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Scrub Typhus in India: A Critical Commentary

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A B S T R A C T

Scrub typhus in India, although, dates back to World War II, was nearly forgotten barring occasional reporting of outbreaks from the Indian Armed Forces, which kept the interest alive in the disease. Scrub typhus at that time was considered a formidable foe. It was credited with inflicting heavy casualties amongst troops in the China-Burma-India operational corridor, which forced the commanders to withdraw troops from these areas. This tended to alter the course of the war itself. An old foe indeed; scrub typhus continues to take a heavy toll on the vulnerable Armed Forces personnel who are posted in areas that enhance their vulnerability to the disease and has predictably also impacted the unsuspecting civil population too who are residing in such areas. Scrub typhus has undoubtedly emerged as a major public health challenge in India. Slow, yet steady, appreciation of the impact of scrub typhus though is being felt, however, professional efforts are still dismal and have failed to bring the disease to limelight and contain its insistent march. Scrub typhus, although an old foe, has reemerged albeit with new challenges.

Keywords: Scrub Typhus, Public Health Challenge, Armed Forces

Introduction

Scrub typhus, a disease vectored by trombiculid mites of the genus *Leptotrombidium* and caused by *Orientia tsutsugamushi* has taken India by surprise in the last decade. It has slowly yet steadily increased its area of activity to include all states of India in addition to four Union Territories (Delhi, Puducherry, Chandigarh, Jammu) which are increasingly reporting its activity with each passing year.[1] The innumerable outbreaks of scrub typhus in India,[2-11] although perplexing, have nonetheless, contributed notably to a better understanding of the complex dynamics of scrub typhus. An interesting facet which has emerged from these reported outbreaks is not only the newer areas reporting rickettsial activity but also the occurrence of the disease in seasons, thus far, not known for vector or rickettsial activity viz. cooler months,[12] which challenges the conventional knowledge of the disease being associated with the post-monsoon period as well as its phenomenal presence in varied terrains especially western India.[13] The dynamic human behavior along with the changing environment and their interplay have led to the re-emergence of scrub typhus globally. Their profound impact on the outcome of military operations has been well documented; however, the frequent occurrence of outbreaks in the civil populations is of immense concern and demands due attention. It is thus pertinent that public health professionals viz. the medical fraternity and the specialists' like entomologists and the epidemiologists are sensitized about the enhanced activity of scrub typhus pan India to ensure capacity building and formulation and implementation of strategies to prevent and/or reduce adverse outcomes of scrub typhus and associated morbidity.

Challenges Impacting Scrub Typhus Re-emergence

The non-specific clinical presentation of scrub typhus i.e.

fever with headache and myalgia adversely impacts the diagnosis of scrub typhus in Indian settings. A systematic review reports that about 66% of scrub typhus cases are likely to be under-diagnosed based on the 'clinical judgment' approach (Laboratory tests based on a high index of suspicion) versus 'complete approach' (Laboratory tests irrespective of the clinical picture).[14] The myriad clinical spectrum with a plethora of serious complications arising in untreated patients ranging from Acute Respiratory Distress Syndrome (ARDS), pneumonitis, shock, hepatitis, acute kidney injury, renal failure, myocarditis, Acute Encephalitis Syndrome (AES), meningoencephalitis, and Multi-Organ Dysfunction Syndrome (MODS) make it a clinicians nightmare and is held mostly responsible for the associated fatality. The treatment guidelines although have been formulated,[15] however, it is important is to have a high index of suspicion based on the history of exposure and endemicity to initiate early and prompt treatment of the cases. The effectiveness of doxycycline in the treatment of scrub typhus is a well-established fact and is advocated as a 'challenge test' i.e. if there is no response within 48h, it can be safely presumed to have some other etiology. To date, there is no report of resistance of *O tsutsugamushi* to doxycycline from India and the same has been rendered unlikely in a recent study investigating the development of resistance to doxycycline.[16,17]

There is a need to map *Orientia tsutsugamushi* antigenic variability in India, to study the association of strains, their differential virulence and the clinical presentation. This vital information will help strategize preventive/containment measures and treatment protocols in areas with virulent circulating strains and in turn ensure reduction in morbidity and mortality in such hot spots. As on date, very limited studies have been undertaken to study the antigenic distribution in our country,[18-22] more studies are required for the preparation of an antigenic map of *O tsutsugamushi* for India. The reports indicate the variable distribution of *O tsutsugamushi* strains in the country but the recent studies demonstrate the predominance of Karp like strains followed by Gilliam like strains in India along with reports of the presence of other strains as well.

The acute paucity or unavailability of diagnostic kits in laboratories and treating facilities limits its reporting and favors delayed treatment which in turn leads to higher morbidity and mortality. The reliance on Weil Felix test for diagnosing scrub typhus needs revisiting; it has been well documented that it has low sensitivity and is reported to yield up to 50% false negatives, however, if positive, the test is considered to be highly specific.[23,24] Immunofluorescence Assay (IFA) is considered to be the gold standard, however, the facilities to undertake the test in most laboratory settings is wanting. To prevent morbidity and mortality due to scrub typhus, it is pertinent that ELISA test kits for scrub typhus, which are the reliable point of care diagnostic kit[25] as well as the facility of PCR for accurate diagnosis of the disease may be made available in all hospital setups and point of care facilities. It is important that the availability of ELISA scrub typhus diagnostic kits even in remote areas with reports of scrub typhus activity should be prioritized to ensure timely diagnosis and treatment. Needless to emphasize that its time India takes a step forward and invests in developing indigenous diagnostic kits to make it affordable and accessible to reduce the burden of the disease.

Figure 1.Distribution of Orientia species outside the 'Tsustugamushi triangle'

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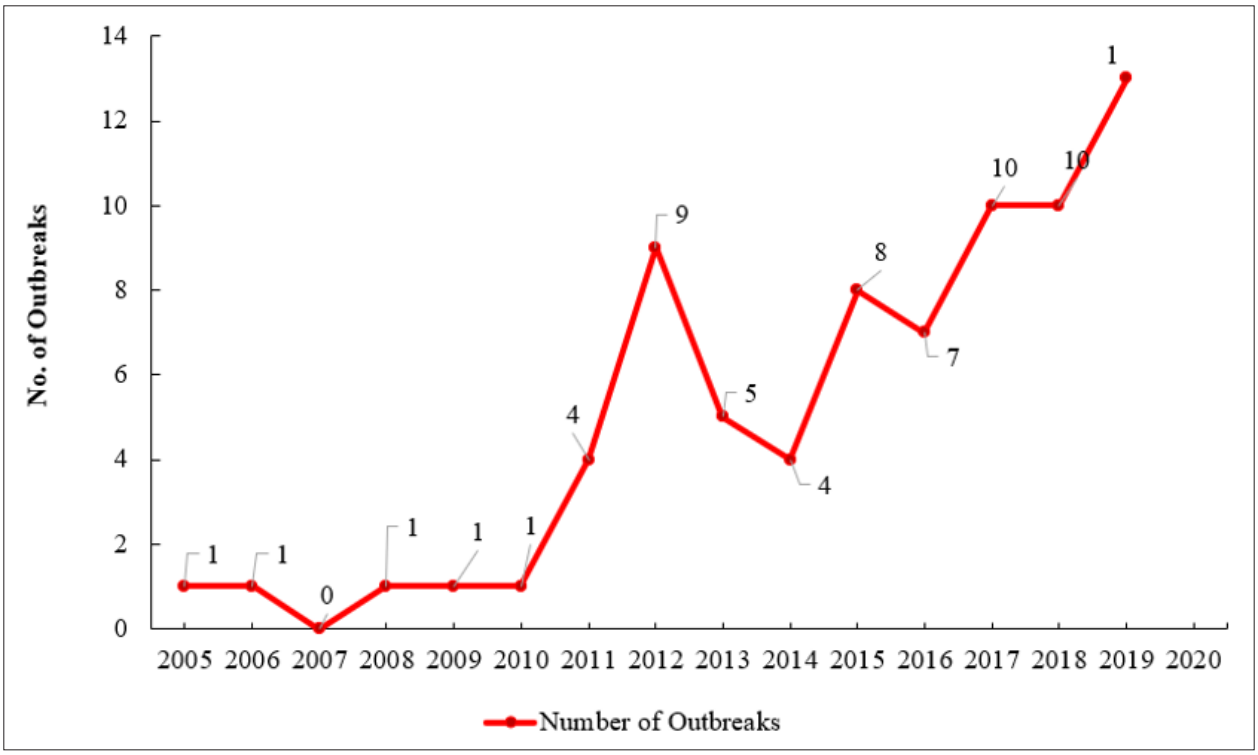
Indian literature, though has been enriched with significant contributions made to vector database,[26-28] still we have a long way to go. *Leptotrombidium deliense* has been reported as the most dominant vector in India in addition to the report of a new vector viz. *Schoengastiella ligula*.[29] With more impetus on research in this area, we await the discovery of more vectors. The published studies reporting entomological data do make a mention about the animal hosts, but there is a need to invest more effort in studying the broader host range in the light of information on the presence of *O tsutsugamushi* in hosts other than trombiculid mites.[30] Equally important is the need for investigation of *O tsutsugamushi* presence in various chigger species and their affinity for humans to assess their risks to human health.

The presence of newly identified *Orientia* species - *Candidatus Orientia chuto* & others[31-35] from areas outside the tsutsugamushi triangle (a triangular area of scrub typhus activity in the Asia Pacific with Russia in the far east, Afghanistan in the west and Australia in the south) viz. Africa and South America call for a concerted focused approach to understand the changing paradigms of scrub typhus transmission leading to its reemergence globally (Figure 1). Undoubtedly, there is a need to devote more resources, inclination, and research into unearthing the many still elusive facets of the epidemiology of scrub typhus in India which has enormous diversity in terms of terrain, geographical attributes, climatic conditions and human vulnerability (occupation, housing conditions, socio-demographic attributes), which enhances the chances of increased exposure.

The need to have trained technicians and skilled professionals cannot be overlooked at this stage when the disease is poised to re-emerge with ensuing heavy morbidity and mortality. Due investment is necessary for this area by identification of Institutes which can take a lead in training personnel in various aspects of the disease ranging from epidemiology, vector and host studies to diagnostic techniques. It is also essential to grant due importance to the disease in the medical curriculum at the graduate as well as postgraduate level with due focus on the training of para medicals as well. Similarly, the curriculum of MSc (Entomology) may also be suitably modified to include the disease and more Ph.D. Entomology students should be encouraged to undertake research in this field. Field training/Hands-on training for In-service professionals should also be encouraged under the aegis of WHO and other competent national professional bodies. The Armed Forces Medical College, Pune India has been a pioneer in organizing specialized field training courses for Public Health specialists as well as para medicals with in-house support and support from WHO, India.



Note: Source – Integrated Disease Surveillance Programme (IDSP)

Figure 2.Reported outbreaks of Scrub Typhus in I ndia (till 03rd week of 2020) by IDSP

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Surveillance of scrub typhus in Indian settings is unheard of barring the Indian Armed Forces which too has very minimalistic surveillance in place. Although the Integrated Disease Surveillance Programme (IDSP) has included scrub typhus outbreaks in its reports (Figure 2), yet the importance to the disease has not been forthcoming from public health professionals, physicians, microbiologists or the entomologists who are hesitant in researching as it is very labour and time-intensive. One encouraging trend, though, which has emerged in recent times is the steady increase in the number of publications on the subject thus establishing the growing interest of professionals albeit a bit late.[36]

The importance of personal protective measures in the prevention of scrub typhus needs advocacy. It is important to disseminate information to the affected communities through concerted efforts of Government agencies and NGOs to reduce the burden of the disease especially when no vaccine is available.

The concept of forming outbreak response teams and its role in swift containment of outbreaks needs deliberation. There is a need to reintroduce the "typhus team" concept in India to combat the growing menace of scrub typhus. The organization and level of functioning may be elaborated if the concept appeals to the stakeholders.

The Way Forward

Its time, the younger generation of scientists, clinicians and the microbiologists take a lead to address the gaps in diagnosis, management, transmission and prevention of scrub typhus in India. There is also a need to have information disseminated through Government resources as done for malaria and dengue.

A private-public partnership can go a long way in achieving the aforesaid targets as well as the development of vaccine against scrub typhus. To achieve this goal a strong and committed political will is essential, which appears grossly apathetic to the morbidity and mortality caused by the disease. It is unfortunate that scrub typhus is majorly deglamorized to malaria, dengue or other vector-borne diseases prevalent in India. The country probably awaits the spiraling of the problem to a dead-end before some considered thought is thrown it's way by the concerned stakeholders.

Key Areas of Future Research in the Field of Scrub Typhus in India

- Preparation of O *tsutsugamushi* antigenic map of India
- Development of Indian diagnostic kit for scrub typhus
- Clinical profiling of scrub typhus vis-à-vis O *tsutsugamushi* strain
- Search for newer hosts with an important role in chigger distribution and transmission of disease
- Exploration of newer vector species and preparation of vector database
- Development of indigenous vaccine of scrub typhus
- Identification of key players in the formulation and implementation of Community Outreach Programs for the dissemination of information on key aspects of scrub typhus – a public-private partnership
- Studies on area-specific risk factors and targeted methods of prevention

Conclusion

Scrub typhus, with an estimated one million deaths and one billion people at risk every year worldwide, is indeed an emerging public health challenge. Urgent initiatives are needed to contain its extent and endemicity. It is the need of the hour that sound management strategies be devised and implemented to reduce the impact of the disease in the Indian subcontinent. The Time to act is NOW.

Conflicts of Interest: None

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