Perspective

# MITE AND TICK-BORNE DISEASES IN INDIA: CHALLENGES AND THE WAY FORWARD

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The tick and mite-borne diseases, notwithstanding their colossal impact on human lives, are yet to stimulate the scientific temperament in India. The last decade has witnessed the emergence of mite-borne scrub typhus and a plethora of tick-borne diseases like Crimean-Congo Haemorrhagic Fever (CCHF), Kyasanur Forest Disease (KFD), tick typhus, Lyme disease etc. It is,

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therefore, arguably surprising that the intelligentsia, still, is reticent to accept their ubiquitous presence in the country. This stark fact is clearly evidenced from the meagre research directed towards this emerging field, which as on date, majorly focuses on outbreak investigations, case reports or some hospital-based studies. The Indian studies available on public domain manifestly depict the wide prevalence of the various tick and mite-borne diseases pan India. The situation indubitably demands an urgent attention and need for initiating dedicated research in this emerging field of medical Arthropodology to curb avertable morbidity and mortality due to the ever-increasing burden of tick and mite-borne diseases globally as well as in the subcontinent.

Scrub typhus caused by an intercellular bacterium, *Orientia tsutsugamushi* (formerly *Rickettsia*) and transmitted to humans by arthropod vectors of *Leptotrombidium* spp. whereas the trombiculid mites *of* other genera such as, e.g., *Euschoengastia*, *Neotrombicula*, *Schoengastia*, and *Schoengastiella* have undoubtedly established their presence in all states of India.[1] Globally, over one billion people are at risk for scrub typhus and an estimated one million cases occur annually with ever increasing incidence[2,3], but surprisingly the Indian data is still woefully wanting in terms of acknowledging the burden of the disease. Scrub typhus, irrespective of its endemicity, constitutes an important cause of pyrexia of unknown origin (PUO) and has rapidly re-emerged to become the major cause of Acute Febrile Illness (AFI) in many parts of the country, and necessitates its inclusion in the list of differential diagnosis in endemic areas.[4] The transmission of scrub typhus is majorly witnessed in the monsoon and post-monsoon seasons in most parts of India but evidence of its perennial transmission is forthcoming and needs validation in all settings. Both trans-stadial and trans-ovarian modes of transmission are known to occur, but there is an acute paucity of evidence on its transmissibility through generations. Absence of an eschar in most of the cases coupled with non-specific symptoms like fever, rash, headache and malaise contributes to its misdiagnosis.[5] Till date, scrub typhus continues to challenge us with newer manifestations of the disease, with its varied impact on the central nervous system, cardiovascular system, renal, respiratory, and gastrointestinal systems with serious complications in the form of myocarditis, pneumonia, meningoencephalitis, acute renal failure, gastrointestinal bleeding, and even acute

respiratory distress syndrome in certain cases, which are not the usual symptoms of the disease.[6,7] Stupendous advancements have enriched the field of diagnostics; yet, it is appalling that even Weil Felix test availability is wanting at most point of care facility. Effective treatment with tetracycline or chloramphenicol remains the mainstay of therapy[7], but challenges to implement chemoprophylaxis globally amongst at risk-groups like armed forces personnel during extended duration of exercise or postings in insurgent areas are a daunting task for a nation. There is a need to develop newer methods of drug delivery for such vulnerable populations to enhance not only the ease of delivery but also compliance. There is pressing priority for continued research in field of disease pathogenesis, transmission dynamics, molecular & immunological markers, novel diagnostic tools, improved therapeutic regimen and effective vaccine to combat the increasing burden of scrub typhus.[8]

Crimean-Congo haemorrhagic fever (CCHF) is the most widespread, emerging tick-borne viral disease affecting humans. The first documented outbreak reported in India was in Ahmedabad, Gujarat in 2011 and, thereafter, outbreaks were reported from other states of the country as well, viz., Rajasthan and Uttar Pradesh.[9] Although, the cases are restricted to few states only, presence of neutralizing antibodies has been nonetheless detected throughout India in sero-surveillance studies.[10] Ixodid (hard) ticks, especially those of the genus, Hyalomma, are known as reservoirs and vectors of CCHF, however, the role of other possible vectors needs exploration. A sero-survey in endemic state of Gujarat to map high risk areas and populations reported a low CCHF seropositivity as against other endemic regions of the world, suggesting a meagre human-to-human transmission rate, explains requirement of further studies into transmission dynamics.[9] High risk groups who acquire infections include abattoir workers, farmers, veterinarians, and healthcare workers; these vulnerable groups need to be targeted on priority for dissemination of preventive strategies and effective implementation of the same. The biggest challenge in tackling CCHF, as on date, is lack of an active surveillance system, which, if established, would indicate the prevalence of CCHF in India. As the anticipation of the viral illness landing in an OPD of a hospital is less, controlling infection in hospital setting is itself challenging. Further, the clinical picture of the illness varies and mimics other viral illnesses, which impacts timely case management. Environmental and climate change along with vector bionomics may be the factors behind emergence of this zoonotic disease in many countries. The time to act is now since there is no specific treatment or vaccine

available as on date. CCHF being a zoonotic disease, the concept of 'One Health' is critical to prevention and management of the disease through a multi-sectoral approach involving medical, veterinary and arthropodology associated field interventions. There is a need to map out the prevalence of the vector Hyalomma ticks, to identify hot-spots in the country to plan preventive strategy against possible outbreaks. Though studies have shown certain clinical and laboratory parameters which may provide a clue to early suspicion of CCHF in endemic areas, nevertheless, further studies are needed to identify specific early markers of the viral illness.[11] It is highly recommended to develop effective anti-viral medication and vaccine to contain this disease with high mortality rate.

KFD or Monkey Fever is a viral haemorrhagic fever caused by a virus of family *Flaviviridae* which is endemic to South-western part of India mainly to five districts of Karnataka. It is transmitted to humans through the bite of infected hard ticks (*Haemaphysalis spinigera*) which act as a reservoir of KFDV.[12] For close to seven decades, this disease was restricted in its distribution but in recent times it has spread to adjacent states of Kerala, Goa, Maharashtra, Gujarat and Tamil Nadu. The evolution and geographical spread of the KFD virus through genome sequencing has been reported in Indian settings, however, information on ecological changes and biological factors driving this virus to newer geographical areas still remain elusive.[13] The challenges in KFD disease lie in the absence of an effective surveillance mechanism for the disease as is true for the other tick and mite-borne diseases. KFD is moving to newer pastures and our ability to tackle the increasing burden of the disease is abysmally limited. Even with the availability of an effective vaccine, we have not been able to control the spread of the disease. Systematic efforts are needed to improve the vaccination coverage of KFD vaccine as well as sensitization of environment for vaccine acceptance.[14] Knowledge gap exists in the KFD disease epidemiology and natural cycle of the disease which mandates further insight into the sylvatic cycle of the disease as well as on the effect of ecological and biological factors in transmission. Improved surveillance measures and vaccination strategies will help in curbing the spread of the disease and prepare us for the future.

The other tick-borne diseases, viz., tick typhus and Lyme disease (vectored by *Rhipicephalus sanguineus* and *Ixodes* spp., and caused by *Rickettsia conorii and Borrelia burgdorferi,* respectively) also suffer from similar challenges in terms of information on prevalence, vector range, epidemiology, transmission dynamics,

impact of climate and other variables on distribution, pathogenic diversity and surveillance. Patients suffering from Lyme disease show multisystem involvement and have reported with various typical and atypical presentations leading to difficulty in ascertaining disease burden.[15-17] Indian tick typhus is an important cause of PUO however, suffers from underestimation due to nonspecific signs & symptoms and lack of adequate diagnostic tool and capacity.[18] Lyme disease and tick typhus are increasingly being reported from many Indian states,[15-20] however, the awareness amongst clinicians, public health workers or acarologists is dismal. In view of above information, it is only opportune that these two diseases are recognized as diseases of public health concern to avert the debilitation due to Lyme disease or morbidity and mortality due to tick typhus.

It is, thus, the need of the hour to undertake in depth field epidemiological studies to better understand the natural history of the disease. This will facilitate development of adequate epidemiological and laboratory capacity to prevent outbreaks and address the rapidly increasing disease burden. The sensitization of clinicians to include these diseases in the list of differential diagnosis for PUO and AFI is vital. Data driven and evidence-based management strategies will go a long way in drafting policies against these emerging groups of mite and tick borne diseases.

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