRMA and Irbesartan Diabetic Nephropathy Trial (IDNT) trials showed that earlier intervention was associated with substantial cost-savings.³⁴ The PREVEND group has also shown the cost-effectivity of the approach of screening the general population for microalbuminuria and treatment of those found positive with ACE inhibitors³⁵. The cost-benefit in the initial years is more in terms of the prevention of cardiovascular events than postponement of ESRD. Information whether of targeted screening and intervention programs as recommended in the west would also be cost-effective in India are lacking, warranting further research.

The earlier enthusiasm about dietary protein restriction for slowing progression of CKD has become muted following demonstration of only minor benefits of low-protein diets³⁶. Coupled with the demands

that adherence to a low-protein diet for several years will place on patients and their families, and the likelihood of development of malnutrition for only a modest benefit, this approach is no longer followed aggressively³⁷. Moreover, low-protein diets decrease blood urea levels, may instill a false sense of security in the minds of patients and doctors. This bears emphasis in India, where the basal protein intake is low in a predominantly vegetarian population, and restriction pushes it down to dangerously low levels.

METHODOLOGICAL ISSUES IN CKD PREVENTION

Who should be screened?

The objective of early diagnosis is the detection of asymptomatic disease at a stage when intervention would have a reasonable potential to have a positive impact on outcome. A key point will be the early identification of *at risk individuals*. The debate here is centered on whether the candidates for screening should be derived from the general population or from certain high-risk groups. Chronic care has tended to screen high-risk individuals. For CKD, these include individuals with diabetes, hypertension, elderly, the obese and those with urolithiasis, recurrent urinary tract infections, and family history of kidney disease. Till date, there is no strong evidence to favor one or the other of the screening approaches [38]. Another suggested approach is to include patients attending the doctor or medical facilities for another reason. In a recent Controversies Conference organized by the Kidney Diseases: Improving Global Outcomes (KDIGO) initiative that was attended by nephrologists and public health personnel from around the world, a targeted approach was preferred over universal screening.

What is the best screening/detection modality?

The two commonest tests for detecting sub clinical disease are: testing for protein in the urine and measurement of GFR using prediction equations such as the MDRD formula³⁹. The latter has not been validated in a primarily vegetarian Indian community that has a significantly different body composition, and is likely to have significantly different rates of creatinine generation. Still, using any formula, even the Cockcroft-Gault equation⁴⁰, is better than not calculating GFR. Standardization and regular validation of the method for estimation of serum creatinine is critical to avoid large variations that are commonly encountered in Indian laboratories.

The Multiple Risk Factor Intervention Trial (MRFIT) investigated the value of a single measurement of dipstick proteinuria and estimated GFR for prediction of end-stage renal disease (ESRD) over a 25-yr period⁴¹. The presence of a 1-2+ proteinuria was strongly associated with renal risk, whereas a baseline GFR < 60, but not of 60 to 75 ml/min per 1.73 m², indicated a poor renal prognosis. Because only subjects with a baseline serum creatinine < 2.0 mg/dl were included, the risk attributable to impaired baseline GFR may have been underestimated. Iseki et al.⁴² in a more general population of Japanese subjects showed that impaired renal function at baseline and dipstick-positivity predicted progression to ESRD. However, testing for an impaired GFR and proteinuria detected only 13% and 19% of the patients who later developed ESRD respectively, whereas the combination of both detected no more than 27%⁴¹.

This suggests the need to have an alternate approach. One suggestion is to use an integrated renal risk score that would take into account other risk factors, such as age, smoking status, BP, cholesterol, and race⁴³. This approach would likely increase the sensitivity and specificity of screening, but at a significantly higher manpower and financial costs. The currently favored approach is to screen for lower

levels of proteinuria (20 to 200 mg/L) using antibody-based techniques as was used in the PREVENT study⁹. Microalbuminuria predicts future CVD, and subjects will therefore benefit from early cardio protective treatment, such as BP lowering and ACEI/ARB use. The cost of this test remains a concern, but can be brought down to as low as Rs 20/test in mass screening. Point-of-care machines are also available, but tests using those cause significantly more (Rs 150-200/test).

Suggestions have been made that the South Asian populations may be especially susceptible to interstitial nephritis. The importance lies in the fact that it has an insidious onset without marked hypertension, proteinuria or hematuria, and hence is likely to be missed if only albuminuria detection strategies are employed⁴⁴. Whether development of new biomarkers, such as markers of tubular damage, would allow earlier detection of this condition remains a research question.

WHAT TO DO TO THOSE WITH ABNORMALITIES?

Primary prevention

Primary preventive measures can be applied to high-risk patients who have not yet developed any evidence of chronic kidney involvement. Some examples include glycemic control in diabetics, management of elevated blood pressure and appropriate management of primary kidney diseases such as glomerulonephritis, vesicoureteric reflux, stones, urinary tract infection, cessation of smoking, lipid control and weight loss. There is sufficient evidence to suggest that this approach reduces the CKD burden. An important example is the dramatic reduction in the incidence of nephropathy due to type 1 diabetes in Scandinavian countries following adoption of strict glycemic and BP control.

Secondary prevention

This is the stage where the current-day preventive strategies are largely concentrated. The strategy here is to institute appropriate measures at the earliest indication of kidney involvement, such as low-level albuminuria or mildly reduced GFR. As stated above, the management goal of CKD in the conservative phase should also include use of all available therapeutic options aimed at preventing or reducing the development of cardiac abnormalities and vascular disease.

Timely referral to nephrologists is an important issue at this stage. Data from North America suggests that an early referral to nephrology specialist care is associated with decreased morbidity and short-term mortality, improved long-term survival on dialysis and leads to significant cost savings¹⁹. Despite this evidence, the epidemiological data indicate that late referral has not decreased in recent years even in the west. At our own center, over 85% of all ESRD patients had their first encounter with a nephrologist less than 3 months before going on dialysis. In India, where there is no formal barrier to referral to nephrology specialists, such a gap suggests that economic issues, coupled with a lack of awareness of the potential benefits of early and regular management by a nephrologist continue to be widespread.

TERTIARY PREVENTION

These measures are aimed at appropriate management of complications related to established CKD, such as correction of anemia, control of abnormal bone mineral metabolism, acidosis, maintenance of growth in children, coronary artery disease and heart failure and preparing patients for renal replacement therapy including addressing the psychological issues. The stress is on improving the quality of life, appropriate education regarding RRT modalities and

suggesting rehabilitation programs. The course of the underlying CKD is not expected to be affected in a big way at this stage.

PREVENTION PROGRAMS IN INDIA

Structured chronic disease prevention programs are lacking in India. The Kidney Help Trust, an organization spearheaded by Dr. MK Mani of Chennai, runs a surveillance and treatment program in an area of approximately 25,000 people. Targeted mainly on hypertension and diabetes, this is mainly based on health workers who are drawn from the local population, and are trained to administer a questionnaire, record blood pressure, check blood glucose levels and protein in the urine by visiting people in their homes. Those who need treatment get cheap drugs such as reserpine and hydrochlorothiazide, metformin and glibenclamide. This approach was effective in bringing down blood pressure to 140/90 or less in 96% of the hypertensives, and in reducing the glycated hemoglobin to 7% or less in 52% of the diabetics⁶.

Perhaps there are lessons to be learnt from ongoing programs in South Africa and Cuba. The South African Chronic Disease Outcome Primary Prevention program has been evolved around an integrated chronic illness model focusing on detecting high-risk patients and controlling their hypertension, diabetes, and risk factors and implemented in primary-care clinics in Soweto and nearby areas.⁴⁵ The first phase had a surveillance component; it also achieved success with blood pressure control, but less control of diabetes and proteinuria reduction was achieved. Nevertheless, the program has provided a better understanding of renal disease and cardiovascular risk and positive short-term treatment outcome. Cuba has developed a National Chronic Kidney Disease Program based incorporating preventive strategies at all levels of care⁴⁶.

World Health Organization's Innovative Care for Chronic Conditions Framework (<http://www.who.int/mediacentre/factsheets/fs172/en/>) provides a model for redesigning health care systems in accordance with local resources. The framework emphasizes a well-defined care plan, self-care, scheduled follow-up appointments, monitoring of outcomes, adherence, and stepwise treatment protocols delivered mainly by primary care practitioners.

CHRONIC KIDNEY DISEASE AS A PUBLIC HEALTH PROBLEM

In a recent publication for the Centers for Disease Control, Schoolwerth et al¹³ suggested that CKD be treated as a public health problem through a public health action plan. For any condition to be called a public health problem, need to fulfill the following criteria was suggested:

1. The burden of the disease should be high, with evidence of recent increase and likelihood of increase in the future. The disease should impact mortality and morbidity, quality of life and cost to the extent of being perceived as a threat by the public.
2. The problem should be distributed unfairly, i.e., it should affect disadvantaged individuals to a greater extent.
3. There should be evidence that upstream preventive strategies could substantially reduce the burden of the condition, and
4. Evidence that such preventive strategies are not yet in place should be present.

The discussion above clearly underlines the fact that CKD meets all four of these criteria, should be treated as a public health problem and should have a public health plan in India. To this end, researchers in India need to generate more data related to the second and third points, which would then need to be presented to the government and other public sector policymakers.

Institution and implementation of the prevention programs requires not only drugs, but also equipment, creation of research institutions, and education and training of health professionals¹. So far, the academic response to the challenge of non-communicable diseases in India has been muted; education institutions and teaching program both at school level and more astonishingly, in medical colleges, have paid scant attention to these issues. Current-day Indian medical graduates are ill prepared for the vital roles they need to play in the changing health environment and deal with the increasing chronic disease burden. In addition to a pertinent medical education, awareness and public health education strategies must be introduced at school level in order to prepare students and general public about the growing burden of chronic disease, and to sensitize them about the need to tackle these conditions at an early stage.

Until the public sector develops, individual practitioners will continue to be the frontline caregivers. These physicians should be required, perhaps even mandated, to participate in continuing medical education programs regarding the management of hypertension, diabetes, and chronic kidney disease⁴⁷.

Professional societies, such as the Indian Society of Nephrology, Indian Academy of Nephrology, Indian Academy of Pediatrics and the Association of Physicians of India need to be engaged in developing early detection and intervention programs that suit the needs and organizational facilities of different regions of our country. Failure to act on their part would hand the initiative to outside agencies and the opportunity to deal with our destiny will be missed. Involvement of statutory bodies such as the Medical Council of India and the Indian Council of Medical Research is crucial and would attract the attention of global agencies such as the World Health Organization.

The role of non-governmental organizations (NGOs) that have done so much to raise awareness and provide better care to HIV-infected individuals cannot be overemphasized. There is some evidence that organizations have turned their attention in this direction; I am aware of at least one Indian NGO (Chronic Care Foundation) that has included reduction of CKD burden in the community as one of its core missions.

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IMSACON 2007 HELD AT MANIPAL, KARNATAKA



ABSTRACTS OF PAPERS PRESENTED AT IMSACON 2007 ON NOVEMBER 2ND-4TH 2007 AT MANIPAL, KARNATAKA

ENDOSCOPIC APPROACH TO BENIGN ORBITAL LESIONS

Dr. Deviprasad. D, Department of ENT, Kasturba Medical College, Manipal, India
Aims: To study the feasibility, prerequisites, advantages and disadvantages of endoscopic management of the benign orbital lesions. **Material & Method:** Retrospective study of 46 cases from Jan 2003 to Sep 2007 who underwent endoscopic orbital procedures including Endoscopic DCR in 39 cases, Orbital decompression in 3 case, Excision of tumor with orbital involvement in 2 cases, Optic nerve decompression in 1 case and Orbital abscess drainage in 1 case. Endoscopic procedures were done with assistance of bipolar cautery, KTP-532 laser as and when required. Regular follow up with endoscopic examination and cleaning of the operated area done. **Observation & Results:** In DCR –Symptom improvement in 93% cases. Recurrence was nil with laser while was seen in 10% with conventional DCR. Complication were minimal in form of granulation in 10% & synechiae in 5%. In other procedures, post op improvement in visual acuity, diplopia & proptosis was good (except in one case). Complication were nil. **Conclusion:** It is an excellent & innovative approach. Advantages- better visualization, decreased, morbidity & operative stress, acceptable cosmetic results, minimal post-op diplopia.

ENDOSCOPIC MANAGEMENT OF THE BENIGN SINO-NASAL TUMORS

Navneeta Gangwar, Asst. Professor, Dept. of ENT Kasturba Medical College, Manipal India
Objectives: To study the feasibility, prerequisites, advantages and disadvantages of endoscopic management of the benign sino-nasal tumors. **Methods:** Retrospective study of 42 cases from 1996 to 2007. Inclusion criteria- all consecutive cases of histologically proven benign tumors, clinical/endoscopic and radiological extent of the tumor confined to- nose, nasopharynx, paranasal sinuses, medial orbit and/or Pterygopalatine fossa. Exclusion criteria- all tumors with intracranial, infratemporal, orbital apex and/or parasellar region extension. Endoscopic excision of the tumors done with assistance of bipolar cautery, microdebrider or KTP-532 laser as and when required. Regular follow up with endoscopic examination and cleaning of the operated area done. **Observations & Results:** Blood loss was minimal (average 250 ml), complete removal of the tumor in the first stage was possible in 39 out of 42 cases. After revision surgery in 3 cases, all are disease free. **Advantages-** less morbidity, quick recovery, cosmetically acceptable, cost effective. **Disadvantages-** piece-meal removal of the tumors, require regular follow-up, may need revision/ planned multiple procedures. **Conclusion:** Endoscopic management of the benign sino-nasal tumors is a suitable alternative to external approach, as complete excision is possible with less morbidity and better cosmesis. But proper pre-operative planning, selection of cases and regular post-operative follow-up is necessary. Bipolar cautery, microdebrider and KTP-532 laser are useful tools.

KTP-532 LASER IN THE MANAGEMENT OF BENIGN CRICOPHARYNGEAL DISEASE.

*Dr Dechu Muddaiah, Prof Dr Deepak Ranjan Nayak, Dr Kailesh Pujary
 Dept. of ENT Kasturba Medical College, Manipal India*

Disorders of the cricopharynx are a relatively common occurrence. Benign conditions like cricopharyngeal dysfunction due to neurological disorders, cricopharyngeal web and stricture and pharyngeal pouch present commonly with dysphagia. Myotomy via an external approach is commonly done for cricopharyngeal dysfunction. We have used laser under microendoscopic guidance for myotomy with good results. Similarly, we have used KTP-532 laser for cricopharyngeal webs, benign strictures and pharyngeal pouch. In this paper we will highlight the advantages of the use of laser in comparison to traditional techniques.

LASER ASSISTED POSTERIOR TRANSVERSE CORDOTOMY

Dr. Kailesh Pujary, Associate Professor, Dept. of ENT, Kasturba Medical College, Manipal
 Tracheostomy is the commonest emergency treatment for bilateral vocal cord paralysis in the adducted position. Various procedures have been done to improve the airway like endoscopic lateralisation and arytenoidectomy which tend to compromise on voice and may lead to aspiration. With the advent of laser newer techniques have been developed other than laser arytenoidectomy. Laser posterior cordectomy was done with good results. Later the incorporation of medial arytenoidectomy had shown that airway improved without the problem of aspiration. We have done KTP laser assisted posterior cordotomy in 25 patients from 1999-2007. Other than bilateral abductor palsy we have also used this technique along with laryngotracheoplasty for laryngotracheal stenosis and in persistent laryngeal oedema following radiation. In this video, the technique is described.

LEIOMYOMA OF NOSE-OUR EXPERIENCE

*Dr Amit Sharma, Prof Hazarika, Dr Kailesh P, Dr Rohit Singh
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Leiomyomas are rare tumors of nasal cavity and paranasal sinuses. Only 23 cases have been reported so far in literature. In our opd we had a case 32 years old male with complaint of right sided nasal block and epistaxis since 2 years. On examining there was a pink lobular vascular mass seen between septum and right middle turbinate. Endoscopic bipolar cautery and excision was done. Biopsy later revealed it to be leiomyoma. I am presenting this case report to you because of it being unique and rare.

RESULTS OF STAPES SURGERY

Dr. Abhishek Sharma, Dr. Prudul Hazarika, Dr. Dipak Ranjan Nayak
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Typically, otosclerosis presents as a slowly progressive conductive hearing loss in the third to fourth decade. Many well-documented studies have demonstrated excellent long-term hearing results with stapedectomy. Although stapedectomy is highly effective, the rare complications may be devastating. Despite a widespread use of stapes surgery, little is known about the long-term durability of hearing results. The present study provides data over a long time frame (5 years) on hearing changes following surgical treatment. During a 5-year period (2002-2006) stapes surgery was performed in 60 consecutive patients in our institution. Postoperative evaluation was performed in the same hospital. The minimum follow-up time at the latest visit was 6 months. At the long-term follow-up, we found that the operative result was very well maintained. Most of the patients reached postoperative (6-12 months) air-bone gap closure less than 20 dB. The result was maintained by the patients. Stapes surgery gives a better social life for the hearing-impaired patient and delays the need for hearing aid in most patients.

A CASE OF MAYER-ROKITANSKY-KUSTER-HAUSER SYNDROME

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14-year-old adolescent, with ectomorphic innocent feminine appearance, presented with congenital absence of right thumb, scoliosis, severe anaemia, primary amenorrhea. She had normally developed breast without any other secondary sexual characteristics. She had history of recurrent episodes of abdominal pain and burning micturition with fever. There was no vaginal orifice. In the genital area there was a pair of ill developed labia majora fused at upper end with a whirling pattern containing inside the urethral opening. The lower end of genitalia had loose skin folds containing adequate amounts of rugae with a raphe mimicking the texture of scrotal skin. Diagnostic work-up included routine haematological studies, skeletal radiography, renal ultrasonography, and renal scan to demonstrate possible associations between the congenital genitourinary and skeletal anomalies. Ultrasound imaging studies confirmed that she had structures close to uterus with hematometra, but vagina and ovary were not found. Sonologically left kidney was non-visualized. Renal scan confirmed agenesis of the left kidney and hypoplastic parenchymally insufficient right kidney. Cytogenetic karyotyping revealed a 46, XX karyotyping and the presence of Barr chromatin body. Based on the clinical examination and investigations, a diagnosis of Mayer-Rokitansky-Kuster-Hauser syndrome was established with associated limb and skeletal deformities.

ATYPICAL PRESENTATION OF A CASE OF Hb E/̂⁰ THALASSAEMIA

Dr. Ranabir Pal¹, Dr. Ankur Barua²
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A 6 year old girl of HbE/̂⁰Thalassaemia presented with moderate anaemia, mild hepatosplenomegaly and normal phenotype without any classical feature of mega hepatosplenomegaly or bronzy discoloration of skin along with typical facial changes. This patient of HbE/̂⁰Thalassaemia with normal phenotype had been followed up in the line of management of ̂⁰Thalassaemia. It is very important to generate awareness among our fraternity regarding subtle presentation and importance of early detection of E/̂⁰Thalassaemia in the cases of unexplained anaemia. Otherwise, they develop irreversible organ damage due to iron overload by iron supplementation. Earliest diagnosis followed by routine follow up as well and timely intervention can help in better prognosis in this treatable disease. Moreover, health education at all levels to care givers and peers would help these patients to lead a productive life in the line of "live with the disease" phenomenon. Professionals related to Community Pediatrics, Clinical Epidemiology and Community Genetics, functioning in unison, has a dominant role to play in preventing the fatal outcome of this genetic disorder.

CAPILLARY HAEMANGIOMA OF NASAL CAVITY

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Although the head and neck is not an uncommon region, the nasal cavity is an extremely rare site for capillary haemangiomas and only few cases have been earlier reported in literature. We report a case of 38 year old female who presented to us with epistaxis and nasal obstruction and was managed successfully with KTP-532 laser assisted excision of the haemangioma. We feel that although capillary haemangioma of nasal cavity is extremely rare, it should be considered as differential diagnosis of bleeding lesions of Nasal cavity.

DEXTRCARDIA WITH SINGLE VENTRICLE

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A 16 years old short stature mesomorphic girl presented with cyanosis, clubbing on twenty nails, progressively increasing generalized weakness, fatigue, breathlessness without exertion. On palpation, right para-sternal lift, systolic thrill and bruit was noted over pre-cordium. On auscultation 1st heart sound was normal; 2nd heart sound was single and loud. The ejection systolic murmur grade III was found in 'Pulmonary area'. Pulse oxymetry showed 67 % Oxygen saturation. General systemic examination delineated no other incidental abnormal or ambiguous visceral arrangement or organomegaly. Haemoglobin level was 10.2 gm/Gm/dL with few reticulocytes and nucleated red cells and microcytes. On chest radiography, a bulge on upper right border of cardiac silhouette in the postero-anterior projection suggested a rudi-

mentary outflow chamber. Pulmonary vasculature was oligoemic suggesting pulmonary outflow obstruction. Electrocardiogram findings were non-specific and did not match with any prototype. There was left axis deviation, normal PR interval and no gross changes in QRS complex in limb leads. P waves were spiked in VR, VF, V₁, V₂. Normal in I, VL, Bifid in II, III, VF, V₃₋₆ - this is a characteristic finding in univentricular heart. A negative P wave in lead I indicated reversed atrial arrangement confirming dextrocardia (atrial situs inversus) QRS complexes were characteristically larger in right chest leads and progressively smaller from V₁-V₆ in left sided leads. In all chest leads there were also additional findings of predominantly rS pattern in QRS complex. There was 'W' pattern of QRS complex in Lead II and V₂. T waves were deeper in I, VR, VL, all precordial leads, taller than normal in others. Absence of ventricular septum was the principal echocardiographic sign with morphology of a normal left ventricle and two inlet valves and the right ventricle was represented by a small rudimentary outflow chamber. It appeared that aorta was arising from the rudimentary chamber and stenosed pulmonary artery from the main chamber. The findings clinically lead to a diagnosis of dextrocardia with single ventricle.

PARTIAL DENYS DRASH SYNDROME, A RARE DISORDER WITH A RARE ASSOCIATION OF CONGENITAL CYTOMEGALOVIRAL INFECTION WITH CHORIORETINITIS

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Congenital nephrotic syndrome is an uncommon cause for nephrotic syndrome in children. Apart from Finnish type, intrauterine infections are other important etiological factors. Denys - Drash syndrome is a rare entity characterised by triad of congenital nephropathy, Wilms tumor and intersex disorders. Incomplete forms are known to exist where congenital nephropathy exists either with Wilms tumor or with intersex disorder. Children with 46XX karyotype can have no intersex disorder. As Wilms tumor develops only later in life, this type of Denys - Drash syndrome may not be considered as a cause in a case of congenital nephropathy initially. Hence all cases of congenital nephropathy without intersex disorder should be considered for molecular study, for detecting WT1 gene mutation at 11p13 locus to diagnose in advance. Bilateral nephrectomy with renal transplant can be life saving in these children. We report a case of incomplete form of Denys - Drash syndrome with no intersex disorder who also had evidence of CMV infection with associated retinitis, which also can cause congenital nephrotic syndrome. To best of our knowledge we have not come across any similar case in the literature.

"UNUSUAL PRESENTATION OF SPINAL CORD INFARCTION IN A PATIENT OF SICKLE CELL ANEMIA : A CASE REPORT"

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Dr. Namita Jajoo, Resident, Deptt. Medicine, Dr. A.P. Jain, Professor & Hod., Deptt. Medicine
Vascular disease of the spinal cord occurs with less frequency than in the brain. Its manifestations are similar, however, and are often abrupt in onset, dramatic in scope, and frequently disabling. The most common serious neurologic complication of sickle cell anemia is occlusive vascular disease with central nervous system infarction. The parenchymal lesions are most often located in the brain, chiefly within major cerebral arterial boundary zones. Spinal cord infarction is extremely rare. Here we report a patient with sickle cell anemia who developed an ischaemic myelopathy secondary to sickle cell anemia.

MANIFESTATION OF DHAT SYNDROME IN THE CONTEXT OF PAKISTAN

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Dhat Syndrome also called semen loss syndrome, is a culture bound syndrome most commonly prevalent in Indian sub continent. This was a pioneering study on a tabooed area in Pakistan. Main objective of the study was to examine manifestation of the syndrome in the Pakistani context. 318 Dhat Syndrome patients comprised the sample and they were recruited from private practice of Hakims, Homeopaths, Fertility Specialists and General Practitioners comprised the sample. Especially designed interview schedule and Dhat Syndrome Symptom Checklist (DSSC) were used to gather data. The patients were interviewed at the clinics of professionals. Analyses revealed that patients were consulting both medical and traditional healers. Majority were single, young, less educated with poor socioeconomic status. They reported masturbation and exposure to pornographic material the major causes of Dhat Syndrome. Though the patients reported physical, psychological and sexual symptoms, manifestation in majority was in physical form. Sex being a neglected and tabooed area in Pakistan, this is the ever first systematic empirical study on the subject. The findings from the study have very important implications for men's sexual health and medical professionals.

INCIDENCE & PATTERN OF NASH IN INDIAN AIRLINES

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Non-Alcoholic Steatohepatitis (Fatty Liver) is an important public health problem because it is more preventable than Hepatitis B, C & Alcoholic liver disease. It is not a harmless condition and may cause fibrosis and cirrhosis. Global prevalence of disease is 10-39% of normal urban population. Usually this condition is found in insulin resistant and obese but many times in normal individual also, and is diagnosed by chance. Present study is aimed to know NASH IN Indian Airlines staff who are rich, well nourished and sedentary workers. Raised SGOT, SGPT mild hyperbilirubinemia and GGT were common findings. Incidence of fatty liver was 22% and NASH was 16%. Which are significant. There is increased intra hepatic production of FFA from glucose which is not taken up by peripheral adipocytes and myocytes. Metabolites of excess lipid stores in liver cell triggers inflammatory response leading to fibrosis. Rosiglitazone, Metformin, Gemfibrozil, Ursodeoxy cholic Acid, Vitamin E along with weight loss form the principles of treatment. The results remains variable.

CLASSIFICATION OF SLOW AND RAPID ACETYLATORS BASED ON ISONIAZID CONCENTRATIONS OF SALIVA IN PATIENTS WITH CHRONIC KIDNEY DISEASE WITH AND WITHOUT TUBERCULOSIS

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Introduction: In India tuberculosis remains the leading cause of death from an infectious agent. Although effective short course treatment with DOTS programme have been introduced for the treatment of TB, still the burden of the disease has not been reduced due to other problem like drug resistance and co infection with HIV. Nevertheless among the effective drug concentration, isoniazid still remains is sheet anchor for the treatment of TB. But one major problem with isoniazid (INH) treatment is the phenomenon of acetylator phenotyping and response to treatment has been found to be much less in rapid acetylator than in slow acetylator. Phenotyping of patients as slow or rapid inactivators of INH is useful to plan treatment with once weekly regimens containing INH and also to avoid the incidence of adverse reactions such as hepatitis and peripheral neuropathy. The incidence of infection with Mycobacterium tuberculosis is significantly higher (10-16 time higher) in patients with end stage renal disease and cases of renal transplant when compared to normal individuals. INH can be estimated in serum by different procedures. Since INH is not bound to plasma proteins and the concentration of INH similar in serum and saliva. **Aim and scope of the study:** The aim of the present study is to find out the acetylator status in patients of chronic kidney disease patients with and without tuberculosis based on isoniazid concentrations using saliva samples. **Materials and methods:** A total of 92 individuals with the age of 18-60 years were included in the study and they were divided into four groups based on creatinine clearance (Cockraft-Gault formula), of them 29 were healthy volunteers (Group I), 27 patients with chronic kidney disease (stage IV) Group II, 25 patients with pulmonary tuberculosis (Group III), 11 patients with both chronic kidney disease and pulmonary tuberculosis (Group IV). INH 100mg (oral dose) was given on an empty stomach and saliva was collected at the 5th hour to determine INH concentration so as to classify acetylator status using the spectrofluorimetric method. The cut off criteria for the classification of slow acetylator status being e^{-} 0.41 μ g/ml. **Results:** In Group I, Group II, Group III, Group IV the number of slow acetylators were 19,18,20,8 respectively and rapid acetylators were 10,9,5,3 respectively. There is no significant change in the phenotyping with regards to the creatinine clearance of all the groups. Among the 92 individuals under various groups, 65 individuals were found to be slow acetylators amounting to 71% and 27 subjects were found to be rapid acetylators amounting to 29%. **Conclusion:** Monitoring of INH concentrations in body fluids is valuable in adjusting the drug dosage and to study the drug-drug interactions when co-administered with other antituberculosis drugs particularly to avoid peripheral neuropathy and hepatitis in those who are slow acetylators. This study shows that it is easy to do acetylator phenotyping of the patients on INH to enable the administration of a proper dosage of the drug using saliva as the test sample.

POLYMERIC ALGINATE FILMS AND BEADS FOR CONTROLLED DELIVERY OF ANTIBIOTICS IN SKIN AND BONE INFECTIONS

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The marriage of biological knowledge with the principles of biomaterial science and engineering will aid the development of innovative biomedical devices. Controlled release technology is one such frontier area that has revolutionized the method of medication by providing many advantages over the existing conventional dosage forms like minimum side effects and maximum therapeutic effect. Novel drug delivery systems (DDS) for localized antibiotic release prepared using biomaterials that are designed for interfacing with the living system without inducing adverse reactions is the need of the hour. In this work alginate which is a natural, biodegradable and biocompatible polymer was selected for the preparation of DDS for antibiotics so that there is no need to remove the drug depleted delivery system by surgical intervention. Calcium cross linked alginate films and beads entrapping antibiotics namely gentamycin, ciprofloxacin and tetracycline were prepared for use as wound cover dressings in skin infections and implants in musculoskeletal infections respectively. The percent drug loading, in vitro degradation behavior and in vitro drug release profiles of the two systems were determined. The antimicrobial efficacy of the two systems was assessed by zone of inhibition technique against gram positive and gram negative bacteria. The high entrapment efficiency and in vitro drug release kinetics showed that the systems could provide controlled delivery of antibiotics for prolonged time periods. The total degradation of the two systems over a period of 10 days was observed in media of various pH values. The clear zone of inhibition obtained around the films and beads in microbial culture demonstrated the bactericidal and bacteriostatic activity of the two systems. The alginate films show good potential as wound cover material with effective antibiotic delivery whereas alginate beads will be very useful as biodegradable implants for localized antibiotic delivery after debridement surgery in infections bone diseases like osteomyelitis.

IMPACT OF HEALTH EDUCATION INTERVENTION ON DIABETES IN ADULTS

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Introduction: Diabetes is a metabolic disease requiring medical diagnosis, treatment and lifestyle changes. But the main risks to health are its characteristic long-term complications. Diabetes is one of the most important risk factors for Coronary Heart Disease (CHD), which is projected by the WHO to become the leading cause of global disease burden by the year 2020. **Objectives:** (1) To assess the existing Knowledge, Attitude & Practice (KAP) regarding diabetes in adults. (2) To assess the impact of a structured health education intervention on KAP regarding diabetes in these adults. **Materials & Methods:** **Study Design:** An experimental study of Non-Randomised Trial. **Study period:** 19th September 2004 (one day activity). **Setting:** Central

Referral Hospital (CRH) of SMIMS, Tadong in East Sikkim of India. **Study Population:** 189 adult individuals in the age group 18 years and above from East Sikkim, who attended the "Diabetes Awareness Camp" at CRH of SMIMS, Tadong in East Sikkim. **Sampling Technique:** Non-probability Purposive Sampling Method was applied using Snowball Technique for selecting the respondents. **Study Instrument:** The Health Education module on Diabetes was developed according to the WHO guidelines. The experts of Community Medicine and Internal Medicine assessed the content validity of the Health Education Module by pre-testing on randomly selected sample of 20 adult visitors of CRH prior to the study for ensuring feasibility, acceptability, time management and reliability. **Statistical analysis:** Proportions were used to derive information on baseline characteristics & Practice aspect of diabetic patients. Paired t-test was applied to the pre-test and post-test results of Knowledge & Attitude on diabetes to assess the impact of health education intervention on diabetes. *P* value <0.05 was considered as statistically significant. **Results & Conclusions:** The mean age of the participants was 45.7 years (\pm 14.8 yrs). Majority were males (63.5%) and belonged to Hindu community (66.7%). Majority of them were literate (69.3%), married (83.6%) and belonged to Middle /High Socio-Economic Status (88.9%). Significant Improvement in Knowledge on Diabetes was observed regarding following aspects: (a) Risk factors of diabetes, (b) Early symptoms of diabetes, (c) Organs affected by diabetes, (d) Warning signs of hypoglycaemia & (e) personal precautions in diabetes. Significant Improvement in Positive Attitude was observed in following aspects: (a) Willing to motivate all family members to get their blood sugar tested once a year after 40 yrs of age, (b) Willing to undergo regular check-up & continue medication once diabetes is detected & motivate other family members to do the same. There were 105 individuals previously diagnosed of diabetes. Majority of them (78.6%) of them were on regular allopathic medication. Though 82.8% of the diabetics were on insulin, but only 18.4% were taking it themselves. Only 7.8% of them were carrying ID card with treatment regimen mentioned and 35.9% were carrying sugar/chocolate in their pocket to prevent hypoglycaemic episode.

STATE ANXIETY AND COPING STRATEGIES OF HEPATITIS C PATIENTS IN RELATION TO INTERFERON THERAPY

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The present study examined state anxiety and coping strategies used by hepatitis C patients. Sample comprised of 100 patients with equal number of patients who had received and those who were waiting to receive interferon therapy. It was hypothesized that the level of state anxiety would be higher among the patients who had received interferon compared to those who had not yet received. It was also hypothesized that there would be difference in the type of coping strategies used by two groups of patients. The patients were recruited from Gastroenterology OPD of Pakistan Institute of Medical Sciences Islamabad (PIMS), Pakistan. State Trait Anxiety Inventory (STAI) and Coping Strategies Questionnaire (CSQ) were used for assessment. Data was analyzed using independent sample t-test and correlation analyses. Results indicated that those patients who had completed interferon therapy were significantly more anxious than those who had not yet received it. Two groups of patients differed significantly on the use of coping strategies. Religious focused coping, active-distractive and active practical coping strategies were used more by those patients who had not yet received interferon therapy, whereas avoidant coping strategies were used more by the ones who had completed interferon therapy. The findings have very important implications for provision of psychological help to Hepatitis C patients in relation to the medical treatment offered to them. **Key terms:** Hepatitis C, Coping Strategies, Interferon Therapy, State anxiety.

"STUDY OF RISK FACTOR FOR CONGENITAL HEART DISEASES IN CHILDREN AT RURAL HOSPITAL OF CENTRAL INDIA."

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Objectives: To determine the risk factor for the development of congenital heart disease in children at Rural hospital of Central India. **Settings:** Study was conducted in the Department of Pediatric, MGIMS, Sevagram. **Design:** It was hospital based study conducted over a period of three year from March 2004 to April 2007. **Methods:** 209 children up to twelve year of age with clinical suspicion of congenital heart disease were subjected to chest X-ray and electrocardiography while the final diagnosis was confirmed by echocardiography. The etiological factors like environmental, teratogens, infections, irradiation, drugs, heredo-familial factors and maternal factors were analyzed. **Results:** Out of 209 cases, 117(56%) were male and 92(44%) female children. 82% of children with congenital heart disease presented at age less than 5 years and only 18% at age above 5 years. 15.78% children were born of related parents, mostly 2nd degree consanguinity. Prevalence of congenital heart disease was maximum among the first born children 42%. Congenital heart disease was highest number of cases (73%) present in children whose mothers were 20-30 years old, while only 15% of mothers aged 30 and more what is considered as high risk age for development of anomalies in general. Chromosomal abnormalities were seen in 4.78% patients. 4.30% cases mothers gave history of antenatal infection in the first half of pregnancy. 6.69% mother gives history of diabetic during pregnancy. Among the acyanotic congenital heart disease group, ventricular septal defect was the commonest lesion found in 25% of cases, followed by atrial septal defect 22%. Tetralogy of Fallot was the commonest cyanotic lesion found in 8.61% followed by transposition of great arteries and tricuspid atresia. **Conclusion:** Majority of patient with congenital heart disease detected in rural hospital have non-cyanotic CHD. Ventricular septal defect is the commonest acyanotic lesion and Tetralogy of Fallot cyanotic lesion. In order to avoid complications, early detection of congenital heart disease is of utmost importance for proper management. Mainly consanguinity, family history, chromosomal abnormality and infection during first trimester are the common risk factor which was present in congenital heart disease children in rural area.

RISK FACTORS OF XEROPHTHALMIA AMONG INDIAN RURAL UNDER-FIVE CHILDREN

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The present cross-sectional study was undertaken to find out the risk factors of xerophthalmia among Indian rural under-five children in January to June 1998 among 4205 preschool children from 14 villages of Bihta Primary Health Center area, Bihar, India. **Interventions:** None. **Main Outcome Measures:** Risk factors of xerophthalmia viz. Socio-economic status, History of Repeated Diarrhoea, Measles, Passing worms in stool and Respiratory Tract Infection. The module was developed on information provided in the WHO publication from the global experts prior to the study for ensuring feasibility, acceptability, time management and reliability with pilot study. Pre-tested questionnaire was then administered to the caregivers of 144 preschool-age children by interview technique. **Results:** Significant difference in magnitude was observed between more affluent families with higher monthly average income and the less affluent ones ($p < 0.01$). History of repeated diarrhoea was more in comparison those without this history. But this difference was not significant ($p > 0.5$). Vitamin A deficient children not passing worms were only 22.50 percent in relation to corresponding value in children passing worms which was significantly high ($p < 0.01$) at 87.50 percent. History of Measles and Respiratory Tract Infection was not at all related as an antecedent risk factor.

CLINICAL EPIDEMIOLOGY OF VITAMIN A DEFICIENCY AMONG PRESCHOOL-AGE CHILDREN OF BIHAR

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Introduction: In India alone, 52 000 children go blind every year on account of vitamin A deficiency. **Objective:** To determine the correlates of vitamin A deficiency among preschool-age children. **Study Design:** Case-Control study. **Study Period:** 1996-1998 (Three years activity). **Setting:** Bihta Primary Health Center area, Bihar, India. **Interventions:** None. **Study Population:** 144 preschool-ages vitamin A deficient children. **Sampling Technique:** Simple random sampling. **Main Outcome Measures:** Correlates viz. Dietary habits, Maternal literacy and Birth order. **Content validity & reliability of study instruments:** The survey module was developed on information provided in the WHO publication from the global experts prior to the study for ensuring feasibility, acceptability, time management and reliability with pilot study. **Data collection procedure:** Pre-tested questionnaire was administered by interview technique to the caregivers of 144 preschool-ages vitamin A deficient children diagnosed by the specially trained investigator from 4205 preschool-age children from 14 villages. **Statistical analysis:** SPSS 10.0 for windows XP was used. **Results and discussion:** Vitamin A deficiency was found significantly higher at 7.14% of the children on vegetarian diet. (O.R. 5.32). Children born to literate mother had a lower prevalence of only 1.35% in relation to illiterate mothers (11%) (O.R. 3.15). Birth order of preschool-age children was significantly related to vitamin A deficiency. Children of birth order less than or equal to three had the prevalence of 2.81% in comparison those with birth order four or more (O.R. 2.08).

BIOFILM, ENTEROAGGREGATIVE ESCHERICHIA COLI AND PERSISTENT DIARRHEA: CURIOSITY UNVEILS

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Dept of Microbiology, Kasturba Medical College- International Center, Manipal- Karnataka **Background:** The EAEC strains have been associated classically with persistent diarrhea which represents a disproportionate share of diarrheal mortality. EAEC strains have been shown to elicit damage to intestinal mucosa and growth retardation in infants. Detection of EAEC strains can make a significant contribution to public health in many areas. The use of biofilm assays as a screening method for EAEC from clinical isolates and multiplex PCR as confirmatory method may be useful. **Methods:** A total of 100 E. coli strains obtained from screening 680 stool samples from children below two years of age with persistent diarrhea in Kasturba Medical College and Hospital, were used to evaluate the usefulness of quantitative micro titer plate method for biofilm production and multiplex PCR to screen and confirm EAEC. E coli isolates from 50 fecal specimens from infants without diarrhea (controls) who attended the same outpatient clinic and who belonged to the same group as the infants with diarrhea were also examined. **Results:** Of the total of 100 E. coli strains which were evaluated, 23 strains showed positive results by PCR and 20 strains showed biofilm production by microtitre plate method. The microtitre plate method for biofilm production showed almost same specificity in comparison with PCR. **Conclusion:** Better diagnostic tools are needed to allow for more standardized laboratory testing on a regular basis. Improved diagnostic tools will help identify epidemiologic patterns of illness and guide treatment recommendations of EAEC illness. Our study showed that biofilm production can effectively be used as a screening method for identification EAEC from persistent diarrheal cases.

PREVALENCE OF PEDIATRIC HEAD AND NECK NEOPLASMS IN EASTERN INDIA

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Introduction: Most of the head & neck childhood neoplasm are benign in nature. However it should never be forgotten that this region is the primary site for about 5% of paediatric malignancies. **Objective:** To determine the prevalence along with age and sex distribution of different Head and Neck neoplasm in paediatric age group attending for treatment in a referral tertiary care hospital. **Materials & Methods: Study Design:** Cross sectional study. **Study Period:** 2001-2004 (Three years activity). **Setting:** Medical College and Hospitals Calcutta. **In-**

terventions: According to international clinical protocol. **Inclusion Criteria:** Children below 12 years attending Oto-Rhino-Laryngology OPD. **Study Population:** 21216 Children below 12 years. **Sampling Technique:** Simple random sampling. **Main Outcome Measures:** Prevalence, age and sex distribution of head and neck neoplasm. **Content Validity & Reliability Of Study Instruments:** The survey module was developed on information provided in the publications from the global experts prior to the study for ensuring feasibility, acceptability, time management and reliability with pilot study. **Data Collection Procedure:** Clinically the children in the sample were examined thoroughly at Oto-Rhino-Laryngology out-patients department. Then all the cases were histopathologically confirmed in the Department of Pathology, Medical College and Hospitals Calcutta. **Statistical Analysis:** SPSS 10.0 for windows XP was used. Percentages were calculated. **Results And Discussion:** We found 161 children below 12 years of age suffering from different Head and Neck neoplasm from a sample of 21216. The prevalence was calculated to be 0.76 percent. The overall sex ratio was 1.40:1 in favour of males. Of the 161 cases 53 cases (32.92%) were malignant neoplasm, 38 cases (23.6%) were benign neoplasm, 46 cases (28.5%) were tumour-like conditions and 24 cases (14.9%) were dysplasias arising from embryonal remnants. Lymphomas were the most common malignant lesion seen. Among the benign tumours, haemangiomas were the most frequent. Dermoid and epidermoid cysts were the most common tumour-like conditions. Thyroglossal duct cysts accounted for the main bulk of the embryonal remnant dysplasias.

CLINICAL EPIDEMIOLOGY OF PEDIATRIC HEAD AND NECK TUMOURS

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Introduction: Pediatric Head and neck tumours present in a variety of ways and require different diagnostic investigations for evidence based management. **Objective:** To determine various clinical presentations, diagnostic investigations, final histopathological diagnosis and treatment modalities of the patients with paediatric head and neck tumour attending for treatment in a referral tertiary care hospital. **Materials & Methods: Study Design:** Cross sectional study. **Study Period:** 2001-2004 (Three years activity). **Setting:** Medical College and Hospitals Calcutta. **Interventions:** According to international clinical protocol. **Study Population:** 161 Children below 12 years with Head and Neck tumours. **Main Outcome Measures:** Clinical presentation, diagnostic investigations, treatment modalities. **Content Validity & Reliability Of Study Instruments:** The management module was developed on information provided in the publications from the global experts prior to the study for ensuring feasibility, acceptability, time management and reliability with pilot study. **Data Collection Procedure:** Clinically 161 Children below 12 years with Head and Neck tumours were examined thoroughly at Oto-Rhino-Laryngology department. Then all the cases were histopathologically confirmed followed by evidence-based management. **Statistical Analysis:** SPSS 10.0 for windows XP was used. Percentages were calculated. **Results And Discussion:** We found 161 children below 12 years of age suffering from different Head and Neck neoplasm with the prevalence of 0.76 percent. The common symptoms of the children were neck swelling (46.8%), nasal blockage (29.7%), and nasal bleeding (23.4%) followed by facial swelling (21.2%) and bulging of eye balls (14.9%). The common clinical findings were nasal (31.9%), nasopharyngeal mass (25.5%), facial swelling (23.4%), proptosis (14.9%). Neck swellings comprised of both lymph node enlargement (29.7%) and other causes (17.0%). Of the various parts of Head and Neck, the cervical region (26%) was most commonly involved, followed by nasal (18%), nasopharyngeal (14%) and ophthalmic regions (8%). Among all the diagnostic investigations undertaken for proper pre-treatment assessment of the extent of the disease, CT scan was most helpful guide to detect the extension of the tumours. All the modalities of treatment were undertaken like surgery, radiotherapy and chemotherapy. International protocols were followed for different type of the neoplasm. Surgery was done in most of the benign conditions (57.4%) and some of the respectable malignancies. Combined chemo-radiation was used for other malignant Head and Neck masses [chemotherapy (38.3%), and radiotherapy (38.3%)] in the present series.

ASSESSMENT OF MATERNAL RISK FACTORS LEADING TO HIGH MORTALITY IN PRETERM NEONATES

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Objective: To assess the maternal risk factors leading to high mortality in preterm neonates. **Design:** Prospective cohort study. **Place and duration:** This study was conducted in two tertiary care hospitals of Lahore, Sir Ganga Ram Hospital (SGRH) in the public sector and Hameed Latif Hospital (HLH) in the private sector. This study was conducted over a period of one year (2002-2003.) **Subjects and method:** A convenient non probability sampling technique was used to select 80 preterm neonates for this study, 50 from SGRH and 30 from HLH. This number of cases was assessed on the basis of including all available preterm neonates of the two hospitals with in the study period. All preterm neonates ranging between 32-37 weeks, irrespective of their birth weight were included in this study. Preterm born with congenital malformation were excluded from the study. The data was collected on a specially designed questionnaire. The mothers of preterm neonates included in this study, were interviewed about their pregnancy and complications faced during this period. All the preterm neonates were followed in neonatal unit to see their outcome. After gathering the data, it was analyzed on SPSS version 10. The Chi-square test was applied to study the relationship of maternal risk factors leading to high mortality of preterm neonates & the P value of d^* 0.05 was used as a cut off point for statistical difference. **Results:** High mortality in preterm neonates was associated with high maternal age ($p = 0.023$) and illiteracy

in mothers ($p=0.03$) Maternal occupation & type of family had no effect on mortality rate of preterm neonates. Smoking in mothers contributed to 50% higher mortality of neonates. ($p=0.076$). Consanguinity of parents showed no association High death rate was observed in Dai handled cases. ($p=0.025$). Maternal complications during pregnancy including premature rupture of membranes, Pregnancy induced hypertension, Diabetes, Anemia, Infections, Bleeding per vagina and past history of abortions were all associated with high mortality in neonates. The mothers having the history of multiple pregnancies showed greater mortality rate ($p=0.125$). Lesser duration of pregnancy was associated with high mortality rate ($p=0.03$) in preterm births. **Conclusion** : High mortality in preterm neonates can be reduced by improving maternal socio demographic profile & improved management of maternal complications during pregnancy.

PRINCIPAL COMPONENT ANALYSIS (PCA) BASED K-MEANS NEAREST NEIGHBOR (K-NN) CLASSIFICATION MODEL FOR OVARIAN TISSUE FLUORESCENCE SPECTRA IN DIFFERENT PATHOLOGICAL CONDITIONS

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Pulsed laser-induced fluorescence spectroscopic studies of pathologically certified normal, benign and malignant ovarian tissues were carried out at 325 nm excitation. The spectral analysis and classification for discrimination among normal, benign and malignant conditions were performed using Principal Component Analysis (PCA) and k-means Nearest Neighbor (k-NN) analysis separately on the same set of spectral data. In the present study we have recorded 97 spectra from 10 normal, 13 benign and 9 malignant ovarian tissue samples. Nine features extracted from each spectrum were used as feature space for PCA. Outlier detection was achieved by 'cluster analysis' method. Finally, k-means Nearest Neighbor classification technique, with the scores of PCs as feature space, was used to classify an unknown sample to that class having most 'similar' or 'nearest' sample point in the training set of data. The classification of fluorescence spectra from pathologically certified normal, benign and malignant tissues gave excellent results. The performance evaluation of classification results were obtained by calculating statistical parameters like specificity, sensitivity and accuracy and they were found to be 100%, 90.90%, and 95.2% respectively. The results indicate that the PCA based k-NN technique appears to be a promising approach for the classification of high dimensional data. The present technique discriminates ovarian malignancy effectively and hence it may be used as an alternative or complementary technique to the existing other conventional methods of disease diagnosis.

DEVELOPMENT AND ADAPTATION OF INDEGENOUS PAIN QUESTIONNAIRE FOR HEADACHES IN PAKISTANI CLINICAL CONTEXT

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 In the present study, a pain questionnaire was developed for headaches in urdu based on Mc Gill (MPQ) pain questionnaire. The MPQ is a leading pain measure which assess 3 component areas e.g. Sensory, affective, and evaluative. Keeping in view the translation and adaptation procedural protocol the MPQ checklist of 78 items documenting different dimensions of pain were translated into urdu by the researcher, with the help of two standard dictionaries given two choices closest in meaning on time to its essence in urdu language were selected. The MPQ and urdu translation was given to five headache patients and bilingual experts to select one of the two words for each description of MPQ. The final list of 78 urdu words was then generated from the most frequently chosen by patients and experts. This list was then back translated into English by two judges using a standard back translation technique. The present study indicates that urdu adaptation of MPQ is a valid tool to assess headaches and pain. It is well suited for use on the Pakistani population and is ready for use in research. It further requires investigation on a more wide range of patient population.

POSTTRAUMATIC GROWTH AND MARITAL SATISFACTION AFTER BREAST CANCER: PATIENT AND SPOUSE PERSPECTIVE

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The present cross-sectional study was carried out to assess the posttraumatic growth and marital satisfaction after breast cancer in patients and their spouses. It aimed to compare patients and spouses on posttraumatic growth and marital satisfaction post diagnosis of cancer. The sample comprised of 60 participants with equal number of patients ($N = 30$) and spouses ($N = 30$) and was recruited from the OPD of the "NORI Hospital, Islamabad, Pakistan. Patients were approached through consultant oncologists and spouses were approached through patients. Posttraumatic Growth Inventory (PTGI) and the Dyadic Adjustment Scale (DAS) were used to assess Post traumatic growth and marital satisfaction respectively. Scales was administered on both patient and spouse separately on the hospital premises. Data was analyzed using Chi-square, Independent sample t-test, and Pearson correlation analysis. Analysis revealed that posttraumatic growth occurs both in patients and spouses after breast cancer however, patients showed higher level of posttraumatic growth and marital satisfaction compared to their spouses. Findings also revealed a significant positive relationship between posttraumatic growth and marital satisfaction. The present study made a significant contribution by looking into positive the outcome of a negative life event and has demonstrated through empirical evidence that positive growth and marital satisfaction post breast cancer diagnosis which can be utilized to help patients and their families to cope with cancer. Key terms: Posttraumatic growth, Marital Satisfaction, Breast Cancer

DEPRESSION IN ELDERLY: META-ANALYSIS ON A MODERN SILENT EPIDEMIC

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Objectives: (1) To determine the Median Prevalence Rates of depressive disorders in elderly population of the world and in India. (2) To conduct a Time-Trend Analysis on prevalence of geriatric depression in India. **Materials & Methods:** Study Design: Retrospective study based on Meta-analysis on prevalence of depressive disorders in elderly population. **Setting:** Community based mental health surveys on geriatric depressive disorders conducted in continents of Asia, Europe, Australia, North America, and South America. **Study Period:** All the studies that constituted the sample were conducted between 1956 and 2005. **Sample Size:** All published articles on prevalence of depressive disorders in elderly population that were available, adequately analyzed and accessible from the internet and the Central Library of Sikkim-Manipal Institute of Medical Sciences (SMIMS) in Sikkim, constituted the study universe. Thus, after applying the inclusion and exclusion criteria, 65 original research studies that surveyed a total of 99,297 elderly individuals in the age group of 60 years and above, residing in various parts of the world were included for the final analysis. **Sampling Procedures:** Simple Random Sampling Method was applied to identify the study subjects in all the individual and independent surveys conducted in these constituent studies. **Inclusion Criteria:** To avoid undesired bias due to design effects from various epidemiological study designs, the researchers had included only community based cross-sectional surveys on prevalence of depressive disorders that were conducted on homogenous community of elderly population in the world, who were selected by simple random sampling technique. **Exclusion Criteria:** All the unpublished reports and unavailable or unanalyzed or inaccessible articles from the internet as well as the Central Library of Sikkim-Manipal Institute of Medical Sciences (SMIMS), Sikkim on studies regarding the prevalence of depressive disorders in elderly population were excluded from the study. But this proportion of excluded reports constitutes less than 3% of the available articles on relevant topic. Hence, it is expected to have minimal impact on the final results. **Study Instruments:** Clinical Diagnosis by Psychiatrists was based on DSM-III-R, DSM IV and ICD-10 criteria. Other standardized study instruments used were GMS, AGECAT, CIDI-SF, CES-D, BDI, HDS, Yesavage Geriatric Depression Scale, Centre for Epidemiologic Studies Depression Scale, Geriatric Mental State Examination, Clinical Rating Scale for Depression, Mini Mental Status Examination and Geriatric Depression Screening Scale. **Statistical analysis:** Median prevalence and its corresponding inter-quartile range. Chi-square for Linear Trend was applied to conduct the time-trend analysis of depressive disorders in elderly population of India. Chi-square test for comparing prevalence rates of geriatric depressive disorders among various countries in the world and in India. P value <0.05 was considered as statistically significant. **Results & Conclusion:** The Median Prevalence Rate of depressive disorders in the world for the elderly population was determined to be 10.3% with Interquartile Range varying between 4.6% and 16.0%. The Median Prevalence Rate of depression among elderly Indian population was determined to be 21.9% with Interquartile Range varying between 11.6% and 31.1%. A Time-Trend Analysis on prevalence of geriatric depression revealed that the prevalence of depressive disorders in elderly population was significantly on the rise from 1956-2005 (r^2 for linear trend = 10.2 and $p = 0.00144^*$). Apart from an increase in stress related injuries of brain due to fast-paced modernization and industrial development, there is also an element of social isolation due to failure of social support and network systems among elderly population of India. The high prevalence rate of geriatric depression could also be attributed to the fact that better diagnostic instruments with optimum validity and reliability had been developed during the recent years to diagnose geriatric depression at an early stage in the community.

KNOWLEDGE AND ATTITUDE ON HEALTH AMONG ADOLESCENT GIRLS

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Adolescent girls at crossroads of childhood and mature adulthood, often experiment in life which may lead to various health problems. This study was undertaken to determine the knowledge and the attitude on health among girl students in three senior secondary schools of North Kolkata by a health education intervention study for two months. By simple random sampling 282 girl students in the adolescent age groups 10 to 19 years studying in these schools were selected. The Health Education intervention module on Adolescent Health was developed on information provided in the Reproductive and Child Health (RCH) Module for Medical Officers and used with audio-visual teaching materials and hand-outs. The mean age of the participants was 15.7 years (± 1.8 yrs). Majority of the respondents belonged to Hindu community (76.7%). Majority of them belonged to Middle Socio-Economic Status (78.9%). Majority participants had poor knowledge and negative attitude regarding Adolescent Health before the intervention. Significant improvement in Knowledge was observed regarding: (a) Sex differences in pubertal spurts of adolescents, (b) Probable causes of health problems in adolescent period, (c) Physical changes in adolescent boys, (d) Physical changes in adolescent girls and (e) Psychological problems in adolescent period. Significant improvement in Positive Attitude was observed regarding following aspects: (a) Opinion regarding substance abuse in adolescent period, (b) Importance of sex education for adolescents. Keywords: Knowledge, Attitude, Adolescent

KAPON CONDOM AMONG ADOLESCENT RURAL GIRLS OF BENGAL, INDIA

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Introduction: The state of sex education programs in Asia is at various stages of development. **Objective:** To determine knowledge, attitude and intended practice of condom among adolescent female students of a rural area of Bengal. **Study Design:** Sex education intervention study. **Study Area:** Haripal block of Hoogly district, West Bengal, INDIA. **Study Period:** 6 months (January-July 2006). **Study Population:** 302 students of adolescent age group 13-19 in that block. **Inclusion Criteria:** Adolescent girls studying in Class VI to XII of three schools. **Exclusion Criteria:** Pre-tested subjects not appearing in post-test session. **Sampling Technique:** Simple Random Sampling. **Study Instruments:** Pre-tested close-ended questionnaires, Audio-Visual aids, Hand-outs. **Data Collection:** Initially, all the adolescents in the inclusion criteria were evaluated by the pre-test questionnaire. Then Health Education Intervention was organized in small groups in interactive sessions lasting 2 hours each and was held by the specialists in Community Medicine. Audio-Visual teaching materials and hand-outs were given simultaneously. Six months later, the post-test questionnaire was administered. **Data Analysis:** SPSS version 10.0 used and paired 't' test was applied. **Results:** Mode age of 302 high school girl students was 16 years with a range of 13-19. Significant improvement in Knowledge and Positive Attitude between pre-test and post-test results was observed regarding the following aspects: (a) Significant Improvement in Knowledge on Condom was observed regarding for sex: (a) While on O.C. always Condom necessary?, (b) With well-known partner, still always need Condom?, (c) Convince peers to use Condom always, (d) While on O.C. convince peers to use Condom always? (e) If well known, still convince peers to use Condom always? (b) Significant Improvement in Positive Attitude was observed in following aspects for sex: (a) Convinced to use Condom always? (b) Asking your friend to use Condom always? (c) Asking newly found relation to use Condom before sex always? (d) While on O.C., convince friend to use Condom to avoid S.T.D.s always? (c) Significant Improvement in correct intended practice was reported in all aspects. The health education module was well accepted. The participatory response was more due to the fact that this health education intervention programme was followed by clinical examination. During interactive sessions, students suggested that the school should provide information about sexuality from the lower grades of secondary schools. **Conclusions:** This study revealed some unknown part of adolescent girl psychology on condom of this part of India.

EVALUATION OF INDIAN VERSION OF WHO-FIVE WELL-BEING INDEX (WHO-5) FOR SCREENING DEPRESSION IN ELDERLY POPULATION

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Introduction: A high prevalence of depressive disorders is seen in old age. The community-based mental health studies have revealed that the point prevalence of depressive disorders among the geriatric population in India varies between 13 and 25 per cent. The WHO-Five Well-Being Index (1998 version) showed a good Internal & external validity and reliability in Primary Health Care of European settings. Since, it is simple and easy to administer, an attempt is made to evaluate the Indian version of this instrument for identifying elderly subjects with depression in Indian community. **Materials and Methods:** Study Design: Cross-sectional study. Setting: Rural area of Udipi taluk, Karnataka in South India. Study period: 8 months (From 1st of March to 31st of October 2002). **Participants:** 627 elderly individuals of age group of 60 years. **Sampling Method:** Simple Random Sampling Method using the PPS technique. **Study Instruments:** Modified Udaï Pareek Scale - Socio-economic status. Depressive Disorders was determined by (a) WHO (five) Well-being Index (1998 version) and (b) Major (ICD-10) Depression Inventory of Mastering Depression In Primary Care Version 2.2. Cognitive impairment - 6CIT Dementia Test. **Statistical Analysis:** Proportions and their 95% Confidence Intervals. Kappa statistics was applied to study the reliability of the screening instrument. *P* value <0.05 was considered as statistically significant. **Results & Conclusion:** The prevalence of depression in elderly population was determined to be 21.7% (95% CI=18.4-24.9). The prevalence rates of depression among the males and females were 19.9% and 22.6% respectively. The Indian Version of WHO-Five Well-Being Index (1998 version) showed a Sensitivity of 97.0%, Specificity of 86.4%, Positive Predictive Value of 66.3% and an Overall Accuracy of 0.89. The Kappa Statistics showed significantly high reliability of *k*=0.71. The total area under the Curve was 0.083 (SE=0.13, 95% CI=5.804-0.109, *p*=0.0001*). Since, the Indian Version of WHO-Five Well-Being Index (1998 version) showed a good Internal & external validity and reliability for identifying Depressive Disorders in elderly population, this could be considered as a useful instrument for identifying elderly subjects with depression in Indian community.

MODIFIED GILBERT'S REPAIR USING HAND SEWN BILAYER PROSTHETIC DEVICE (HSBP)

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Objective: To study the outcome of the Gilbert's repair by using HSBP for inguinal hernia and to compare the results with the conventional Gilbert's repair. **Methods:** This was an observational prospective clinical study on 52 patients with unilateral inguinal hernia, where the surgical repair was done by Gilbert's repair using HSBP (Hand Sewn Bilayer Prosthesis constructed by sewing 3"x6" and 6"x6" polypropylene mesh). The patients were observed postoperatively using pain scoring, retention of urine, hemorrhage, wound infection, cord edema/hematoma and duration of hospital stay and followed up after six weeks and one year using the following parameters testicular atrophy, residual neuralgia & recurrence. **Results:** Infection-1 cases, hematoma-1 cases, seroma-4 cases, neuralgia-2 cases, testicular atrophy-0 cases, recurrences-0 cases out of 52 total cases after 1 year of follow up. No statistically significant difference could be found between the studies done by Gilbert's PHS and the

author's HSBP in the variables studied. **Conclusion:** From the above comparison it is observed that operating the inguinal hernia by Gilbert's repair using HSBP device is having results and complications which are on par with that obtained using prolene hernia system [PHS]. Hence it is concluded that the modified Gilbert's repair using the HSBP is the most cost effective approach (since the cost of the later is only 2000Rs where as that of the former is 11000Rs) and it is particularly true in the Indian subcontinent where the type of the operation is tailored to patient's financial status.

DELINEATION OF LYMPHATICS IN FILARIAL LYMPHOEDEMA -K.J. EXPERIENCE

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Introduction: It is estimated that in India there are about 16 million cases are suffering from chronic disease of lymphatic filariasis; the most common type of the disease is Bancroftian. Lymphatic dysfunction may be present even in the early stage of the infection. By doing lymphoscintigraphy using a radiotracer like 99m Technitium labeled Human Serum Albumin (99mTc HSA) and a gamma camera, it was possible to visualize the lymphatic system. The technique is simple with less discomfort to the patient. K.J.Hospital, Chennai being the pioneers in perfecting this procedure, starting from 1990, it had investigated over 500 cases of lymphatic filariasis for the past 15 years. **Materials & Method:** In the tracer, HSA (imported) kit was used to tag 99m Technitium radio nucleotide extracted from 99 Molybdenum (supplied by BRIT, Mumbai). Tagged radiotracer was estimated to give strength of about 10 mci per ml. A dose of 0.5 mci in about 0.05ml was injected intradermally in the 2nd web space in the upper or lower limb as the case may be bilaterally. Radiotracer markers were kept at knee level and super sternal notch. The gamma camera is in sweep mode and the patient lies under the camera in supine posture. Images were obtained immediately after injection, 15mts after massage, 1 hour and 3 hour post injection. These images depicted the transport of tracer at stipulated intervals. Out of 165 cases of positive filarial disease 20% gave a normal morphology, 66 showing severe abnormalities with dermal back flow with dysfunction varying in between. **Results & Discussions:** Results show that in normals the tracer reaches at groin level in about 10 minutes after injection. Reduced function of the lymphatics results in slower transport, which is a consequence of obstructions and dilations of the lymphatics, which are evident from the flow pattern. Collaterals and multi channels, dermal back flow, lack of concentration of tracer in nodes etc., may also be visualized. Recently attempt was made in the development of Lymphoscintigraph, which uses micro detectors at various anatomical points on the skin corresponding to the lymphatic channels to pick up the activity with a help of a P.C. This attempt was made under MoU in collaboration with scientist from Indira Gandhi Centre for Atomic Research, Kalpakkam. It was possible to correlate the counts that are plotted as histograms with the gamma camera images. **Conclusion:** The procedures is very much helpful in the management of the disease and follow-up, the morphology of lymphatic is very clear, clinician shall be able to point out the level of abnormality and type of dysfunction. The portable system developed in our hospital can be used for field trials and that would reduce the cost since gamma camera is dispensed with.

ESTIMATION OF FRACTURE AND COMPRESSIVE STRENGTH OF NATURAL URINARY STONES

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Objectives: Urolithiasis has been found among the human race ever since the early days of civilization and it is one of the common causes of disease of the urinary system. Treatment modality for urinary stone disease has been revolutionized since the introduction of extracorporeal shock wave lithotripsy and it has become primary treatment modality, eliminating the need for surgical intervention. Hence, a knowledge of physical properties of renal calculi is important to understand shock-wave stone interaction and the mechanism of stone fragmentation. Fracture refers to the failure of a material under load by breaking into two or more pieces. Compressive strength is defined as the stress calculated at the maximum load. **Materials and Methods:** A total of fifteen cylindrical stone samples were prepared for the study of fracture strength and compressive strength. The length and diameter of the samples ranged from 0.7-1.79 cm and 0.39-0.68 cm respectively. To determine the fracture strength of urinary stones in the present study, a simple device was fabricated and the fracture strength was calculated. The instrument works on the principle of lever arrangement. Fracture strength of five urinary stones were studied in the equipment designed in the laboratory and for remaining ten samples, Hounsfield test equipment was used to find the compressive strength. **Results and Discussion:** The fracture strength of five stones tested in the fabricated instrument was in the range 0.886 to 2.9 MPa. The fracture strength was found to be higher for calcium oxalate stones and less for apatite and MAPH mixed stones. The compressive strength of ten samples with predominantly calcium oxalate or a mixture of calcium oxalate with any of the constituents like apatite, MAPH and UA were found to have values in the range 2.212 - 11.108 MPa. No particular trend was observed in this study. The reason for the variation in compressive strength may be due to the structural inhomogeneity of the stones. Different stones responded differently while determining their compressive strengths. Tensile strength studies on urinary stones were not attempted due to the lack of large sized specimens. But tensile strength is found to have an indirect relation with compressive strength. Hence, tensile strength of the ten samples was computed and it was found to be in the range that falls under the category of composites. **Conclusion:** In conclusion to improve the efficacy of ESWL treatment with optimum parameters, studies on the physical properties on a quantitative basis have shown to be helpful. The data could be used in the refinement of lithotripsy technology to achieve maximal stone fragmentation efficacy while minimizing the side effects on the surrounding tissue. Especially compressive strength tests which can be done on a small specimen provide a simple and convenient method to characterize the complex mechanical properties of renal calculi to a great extent.

ERYTHROCYTE MARKERS OF OXIDATIVE INSULT IN THE ACUTE PHASE OF GRADED TRAUMATIC HEAD INJURY IN HUMANS

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Objective: Acute oxidative stress following a traumatic head injury (HI) has been implicated to induce severe secondary brain damage and to influence the clinical outcome of HI patients. This study was performed to evaluate and compare the oxidative changes in patients with varying severity of head injury in the early posttraumatic period using the erythrocyte markers. **Methods:** Head injury (HI) patients were divided into two groups based on their Glasgow Coma Scale (GCS) scores recorded at admission to the hospital on the day of trauma itself. Accordingly, the study included 30 severe HI (SHI, GCS scores 8 or less) and 25 Mild HI (MHI, GCS scores more than 8) patients. Thirty age and sex matched healthy individuals were included in this comparative study as controls (NC). Venous blood samples were withdrawn from NC and HI patients (within 24 hours of trauma onset). Erythrocyte oxidative changes were studied by estimating thiobarbituric acid reactive substances (TBARS) and glutathione (GSH) levels and by assaying the activity of superoxide dismutase (SOD). **Results:** Erythrocyte TBARS levels were significantly higher and GSH levels were significantly lower in SHI and MHI patients as compared to NC. SOD activity was significantly increased only in SHI patients and remained unchanged in MHI patients as compared to NC. As compared to MHI patients, erythrocyte TBARS levels were significantly higher, GSH levels were significantly lower and SOD activity was markedly elevated in SHI patients. **Conclusion:** Early oxidative changes were found to vary relatively with the severity of trauma in HI patients. These early changes could thus have a significant impact on the neurological recovery of HI patients.

GEMCITABINE AND CISPLATIN COMBINATION CHEMOTHERAPY AS FIRST LINE TREATMENT IN METASTATIC BREAST CANCER (MBC) PATIENTS WITH LOW KPS

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Background: We have previously reported an overall response rate of 61.9% with gemcitabine and cisplatin in second line setting (ASCO 2003; abstract 212) and 76.7% in first line setting in patients with metastatic breast cancer (ASCO 2005; abstract 713). All these patients had KPS > 70. As many patients with MBC have a low KPS, we devised a different dose and schedule of gemcitabine and cisplatin for these patients. The objective of this study was to evaluate the efficacy and toxicity of this protocol as first line treatment of MBC patients with low KPS. **Methods:** Female breast cancer with visceral or visceral and bone metastases and a KPS of 60-70 were eligible. Adequate marrow, renal and hepatic function was required. Metastatic brain disease and bone as the only site of disease were excluded. Informed consent was taken from all the patients. Gemcitabine 1250 mg/m² and cisplatin 50 mg/m² were given on day 1 only. Cycles were repeated every 3 weeks. CTCAE version 3.0 of NCI and RECIST was used. **Results:** From January 2005 to April 2006, 42 patients were enrolled. Median age was 48 years (Range 28-70). A total of 246 cycles were delivered with a median of 5 cycles. 12 patients received 8 cycles. CR was seen in 19% patients and PR in 50% with an overall response rate of 69%. Stable disease was seen in 14.3% and PD in 16.7%. Three patients with progressive disease have died. Grade I alopecia and hyperbilirubinemia was seen in 50% and 9.5% patients respectively. Grade II neutropenia, thrombocytopenia, vomiting and serum creatinine elevation was seen in 31%, 9.5%, 28.6% and 12% respectively. Grade III neutropenia and vomiting was seen in 21.4% and 4.8% respectively. **Conclusion:** This treatment schedule is an effective first line treatment of MBC patients with poor Karnofsky performance status patients and provides a good overall response rate and manageable toxicity.

CLAVICLE RADIOGRAMMOMETRY – A SIMPLE TOOL FOR PREDICTING BONE MINERAL DENSITY

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Objectives: To investigate the efficacy of the empirical formula derived at our K. J. Research Foundation, K. J. Hospital, Chennai, which is termed as KJH: Anburajan's empirical formula (involving simple clavicle radiogrammetry measurements from chest radiograph) for predicting total hip bone mineral density (BMD) in g cm-2 in women and men in the evaluation of osteoporosis as compared to a sophisticated technique like Dual-energy X-ray Absorptiometry (DXA), a "gold" standard for measuring BMD. **Materials & Methods:** Subjects A total number of 116 patients, aged above 35 years (women=66, and men=50), who participated in "Free Osteoporosis Screening Camp" conducted at K. J. Hospital, Chennai during the period June 1 and 2nd, 2006 were included in this study analysis. Patients with secondary bone diseases were excluded. **Measurements** A total hip BMD (g cm-2) was measured in all the patients using DXA bone densitometer (QDR-4500, Hologic Inc., Waltham, Massachusetts, USA). Also, a standard postero-anterior (PA) chest radiograph was taken in all the individuals. Using these measurements, cortical bone mass indices of the clavicle are calculated as follows: Combined Cortical Thickness (CCT) = (D-d) cm; and Percentage Combined Cortical Thickness (%CCT) = [100(D - d) / D]. The sensitivity and specificity of this formula was found to be 82.4% and 94.0% respectively, when compared to DXA as a "gold" standard for measuring BMD (g cm-2). **Statistics** Linear regression analysis was used to study the dependence of predicted hip BMD (g cm-2) using KJH: Anburajan's empirical formula and measured hip BMD (g cm-2) by DXA. **Results** The predicted hip BMD (g cm-2) using the formula was correlated statistically significant with the measured hip BMD (g cm-2) using DXA in women (r²=0.423, p<0.001) and men (r²=0.21, p<0.001); but, this correlation was greater in women than in men. **Conclusion** The preliminary study analysis showed that the KJH: Anburajan's empirical formula predicted total hip bone mineral density (BMD) in g cm-2 in women very well than in men in the evaluation of osteoporosis as compared to a sophisticated technique like Dual-energy X-ray Absorptiometry (DXA), a "gold" standard for measuring BMD.

RADIOPROTECTIVE EFFECT OF THYMOL IN CHINESE HAMSTER LUNG FIBROBLAST CELLS: A MICRONUCLEUS STUDY

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The radiomodulatory potential of Thymol (TOH) against radiation-induced micronuclei formation was analyzed using Chinese hamster lung fibroblast cells (V79) growing *in vitro*. The micronuclei frequency was evaluated in cytokinesis blocked binucleate V79 cells. The TOH rendered protection against the radiation induced DNA damage, as evidenced by the significant reduction in micronuclei after various doses of TOH treatment. The optimum protective dose of TOH was selected by treating V79 cells with 10 - 300 mg/ml, 1 hr before exposure to 3 Gy of gamma radiation. The dose of 25 mg/ml TOH with the greatest reduction in micronuclei was further used in combination with various doses (0.5, 1, 2, 3, and 4 Gy) of gamma radiation exposed 1 hr after TOH treatment. There was a linear dose dependent increase in the micronuclei in the radiation alone group, while 25 mg/ml TOH significantly protected the cells from the induction of cytogenetic damage as observed by the reduction in micronuclei compared to the respective radiation alone groups. TOH produced a dose-dependent increase in free radical scavenging ability against various free radicals viz., 2,2-diphenyl-1-picrylhydrazyl (DPPH), 2,2-azino bis (3-ethylbenzothiazoline-6-sulfonic acid) (ABTS), superoxide anion (O₂⁻), hydroxyl radical (OH) and nitric oxide radical (NO) generated *in vitro*. Besides, an excellent (70%) inhibition of lipid peroxidation *in vitro* was observed at a dose of 100 mg/ml TOH and attaining saturation point at higher doses. The present findings demonstrated radioprotective effect of TOH rendering protection against radiation induced genomic instability and DNA damage. The observed radioprotective effect may be partly attributed to the free radical scavenging and anti-lipid peroxidative potential of Thymol.

REDUCING THE CYTOTOXICITY TO LYMPHOCYTES OF CR(III) PICOLINATE, A PREVALENT NUTRITIONAL SUPPLEMENT.

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The importance of the role of chromium (III) in glucose and fat metabolism has been recognized very early, yet the mode of action is being realized only in the recent times. Chromodulin the biologically active form of chromium is a Cr(III) complex liganded to amino acids such as glycine, aspartate, cysteine, glutamic acid and is a small molecular weight protein. Chromodulin has been demonstrated to activate fully, the partly activated insulin bonded insulin receptor. Currently Cr(III) picolinate is used as a nutritional supplement as also in treating diabetics. Our earlier work has indicated that redox active Cr(III) complexes are cytotoxic and are capable of inducing apoptosis of lymphocytes. Since Cr(III) picolinate is also capable of undergoing redox actions, we have now investigated the effect of Cr(III) picolinate in human blood peripheral lymphocytes. Lymphocytes have been purified using Ficol-Histopaque density gradient centrifugation and cultured in the presence of RPMI-1640 medium and 5% CO₂ in a humidified atmosphere at 37°C. Cytotoxicity to lymphocytes has been observed through thymidine incorporation, viability studies, and morphological assessment. The observed chromatin condensation and apoptotic bodies and DNA fragmentation patterns indicate that the cells undergo apoptotic cell death. A number of cells with vacuoles in the cytoplasm are also seen, indicative of possible cell death through autophagy also. At high concentrations of Cr(III) picolinate, necrotic cells can be observed. Picolinic acid which is formed from Cr(III) picolinate is toxic at concentration higher than 2000M. Apoptosis and necrotic cells can be differentiated with fluorescence microscopy using a combination of acridine orange and ethidium bromide. The various cell death processes may be initiated by a common mechanism and this is indicated. Treatment with antioxidants reduces the toxicity to lymphocytes. It may thus be essential to look for some non-redox active chromium compounds as a chromium supplement or alleviate the toxicity by including an agent which may aid in suppressing the toxicity of Cr(III) picolinate.

TRABECULAR BONE ASSESSMENT IN THE EVALUATION OF OSTEOPOROSIS.

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To quantify the trabecular micro-architectural network as it appears in the lateral radiograph of the calcaneum in the evaluation of osteoporosis in women as compared to the Dual-energy X-ray Absorptiometry (DXA), a "gold" standard tool for measuring osteoporosis. **Subjects:** A total number of 30 women subjects, aged between 48 to 63 years (18 normal (age and SD is 54 ± 6 years and 12 osteoporotic (age and SD is 56 ± 7)) were participated in this study. Patients with secondary bone diseases were excluded; further, patient's who had undergone previous major surgery, like kidney transplantation was excluded. Also, excluded were those taking any drugs known to affect calcium metabolism, example: thiazide, diuretics, oestrogen, and calcium. **Measurements:** A total hip BMD (g cm²) was measured in all the patients using DXA bone densitometer (QDR-4500, Hologic Inc., Waltham, Massachusetts, USA). Also, a standard lateral radiograph of the calcaneum was taken in all the individuals. The radiographs are digitized and stored for texture analysis. The programs developed by us in Matlab software automatically compute the texture parameters. **Results:** The Discriminant analysis shows significant alterations of the trabecular micro architecture between the normal and osteoporotic subjects (p<0.08) who are classified based on the T-Score obtained by DXA. The results obtained show that there is considerable alterations of the trabecular network as there is depletion in the bone mineral density. **Conclusion:** The preliminary study analysis showed that the textural modification is evident which proves that in addition to decrease in the bone mineral density (BMD) (which is the quantitative change) and there is a significant alterations

of the micro-architecture of bone trabecular network (which is the qualitative change) in accordance with the decrease in BMD in the osteoporosis.

A COMPARATIVE STUDY OF THE HEMATOLOGICAL PARAMETERS IN D – DIMER POSITIVE PATIENTS WITH DISSEMINATED INTRAVASCULAR COAGULATION(DIC) OR THROMBOSIS

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Introduction - D – Dimer test is one of the most important diagnostic tools for the diagnosis of DIC and thrombosis. The interpretation of d – dimer in DIC and thrombosis depends on the clinical picture and correlation with other lab parameters. The relevance of the present study is to identify the hematological markers which would be helpful in the early diagnosis and differentiation between DIC and thrombosis. **Objectives** 1. Compare the significance of the hematological parameters in patients with DIC and thrombosis with D – Dimer positivity. 2.

Evaluation of the significance of hemolysis and infection in patients with DIC and thrombosis with D – Dimer positivity. 3. Study the relationship of thrombocytopenia in DIC and thrombosis with D – Dimer positivity. **Materials and methods** - A retrospective study of 72 patients diagnosed clinically as DIC or thrombosis with positive D – Dimer test during 2005 – 2006 was done. The clinical data was taken from medical records department of Kasturba Hospital, Manipal. The hematological parameters including peripheral smear done on the same day, complete blood counts and coagulation profile of all these patients were taken. The clinical and lab data were analyzed. **Results** - In the present study, out of 72 cases, 58 cases were clinically DIC while 14 were cases of thrombosis. Out of 58 D – dimer positive cases of DIC, 44(75.8%) cases were due to sepsis, 4(7%) were of malignancies, 5(8%) were due to obstetric causes and 2(3%) were due to snake bite. Thrombocytopenia was present in 50% cases of sepsis and malignancy while it was 100% in the obstetric cases. Polychromasia was seen in 33(56.8%) cases either alone or in combination with other features of hemolysis. Microangiopathic hemolytic anemia was seen in 17/58 (29.3%) cases of DIC. Out of 58 cases, 39 (67.2%) cases showed evidence of leucocytosis and neutrophilia. In sepsis and obstetric cases the evidence of infection was seen in 68.2% and 60% respectively. Deranged coagulation parameters were seen in 37(63.8%) cases with derangement of both PT and APTT in 19(32.7%) and PT alone in 15(25.8%) cases. Out of the 14 D – Dimer positive cases with thrombosis, 10 (71.4%) were venous while 4 (28.6%) were arterial. Polychromasia was seen in 13(92.8%), out of 14 total cases considered while thrombocytopenia was seen in only 2 (14.2%) cases. Leucocytosis alone or in combination was seen in 10 (71.4%) of the cases. Coagulation parameters were deranged in 10 (71.4%) cases with 8 (80%) of these having venous thrombi. **Conclusion** 1. Sepsis was the most common cause of D – Dimer positive DIC. The reliable markers for DIC include thrombocytopenia and deranged coagulation parameters. 2. In D – Dimer positive cases of thrombotic deranged coagulation parameter was a consistent finding while thrombocytopenia was not a significant feature. 3. Leucocytosis with neutrophilia was a prominent feature in DIC due to sepsis and obstetric cases while leucocytosis alone was significant in the thrombotic cases. 4. Microangiopathic hemolytic anemia and the evidence of hemolysis were seen in DIC while polychromasia was the only feature noted in thrombosis.

EFFECT OF TRACE METALS ON CELL SURFACE HYDROPHOBICITY OF STAPHYLOCOCCUS EPIDERMIDIS.

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Aim: To study the effect of trace metals on cell surface hydrophobicity of *Staphylococcus epidermidis*

Material and methods: *Staphylococcus epidermidis* strains N- 203 and MTCC- 435 were grown in chemically defined medium. The trace metals used in the study were Ca^{2+} , Co^{2+} , Cu^{2+} , Fe^{3+} , Mg^{2+} , Mn^{2+} , Ni^{2+} and Zn^{2+} . Different concentrations (0.01mM, 0.05mM and 0.25mM) of trace metals are incorporated in the CDM. The cell surface hydrophobicity was determined using Rosenberg et al method. **Result and conclusion:** Bacteria grown in CDM without trace metals showed less hydrophobic properties. Though all the metals tested enhanced the hydrophobicity, Ca^{2+} and Mg^{2+} significantly enhanced the hydrophobicity of *S.epidermidis*. Bacteria grown in the presence of increased concentration of Mn^{2+} had less hydrophobic property. Since cell surface hydrophobicity of bacteria is the initial step of colonization, these findings could help to understand catheter related infections caused by *S.epidermidis*

EFFECT OF TRACE METALS ON SUSCEPTIBILITY OF SALMONELLA TYPHI TO HUMAN SERUM

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Background and Objectives: Resistance to the bactericidal effect of human serum is a virulence trait encountered in bacteria having propensity to invade blood stream. This study was designed to study the effect of trace metals on susceptibility of *S.typhi* to human serum.

Methods: Serum bactericidal activity was determined using the method described by Hughes. The kinetics of interaction of human serum with *S.typhi* grown in varying concentration of metals was assayed and percentage survival was determined.

Results: Calcium and magnesium did not have any significant effect on susceptibility of *S.typhi* to PNHS. Copper ions provided resistance to bacteria against lethal effect of human serum. Iron and zinc were found to enhance killing by PNHS.

Conclusions: Trace metals occupy a central role in the battle between host and the parasite. The findings illustrate that the metal ions influence bactericidal effect of human serum in different ways.

GLANZMANN'S THROMBASTHENIA: THE MANIPAL EXPERIENCE.

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Introduction: Glanzmann's Thrombasthenia (GT) is an autosomal recessive disorder of platelet aggregation causing life long bleeding. It is a common disorder of platelet function in the young especially in Southern India where consanguineous marriages are common. The present study is undertaken to evaluate the magnitude of the disease in a tertiary care hospital in South India .

Objectives: 1) To study the clinical spectrum of patients with GT in a tertiary care hospital in South India 2) To correlate clinical and laboratory parameters of GT including the platelet aggregation studies. 3) To identify the sub-groups of patients requiring specialized tests for the diagnosis.

Materials Methods: A retrospective study of 15 patients diagnosed as GT in the Hematology Laboratory of Kasturba Hospital, Manipal during a 2 year period was undertaken . The clinical and the lab parameters were compared. The Lab parameters studied include haemostatic screening tests (BT, PT, APTT, TT, Factor XIII, clot retraction, platelet count, direct smear) and platelet aggregation studies with ADP, Collagen and Epinephrine. Von Willebrand factor assay and platelet aggregation with Ristocetin were done in some cases. **Results:** 1) 14/15 (93%) patients were less than 20years of age.

2) Consanguineous marriage was found in 4 (26.6%) cases. 3) The common clinical presentations were epistaxis and skin bleeds. Majority of the females also presented with menorrhagia. 4) Bleeding Time(BT) was prolonged in 14/15 (93%). Clot retraction was reduced or absent in 10/15 cases (66.67 %). Platelet clumps were absent in 10 cases (66.67%). 5) In 5/15 (33.33%) cases the clot retraction was normal. But 80% of these cases showed increased BT. 6) In 5/15(33.33%) cases small clumps of platelets were seen. 7) Platelet aggregation studies were characteristic of GT in 13 patients (100%) in whom it was done 8) VWF assay was normal in all 11 cases in which it was done. 9) 8/15 (53.33%) cases showed decreased aggregation with Ristocetin.

Conclusion: Consanguineous marriage in 26.67 % of patients was responsible for increased prevalence. Platelet aggregation studies are necessary for a confirmed diagnosis of GT. VWF assay & Platelet aggregation with Ristocetin are other helpful tests to differentiate GT from other common platelet functional disorder

HIGH LEVEL AMINOGLYCOSIDE RESISTANCE AMONG ENTEROCOCCAL ISOLATES

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Background and Objectives: Enterococcal isolates are increasingly being reported as resistant to the routinely used antimicrobial agents. This study was undertaken to determine the incidence of high level aminoglycoside resistance (HLAR) among enterococci, isolated from various clinical specimens at the Department of Microbiology, Kasturba Medical College Hospital, Manipal, India. **Methods:** 192 strains of enterococci, isolated from clinical specimens, over a period of two years were used in this study. Standard techniques were used for isolation and identification. HLAR was detected using agar dilution method. **Results:** HLAR was observed in 45.8 % of *E.faecalis* and in 33.9 % of *E.faecium* strains. **Conclusions:** Routine evaluation of HLAR is essential in formulating treatment guidelines.

INDUCIBLE CLINDAMYCIN RESISTANCE AMONG STAPHYLOCOCCI

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Background and Objectives: Multiple mechanisms which confer resistance to macrolide, lincosamide and streptogramin antibiotics have been reported. This study was undertaken to detect the presence of inducible clindamycin resistance among staphylococcal isolates.

Methods: D-test was performed in accordance with the CDC guidelines for detection of inducible clindamycin resistance. **Results:** Around 13 % of the staphylococcal isolates showed inducible clindamycin resistance and belonged to the MLS_Bi phenotype. Among the MLS_Bi phenotypes, 38% were methicillin resistant *Staphylococcus aureus* and 13% belonged to methicillin sensitive *Staphylococcus aureus* **Conclusions:** Testing for inducible resistance to clindamycin should be done on a regular basis, as it helps in providing accurate therapy.

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