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Original Research Article

A descriptive study to quantify severity in patients with severe scrub typhus in hilly city of Northern India

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ABSTRACT

Background: Himachal Pradesh is an endemic area for scrub typhus. If not treated early, it can lead to life threatening complications. Therefore, more emphasis needs to be laid on the diagnosis and prompt treatment, so that mortality due to severe scrub typhus can be prevented. So, this study was done with an objective to study the clinical profile of patients diagnosed with severe scrub typhus and assess their severity using APACHE II score in IGMC, Shimla.
Methods: Authors conducted a descriptive cross-sectional study in Indira Gandhi Medical College, Shimla over one year (June 2016-May 2017). Out of 538 confirmed scrub typhus cases, 58 severe cases were reported, and their severity was assessed with predefined criteria of sepsis and APACHE II score.
Results: Mean age of males (50.18±18.6 yrs) was found to be more than that of females (45.52±14.5 yrs), the difference being statistically insignificant t(56)= -1.01, (P=0.32). Fever (100%), headache (84.5%), vomiting (79.3%) were the major presenting symptoms and tachycardia (96.5%), hypotension (87.9%), tachypnoea (94.8%) were the main clinical signs. The mean APACHE II score on admission was 16.25±5.0 with a predicted mortality of 23.5%, that was found to be less than actual reported hospital mortality (25.8%).
Conclusions: APACHE II score was found reliable tool for risk stratification**.** Case fatality in diagnosed cases of severe scrub typhus was found high. Early diagnosis and prompt treatment according to guidelines would help in decreasing the mortality, financial burden on patient, society and health system.

Keywords: APACHE II, Mortality, Scrub typhus, Severity

INTRODUCTION

As evident from the reports across the world, the rickettsial infections are re-emerging and their burden is on the rise. Scrub typhus is such a rickettsial zoonotic infection caused by an obligate intracellular parasite orientia tsutsugumashi and transmitted by the bite of the larval trombiculid mite.[1] scrub typhus is endemic to a part of the world known as the "tsutsugamushi triangle" extending from japan and russia in the north, to australia in the south and to Pakistan in the west.[2] it is a major pathogen in the Asia-Pacific region, contributing up to up

to a 23% of all febrile episodes.[3] though once a neglected disease in india as compared to other infections, recent trends indicate that there is a resurgence of infection in Maharashtra, Tamil Nadu, Karnataka, Kerala, Jammu And Kashmir, Uttaranchal, Himachal Pradesh, Rajasthan, Assam and West Bengal.[4-9] In the state of Himachal Pradesh, during monsoons average temperature at lower altitudes is nearly 20 to 35 deg. C, which provides an optimum environment for the vector of scrub typhus to spread.[10] The highly variable nonspecific presentations of this infection pose a mammoth challenge to the physicians in diagnosing it early in the clinical course when the drug therapy is quite effective.[11] with common symptoms such as fever, rash, headache, nausea, vomiting, and thrombocytopenia, it is quite difficult to differentiate it from spectrum of other infections like malaria, chikungunya, dengue, enteric fever, leptospirosis, and brucellosis.[12] Subsequently in due course the life-threatening complications such as pneumonitis, meningoencephalitis, hyperbilirubinemia, renal failure and myocarditis may also develop. The spectrum of infection ranges from mild nonspecific features to multiorgan failure and death.[13] The case fatality rate in untreated cases has been found to be 3% to 60%.[14] In Himachal too the disease causes substantial mortality as indicated by the recent trends and reports.[15]

Due to the lack of licensed vaccines, unreliable diagnostics and poor vector management strategies, more and more cases are turning out to be severe form of infection leading to the poor clinical outcomes. With this background in mind the present study was conducted to capture the severity profile of diagnosed scrub typhus patients in a tertiary care hospital of Himachal Pradesh, India.

METHODS

The study was conducted among the patients of severe scrub typhus admitted at Indira Gandhi Medical College (IGMC), a tertiary care centre in Shimla, Himachal Pradesh. It was a descriptive analytical cross-sectional study that was conducted over a period of one year (June 2016-May 2017). Out of total 538 scrub typhus cases, 58 severe scrub typhus cases were enrolled in the study. IgM scrub positive and those fulfilling the criteria of severe sepsis were categorised as severe scrub typhus cases.

Inclusion criteria

- Who consent to be part of the study
- Age >18 years
- All patients admitted with Severe Scrub typhus (IgM scrub positive) with criteria fulfilling severe sepsis.

Exclusion criteria

- Unconfirmed Cases.

Study tool

The clinical severity of scrub typhus was assessed both by pre-defined severe complications and by the Acute Physiology and Chronic Health Evaluation (APACHE) II score at the time of admission.

APACHE II

APACHE II (Acute Physiology And Chronic Health Evaluation II) is a severity-of-disease classification system, one of several ICU scoring systems. It is applied within 24 hours of admission of a patient to an intensive care unit (ICU): an integer score from 0 to 71 is computed based on several measurements; higher scores correspond to more severe disease and a higher risk of death. APACHE II was designed to measure the severity of disease for adult patients admitted to intensive care units. It has not been validated for use in children or young people aged under 16.[16] The point score is calculated from a patient's age and 12 routine physiological measurements: PaO_2 (depending on FiO_2), Temperature (rectal) , Mean arterial pressure , pH arterial, Heart rate, Respiratory rate, Sodium (serum), Potassium (serum), Creatinine, Haematocrit, White blood cell count, Glasgow Coma Scale. These were measured during the first 24 hours after admission and utilized in addition to information about previous health status (recent surgery, history of severe organ insufficiency, immunocompromised state) and baseline demographics such as age.

Operational definitions[17]

Severe scrub typhus patients are those with IgM scrub typhus positive, clinically SIRS i.e. any ≥2 of following:

- Fever >100.4ºF (38ºC) or hypothermia <36ºC (<98.6ºF)
- Tachypnoea (>24 bpm)
- Tachycardia (>90 bpm)
- Leucocytosis (>12,000/µl), leukopenia (<4000/µl).

With either of following organ dysfunctions

- Cardiovascular (SBP <90 or MAP ≤70)
- Respiratory (PaO2/FiO2 ≤250)
- Haematological (Platelet: <80,000/ µl or 50% dec. over 3 days)
- Renal (UO <0.5ml/kg/hr for 1hr)
- Metabolic acidosis (pH ≤7.30 or base deficit ≥5 mEq/l).

Sepsis is defined as at least two of the following signs and symptoms (SIRS) that are both present and new to the patient and suspicion of new infection

- Hyperthermia >38.3ºC or Hypothermia <36ºC
- Tachycardia >90 bpm

- Leukocytosis (>12,000 µL-1) or Leukopenia (<4,000 µL-1) or >10% bands
- Acutely Altered Mental Status
- Tachypnoea >20/min
- Hyperglycemia (>120 mg/dl) in the absence of diabetes.

Severe sepsis includes SIRS and at least one of the following signs of hypo perfusion or organ dysfunction that is new and not explained by other known aetiology of organ dysfunction

- Cardiovascular: Arterial systolic blood pressure ≤ 90 mm of Hg or mean arterial pressure ≤70 mm of Hg that responds to administration of IV fluids
- Renal: Urine Output <0.5 ml/kg/hr for 1 hr despite adequate fluid resuscitation.
- Respiratory: Pao2/Fio2 ≤250 or, if lung is only dysfunctional organ ≤200.
- Haematological: Platelet count <80000μl or 50% decrease in platelet count from highest value recorded over previous 3 days.
- Unexplained metabolic acidosis: A pH ≤7.30 or a base deficit ≥5.0 mEq/L and plasma lactate level >1.5 times upper limit of reporting lab.
- Hepatic dysfunction as evidenced by Bilirubin>2 or INR >1.5.

Statistical analysis

The data was entered and cleaned in Microsoft Excel spreadsheet. The quantitative variables were presented as mean scores and standard deviations and qualitative variables presented as percentages and proportions. The analysis was done using Epi info version 7.2.4. Student T-test was used to compare mean scores between two groups. Chi-square and Fischer exact test were used to compare the proportions as applicable. Two tailed P value less than 0.05 taken as statistically significant.

Prior ethical approval to conduct the study was taken from institutional ethics committee. Patients were provided with complete information about the study and potential harms to them. No incentive was given to the patient and not out of pocket expenditure was incurred by the patient for the research purpose. All information collected was for research purpose only and individual identifiers were omitted to maintain anonymity and confidentiality.

RESULTS

During the study period, out of total 538 IgM positive scrub typhus patients, only 58 patients who fulfilled the criteria for severe scrub typhus were included in the analysis. The mean age of the patients was found to be 46.8±15.7 years. Of the total participants, majority were (72.4%) females (Table 1 and Figure 1).

Table 1: Demographic Profile: Age (mean years ±SD).

Gender	Age (years)	P value
Males	50.2±18.69	0.32*
Females	45.5±14.55	

*Student's t test; t (56) = -1.01

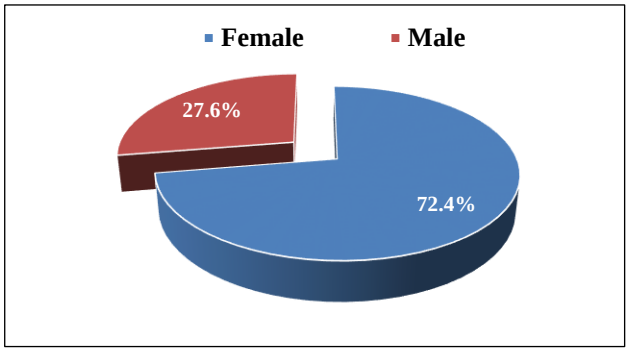

Figure 1: Gender Distribution of study participants.

Nearly one third of the participants were in the age group of 41-50 years (Figure 2). Maximum patients of severe scrub typhus were admitted in the tertiary care hospital in the month of September (40%), followed by august and July (Figure 3). On history, 100% of the patients presented with fever, followed by headache, nausea, myalgia. Only 7% of the patients of severe scrub typhus were in altered sensorium and 3.4% had seizures at the time of admission (Table 2). On clinical examination 96% of the patients had tachycardia, 88% had hypotension, followed by raised temperature (102-degree F). 25.8% severe scrub typhus patients had eschar on examination (Table 2). At the time of admission, sepsis was confirmed in scrub typhus patients by considering the signs and symptoms that fulfil the criteria of definition of severe scrub typhus. (Table 3).

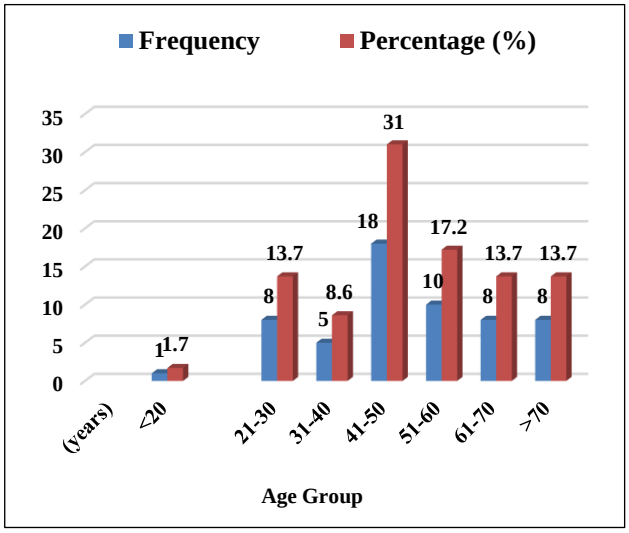

Figure 2: Distribution of the study population by age (N=58).

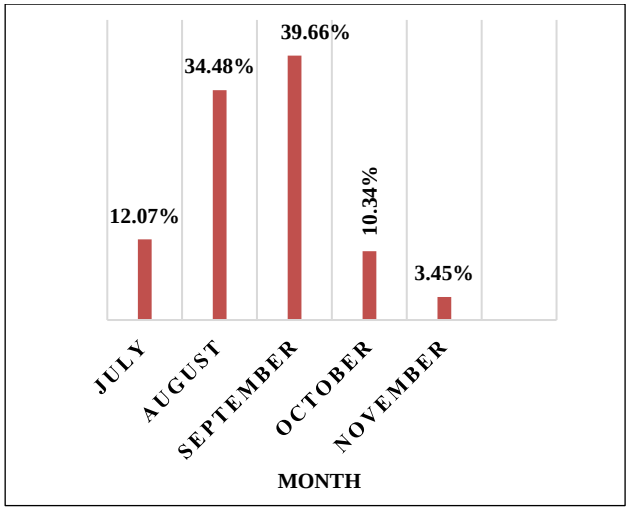

Figure 3: Month wise distribution of cases.

Table 2: Symptoms and signs.

Symptoms and Signs	N (%)
Fever	58 (100)
Headache	49 (84.4)
Vomiting	46 (79.3)
Myalgia	39 (67.2)
Shortness of breath	34 (58.6)
Cough	25 (43.1)
Chills and rigors	20 (34.4)
Loose stool	10 (17.2)
Altered Sensorium	4 (6.9)
Seizure	2 (3.4)
Abdominal Pain	1 (5.5)
Tachycardia (>90/min)	56 (96.5)
Hypotension	51 (87.9)
Temperature (>102F)	44 (75.8)
Pallor	15 (25.8)
Icterus	15 (25.8)
Skin Rash	15 (25.8)
Eschar	15 (25.8)

Table 3: Severe scrub typhus characteristics.

Variables	N (%)
Fever (>100.4 deg. F)	58 (100)
Tachypnea (>24 breaths/min.)	55 (94.83)
Tachycardia (>90 beats/ min.)	56 (96.55)
Leukocytosis (>12,000/µl)	47 (81.03)
Leukopenia (<4000/µl)	1 (1.72)

Clinical severity assessment

To assess the clinical severity of scrub typhus, the mean APACHE II score on admission of 58 patients was calculated as 16.25±5.0, with a predicted mortality of 23.5%. However, the actual reported hospital mortality was found to be 25.8%. This diff. was found to be statistically insignificant (P value-0.931). The parameters used to calculate the clinical severity has been summarised in Table 4.

Table 4: Characteristics to assess APACHE II score.

Variable	Values (mean±SD)
Haemoglobin	11.4±1.84
Temperature	102.5±1.11
PaO2	70.1±12.7
Mean Arterial Pressure (MAP)	65.2±16.47
pH	7.3±0.09
Heart rate (HR)	118.2±9.46
Respiratory rate (RR)	29.7±4.84
S. Sodium levels	138.2±4.63
S. Potassium levels	4.08±0.58
S. Creatinine levels	2.15±1.24
Haematocrit	33.8±5.78
White blood cells (WBC) count	15.4±5.57
Glasgow coma scale (GCS)	14.6±1.53
Admission APACHE II score	16.2±5.0

APACHE II score was found to be <10 in 6 patients of severe scrub typhus. And in 52 patients it was ≥10, indicating increased risk of mortality in these severe scrub typhus cases.

DISCUSSION

The median age was 47.0 (IQ range: 34.25-58.25) in the present study. In contrast Varghese et al reported that median age of scrub typhus patients in the Southern part of India 36.5 (range: 12-75 years).[18] In these findings, 31.03% of patients were in age group of 31-40 years and majority comprised of females (72.4%). This corroborated with study of Sharma et al, where the highest incidence of scrub typhus was reported in the age group of 30-40 years, with higher incidence among females.[19] The higher incidence in females may be attributed to their active participation in the agricultural or horticultural work. Moreover, females tend to work with bare hands usually in the fields or cutting grass. Therefore, they were more likely to be exposed to infected mites which inhabit the soil and scrub vegetation. Most of the cases were reported in the month of September 23 (39.66%). Sharma N et al, also reported that most of the cases presented in September (31%) followed by October (26%) and August (24%).[20] Fever was present in all (100%), headache in 84.48%, vomiting in 79.31%, and seizures in 3.45% of the patients. Almost similar findings were reported by study done Tsay et al.[21] Nearly 7% patients presented with altered sensorium, with GCS <15 in 6.8% at time of admission, compared to study by Griffith et al where altered mental status (GCS <15) was observed in 30% at admission.[22] About 46.5% had low Hb, leucocytosis in 77.58%, leukopenia in 5.17% and thrombocytopenia in 93.1%. Vikrant et al, in their study found leucocytosis in 44.3% and thrombocytopenia in 61.5% patients.[23] Mean APACHE II score was found to be 16.25±5.0 with predicted mortality of 23.5%.

Whereas actual reported hospital mortality was found 25.8%. Griffith et al, found mean APACHE II score on admission as 23.2 (8.3) with predicted mortality of 46%.[22]

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Ethical approval: The study was approved by the Institutional Ethics Committee

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