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ORIGINAL RESEARCH

Clinical profile of patients with scrub typhus; cross sectional study, at Maharishi Markandeshwar Medical College and Hospital, Solan

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Abstract

Background: Conducted a study to know the demographic, clinical and biochemical profile of scrub typhus patients.

Material and Method: This prospective, cross sectional study was conducted in the Department of General Medicine at Maharishi Markandeshwar Medical College and Hospital, Kumarhatti, Solan and included 50 cases patients with scrub typhus. The detailed clinical history in which particulars of the patient, chief complaints, history of present illness, past history and family history was taken and physical examination was recorded. Their Complete blood counts, liver function test, kidney function test and serum albumin were done and analysed to find the relation with investigations, symptoms and outcomes of the patient.

Results: The majority of patients presented with scrub typhus belonged to 41-50 years age group, with a sex ratio of 1:1. Major presenting symptom was fever, rest of the symptoms were generalized, eschar was present in only one fourth of the patients, hence the diagnosis cannot be ruled out in the absence of eschar. Transaminitis and thrombocytopenia were important investigation finding present in more than three fourth of the patients. Acute hepatitis, AKI, pneumonitis were important complications which lead to MODS.

Conclusion: Presence of transaminitis, hypoalbuminemia, thrombocytopenia, AKI, and MODS was associated with poorer outcomes and mortality.

Keywords: scrub typhus, prevalence, thrombocytopenia

Introduction

More than a billion people live in the "tsutsugamushi triangle," where scrub typhus is a common acute fever sickness[1]. This region includes large portions of south and southeast Asia, the Asian Pacific Rim, and northern Australia.There are an estimated one million cases of scrub typhus each year around the world, and unless properly treated, it is likely responsible for more deaths than dengue. This zoonotic illness is widespread in Himachal Pradesh. This condition is caused by O. tsutsugamushi bacteria, which are gram-negative obligate intracellular bacteria. Leptotrombidium chiggers are a major vector of illness[2].

In addition to a high temperature, patients may also have shortness of breath, cough, nausea, vomiting, muscle aches, and a headache[3-4]. When looking for an eschar at the immunization site, you might find one in anywhere from 10 percent to 92 percent of persons[5].

Scrub typhus can cause symptoms ranging from a mild illness to multi-organ failure and death[6]. Myalgia, arthralgia, rash, lymphadenopathy, hepatosplenomegaly, jaundice, thrombocytopenia, acute kidney injury, capillary leak phenomenon, and acute respiratory distress syndrome are all symptoms that can present themselves alongside a high temperature and be considered a differential diagnosis of Acute Undifferentiated Fever[7].

Complications from scrub typhus include pneumonia, low blood counts, and potentially acute respiratory distress syndrome[8]. Other neuropsychiatric and delirium-related symptoms may occur as a result. However, this seemingly insignificant illness has been linked to cases of multi-organ failure and even death[9]. Scrub typhus has been rediscovered in countries like India, Sri Lanka, the Maldives, and Micronesia where it had been all but forgotten. Not only has it become well-known as a cause of acute respiratory distress syndrome (ARDS) in tropical nations during the monsoon seasons, but it is also responsible for a disproportionate share of deaths in these regions if it is not recognized and treated promptly.

Complete blood count tests and other fundamental laboratory tests that are depended on to provide diagnostic clues are often normal, despite the prevalence of thrombocytopenia[10-11]. Mild transaminitis is a common laboratory result in scrub typhus, occurring in between 66.7% and >90% of patients across multiple investigations[10]. Creatinine increase, an indicator of renal failure, has been observed in 10–20% of studies with a wide range of prevalence estimates[10]. The Weil-Felix test, like many others, is a relatively insensitive and non-specific diagnostic tool. IgM ELISA testing or immunofluorescence assay (IFA), the gold standard but less often available, are currently the tests of choice for the serologic diagnosis[12].

Due to its effect on numerous organ systems and development to severe consequences if not recognized early and managed properly, this re-emerging infectious illness in India has gained clinical importance. Many patients develop life-threatening complications and die from their sickness because of the disease's lack of unique clinical symptoms, which overlap with other prevalent tropical fevers and make identification difficult. Safe and highly effective medications give hope for a rapid recovery from disease, but only if treatment is started right away. Therefore, defining the clinical variables that aid in disease severity prediction is crucial. So, researchers at Solan's Maharishi Markandeshwar Medical College and Hospital set out to examine the clinical profile of scrub typhus patients.

Materials and methods

The research work was carried out as part of a cross sectional study for the study period 2021-2022 in the "Department of Medicine, MMMC&H, Kumarhatti".The study was carried out after taking the prior approval of the Ethical committee of the MMMC&H. An informed written consent was taken from all the participants.

Selection of Patients

50 patients with Scrub Typhus presenting to the Department of Medicine was considered for the study. Patients that fulfill the inclusion criteria were taken up for the study.Patients with history of alcohol intake >10gm/day. (30ml of 40% alcohol (spirits), 100 ml of 13% alcohol (wine), 285ml of 4.9% alcohol (beer), 425ml of 2.7% alcohol (beer)), patients with alcoholic or chronic liver disease, patients with viral or ischemic hepatitis, patients with infectious mononucleosis and those who didn't give their consent for the study were excluded.

Investigations

All the patients that are enrolled for the study were subjected to detection for scrub typhus, total and direct bilirubin, SGOT, SGPT, alkaline phosphatase levels and complete blood count.

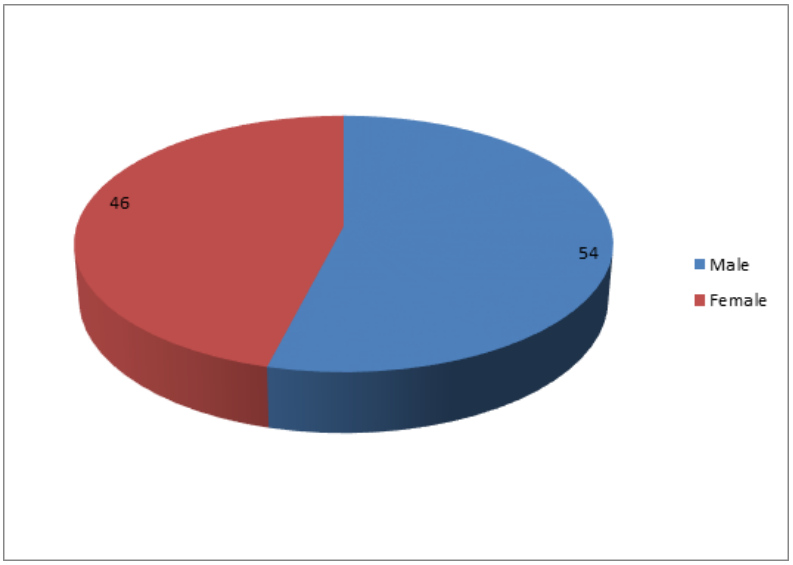
Our hospital has a microbiology lab where they test for scrub typhus IgM antibodies in the blood. Tests of biochemical processes were documented, such as those of renal and liver function. Patients with multi-organ failure were given the usual medical treatment, including mechanical ventilation and renal replacement therapy.

Scrub typhus systemic complications were defined according to the following criteria:

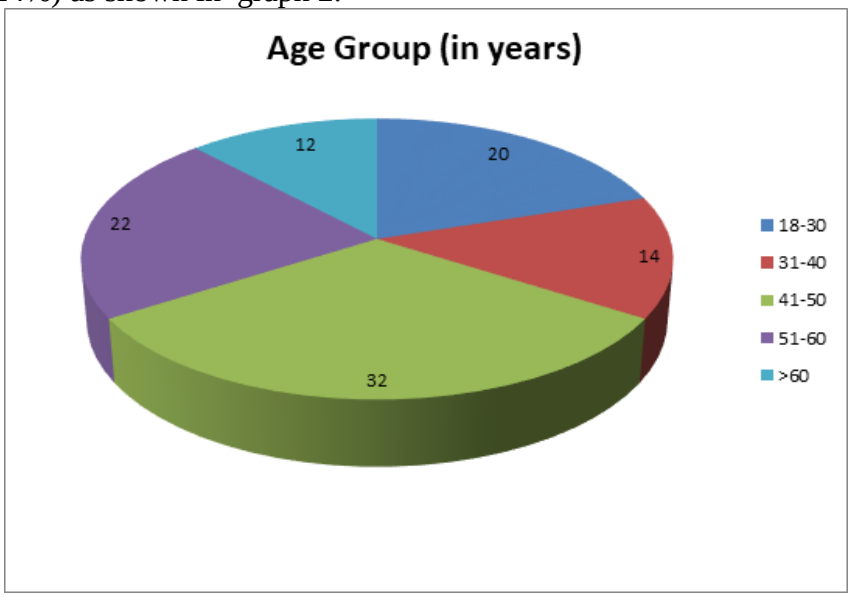
1. Acute kidney injury (AKI) is defined as a rise in serum creatinine (S. Cr) of at least 0.3 mg/dl or a decrease in urine output to 0.5 mL/kg per hour for more than 6 hours.
2. Serum transaminase elevation of more than 6 times the upper limit, indicative of acute hepatitis.
3. Noncardiogenic pulmonary edema presenting as acute onset, bilateral alveolar or interstitial infiltrates on chest radiograph, and PaO2/FIO2= 200 mmHg on arterial blood gas analysis; this is the diagnostic criteria for acute respiratory distress syndrome (ARDS).
4. Acute onset of non-cardiogenic pulmonary edema appearing as unilateral or bilateral alveolar or interstitial infiltrates on chest radiograph and arterial blood gas PaO2/FIO2 > 200 mmHg is diagnostic of pneumonia
5. The presence of schistocytes (fragmented red cells) in a blood smear, higher levels of fibrin breakdown products are diagnostic of disseminated intravascular coagulation (DIC) (FDPs).
6. An rise of serum amylase/lipase >3 times the upper limit of normal, along with the sudden onset of clinical symptoms including abdominal pain, vomiting, guarding/tenderness, is diagnostic of acute pancreatitis.
7. Systolic blood pressure of 90 mmHg or below for 1 hour despite sufficient fluid resuscitation indicative of septic shock.
8. CSF analysis reveals normal or low sugar levels alongside high protein and lymphocytic/neutrophilic cytology, suggesting meningitis.
9. When more than one organ is affected by dysfunction, the term "multiple organ dysfunction syndrome" (MODS) is used to describe the condition.

Results

The aim of the study was to analyse the clinical profile and severity of disease in patients diagnosed with scrub typhus and to study the relation of Liver Function Test with the disease severity. Out of 50 subjects, 54% were males and 46% were females (graph 1).



In this study, maximum subjects were from 41-50 years (32%) followed by 51-60 years (22%) and 18-30 years (20%). Minimum subjects were from >60 years (12%) followed by 31-40 years (14%) as shown in graph 2.



Complaints	N	%
Fever	50	100
Chills	15	30
Body ache	8	16
Headache	8	16
Vomiting	6	12

Fever, chills, body ache, headache and vomiting was reported among 100%, 30%, 16%, 16% and 12% of the subjects respectively (table 1)

Variables	OR	p value
Gender (Male vs Female)	0.89	0.71
Age>60 years	1.27	0.62
Total leucocyte count >11000/cmm	1.21	0.68

Platelet count <100 000/cmm	2.14	0.032*
Bilirubin>1.3 mg/dl	1.49	0.17
Asparate Aminotransferase>40 IU or Alkaline phosphatase >130 IU/L or both	3.69	0.008*
Serum creatinine >1.6 mg/dl	2.73	0.013*
Serum albumin < 3 g%	2.07	0.06
Bilirubin Direct >0.2 mg/dl	3.05	0.021*
Alanine Aminotransferase >78 IU	3.11	0.018*

*: statistically significant

Table 2 showed the predictors of mortality among the study subjects. Univariate analysis revealed that factors related to mortality in increasing order were Asparate Aminotransferase>40 IU or Alkaline phosphatase >130 IU/L or both, Serum creatinine >1.6 mg/dl Platelet count <100 000/cmm, Alanine Aminotransferase >78 IUand Bilirubin Direct >0.2 mg/dl.

Findings	**N**	**%**
Eschar	13	26
Edema	15	30
Lymphadenopathy	8	16
Pallor	7	14
Icterus	6	12
Hepatomegaly	4	8
Spleenomegaly	5	10

Examination findings revealed presence of Eschar, edema, lymphadenopathy, pallor, icterus, hepatomegaly, splenomegaly in 26%, 30%, 16%, 14%, 12%, 8%, and 10 % respectively, as depicted in table 3.

Variables	**N**	**%**
Bilirubin>1.3 mg/dl	13	26
Bilirubin Direct >0.2 mg/dl	31	62
Alanine Aminotransferase >78 IU	33	66
Asparate Aminotransferase>40 IU	50	100
Alkaline phosphatase >130 IU/L	48	96

LFT profile viz. Bilirubin>1.3 mg/dl, Bilirubin Direct >0.2 mg/dl, Alanine Aminotransferase >78 IU, Asparate Aminotransferase>40 IU and Alkaline phosphatase >130 IU/L was found in 26%, 62%, 66%, 100% and 96% of the subjects respectively (table 4).Complications viz. acute hepatitis, pneumonitis, AKI and multisystem involvement was shown in 16%, 14%, 12% and 10% of the subjects respectively.

Discussion

Scrub typhus has recently emerged as a killer disease where disseminated vasculitis and peri-vasculitis result in end-organ injury among febrile patients. Very few studies have tried to study the overall clinical profile of this dreadful but potentially treatable disease. Owing to frequent outbreaks witnessed in different parts of the country in the recent past, scrub typhus is thought to be the commonest occurring rickettsial infection in India and the mortality from untreated scrub typhus remains unknown[13] .

Total 50 patients with serologically proven scrub typhus who presented to Maharishi Markandeshwar Medical College and Hospital, Kumarhatti, Solan were recruited in the single, prospective, observational, cross sectional study over the period of 2 years, after applying inclusion and exclusion criteria. The sociodemographic, clinical profile, complete blood counts and liver function tests were analysed in this study and their disease severity was compared with their liver function test.

Age

In this study, maximum subjects were from 41-50 years (32%) followed by 51-60 years (22%) and 18-30 years (20%). Mean age of the patients was 44.8 years which was comparable to the mean age of patients in a study conducted by Sarah S. Premraj et al[14] in the south India, where the mean age of patients was 39.6 years.

Similarly in a study by Varghese et al[15], Vellore, India, the mean age of the patients was 36.5 years. In this study maximum number of patients were between 41-50 years of age (32%) and minimum were in the ages of more than 60 year.

Clinical Presentation

The clinical manifestations of this disease vary from minimal disease to severe fatal illness with multiorgan dysfunction. The commonest presenting symptoms were fever, cough and shortness of breath. It was found that in the present study that 100% of the patients presented with fever, 30% had chills, 16% complained of bodyaches, 16% complained of headaches, 14% of the patients had cough and around 12% of patients complained of vomiting.

In a study conducted by Sharma et al[16] 100% of the patients had a history of fever. In a similar study conducted in Himachal Pradesh fever was the presenting complain in 99.9% of patients. Similarly in a study conducted by Kumar et al[17] and Palanivel et al[18], all (100%) the patients had fever. In a study done by Dodake et al[19] cough was seen in 15% of the patients.

Complications

Among the patients in this study major complications seen were acute hepatitis seen in 16% of patients, pneumonitis seen in 14% of patients, acute kidney injury in 12% of patients and out of the total 10% patients had multi system involvement, which was taken as involvement of more than 1 organ system.

In a study done by Premraj et al[14] and other similar studies found evidence of AKI in 16% of the patients which is similar to findings in our study.

Similarly in a study done by Sivarajan et al[20] acute hepatitis was seen in 16.7% of the patients, pneumonitis in 15.6% of the patients, AKI in 12.2% of the patients and multiorgan involvement was seen in 14.4% of the patients.

Lft

Among the patients in this study 100% patients had values of Aspartate aminotransferase >40 IU, 66% had values of Aspartate aminotransferase >78 IU. Bilirubin levels signify that direct bilirubin was more increased in these patients however total bilirubin stays in the normal range.

In a study by Sivarajan et al al[20] (100%) of the patients had liver enzymes (AST, ALT, ALP), hyperbilirubinemia was seen in 25% of the patients.

Mortality

The mortality in patients with scrub typhus had wide variations and depends on the circulatory load of O. tsutsugamushi, early or late presentation and treatment modality. Deaths are attributable to delayed presentation or diagnosis, and development of MODS. Complications such as ARDS, renal failure and hepatic involvement are independent predictors of mortality.

In the present study, mortality was found in 6% of the patients, most of which were elderly patients with multi-organ involvement. Platelet count less than 1 lakh cells/mm^{16}, raised Tansaminases (AST, ALT, ALP), and serum creatinine value >1.6 mg/dl were associated with mortality (p-value <0.05). Longer duration of symptoms, late diagnosis and treatment, leads to multi-organ involvement and once multi-organ involvement sets in it leads to poor prognosis, delayed recovery and more chances of mortality.

Overall mortalty rate in a study done by Sivarajan et al[20]was and various other studies was 5.15% and mortality was associated with thrombocytopenia, raise transaminases, and raised creatinine (p-value <0.05).

Conclusion

Present study is a prospective, observational, and cross sectional study conducted over a duration of 1 year. Total 50 patients with scrub typhus were analysed in this study, and their laboratory findings were compared for profile and and assessing severity of the disease.

Our Study shows that Acute febrile Illness presenting in Himachal Pradesh has a 10% incidence of scrub typhus. Patients present with fever, and other symptoms (chills, cough, headache, myalgia, vomiting), which can be difficult to differentiate from other febrile illnesses (dengue, pneumonia, malaria). Presence of Eschar should prompt the diagnosis of scrub typhus, but its absence should not be used to rule out scrub typhus. Middle aged patients working in agriculture and horticulture are more exposed to this disease.

Our findings show a link between scrub typhus and transaminases. And involvement of multiple organs, transaminitis, thrombocytopenia, and raised serum creatinine have been linked with MODS, poorer outcomes and mortality.

It is suggested to keep scrub typhus a possibility in cases presenting with acute fever, and other symptoms, with transaminitis, and a IgG/IgM testing for scrub typhus should be done for early detection and treatment to reduce morbidity, hospital stay, and mortality.

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