

EMERGING INFECTIONS: EDITOR'S PERSPECTIVE

While the world is deeply engaged in solving global warming & financial crisis other global or regional issues like health related are moving to the back burner. However, multidrug resistant infections or newer geographical locations with newer infections earlier known to be only prevalent elsewhere can be considered as no less than a part of the global warming phenomenon. In fact it is more of the demographic changes with earlier known infections than the newer emerging ones in the true sense of the word that are viewed as emerging infections. The data when reviewed as below does not make it difficult to understand that we in fact do not need infections to emerge but are inundated with newer & newer aspects of already known and forgotten infections that are seen with different presentations at newer locations.

Over 1.1 billion people do not have safe water to drink and over 2.4 billion people are without proper sanitation¹. The global burden of water-related infections alone are no less : approximately 4 billion cases of diarrhoeal diseases each year lead to 2.2 million deaths, which includes children under the age of 5. This is equivalent to 20 jumbo jets crashing every day. This represents approximately 15% of all child deaths under the age of 5 in under-developed countries¹. Out of seven billion USD drugs market, anti-infectives constitute 23% of it and most of these are gastrointestinal products. By simply improving the quality of water we can reduce diarrhoeal diseases by 16%, whereas improving sanitation can result in a reduction by about 32%, and hand washing with soap a further reduction of up to 45%¹. Only 2% GDP of Indian budget is spent on health. And it needs 78 toilets to be built every minute for 4 years to provide adequate sanitation. Such figures reveal the odds that we are facing in preventing re-emergence of infections.

Poverty besides being a curse also encourages diseases to grow exponentially. The economic system that we live in today is focused on high profits. The high-technology products such as those generated from the electronic, pharmaceutical, and chemical industries, together with the financial markets are the highest profit areas today. Investment in public health more so in infection related issues has a low priority. It has to be realised that once you prevent illnesses it is bound to result in economic growth of a country.

Opportunistic fungal infections have emerged as important causes of morbidity & mortality in immunocompromised patients and remain a major challenge for treating infections. Invasive fungal infections besides their increased frequency, are still associated with unacceptably high mortality, up to 40% in bloodstream infections caused by *Candida albicans* and more than 50% in invasive aspergillosis². However, the trend is currently changing in yeast infections where *Candida non-albicans* is ruling supreme. At our centre we are finding *C. haemulonii* emerging as one of the leading yeast fungal infection in our ICU which has significantly reduced MIC to Amphotericin B.

The drug resistant HIV infection claiming lives in Africa and elsewhere has a potential to cause disaster in countries where infants even before achieving the productive years of life are getting eliminated by this disease. As it appears India is sitting over a volcano (2.4 million cases) if WHO figures are to be believed. However, with government support for HAART in our country we are bound to find illnesses related to the immune-reconstitution syndrome. The knowledge of such infections in such patients are necessary for the appropriate follow up therapy in such patients. Moreover lack of viral load monitoring seems to be associated with resistance in patients

with viral failure after first year of HAART, therefore early identification of such patients might be the best way to employ viral load testing which has been abandoned in favour of CD 4 assay in our country³.

Malaria is the world's most important parasitic infection & ranks foremost among the major health and developmental challenges in the developing countries of the world⁴. The mortality caused by *Plasmodium falciparum* has been documented as 85%⁵. On studying the evolution of *P. falciparum* 8 new isolates of Chimpanzee malaria *Preichenowi* were found closest related to it⁵, thereby suggesting that humans acquired it from non-human host as a result of changing demographics. There is ever increasing trend of multi-drug resistance in *P. falciparum* & *vivax* malaria. Effective interventions remain a formidable challenge. India shares with China the burden of *P. vivax* preponderance therefore cannot be ignored now & latter be recognized as emerging infection. In fact may be seen more often if adequate attention is not given towards the gaps in our understanding of this parasite⁶. Despite global economic development, more people die from malaria nowadays than 40 years ago⁷. Estimate for annual malaria mortality range from 0.5 to 3.0 million people⁸. In a well-documented study it was concluded that chloroquine resistance has resulted in 4 to 8 fold increase in mortality⁹. Every year we are visited by Dengue, another mosquito born scourge of mankind directly related to our public hygiene and such re-emerging infections are totally preventable. The emergence of a variety of influenza virus (H1N1, H5N1) have visited us & the reaction towards its preparedness has taught us a few lessons. Though the world community did a commendable job by way of speedy characterisation & vaccine development, this needs to be matched by the local response as well. Continued circulation of avian & swine influenza viruses in Asia & other parts of the world shows that a future pandemic from non-human influenza viruses is a distinct possibility & complacency has no scope. This assumes more significance when oseltamivir resistant strains of H1N1 have already emerged (10).

The incidence of sepsis has increased by 329% over a period of 20 years between 1979 and 1999, according to new research presented at the American Thoracic Society's 98th International Conference (May 17-22, 2002 Atlanta, GA, USA). "Although better supportive care for patients with sepsis has lowered the mortality rate, many more patients are now actually dying from sepsis," (Dr. Greg Martin, Emory University School of Medicine, Atlanta, GA, USA)¹¹. There are now more people with altered immunity because of organ transplantation, bone marrow transplantation, chemotherapy, and HIV infection, which lowers immunity in patients. Add to this the relative rise in the average life span resulting in a geriatric population pool.

Despite significant advances in the fight against tuberculosis over the past 10 years, formidable challenges still remain. Laboratory research over the past decade has transformed tuberculosis research including progress in the understanding of multi-drug resistance. The development of rapid DNA-typing techniques (HAIN-Test), and the genetic sequencing of *Mycobacterium tuberculosis* has added value to molecular tests and have taken a step further ahead in initiating appropriate therapy and tracing the cases. HAIN-Test can detect mycobacteria directly from the samples both pulmonary and extrapulmonary, smear negative as well as positive. The assay that detects MDR TB though detects mutated genetic sequences only from smear positive sputum. This application detects rpoB-WT I-8

(Wild Type sequence) and rpoB – MUT 1-3, sequences and similarly detects katG and inhA wild and mutant sequences. It is the deletion of WT and replacement with mutant sequence in one or more drug related sequence that indicates presence of MDR TB in a patient directly from his/her smear positive sputum. This can make a lot of difference to the clinician in starting the therapy on MDR cases. Moreover, it takes only five hours to complete the procedure. Genetic sequencing can further provide the epidemiological lineage of the spread of the disease. Experts addressing the tuberculosis control noted that 23 “high-burden countries” account for 80% of the world’s tuberculosis cases & India figures one among them. Nevertheless, the incidence of tuberculosis is still rising. It is estimated that one in three people worldwide is infected with tuberculosis and that there are 9 million active cases each year, resulting in 2 million-death¹². At our centre 9 – 15% MDR tuberculosis cases have been documented in the year 2008-09 besides a few XDR-TB. Around 50,000 of 9 million new cases of tuberculosis seen worldwide each year are now due to multi drug-resistant (MDR) strains. Countries that have highest percentage of XDR among their MDR cases include Azerbaijan (12.8%), Ukraine (15%) & Estonia (23.7%) reported by Philip LoBue (Div. of Tuberculosis Elimination, CDC, Atlanta, GA, USA)¹³⁻¹⁴. Hepatitis B virus (HBV) infection is prevalent in Asia, Southern Europe, and Latin America, where the rate of hepatitis B surface antigen (HBsAg) carriage in the general population ranges from 2% to 20%¹⁵. Roughly 2 billion people, one third of the world’s population, have serological evidence & develop liver diseases. Worldwide, the 350 million people with chronic HBV infection have a 15% to 25% risk of dying from HBV-related liver disease, including end-stage cirrhosis and hepatocellular carcinoma (HCC)¹⁶. Each year, acute and chronic HBV infection causes roughly 1 million deaths¹⁷. It is these cases that are going to make the pool of transplant patients. The newer & difficult to diagnose infections in this group of patients determines to a large extent the outcome of transplant surgeries. Unfortunately vaccines for many pathogens worldwide, including HIV, hepatitis (HCV, HEV), malaria (*Plasmodium falciparum*), and *Mycobacterium tuberculosis* are either ineffective or unavailable. The traditional immunisation arsenal includes vaccines that use live attenuated or inactivated organisms. From an immunological standpoint, live attenuated vaccines still represent the vaccines of choice.

Methicillin resistant *Staph.aureus* (MRSA) has long been recognized as a human pathogen causing a variety of disease syndromes. However, community acquired MRSA (CA-MRSA) prevalence has been increasing over the past decade. These organisms have the commonest genotype, USA 300 & are distinct from hospital acquired MRSA. CA-MRSA frequently causes skin & soft tissue infections & produces Panton-Valentine Lenkocidin fusion protein. The recognition of such organisms may prevent treatment failures & lower morbidity.

An attempt has been made in this supplement to highlight some of the important emerging infections. The readers shall appreciate the endeavor of every author by its quality besides these being thought provoking to us. I am hopeful that topics like drug resistance in typhoid reviewed by Dr. Reena Raveendran, CA-MRSA by Dr Neeraj Goel, emerging & re-emerging parasitic infections by Dr K. J. Prasad, significance of Candida (non-albicans) by Dr. J. K. Oberoi and XDR Tuberculosis by Dr. B. L. Sherwal and his team shall be an interesting reading.

As the Organ Transplants have gained momentum in our country it is important for us to understand its outfalls (collateral damage) by way of immunosuppressive therapy. Opportunistic pathogens play a

dominant role in the immediate as well as delayed onset infections affecting morbidity and mortality of the transplant patients. Distinguished authors with a long-standing reputation in this field Dr. V. Kher & Dr Shyam B Bansal have done full justice to the topic.

As we know every season we are visited by quite a few viral illnesses like, dengue, chikungunya, swine flue, SARS etc. and Dr. Lalit Dar has aptly driven the point home brought the fact home who is passionately pursuing the human viruses.

Emergence of carbapenemase producing multi-drug resistant gram negatives organisms are causing most infections in most of the tertiary care ICU and are the cause of treatment failures. Multiple antibiotic hydrolyzing enzymes are produced by a variety of organisms, predominantly GNB, have been reviewed with their clinical implications by me & my colleague Dr. S. Datta. Emergence of such rouge bugs urges us to be more discrete in usage of antibiotics since none are in pipeline.

Since India does have a reasonable burden of HIV its outfall of therapy by way of immune reconstitution Syndrome would be worth understanding & Dr. Sarman Singh has done full justice to the topic. Rarer presentations can be appreciated in the images section provided by Dr. Kamalender Singh & case report by Dr. Atul Gogia & others. For the readers delight some of the interesting case studies have been included in this supplement provided by Dr Camilla Rodrigues and her team who are pursuing Clinical Microbiology & infectious diseases in our country with passion.

However, it has been a pleasure as well as a learning experience to be associated with this special issue of JIMSA as its Guest Editor. Guest Editor once again wish to thank Dr. P. D. Gulati for giving me a chance. My sincere thanks are due to all the contributors especially Dr. Neeraj Goel who very readily agreed to my request and have put in lot of efforts in helping me produce this issue in time.

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