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Scrub Typhus: One of the Common & Neglected Causes of Bilateral Pneumonitis in Central India.

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Abstract
Background: *Scrub typhus, a bacterial disease caused by Orientia tsutsugamushi, that cause systemic vasculitis thus leads to multiorgan dysfunction syndrome (MODS) and significant mortality. This study was conducted to assess the clinical and laboratory profile and complications in typhus patients.*
Methods: *We conducted this observational study on 16 scrub typhus positive patients who presented to the Department of Medicine at N.S.C.B Medical college, Jabalpur between n August, 2019 and October, 2019.*
Results: *Females: males ratio-- 4.3:1(81.2% vs. 18.75%). Mean age of patients was 34.1±13 years; mean duration of illness before admission was 9.33±6 days. Agricultural laborers comprised 75.0% of patient population. Most common presenting symptoms were fever (100%), cough & shortness of breath (94%), headache (75%), skin rashes(27%), bleeding manifestation (20%) and eschar in (6.67%) patients. Common laboratory findings included Haemoglobin--09.35±2, WBC count--12.48±10, platelet count—1.37±1, AST--199±135 IU/L, ALT--195±165 IU/L, Bilirubin(mg/dl)--2.42±2, serum albumin(g/dl)--3.2±0, serum creatinine(mg/dl)—1.87±0.9, blood urea(mg/dl)—83.20±41. Most common complication included pneumonia (94%), hepatitis (81.2%), Shock (68%), renal failure(54%) and Bleeding manifestation(20%) in such patients. No case mortality reported.*
Conclusions: *Patients presenting after 7 days of onset of constitutional symptoms developed more complication. Thus early diagnosis and treatment prevent the severe complication and mortality.*

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I. Introduction

Scrub typhus is a infectious disease which is caused by mite Orientia tsutsugamushi. It is characterized by the endothelial inflammation which lead to generalized vasculitis, thus it can affect any organ of the body[(1,2)]. In its initial stage has non specific clinical manifestation like fever, chills, headache and myalgia. So early diagnosis and management can prevent the development of various complication like interstitial pneumonia, renal failure, bleeding and multi organ failure[(3-6)]. Recent studies on scrub typhus have reported many abnormal laboratory finding[(2,7)]. However, there has been a few studies on the atypical presentation and indicator of the severity of the disease. By assessing such indicator and atypical presentation[(8)] , proper care can be given to patients who are prone for the life threatening severe disease. Thus this study was done to identify the various presentation of the disease.

II. Methods

We conducted the observational study in the Department of Medicine N.S.C.B Medical College Jabalpur, between August 2019 to October 2019.

Patients aged ≥ 14 years who presented with complaint of fever, cough, SOB were admitted in medicine ward. After taking proper history and thorough examination all routine investigation like complete blood count, renal function test, liver function test, Ultrasonography abdomen, X ray chest PA view was done. Throat swab was also send to rule out H1N1-one of the common cause of bilateral pneumonitis. Once H1N1 test came negative. Thus the diagnosis of scrub typhus was confirmed with IgM ELISA titre against O. tsutsugamushi increased four time or more.[(9)]

Severe tsutsugamushi disease was defined if it showed the subsequent conditions: (1) pneumonia that exposed parenchymal lung lesions on chest radiographs and cough or dyspnoea, (2) renal failure that exposed serum creatinine clearance value ≥2 mg/dl [(10)], (3) meningoencephalitis that exhibited altered mental states like confusion, obtundation, stupor, or coma without evident causes like shock or hypoglycemia, or the presence of both severe headaches and neck stiffness, or spinal fluid (CSF) counts of ≥5 leukocytes/mm^3, (4) shock, which is defined by a systolic pressure less than 90 mmHg (or a fall in systolic blood pressure of > 40 mmHg), (5) myocarditis, (6) GI bleeding, or (7) death.

In addition, scrub typhus-like diseases, including swine flu, endemic typhus, leptospirosis, epidemic viral haemorrhagic fever, and malaria were excluded supported the laboratory tests and clinical features. Signed consent was obtained for every patient before the patients were included within the study.
The collected data were stored using the pc program. Continuous data are expressed as mean ± SD.

III. Result

Patients clinical and laboratory profile and complication are summarized in Table 1-2. Total 16 patients admitted with scrub typhus disease between August 2019 to October 2019. The proportions of females patients were more than males (81.2% vs. 18.75%). The mean age of patients was 34.1±13 years and the mean duration of illness before presentation to the hospital was 9.33±6 days. Agricultural laborers comprised 75% of the total patient population. The most common presenting symptoms were fever (100%), cough (94%), shortness of breath (94%), headache (75%), skin rashes (27%), and bleeding manifestation (20%). An eschar was noted in 6.67% of patients but it was absent in severe cases.

USG Finding included hepatomegaly (34%), pleural effusion (27%), splenomegaly (20%), and ascites (6.6%).

Common laboratory finding include Haemoglobin— 09.35±18, Wbc count— 12.48±10, platelet count—1.37±1, AST-- 199±135 IU/L, ALT--195±165 IU/L, Bilirubin (mg/dl)— 2.42±1, serum albumin (g/dl)— 3.2±0, serum creatinine (mg/dl) — 1.87±0.9, blood urea (mg/dl)—83.20±41.

About a two third patients (66.6%) had evidence of MODS. Complication occurring in scrub typhus patients included respiratory system dysfunction most commonly in 94% patients. AST And ALT ≥ 3 time the upper limit of normal seen in 81.2% patients, Hepatic dysfunction with bilirubin >2 mg/dl was found in 53.3%, Shock was present in 68% of cases, and renal failure with creatinine >2 mg/dl in 54% of the patients.

IV. Discussion

Scrub typhus is a fatal bacterial infection that affects about one million people every year.[10] Mean age of typhus patients in study was 34.1±13 years. This belong to the age group actively involved in occupational activities, putting them to risk of the disease. It is similar to Suman Suryanarayana Karanth et al.[11] and GM Varghese et al.[12] This is different from study done by Kim et al[13], who found that age >60 years was most common in severe case.

Patients presented to hospital with mean duration of illness before admission of 9.33±6 days, which show similarities with G.M. Varghese et al.[12] and Kim et al[13], with symptoms of fever(100%), shortness of breath (94%), cough (94%), headache (75%), skin rashes (27%) etc. About two-third (66.6%) of patients had evidence of MODS , with shock requiring vasoactive agents, and renal failure which reversed on aggressive treatment, which is higher than G.M. Varghese et al.[12] There was no case-fatality in this study which is different from the 9% reported from G.M. Varghese et al.[12] study. This trend may primarily be due to increased awareness and early recognition and treatment of the cases by physician and also due to less number of cases.

In this study, Pulmonary dysfunction was the most common complication (94%), and the majority of these patients require high flow oxygen support, While G.M. Varghese et al.[12], show Pulmonary dysfunction in 33.7% cases. Acute renal failure was seen in 54% of our patients. This incidence of renal impairment is greater than the 23.2% incidence reported by Attur et al.[14] and much lower than the 66.4% incidence reported by Mahajan et al.[15] The occupation and scrub vegetations surrounding the house of the patients are known to have a strong association with acquisition of the infection.[16] In this study, 75% of the patients were agricultural laborers and 26.3% housewives, indicating an increased risk of infection in those who encounter scrub vegetation in their daily life. Our rate of finding an eschar, in 6.66% of patients, is lesser than noted in 46% of patients by Vivekanandan et al in Pondicherry.[17]

Table No.–1 Clinical and laboratory profile and complication of scrub typhus patients

Characteristic	Scrub typhus case
Demographic profile Values	
Age (mean years ± SD#)	34.1±13
Male (%)	18.75%
Female(%)	81.2%
Duration of illness before admission, mean days ±SD#	9.33±6
Duration of hospitalization, mean days ± SD#	7.46±2
Symptom and Sign	
Fever with chills and rigor (%)	15(100%)

Headache(%)	12(75%)
Cough(%)	14(94%)
Shortness of breath(%)	14(94%)
Skin rash(%)	04(27%)
Bleeding manifestation(%)	03(20%)
Eschar(%)	01(6.66%)

Ultrasonography finding

Hepatomegaly(%)	05(34%)
Splenomegaly(%)	03(20%)
Pleural effusion(%)	04(27%)
Ascites(%)	01(6.6%)

Laboratory profile Value(mean±SD[#])

Haemoglobin (g/dL)	09.35±2
WBC count (no. of cells × 1, 000/µl)	12.48±10
Platelet count (no. of cells × 10^9/l)	1.37±1
AST (Aspartate aminotransferase IU/L)	199±135
ALT(Alanine aminotransferase IU/L)	195±165
Bilirubin (mg/dL)	2.42±2
Albumin (g/dL)	3.2±0
Serum creatinine (mg/dL)	1.87±0.9
Blood urea (mg/dl)	83.20±41

Complication of scrub typhus Values(%)

Pneumonia	14(94%)
Hepatitis	13(81.2%)
Renal failure	08(54%)
Shock	10(68%)
Bleeding manifestation	03(20%)
Seizure	01(6.25%)
Myocarditis	00
Death	00

[#]standard deviation

However, in North India, Mahajan et al reported finding an eschar in just 9.5% of patients,[(15)]. while in Korea an eschar has been documented in as many as 90% of patients.[(18)] The variation in prevalence of an eschar may represent the different geographic distribution of the various strains of the organism, or inadequate search for the eschar; further research is warranted in this area.[(19)] the presence of eschar is related with less severe disease.[(11)] The finding of mild hepatitis in 81.2% of our patients is consistent with reported from G.M. Varghese et al[(12)] in Tamil nadu. Thrombocytopenia was noted in 67% of patients in our study. However, data reported from northern China suggest significantly lower rates of thrombocytopenia, starting from 4.6% to 48.9%.[(20)] This might partly be explained by the lower threshold used in their study (100 vs. 150x10^9/l), as studies done in Pondicherry, also found lower rates (10%) with the same lower threshold. Leukocytosis (>11x109 /l), a common indicator of bacterial etiology, was found in less than 40% of our patients. This finding was present in an even lower percentage of patients in the study by Liu et al. in northern China (10.5%).[(20)] However, the result of the leukocyte count was very inhomogeneous in our study, with a range from minimum 2.8 X 10^9 /l to maximum 38 X 10^9 /l. We observed haemoglobin <12 g/dl in 80% of cases which had similarities with Suman Suryanarayana Karanth et al.[(11)] study.

One of the limitations of our study is that it included less number of cases and short duration of study. The study may also be limited by the inherent disadvantages of a retrospective study design from a single medical centre, such as the bias in patient selection or referral and the potentially incomplete data available for some of the patients.

SEVERITY SCORING:

This scoring system **(Table 2)** was designed to assess the severity of disease on the basis of several clinical and laboratory feature. Scrub typhus was categorised into mild, moderate and severe disease on the bases of sum total of points given against each feature. Point score of 1-3, 4-6, and 7-10 consider as mild, moderate and severe disease respectively.

Out of 16 cases, 4 and 12 cases were categorized under moderate and severe disease category by using scoring system. Thus early diagnosis and treatment of severe disease may halt the progression of disease toward life threatening complication.

Table 2: Severity scoring*

Feature	Points
Hypotension(≤90/60 mmHg)	1
AKI(S. creatinine ≥ 2 mg/dl)	1
W.B.C ≥ 10,000/mm^3	1
Haemoglobin(Hb≤10 g/dl)	1
Thrombocytopenia(≤1 lakh/mm^3)	1
Absence of eschar	1
Bilateral pneumonitis	2
Hepatitis(AST & ALT ≥3xULN)	2

***Mild disease: 1-3 score;**
Moderate disease: 4-6 score;
Severe disease: 7-10 score

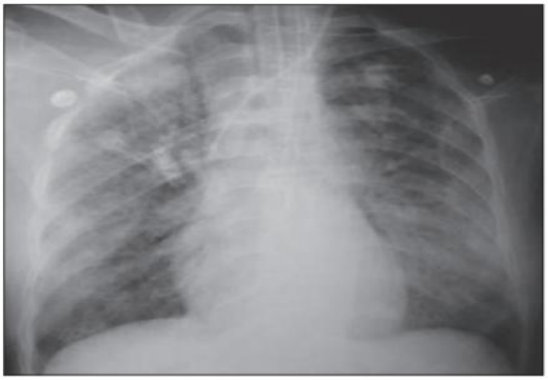

Fig. 1: Chest X Ray showing bilateral pneumonia in scrub typus patient

V. Conclusion

Scrub typhus may be a serious acute febrile illness related to significant mortality. Respiratory dysfunction, shock, and acute renal failure are serious life-threatening complications of this disease. Scrub typhus is present in regions that are co-endemic for various infectious diseases that may present with similar clinical syndromes, such as influenza infection, malaria, dengue, typhoid, and leptospirosis.

The mortality from this infection does appear to have been decreasing over the last several years. However, developing increasing awareness of this infection among clinicians in endemic settings and reliable methods for more rapid diagnosis and early treatment are going to be the key to further reducing the mortality caused by this deadly disease.

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Conflict of interest: the author declare no conflicts of interest

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