

To determine the clinical profile and manifestations of scrub typhus among people

Abstract:

Introduction:

In developing countries acute febrile illness (AFI) is the most common presenting complaint in emergency and outpatients department. Usually in the rainy season and post rainy season Outbreaks of AFI occur in India. Outbreaks like Dengue, Malaria, Typhoid, Scrub typhus and several viral infections have been classically responsible. *Orientia tsutsugamushi* is an obligate intracellular gram negative bacteria which cause Scrub typhus. Scrub typhus is the infection caused by the bite of infected chiggers. The clinical manifestation is characterised by the presence of fever, body pain, headache and and rarely can cause rashes. Scrub typhus is mite borne rickettsiosis and is an endemic infection in area unique to Asia, with an estimated one billion people. In recent years, many parts of India scrub typhus have rapidly reemerged to become the major cause of AFI during monsoon seasons. In India, of the 29 states, 23 have reported the presence of scrub typhus.

Aim: The main aim of this study is to determine the clinical profile and manifestation of scrub typhus infection among people. **Material and method:** Total 72 patients with conform cases of scrub typhus fever were included in this study. The evaluation of fevers were undergone clinically initially serological test and Weil–Felix test followed by immunoglobulin M (IgM) scrub typhus and positive cases were included in this study. Consideration was taken of their clinical appearance and investigations.

Result: Total 72 positive cases were included in this study. Among the total IgM positive for scrub typhus were analyzed with their age and sex variation. From each and every patient different clinical manifestations and complications were analyzed and recorded. The common symptoms were fever; myalgia, breathlessness, rash, and abdominal pain were recorded as 100%, 66.7%, 8.3%, 13.9% and 36.1% respectively. Renal failure was the most common complications followed by pneumonia as 19.4% and 9.7% respectively. In laboratory findings high C-reacting protein and leukocytosis are also found in 81.9% and 33.3% respectively.

Conclusion: Scrub typhus is a widespread tropical infection and often occurs as pyrexia of unknown origin. However sometime it is under diagnosed due to low indication of suspicion and due to non-specific clinical manifestation and also in most of clinical settings due to lack of diagnostic procedures. If there was early diagnosed then treatment will be easy and cost effective due to good response of antibiotics.

Keywords: scrub typhus, *Orientia tsutsugamushi*, Immunoglobulin M scrub typhus, Doxycycline

Introduction:

In developing countries acute febrile illness (AFI) is the most common presenting complaint in emergency and out patients department. Usually in the rainy season and post rainy season Outbreaks of AFI occur in India^{1,2}. Outbreaks like dengue, Malaria, typhoid, scrub typhus and several viral infections have been classically responsible. Unlike fever of unknown origin (FUO), which has a common definition, AUF, also known as “acute febrile illness”, or “acute fever” lacks a definition of universal consensus.³ Because FUO allows the fever duration to exceed three weeks, some authors have described AUF as a fever that will resolve in three weeks time. Thus the word AUF is used to describe fever that do not usually last beyond 21 days, and lack clinical features that are localizable or unique to the organ⁴.

Scrub typhus affects an estimated 1 billion people globally, with 1 million cases reported each year. The illness is seen in rural areas of South and Southeast Asia, the Western Pacific (from Korea to Australia), and India and Pakistan.⁵ Scrub typhus is a dangerous disease that kills around 6% of patients if left untreated and 1.5 percent if treated, although mortality can reach 13% in locations where the standard treatment does not always work.⁶

Orientia tsutsugamushi is an obligate intracellular gram negative bacteria which cause Scrub typhus. Scrub typhus is the infection caused by the bite of infected chiggers. The clinical manifestation is characterised by the presence of fever, body pain, headache and rarely can cause rashes. Scrub typhus is mite borne rickettsiosis and is an endemic infection in area unique to Asia, with an estimated one billion people.⁷ Though this scrub fever is zoonotic disease, and is a more prevalent in mite infested areas, human beings get in contact with these mites as a result of recreational and, occupational or agricultural exposure.

In historic era scrub typhus was considered as a lethal disease and after the introduced of several antibiotics, especially doxycycline, this infection is mostly controlled. Since World War II in Southeast Asia Scrub typhus has been present.

However in India there has been a resurgence of the infection in the last few years. The disease become a major occupational hazard in farm workers, adults engage in agriculture, occupation in forest, soldiers in temporary camps and those living near bushes and wood piles.⁸ In recent years, during monsoon seasons, many areas of India scrub typhus have rapidly reemerged to become the key cause of AFI. In India, Of the 29 states, 23 have reported the presence of scrub typhus. Clinically scrub typhus ranges from subclinical disease to systemic failure and death.⁹ This disease usually presents with fever, myalgia, rash, jaundice, diffuses lymphadenopathy, thrombocytopenia, hepatomegaly, splenomegaly and capillary leak syndrome. Severe complications can be caused by this disease in various proportions of patients, such as acute

respiratory distress syndrome (ARDS), acute kidney injury, hepatitis, myocarditis contributing to heart failure and meningoencephalitis.¹⁰

Sometime in delay presentation, delay in treatment and diagnosis and increasing in antibiotic resistance exhibited by the organism are factors responsible for high mortality. About scrub typhus infection there are very less awareness among doctors and public.¹¹ Therefore, the clinical presentation of scrub typhus fever in the rural areas less with suspicion among clinicians as well as private practitioners. The main aim of this study is to determine the clinical profile and manifestation of scrub typhus infection among people.¹²

Material and method:

This is cross sectional study which was conducted in department of microbiology of Datta Meghe Medical College and Hospital in collaboration with Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Wardha, in a period of four months. Total 72 patients with conform cases of scrub typhus fever were included in this study. In this study every patients with suspected cases who visit in the department of medicine followed by the evaluation of fevers were undergone clinically initially Weil–Felix test and followed by serological test like immunoglobulin M (IgM) scrub typhus test by IgM ELISA, (Merile) in the department of microbiology and positive cases were included in this study. In some cases IgM scrub typhus only positive were found. Consideration was taken of their clinical appearance and investigations and analyzed spectrum of clinical manifestations.

Result:

Total 72 positive cases were included in this study. Among the total IgM positive for scrub typhus were analyzed with their age and sex variation. From each and every patient different clinical manifestations and complications were analyzed and recorded. In this study showed males were more in compare to female. Males were 63.9% and females were 36.1%. In all the age group also males were more than female. Most of the cases 23 (31.9%) belong to age group 31–40 years followed by 18 (25%) in age group of 21–30 years. In this study also showed males are predominate with respect to the age group too. In the age group 13-20 years old and 51-60 years old showed less no of cases as shown in table no 1 below.

Table no: 1 Age and sex variation

Age group	Male	Female
13-20	4	2
21-30	12	6
31-40	16	7
41-50	8	7

51-60	6	4
Total (%)	46 (63.9)	26(36.1)

In this study almost all the cases showed fever as common mode of presentation. Out of 72 cases all patients showed fever and among total fever cases 68.1% showed more than 7 days of fever whereas 31.9% showed fever less than 7 days which followed by 66.7% with malaise as a common symptom. Headache is also a common symptom which showed 55.6%. 9.7% cases showed jaundice and 6.9% showed CNS symptoms/confusion which was rare among the patients. 33.3% cases showed cough. Other clinical presentations included nausea and vomiting in 44.4%, abdomen pain in 36.1%, 8.3% in respiratory difficulty and rash in 13.9%. Uncommon symptoms such as rash were noted mostly maculopapular found in limbs followed by abdomen and thorax. The most diagnostic clinical presentation as Eschar found in 23.6% of cases. In extremities most of eschars were found followed by abdomen and thorax. Groin and axilla is the next site of intimacy and one case has been found in male patient genitalia. Clinical presenting signs such as splenomegaly were found in 20.8%, hepatomegaly in 37.5% and Lymphadenopathy (local or generalized) found in 23.6% cases as shown in table below.

Table 2: Clinical presenting with signs and symptoms

Signs and Symptoms	Number of cases (n)= 72	Percentage
Fever >7 days	49	68.1
Fever <7 days	23	31.9
Fever	10	13.9
Headache	40	55.6
Pain abdomen	26	36.1
Nausea/vomiting	32	44.4
Respiratory difficulty	6	8.3
Central nervous system symptoms/confusion	5	6.9
Cough	24	33.3
Malaise	48	66.7
Jaundice	7	9.7
Eschar	17	23.6
Hepatomegaly	27	37.5
Splenomegaly	15	20.8
Lymphadenopathy	9	12.5
Anemia	17	23.6

In this study the most common complication observed were Renal failure in 19.4% followed by pneumonia in 9.7%, acute respiratory distress syndrome (ARDS) in 6.9%, multiple organ

dysfunction syndrome (MODS) in 5.6%, meningoencephalitis in 4.2%, shock in 1.4%, myocarditis in 1.4%, and pancreatitis in 1.4% as shown in table below.

Table 3: Complications of the patients

Complication	Number of cases (n) =72	Percentage
Renal failure	14	19.4
Pneumonia	7	9.7
*ARDS	5	6.9
*MODS	4	5.6
Meningoencephalitis	3	4.2
Shock	1	1.4
Pancreatitis	1	1.4
Myocarditis	1	1.4

* Note: ARDS: Acute respiratory distress syndrome, MODS: Multiple organ dysfunction syndromes

Laboratory findings in this study, all patients showed as 100% positive in IgM scrub. In this study as laboratory finding suggest that CRP is high in 81.9% positive patients followed by leukocytosis (>11,000) in 33.3% cases. In 29.9% hepatopathy in the form of raised liver enzymes 3 times above normal range showed by patients and nephropathy in 16.7%, proteinuria in 22.2%, anemia in 23.62%, and pulmonary infiltrates in chest X-ray in 8.3% cases. Thrombocytopenia also found in 20.8% of cases as showed in table below.

Table 4: Laboratory investigation findings

Investigation	Number of cases (n) =72	Percentage
IgM scrub	72	100
CRP	59	81.9
Leukocytosis (TLC >11000)	24	33.3
Hepatopathy	21	29.2
Nephropathy	12	16.7
Proteinuria	16	22.2
Pulmonary infiltrate	6	8.3
Thrombocytopenia	15	20.8
Anemia	17	23.6

Note: IgM: Immunoglobulin M, CRP: C-reacting protein, TLC: Total leukocyte count

Discussion:

In India Scrub typhus is increasingly noticed as an emerging disease of clinical importance. Scrub typhus is an acute febrile disease with often non-specific constitutional signs making it difficult to diagnose if an eschar that is most pathognomies is not observed.¹³ Scrub typhus is usually diagnosis by history and clinical presentation. The huge variation and frequent clinical symptoms of the disease that similar to other febrile disease pose a challenge to clinical diagnosis. Indoor admission was reported as high as 12%. However load of disease may be under reported as most of the studies were hospital based. Furthermore, Weil–Felix is not available in most of the endemic areas other than serological testes.¹⁴ Non-specific febrile illness which present as infection presents with rash, gastrointestinal, respiratory, lymphadenopathy and central nervous symptoms which if not diagnosed and treated early can lead to complications such as pneumonia, myocarditis, gastrointestinal bleeding, meningoencephalitis, acute renal failure and ARDS. In this study total 72 cases were included with the age above 13 years and showed male predominant in all of age groups with more than 2:1 proportion in age groups 21–30 and 31–40 years of age which was comparable to the study of Kumar *et al*¹⁵ however studied of Wei *et al*¹⁶ showed the prevalence of female over 50 years of age in their research. In this study out of 72 cases all patients showed fever and among total fever cased 68.1% showed more than 7 days of fever whereas 31.9% showed fever less than 7 days.¹⁷ Patients with fever less than 7 days showed 31.9% which followed by 66.7% with malaise as a common symptom. Headache is also a common symptom which showed 55.6%. Jaundice was seen in 9.7% cases and 6.9% showed CNS symptoms /confusion which was rare among the patients and 33.3% cases showed cough. Other clinical presentations included nausea and vomiting in 44.4%, abdomen pain in 36.1%, 8.3% in respiratory difficult and rash in 13.9 % which was comparable to the studied of Sirisantha *et al*¹⁸ The most common complication observed were renal failure in 19.4% followed by pneumonia in 9.7%, acute respiratory distress syndrome (ARDS) in 6.9%, multiple organ dysfunction syndrome (MODS) in 5.6%, meningoencephalitis in 4.2%, shock in 1.4%, myocarditis in 1.4%, and Pancreatitis in 1.4%. Similar findings were observed by Varghese *et al*¹⁹, Bhat *et al* in this study 81.9% patients had high CRP, leukocytosis in 33.3% cases in 29.9% hepatopathy in 16.7%, proteinuria in 22.2%, anemia in 23.62%, and pulmonary infiltrates in chest X-ray in 8.3% cases. This can be comparable to the studied of Palanivel *et al*²⁰ without proper diagnosis antibiotics are often used indiscriminately in fever of unknown origin, leading to most species becoming multidrug resistance.¹⁵ Doxycycline is the most effective, and cost effective antibiotic in scrub typhus. Hence, doxycycline should be used with proper diagnosis of scrub typhus. Nevertheless, doxycycline should be an effective treatment in the suspected scrub typhus situation.²²⁻²⁴

Conclusion:

Changing epidemiology in India now scrub typhus became the commonest causes of AFI. Scrub typhus is a widespread tropical infection and often occurs as pyrexia of unknown origin. However sometime it is under diagnosed due to low indication of suspicion and due to non-specific clinical manifestation and also in most of clinical settings due to lack of diagnostic procedures. A high indication of suspicious should be maintained for the early diagnosis and management to prevent complication. If there was early diagnosed then treatment will be easy and cost effective due to good response of drugs such as doxycycline and azithromycin.

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Conflict of Interest: Nil

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