

Challenges in Tropical Infections

— Nandini Chatterjee

MD, FRCP (Glasgow), FICP
Professor, Department of Medicine,
IPGME&R and SSKM Hospital, Kolkata 700020 and
Hony Editor, JIMA

The Indian subcontinent represents one of the largest tropical and subtropical regions, which is the seat of multifarious infections causing acute febrile illnesses. Nearly 15 million people die every year because of tropical infections and parasitic diseases. The predisposing factors are many – notably, hot & humid climate with less seasonal variation in temperatures, higher rainfall, Poor living condition, higher population with limited resources and greater coverage of land by vegetation.

It could be expected that with the advancement of medical science, the infectious diseases would have taken a back seat by now. However contrary to popular belief, tropical infections continue to thrive and physicians are facing many new challenges with the passage of time.

Changing epidemiology :

The new challenge facing humanity is the spread of tropical infections to temperate zones.

This is the resultant from increasing migration, international air travel, tourism and work visits to the tropical regions from the West. As a result, Chikungunya Virus (CHIKV) cases that have been reported in Italy and France throughout the past years while ZIKA virus infections are being diagnosed in the United states.

Moreover, urbanization and deforestation coupled with climatic alterations have an impact by influencing the geographical and temporal distribution of arthropods and/or reservoir hosts. This affects the transmission chains and leads to the emergence of new epidemics in non endemic zones.

Increase in ambient temperature and prolongation of monsoon months lead to survival of mosquito vectors for a longer period in hilly regions that used to have extreme climates in the past.

Changing Clinical spectrum :

The clinical presentation of most infections are undergoing a sea change. Atypical manifestations are being seen in common acute febrile illnesses like malaria, dengue, scrub typhus, leptospirosis and enteric fevers. More asymptomatic and subclinical infections are having an enhancing effect on transmission dynamics .

Common trends indicate an increase in severe disease manifestations like Expanded Dengue Syndromes (EDS), complicated Vivax malaria infection, AES due to Scrub typhus, JE and enteric fever as well as fulminant Hepatic Failure in Leptospirosis and Hepatitis A & E.

The changes in clinical profile are being attributed to genetic changes in the organisms or the presence of non-neutralizing antibodies that cross react and lead to Antibody Dependant immune Enhancements (ADE)

Coinfections :

Also baffling the physicians are overlapping and nonspecific symptoms in different infections as well as Mixed Infections or Coinfections.

In India, certain geographic regions witness simultaneous outbreaks of two or more diseases like scrub typhus, dengue fever, malaria, leptospirosis and chikungunya during monsoon and post-monsoon period.

In published literature various permutation and combination of infections have been reported.

The most common coinfection found are scrub typhus and dengue, Scrub typhus and leptospirosis, Dengue and chikungunya .Even simultaneous Scrub typhus, dengue and vivax malaria together were detected in some series. Malaria- dengue – chikungunya combinations are also common.

Himachal Pradesh, Uttarakhand, Central India, Puducherry have all documented serious mixed infections.

Mixed infections are responsible for diagnostic conundrums with prolonged disease courses and increased morbidity.

Diagnostic challenges :

Acute undifferentiated fevers pose great dilemmas for physicians because of the non-specific similar and overlapping symptomatology in various infections.

A greater problem is the short window of detection after clinical symptom onset due to the short viremic phase in case of arboviruses. So antigen detection assays by ELISA, though a definitive test, has time constraints.

Serology is the next tool at our disposal but serology-based differential diagnosis is complicated by cross reactivity by other organisms (scrub typhus, dengue and salmonella) or by previous infections of separate strains eg, dengue virus

In endemic zones, high baseline titres are also a deterrent to accurate diagnosis as in enteric fever.

Apart from the diagnostic challenge, patterns of cross-reactivity are also important because cross-reactive pre-existing heterotypic arbovirus antibodies of a previous infection can lead to an enhanced immune reaction via Antibody Dependent Enhancement (ADE), as seen between different DENV serotypes. This was recently demonstrated in the Zika virus epidemic demonstrating elevated risk of DENV severe disease by either a prior ZIKV or DENV infection or both.

Thus the desirable diagnostic modalities are culture of the organism or Genome detection by PCR technology. The differentiation of cross reactivity and serological dual positivity requires molecular diagnostic tests. But in low resource countries like ours there is scarcity and poor accessibility of sophisticated facilities.

Culture of organisms also suffers from limitations, as it is time consuming, yield is often unsatisfactory and affected by prior empirical therapy, which is rampant in the Indian subcontinent.

Therapeutic challenges :

The therapy of tropical infections too have many impediments.

Firstly arboviral infections rely on supportive therapy as there are no specific drugs for them.

Moreover, for other infections development of drug Resistance is a scourge with far reaching consequences.

Many factors have contributed to that, the foremost of which is empirical therapy. In rural or under developed set ups sometimes empiric therapy is inevitable but there should be some guideline or algorithm for empiric therapy.

Other reasons for resistance are use of improper dosing, under or overuse of drugs and over the counter purchase of Medicine and their application.

Preventive Challenges :

The basic and most important intervention in preventing infectious diseases is to improve the quality of water, sanitation and hygiene (WASH). Unfortunately handwashing facilities are available to 87.5 per cent of our population. Population density and overcrowding are the main hurdles in ensuring adequate sanitation .

Availability of vaccines is another major issue .Most of the infections either do not have vaccines or the vaccines are not up to the mark in efficacy and safety.

Large field efficacy trials are the need of the hour but cost and logistic difficulties need to be surmounted. Vaccination also entails availability of storage and cold chain space, workforce allotment, training of frontline health workers.

Thus it is evident that tropical infections have multifaceted problems and tackling them requires meticulous clinical, infrastructural and therapeutic strategies. We need to develop disease burden extrapolation models through surveillance data to choose the sites that need to be prioritized for routine intervention and this requires long-term financial and administrative commitments.

In this issue we are publishing a case report of a patient presenting with icterus who was diagnosed to have a co infection of Dengue and Leptospirosis. The co infection led to the prolongation of the illness with enhanced severity. Also this case emphasizes the fact that exclusion of all the possibilities by testing is necessary as there is an overlap of signs and symptoms in tropical diseases.

Coinfections are a significant public health issue in tropical countries. These scenarios need to be reported more often and studies should be designed for evaluation of clinical atypia and patient outcomes and also to explore the extent of cross reactivity between various pathogens in tropical regions.

FURTHER READINGS

- Yeolekar ME— Tropical infections: Clinical implications. *J Assoc Physicians India* 2018; **66**: 68-9.
- Shelke YP, Deotale VS, Maraskolhe DL — Spectrum of infections in acute febrile illness in central India. *Indian J Med Microbiol* 2017; **35**: 480-4.
- Morch K, Manoharan A, Chandy S, Chacko N, Alvarez-Uria G, Patil S, *et al*— Acute undifferentiated fever in India: a multicentre study of aetiology and diagnostic accuracy. *BMC Infect Dis* 2017; **17**: 665.
- Salam M, Mustafa S, Hafiz A, Chaudhary AA, Deebea F, Parveen S — Global prevalence and distribution of coinfection of malaria, dengue and chikungunya : a systematic review. *BMC Public Health* 2018; **18**: 710.
- Raina S, Raina RK, Agarwala N, Raina SK, Sharma R — Coinfections as an aetiology of acute undifferentiated febrile illness among adult patients in the Sub Himalayan region of North India. *J Vector Borne Dis* 2018; **55**:130-6.
- Ahmed S, Dhar M, Mittal G, Bhat NK, Shirazi N, Kalra V, *et al* — A comparative hospital based observational study of mono and coinfections of malaria, dengue virus and scrub typhus causing acute undifferentiated fever. *Eur J Clin Microbiol Infect Dis* 2016; **35**: 705 11.
- Basheer A, Iqbal N, Mookkappan S, Anitha P, Nair S, Kanungo R, Kandasamy R — Clinical and laboratory characteristics of dengue-orientia tsutsugamushi co-infection from a tertiary care center in south india. *Mediterr J Hematol Infect Dis* 2016; **8**: e2016028
- Borkakoty B, Jakharia A, Biswas D, Mahanta J — Co-infection of scrub typhus and leptospirosis in patients with pyrexia of unknown origin in Longding district of Arunachal Pradesh in 2013. *Indian J Med Microbiol* 2016; **34**: 88-91.
- Sivamani K, Dhir V, Singh S, Sharma A— Diagnostic dilemma— dengue or Japanese encephalitis? *Neurol India* 2017; **65**:105-7.
- Gupta N, Chaudhry R, Mirdha B, Das B, Dar L, Kabra S, *etal*. Scrub Typhus and Leptospirosis: The fallacy of Diagnosing with IgM Enzyme Linked Immunosorbant Assay. *J Microb Biochem Technol* 2016; **8**.