

# Scrub typhus: Emerging cause of multiorgan dysfunction

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Scrub Typhus is a zoonotic infectious diseases caused by obligate intracellular gram negative, non-flagellate, and non-spore-forming Cocco-bacilli - the rickettsae *Orientia Tsutsugumoshi*. The disease is contracted via the bite of trombiculid mite larvae (chiggers). The chiggers live in wide range of vegetation type from scrubs (terrain between woods and clearings), primary forests to gardens, beaches etc. The epidemic period is influenced by activities of the infected mite which appear to occur more frequently during or after rainy seasons. This leads to in a spurt in cases during and after monsoon in India. Humans are accidental hosts and seen in people where activities bring them into contact with vector chiggers.<sup>[1]</sup>

Scrub typhus is grossly under-diagnosed in India due to its non specific clinical presentation, limited awareness and low index of suspicion among clinicians and lack of diagnostic facilities.<sup>[2]</sup> Scrub Typhus manifests clinically as a non-specific febrile illness often accompanied by headache, myalgia, nausea, vomiting, diarrhea, cough or breathlessness. Severity varies from subclinical illness to severe illness with multiple organ system involvement which can be serious unless diagnosed early and treated.

Eschar at the site of attachment of the larval mite or chiggers the most characteristic feature of scrub typhus, but it is not seen in all patients. It is a black necrotic lesion resembling a cigarette burn usually found in areas where skin is thin, moist or wrinkled and, where the clothing is tight. Eschar is found in about 50% cases. However, this detection requires careful and diligent search. The common sites involved are axilla, groin and breast. Often

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patients are not aware of the presence of the eschar, as it hardly produces any symptoms of discomfort. Diagnosis is confirmed by a positive IgM ELISA and/or pathognomonic eschar with PCR confirmation where feasible.<sup>[3-5]</sup>

Across the globe, more than one billion people are exposed to the risk of the disease and live in endemic areas. India has an annual incidence of approximately one million cases.<sup>[4]</sup> The disease was first reported in army barracks during World War II in Assam and West Bengal, again during Indo-Pak war in 1965. Data in India is scanty, but interest was renewed with outbreaks in the Sub-Himalayan belt from Jammu to Nagaland and Haryana,<sup>[1,3,5]</sup> and in 2012 from Rajasthan.<sup>[4]</sup> We ourselves were surprised to see large number of Scrub typhus cases during the last 2 yrs in the post monsoon period in Rajasthan with significant morbidity and morbidity from multiorgan failure.<sup>[7]</sup> Since these cases occurred during the same period and with almost indistinguishable clinical presentation from malaria, typhoid, dengue and Leptospirosis, these have been clubbed together as the "tropical fever syndrome". Thrombocytopenia, Pneumonia, Meningitis like syndrome and renal failure have been part of MODS that has been observed in this disease. However, the studies though very small in number have revealed that there are clinical and laboratory features which may help early differential diagnosis of this disease. It is possible that during the

outbreaks of dengue and malaria in India, clinicians might have missed cases of scrub typhus all these years due to low awareness of the infection. However the recent resurgence of this infection in epidemic proportions with confirmed diagnosis has been an eye opener.

In one series published in 2010 MODS was reported in one third of patients (17 out of 50). Hypotension (16%), renal impairment (12%), ARDS (8%) and meningitis (14%) were some of the important complications. They reported dramatic response to doxycycline in nearly all the patients.<sup>[2]</sup>

In a retrospective study of scrub typhus cases, conducted at a university teaching hospital, including 623 patients admitted between 2005 and 2010, most common presenting symptoms were fever (100%), nausea/vomiting (54%), shortness of breath (49%), headache (46%), cough (38%) and altered sensorium (26%). An eschar was present in 43.5% of patients. Common laboratory findings included elevated transaminases (87%), thrombocytopenia (79%) and leukocytosis (46%). MODS was seen in (34%) of patients. The overall case-fatality rate was (9%). Features of acute lung injury were observed in (33.7%) and (29.5%) required ventilator support. Shock requiring vasoactive agents, CNS dysfunction and renal failure were independent predictors of mortality.<sup>[5]</sup>

In this issue, Griffith et al from the same institute<sup>[6]</sup> report on patients of scrub typhus presenting with MODS. Respiratory organ dysfunction predominated and was present in 112 patients (96.6%). Cardiovascular dysfunction was present in 61.7% and renal and hepatic dysfunction in 63.8% of patients. Sixteen patients (15%) had evidence of dysfunction of all six organs during the course of hospitalization. Ventilatory support was required in (87.9%). Despite MODS the survival of 76% was surprisingly good. APACHE-II score and duration of fever were independently associated with mortality.

ISCCM launched its own collection of data through its ISCCM research net from as many ICUs of country as possible. The data was presented in the Annual conference of ISCCM in 2014<sup>[7]</sup> and following observations were made of all cases admitted in ICU with suspected diagnosis of Tropical Fever. Scrub typhus formed >15% of cases. The peak was noted between July and December a total number of 327 cases were entered out of which >25% were paediatric patients. Males were more than females, included both urban and rural population with rural preponderance. Mean age of adults was 36.5 years and in paediatric patients 6.3 years. Mean Apache score

was 18. All scrub typhus patients had presented with fever (75.55%) and respiratory distress (Pneumonia) (33%), significant Thrombocytopenia (26%) Jaundice with or without rise of SGOT and SGPT (22%), variable degree of renal failure (9%), Encephalopathy and Multiorgan failure syndrome (8.88%). Thirty-seven percent of Scrub typhus patients with hypoxemia required mechanical ventilation, 15.55% patients could be supported with non invasive ventilation Mortality was 13.33%. Highest mortality (21%) was noted in malaria followed by scrub typhus. Cases with ARDS and renal failure had higher mortality. Encephalopathy was another independent predictor of mortality.<sup>[7]</sup>

Sporadic complicated scrub typhus has been reported off and on.<sup>[8-11]</sup> Scrub typhus is thus an age old infection now appearing to be in resurgence, Epidemics are observed during the post monsoon season. Its manifestations are indistinguishable from those of other tropical fevers like dengue, malaria, typhoid and Leptospirosis. Diagnosis is made by clinical picture, eschar, Elisa and PCR. It is an important cause of multiorgan failure with 10 to 13% incidence. Severe ARDS, Meningo-encephalitis and Renal failure appear to be independent predictors of mortality.<sup>[5,6,12-15]</sup> However, further epidemiologic studies and data will throw more light on this subject in the coming years.

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