



International Journal of Medicine and Health Profession Research

Journal home page: www.ijmhpr.com

<https://doi.org/10.36673/IJMHPR.2021.v08.i02.A25>



STUDY OF CLINICAL CHARACTERISTICS OF PATIENTS OF SCRUB TYPHUS IN MULTI SPECIALITY HOSPITAL IN EASTERN INDIA OF AGE GROUP MORE THAN 13 YRS: AN EPIDEMIOLOGICAL CROSS-SECTIONAL STUDY

Sujoy Mukherjee¹, Aditi Munmun Sengupta^{*2}, Radhakrishna Mishra³

¹Department of Internal Medicine and Critical Care, Calcutta Medical Research Institute, Kolkata, India.

^{2*}Department of Critical Care, Calcutta Medical Research Institute, Kolkata, West Bengal, India.

³Department of Family Medicine, Family Medicine from Calcutta Medical Research Institute, Kolkata, India.

ABSTRACT

Recent reports from all over India indicated a resurgence of the disease, scrub typhus which is associated with morbidity and mortality becoming a serious cause of concern especially in eastern India. Although this disease is in rural areas, it is now urbanized and prevalence has further broadened affecting children all over the country. Due to overlapping presentations with other diseases and varied presentations, scrub typhus required a high degree of suspicion. The present study has attempted to estimate the prevalence of clinical features, complications, and the health impact of scrub typhus on children. Around 34 patients admitted in the Calcutta Medical Research Institute, Kolkata, West Bengal who were diagnosed for scrub typhus were considered for the study and descriptive, observational, cross-sectional methodology was employed. SPSS and Minitab 17 were conducted. The results of the study showed that children get infected with scrub typhus disease presented with fever, eschar, thrombocytopenia and mild hepatitis. Lack of diagnostic procedures and knowledge about the disease delays the diagnosis and early treatment in the Indian scenario and prompt empirical therapy along with clinical suspicion are required to reduce the mortality from scrub typhus among children. Future studies are required with larger samples for the generalizability of the study results.

KEYWORDS

Scrub typhus, Children, Fever, Eschar, Thrombocytopenia, Mild hepatitis, Clinical suspicion and Empirical therapy.

Author for Correspondence:

Aditi Munmun Sengupta
Department of Critical Care,
Calcutta Medical Research Institute,
Kolkata, West Bengal, India.
Email: sengupta2aditi@gmail.com

INTRODUCTION

Scrub typhus (ST) is a vital reason for acute undifferentiated febrile illness (AUF) that is emerging in the last decade found in various parts of India. Scrub typhus belongs to Rickettsial diseases group caused by a gram-negative, obligate intracellular bacterium named *Orientia*

tsutsugamushi (tsutsuga meaning dangerous and mushi meaning mite or insect) and is maintained inside trombiculid mites through transovarial and transstadial transmission (Peter *et al*, 2015)¹. Clinical spectrum ranges from asymptomatic to becoming severely fatal in humans as they acquire the infection through trombiculid larval stage called chiggers. Scrub typhus is endemic and found in certain parts of the world comprising East and South Asia and Southwest Pacific called “tsutsugamushi triangle” (Luce-Fedrow *et al*, 2018)². In India, the Scrub typhus cases suggested majority from north-eastern hilly and heavily forested parts of India like Himachal Pradesh, Himalayas, Sikkim, Assam, Meghalaya, Nagaland, West Bengal and Uttarakhand as well. According to the World Health Organization (WHO) ST is one of the most under-reported and underdiagnosed febrile illnesses that requires hospitalization (Bonell *et al*, 2017)³. Scrub Typhus accounts for 23% of all the febrile cases with ~1 million that occur annually in the endemic areas (Bonell *et al*, 2017)³. In India, ST is an important reason for the febrile cases in the eastern part of the country and found more prevalent during winter and rainy seasons as the increased humidity favours mite eggs hatching into chiggers that results in transmission of Scrub typhus (Nallasamy *et al*, 2020)⁴. Four factors are essential for the microfocus infection namely intimate and coexistence relationship among *O. tsutsugamushi*. Rats, chiggers, transitional or secondary forms of vegetation are called zoonotic tetrad. During the rainy season, lower altitudes like hilly areas have an average temperature of 20°C to 35°C that is quite conducive to arthropod vectors spread and thus, such areas have been reported to have high Scrub typhus cases. Moreover, it has been observed that seropositive individuals belonged to active groups working physically in outdoor activities like agriculture and farming (Chakraborty S and Sarma N (2017)⁵. Rat burrows and granaries were found to be common in the majority of dwellings. ST prevalence is associated with climatic changes that potentially provides a niche suitable for rickettsial vectors viz fleas, ticks, mites, etc to dissipate and proliferate the rickettsial infection. This makes north east parts of

India highly vulnerable to ST infection due to climatic change with visible bearing on forest sectors and agriculture (Khan *et al*, 2015)⁶.

In recent years, Scrub typhus infection has re-emerged as AFI in many parts of India during the monsoon and post monsoon seasons. Scrub typhus is a rural disease which usually affects the individuals and children who are highly exposed to mites, although it can also occur in urban areas. The scope of clinical presentation is from subclinical to organ dysfunction, failure and death usually presented with myalgia, rash, fever, diffuse lymphadenopathy, thrombocytopenia, jaundice, splenomegaly, hepatomegaly and capillary leak syndrome (Saluja *et al*, 2015)⁷. The pathognomonic feature of Scrub typhus is necrotic eschar at the site of mite bite and progresses to severe complications like hepatitis, myocarditis, acute kidney injury (AKI), acute respiratory distress syndrome (ARDS), and meningoencephalitis in patients at different proportions. The characteristic lesion is called eschar that originates as a vesicular lesion on skin at the mite feeding site which later forms an ulcer having a black necrotic center, regional lymphadenopathy and an erythematous border (Kundavaram *et al*, 2013)⁸. Maculopapular rash, fever starts from the trunk and spreads to limbs. This affects the cardiovascular system, central nervous system, gastrointestinal and respiratory systems.

The clinical symptoms of Scrub typhus in children get misdiagnosed as they mostly remain nonspecific. Scrub typhus presents as a febrile illness that may become mild or severe in children presenting generalized or regional lymphadenopathy and fever (Sapkota *et al*, 2017)¹¹. Vomiting, abdominal pain and diarrhoea should also be considered as one of the differential diagnoses in children due to Scrub typhus. Children get affected by Scrub typhus due to less pre-existing immunity predisposing them to a greater risk for developing the infection. In general, fever accompanied by capillary leak is considered a vital clinical sign of Scrub typhus infection to differentiate it from dengue fever. Other signs and symptoms that appear in children include rash on soles and palms, upper respiratory problems, seizures, arthralgia, altered sensorium, eschar,

periorbital oedema, retinal, vasculitis, hepatomegaly and splenomegaly (Bhat *et al*, 2014)¹². In addition, the presence of eschar is also a valuable clinical sign in the Scrub typhus diagnosis, however, its absence does not rule out the infection. Serious complications in children usually occur during the second week of the infection that includes pneumonia, acute respiratory distress syndrome, GI bleeding, meningoencephalitis, severe thrombocytopenia and acute renal failure (Rapsang and Bhattacharyya, 2013)¹³. It is considered a life-threatening disease in children and requires immediate mediate interventions.

AIMS AND OBJECTIVES

This section will include the objectives to be studied in the paper which are illustrated as:

To estimate the prevalence of various clinical features of scrub typhus among children in Eastern India.

To estimate the prevalence of complications of scrub typhus among children in Eastern India

To examine the health impact of scrub typhus among children of Eastern India.

To determine the diagnostic manifestations, treatment, and related outcome of scrub typhus among children of Eastern India.

LITERATURE REVIEW

Epidemiology and prevalence of scrub typhus

According to Chunchanur, (2018)¹⁴ Rickettsial diseases like Scrub typhus is one of those infections that is re-emerging in India at present times. The term “Scrub typhus” is commonly used due to the vegetation type i.e. terrain between clearing and woods where the vector harbours. However, this given name is not entirely true as Scrub typhus infection can occur in varied habitats such as semi-deserts and seashore. The larval mites usually feed on the wild rats and humans are infected accidentally as they encroach the mite present in the infested areas called mite islands through agricultural or occupational exposure. Scrub typhus is highly prevalent in rice fields considered a crucial reservoir for mite transmission and this is the reason, the infection is quite dominant in hilly parts located in

eastern India. In the past few years, in the eastern India, scrub typhus has increased especially during post-monsoon and the cooler months of the year. The mountainous states in Northern India have been recently reported to have Scrub typhus outbreak as the vector species that causes the disease, *Gahrliepia* (*schoengastilla*) and *Leptotrombidium deliense* sp. were recorded through entomological study conducted in these regions of Eastern India. The recognition of Scrub typhus infection in children adds to the differentials in a febrile child in the north-eastern parts of India.

According to Khan *et al*, (2012)¹⁵ northeast India is situated at latitude 21.578-29.308 N and longitude 89.468-97.308 E which has predominantly a sub-tropical and humid climate with humid, hot summers, mild winters and severe monsoons. This makes the climate favourable for the scrub typhus re-emergence in the region of northeast India after a long gap of almost 65 years.

According to Das *et al*, (2019)¹⁶ Scrub typhus infection has also been reported in the state of Orissa from eastern part of India. Peak transmission in Orissa was observed among individuals residing close to wood piles and bushes, raising domestic animals and working on farms being the high risk factors especially during the rainy season. According to Varghese *et al*, (2016)¹⁷ cases of Scrub typhus have also been reported from southern parts of India like Andhra Pradesh, Tamil Nadu, Karnataka and Telangana. The coastal areas of these states reported high numbers of Scrub typhus cases especially during the cooler months from September to December. The increase in agricultural laborers in these endemic regions of Southern India have a higher risk of developing Scrub typhus infection as they are involved in agriculture which increases their exposure to trombiculid mites that acts as a reservoir for *O. tsutsugamushi*. A study conducted by Digra *et al*, (2010)¹⁸ showed that Scrub typhus is quite common in Jammu and Kashmir including children due to its hilly regions. The age group of children between 5 years to 18 years belonging to Sunderbani-Naushera - Rajouri belt were presented with high grade fever, generalized maculopapular rash predominantly on the soles and palm peripheries

in all the paediatric Scrub typhus cases. Scrub typhus has also been reported in South India and Thomas *et al*, (2016)¹⁹ conducted a study to investigate the rickettsial fevers among children from Southern India and the results of the research showed that children below the age of 13 years were clinically-diagnosed with rickettsial fever and were hospitalized with prevalence of fever, rash, retinal vasculitis between the months September and January. The states like Kerala, Karnataka, Maharashtra also reported ST cases as the infection established as an endemic disease in these states, however, the occurrence among children is often overlooked.

Related risk and complications of scrub typhus

A study conducted by Mohanty *et al*, (2020)²⁰ revealed that scrub typhus complications involve respiratory involvement, hepatic and gastro-intestinal involvement, neurological involvement, complications in soft tissue and skin. In the study, patients presented with dry cough, breathlessness, pleural effusion and in some cases, mechanical ventilation and support may be required due to ARDS. Hepatic and gastro-intestinal involvement includes vomiting, jaundice, splenomegaly, hepatomegaly and ascites at the time of presentation. Neurological involvement consists of headache, altered sensorium, neutrophilic predominance having elevated proteins, pedal oedema, eschar over the anterior of the trunk with conjunctival congestion and axillary lymphadenopathy. Associated complications with scrub typhus include liver dysfunction, acute kidney disease, shock, meningoencephalitis, ARDS and multi-organ dysfunction syndrome (MODS).

Rapsang and Bhattacharyya, (2013)¹³ also studied the risk and complications in scrub typhus and reported that there is risk of involvement of the pulmonary system which is well-documented and pleural effusion seen in the majority of patients. Pulmonary manifestations also include varying degrees of interstitial pneumonitis or bronchitis that progresses to ARDS, pneumonitis with patchy consolidation, hilar adenopathy, reticulonodular opacities, focal atelectasis, centrilobular nodules and bronchial wall thickening that increases the length of

stay in hospitals and requirement for ICU. The risk factors for the ARDS development include thrombocytopenia and early pneumonitis. Acute pancreatitis is also a complication associated with pancreatic abscess in patients with multi-organ dysfunction and failure. ST is a killer disease in which perivascular and vasculitis inflammatory lesions result in MODS that may prove fatal. Aggressive management includes dialysis, ventilator strategy and management of haematological abnormalities to prevent the mortality that is associated with the scrub typhus risk and complications.

Dass *et al*, (2011)²¹ studied the complications in paediatric scrub typhus where meningoencephalitis was the most common and major complication observed followed by pneumonia, subconjunctival haemorrhage. Septic shock, cortical blindness, peritonitis, prolonged oxygen dependency, coagulopathy, pancytopenia, urinary tract infection (UTI) and myocarditis. The authors found some complications in scrub typhus like cortical blindness that revealed bilateral occipital lobe necrosis, peritonitis, acute pain abdomen, simulated acute appendicitis that mimicked acute cholecystitis. Kalal *et al*, (2016)²² conducted a study to describe the clinical and epidemiological profile of paediatric scrub typhus below the age of 18 years. The neurological complications involved in scrub typhus in children were meningoencephalitis, retinal vasculitis, shock and purpura fulminans. The infection manifests clinically as nonspecific febrile illness accompanied by occasional rash, headache, myalgia accompanied by involvement of (CNS), gastrointestinal and respiratory symptoms that may result in MODS and failure. Renal failure, shock and CNS involvement are the major complications that are associated with morbidity and mortality. Clinical manifestations of Scrub typhus are variable due to the strains differences that infect and result in high antigenic variation levels.

Health impact of scrub typhus among children

Scrub typhus is life threatening among children. Balaji *et al*, (2017)²³ studied the clinical profile of scrub typhus in children in South India. This infection has affected the children leading to

morbidity and mortality. Majority of children from the rural areas in India present with high-grade fever exceeding 5 days with cough, chills, cold, vomiting that has a major impact on their health. The children also suffer from headache, lethargy, abdominal pain, myalgia, convulsion, diarrhoea and incessant cry affected by scrub typhus. Eschar is formed in the skin folds of genitalia, axilla, groin, perianal areas, inguinal areas, umbilicus, behind the ear and scalp. Oliguria, generalized anasarca and GI bleeding are important clinical characteristics of ST that affect children majorly. Children with Scrub typhus infection also develop complications when they are not treated on time and thus, timely prognosis is quite important as the complications develop during the second week of the illness. Wide pulse pressure shock is the most common finding in ST disease and therefore, diastolic BP needs to be monitored in critically ill children.

Bhat *et al*, (2016)²⁴ reported that children with scrub typhus presented meningeal signs which is an early and common complication of paediatric scrub typhus. Analysis of cerebrospinal fluid (CSF) revealed that total leukocyte count and proteins were elevated and mononuclear pleocytosis confirmed meningitis, an early complication in paediatric scrub typhus. This shows that neurological involvement is a prominent clinical manifestation that affects children with scrub typhus. The results of a recent study conducted by Williams *et al*, (2021)²⁵ is a breakthrough that revealed hyperferritinemia, a complication associated with paediatric scrub typhus, is quite prevalent, however, limited studies are available. The results of the study showed that hyperferritinemia from mild to severe had been observed in children, but its association with mortality has not yet been established. However, hyperferritinemia is an indication and an attractive marker for the haematological dysfunction prominent in children infected with scrub typhus.

Bal *et al*, (2019)²⁶ also investigated the clinical and distribution profile of paediatric scrub typhus presented with acute febrile illness in eastern part of India. Systemic complications developed among the children found positive for scrub typhus and became one of the major causes for the high morbidity

among the children in Orissa. A delay in diagnosis, late presentation and treatment may cause death among children below the age of 10 years because of non-specificity of scrub typhus signs and symptoms and low suspicion index. Acute encephalitis syndrome (AES) outbreaks among children aged below 15 years have been reported in paediatric scrub typhus cases. This shows that Scrub typhus is a crucial clinical feature and cause of AFI and AES among children in eastern India. High index of suspicion of Scrub typhus and its early diagnosis with effective management of the risk and complications would help to reduce the morbidity and mortality in children due to ST disease.

Clinical feature and analysis of scrub typhus

According to Pathak *et al*, (2019)²⁷ scrub typhus is presented as an undifferentiated acute fever and the incubation period for the clinical symptoms is between 6 and 21 days from the time of exposure. Scrub typhus is characterized by the sudden onset fever, headache, chills, myalgia, backache, vomiting, profuse sweating, enlarged lymph nodes and vomiting. According to Kim *et al*, (2007)²⁸ in some Scrub typhus patients, eschar may develop at the feeding site of chigger, usually at sites of skin folds like groin, inguinal and axillary areas. Eschar has been reported less frequently in Scrub typhus patients from East Asia, patients from South India present themselves frequently with eschar and there is significant difference in the eschar distribution among females and males. In males, it is primarily present in the groin, axilla and genitalia and in females, it is present in the abdomen and chest. Unusual sites for the eschar formation are also reported in the ear lobe, cheek and dorsum of the feet. 5 to 8 days after the onset of fever, a maculopapular or macular rash may appear on the trunk that later extends to legs and arms in a small proportion of Scrub typhus patients. Related complications include ARDS, pneumonia, encephalitis, myocarditis, DIC, hepatitis, acute kidney injury, hemophagocytic syndrome, transient adrenal insufficiency, acute pancreatitis and painful subacute thyroiditis.

Misra, Kalita and Mani, (2015)²⁹ have outlined the neurological manifestations observed in scrub typhus

patients as in meningoencephalitis, encephalitis or meningitis. Other symptoms include Guillain-Barre Syndrome, cerebral venous thrombosis, opsoclonus, transient Parkinsonism, cerebellitis, abducens nerve palsy, transverse myelitis and bilateral optic neuritis. In severe ST infection, MODS is common where respiratory dysfunction is predominant with requirement of ventilation support, cardiovascular and hepatic dysfunction and duration of fever is associated independently with mortality. Vikrant *et al.*, (2013)³⁰ studied the acute kidney injury (AKI) that is associated with scrub typhus infection. Retrospective study of the patients diagnosed with acute febrile illness also had AKI. Laboratory abnormalities have also been observed in patients with ST like anaemia, thrombocytopenia, leucocytosis, hypernatremia, hyponatremia, hyperkalaemia, hypokalaemia, metabolic acidosis, hepatic dysfunction and hypoalbuminemia. Physical examination of patients with scrub typhus presented with interus, conjunctival suffusion, facial puffiness, lymphadenopathy, pedal oedema, eschar and skin rash. Venkategowda *et al.*, (2015)³¹ ST is one of those rickettsial diseases that has differential diagnoses presented with fever and thrombocytopenia and ARDS associated with high morbidity and mortality. Weil Felix test or Immune-chromatography test tested positive in patients showed clinical features like cough, low blood pressure, dyspnoea and decreased haemoglobin. According to Wangrangsimakul *et al.*, (2020)³² the clinical symptoms of scrub typhus include fever, eschar, tachypnoea, cough, headache and lymphadenopathy. Complications include severe thrombocytopenia, hepatitis, circulatory shock and ARDS.

METHODOLOGY

The study was conducted in a tertiary care centre at the Calcutta Medical Research Institute, Kolkata, West Bengal. The centre has 450 bedded centres with multiple ICU and various super speciality departments. The study was conducted over a period of 19 months from 1st May 2018 to 10th December 2019.

As the study is aimed at analysing the clinical profile and complications of the scrub typhus patients admitted in tertiary care centres, a quantitative research approach is appropriate for the present study. This approach would help in studying the clinical symptoms of the scrub typhus patients in a multispecialty hospital. The study also adopted a deductive research approach as the study is associated with scientific investigation where the clinical characteristics of scrub typhus patients were studied in hospitals in eastern India.

The present study adopted a prospective, descriptive observational cross-sectional research design. This research design is appropriate for the present research as it helps to study the disease or condition of scrub typhus and the potentially related clinical characteristics at a specific point of time for a defined age group, i.e., children above 13 years of age. Cross-sectional study employed in the present study is observational in nature and also descriptive research, not being relational or causal in nature. Moreover, for the present study, descriptive, cross-sectional study would help to inspect the prevalence of scrub typhus among children in eastern India at a specific period or point of time without attempting to provide causes for such prevalence or draw any conclusions or inferences. During the study, the researcher did not interfere with the management protocol and decision making with regards to patient treatment.

For the present study, a primary data collection method was chosen where original data has been collected and used commonly in descriptive or experimental research design as employed in the present study. Interviews in the form of questionnaires-based surveys having close-ended questions in offline or online mode can be used for quantitative data collection methods. For the present study, closed-ended questionnaires were used having close-ended questions with major sections: one section for obtaining demographic information and the next section about the complications, risk, clinical analysis, diagnosis, and possible outcome in scrub typhus. The primary data was collected from traders from the hospitals with the consent of patients and doctors. Hence, for the present study,

the primary data collection method has been chosen as it is quite pertinent and relevant to the research question being investigated or addressed.

For the present study, ethical approval was taken from the Ethics and Scientific Committee and informed consent was collected from the study participants. After seeking approval, based on a predesigned data abstraction form, required information was taken from the patients. Moreover, basic laboratory tests were done, patients were screened and examined clinically for the distinguishing signs and symptoms of scrub typhus. IgM ELISA was also performed on the serum samples using the Scrub Typhus Detect test with additional investigations like rapid test, blood culture and other physical examinations. Scrub typhus associated complications were also diagnosed like MODS, AKI, ARDS, meningitis, hepatitis and shock. Diagnosed patients with strong clinical suspicion for scrub typhus were treated with Doxycycline and in other cases, Azithromycin. Moreover, during the hospital stay patients diagnosed with scrub typhus were followed up for complications and treatment outcome was recorded. Finally, 34 patients admitted in the Calcutta Medical Research Institute who were diagnosed for scrub typhus fitting into the inclusion and exclusion criteria were included for the study through a simple random sampling method. All patients above the age of 13 years who presented with symptoms suggestive of scrub typhus and IgM (Immunochromatography) positive for scrub typhus were included for the study. Patients who were already diagnosed with other febrile illnesses like malaria, dengue fever, chikungunya, leptospirosis, pneumonia, cellulitis, UTI, typhoid were excluded from the study. As the study is aimed at analysing the clinical profile and complications of patients diagnosed with scrub typhus admitted in a tertiary care centre, the sample size was selected based on a previous study.

Method for calculation of sample size

Population (N): 61

Proportion (p): 94.91%

Confidence limits (d): 5%

Design effect (for cluster surveys DEFF): 1

Equation:

$$\text{Sample size (n)} = \frac{[DEF * Np(1-p)]}{[(d^2 / Z^2(1-\alpha)) * (N-1) + p*(1-p)]}$$

For confidence interval of 95% sample size calculated by Open Epi version 3 was a minimum of 34.

Statistical analysis of the collected data was performed on a computer by SPSS version 20 (statistical package for the social sciences) and Minitab 17 were used for calculations. The continuous variable was expressed as Standard and Mean deviation for descriptive analysis. Categorical variables were expressed as percentage and frequency. In inferential Statistics, Chi-square test and fisher's exact test was done to find out relations between the categorical variables. It was observed that P value less than 0.05 was considered as statistically significant.

RESULTS

Demographic profile of patients with scrub typhus

From Table No.1 and Table No.2, of the 34 patients recruited for this study, about 10 participants (29.4%) were in the age group between 41 to 50 years showing maximum peak age of incidence. The age group between 13 to 30 years showed a second peak where 7 participants (20.6%) belonged to this age group. 4 participants (11.8%) were observed in the age group 31 to 40 years having the least number.

From Table No.3, of all the 34 study participants, it can be observed that scrub typhus was predominant among males having 19 patients (55.9%) as compared to 15 females (44.1%).

Table No.4 displays the occupational distribution of the study participants. From the results, it can be observed that of all the study participants, maximum number of cases were seen among 11 housewives (32.4%) followed by 8 others (business man, retired person) (23.5%), 7 office employees (20.6%) and farmers and students (11.8%).

Table No.5 displays the scrub typhus cases district-wise in West Bengal. It was observed that maximum number of scrub typhus patients were from Kolkata having 16 patients (47.1%) followed by 8 patients from Howrah (23.5%), 5 patients from Medinipur

(14.7%), 4 from Hooghly (11.8%) and one patient from Purulia (2.9%).

Table No.6 displays the distribution of the cases in the rural and urban areas of eastern India. From the results, it can be observed that the majority of the scrub typhus cases were from rural areas as compared to urban areas having 52.9% (rural) and 47.1% (urban).

Table No.7 displays the distribution of patients according to ward and ICU setting and the results showed that the majority of the patients were managed in the ICU i.e. (58.8%) and about 41.2% in wards.

Table No.8 displays the majority of scrub typhus cases seen during the cooler months (post monsoon period) having the maximum percentage of cases seen in the month of October (26.5%) followed by September and November (23.5%).

From Table No.9, it can be deduced that about 8.8% of patients presented with fever with a duration less than 7 days, maximum number of cases (58.8%) presented with a duration of 7 to 13 days and 32.4% of cases presented with 14 days or more days with fever.

Table No.10 presents the distribution of signs and symptoms of scrub typhus observed in the sample patients. Fever was observed in 100% of the cases followed by myalgia being the second commonest symptom seen in 52.9% of the cases, followed by breathlessness in 38.2% of cases and cough and headache being the next common features having 35.2% of each cases.

Looking into the gastrointestinal symptoms, Table No.11 showed that vomiting (29.4%) was the most common complaint among GI symptoms followed by abdominal pain (23.5%) and loose stools (5.8%).

Table No.12 showed the signs of scrub typhus mostly observed in the sample patients. The results of the study showed that eschar was the pathognomonic sign of the scrub typhus observed in 8.8% of the cases. Other common signs observed were pallor (35.2%), Icterus (11.7%), lymph node enlargement (2.9%).

Table No.13 displays the cases of liver symptoms where hepatosplenomegaly (32.3) were maximum

followed by cases of hepatomegaly (17.6%), splenomegaly (11.7%).

Table No.14 shows the haemoglobin count, platelets and leukocyte counts of the patients diagnosed with scrub typhus. Anaemia was seen in almost 38.2% of the cases with leukocytopenia in 32.3% cases and thrombocytopenia in 5.8% of the cases.

Table No.15 showed the renal abnormalities in which raised serum creatinine was observed in 10 patients (29.4%), urea was raised in 6 patients (17.6%), 17.6% of oliguria cases, haematuria and proteinuria was seen in 11.76% and 14.7 % respectively.

Table No.16 shows the complications associated with scrub typhus observed in the sample patients. The results of the present study showed hepatitis (32.4%), AKI (20.6%) and heart failure (23.5%) being the most common complications of ST. Other complications were MODS (23.5%), shock (17.6%), ARDS (11.4%) and meningoencephalitis (5.9%) that affected liver, kidney and heart.

Table No.17 showed the pulmonary findings through X-ray of the chest and it was found that 32.3% patients had pleural effusion while 14.7% had pneumonitis like condition. 50% of the patients showed normal chest X-ray findings.

Table No.18 shows the distribution of organ support during T/T and it was found that 29.4% of patients required organ support during the treatment in various forms like ventilation, vasopressors and hemodialysis.

Table No.19 shows the distribution of duration of hospital admission. It reveals that 53% of the patients needed 8 to 13 days, 47% of the patients required less than 7 days of hospital stay and none of the patients required more than 14 days.

DISCUSSION

In the present study, the clinical features and complications of Scrub Typhus were analysed. 34 patients who were Immuno chromatography IgM positive for scrub typhus were included in the study conducted at the Calcutta Medical Research Institute, Kolkata, West Bengal during the period from 1st May 2018 to 10th December 2019. The observations found are discussed below.

The incidence of scrub typhus is re-emerging in India especially in the eastern parts of India. However, the disease presentation and severity are low in the country due to lack of awareness among people, under-diagnosis and reporting especially in the children group. In the present study, the percentage of male patients (55.9%) were more than female patients (44.1%) and this trend has also been reported in a study conducted by Jyothi *et al*, (2015)³³ stating that they spend most of their time outdoors. Moreover, in the present study, maximum patients were from the age group between 41 to 50 years (29.4%). This is not much consistent with the majority of Indian studies as it was found that young adults in the age group 20 to 40 years were mostly affected as they are the most active group (Subbalaxmi *et al*, 2014)³⁴. Looking into the occupation, in the present study, housewives (32.4%) were mostly affected. This trend is also consistent with other studies done earlier in Indian context where it was found that housewives had the maximum scrub typhus cases as they are seen to work in open fields for activities like agriculture and collecting firewood also reported by Trowbridge, Premkumar and Varghese, 2017³⁵ in their study. Majority of the patients were from rural regions (52.9%) in the districts of West Bengal and about 47.1% from urban areas. Previous studies done in India are also consistent with the result of the present study where the sample patients hailed from hilly areas in the eastern part of India reported by Sethi *et al*, 2014³⁶. Scrub typhus infections are greatly affected by seasonal variations. In the present study, it has been observed that majority of cases were during the cooler months post (monsoon period) (26.5%) which is consistent with other studies where post monsoon surge of scrub typhus cases has been witnessed in the months of September and October as it is the favourable season for the breeding of mites and its transmission as reported by Rungta N, 2014³⁷.

In all the 34 cases, patients with scrub typhus presented with fever between 7 to 13 days and myalgia as the second commonest symptom seen in 52.9% of cases being the most common clinical presentations. Cough (35.2%), headache (35.2%) and

breathlessness (38.2%) were the common clinical features of scrub typhus presented by the cases. Patients may also present with other symptoms that are nonspecific and may often lead to a dilemma in diagnosis. Vomiting (29.4%), abdominal pain (23.5%) and symptoms of renal, hepatic, lung and blood were witnessed in almost all the scrub typhus cases. Other studies conducted by Sivarajan *et al*, (2016)³⁸, Narvencar *et al*, (2014)³⁹ in India also showed similar trends in the symptoms of scrub typhus. Gastrointestinal symptoms like loose stools (5.8%) were common among the patients. Eschar (8.8%), a black necrotic lesion found at the chigger attachment site in the folds of the skin is one the distinguishing clinical feature of scrub typhus mostly observed in the sample patients in the present study. These results correlated with the findings of Sarkar *et al*, (2020)⁴⁰. Pallor was observed in 35.2% of the patients which is comparable with the reports by Pathania, Amisha and Rathaur, (2019)⁴¹. Liver symptoms like hepatosplenomegaly (32.3%) was seen in the majority of the cases in the present study which correlates with the findings of Sariga, Karthik and Ratnam, (2018)⁴². Low haemoglobin count (less than 10gm/dl) or anaemic condition was seen in almost 38.2% of the cases in the present study sample followed by leukocytopenia in almost 32.3% of the cases. 32.3% patients had pleural effusion that provided evidence of pulmonary abnormalities witnessed in the sample patients. These findings when compared to previous studies by Goswami *et al*, (2013)⁴³ also showed that pulmonary involvement is there in scrub typhus disease that may lead to major complications like ARDS.

Some of the scrub typhus patients in the sample also developed complications and the most common complications found were hepatitis (32.4%), AKI (20.6%) and heart failure (23.5%) followed by MODS (23.5%), shock (17.6%), ARDS (11.4%) and meningoencephalitis (5.9%) that affected kidney, liver and heart. 29.4% of patients required organ support during the treatment in various forms like ventilation, vasopressors and haemodialysis in the present study. These findings when compared to other reports by Kumar *et al*, (2014)⁴⁴ showed that ARDS is the most common complication in scrub

typhus infection. In the present study, 53% of the patients required ICU (58.8%) had 8 to 13 days hospital stay followed by 47% patients who stayed from less than 7 days. This result is consistent with a study conducted by Premraj *et al*, (2018)⁴⁵ which showed that the mean duration for hospital stay was 7.7±3.6 days.

Limitations and Contributions

The present study was aimed at estimating the prevalence of various clinical features and complications of scrub typhus in the eastern part of India. This contributed in bridging the knowledge gap regarding differential diagnosis in scrub typhus that may reduce the chances of related complications and delay in treatment especially among children and in cases where eschar or maculopapular rash is not present. Moreover, the present research could guide the primary care physicians in preventing the potentially fatal infection, scrub typhus disease from spiralling into a serious health issue in the country. Moreover, this study may serve as guideline for the healthcare professionals for early recognition, diagnosis and treatment based on the clinical symptoms presented in the present study especially in rural regions of India where people are unaware about this disease and in absence of "gold standard" confirmatory tests to be performed in the laboratory due to lack of resources in poor settings.

The major limitation of the study is the small sample size that the results could not be generalized to other populations as the study was done in a single centre and the results may vary with respect to other regions because of the differences in the geographical regions in the prevailing serotype. The diagnosis of the patients for scrub typhus was done based only on the serologic analysis and not by culture or immunofluorescence assay (IFA) or Polymerase Chain Reaction (PCR) technique considered the "gold standard" confirmatory test for scrub typhus. Moreover, mortality risk factors could not be assessed due to lack of deceased patients and the differences in the mortality or severity or virulence difference as per serotypes or genotypes of *O. tsutsugamushi* was also not evaluated in the present study due to lack of resources. In addition, only the hospitalized patients were included in the study and the prevalence of the rickettsial diseases in the neighbouring communities were not assessed.

Table No.1: Age distribution

S.No		Variable	Frequency	Percentage
1	Age	13 - 30	07	20.6
		31 - 40	04	11.8
		41 - 50	10	29.4
		51 - 60	06	17.6
		> 60	7	20.6
		Total	34	100.0

Table No.2: Mean age distribution

S.No	Age	
1	Mean	45.88
2	STD	16.48
3	Medium	48.00
4	Minimum	15.00
5	Maximum	76

Table No.3: Sex Distribution

S.No	Variable	Patients	Percentage (%)
1	Males	19	55.9
2	Females	15	44.1
3	Total	34	100

Table No.4: Occupational distribution

S.No	Variable	Frequency	Percentage (%)
1	House wife	11	32.4
2	Farmer	04	11.8
3	Student	04	11.8
4	Office employee	07	20.6
5	Others (business man, retired per)	08	23.5
6	Total	34	100

Table No.5: District wise distribution

S.No	Ad Address	Frequency	Percentage (%)
1	Hooghly	4	11.8
2	H-Howrah	8	23.5
3	Kolkata	16	47.1
4	Medinipur	5	14.7
5	Purulia	1	2.9
6	Total	34	100.0

Table No.6: Distribution in rural vs urban area

S.No	Area	Frequency	Percentage
1	Rural	18	52.9
2	Urban	16	47.1
3	Total	34	100

Table No.7: Distribution in ward and ICU setting

S.No	ICU/ward	Frequency	Percent
1	Ward	14	41.2
2	ICU	20	58.8
3	Total	34	100.0

Table No.8: Seasonal distribution

S.No	Month	Frequency	Percentage
1	May	3	8.8
2	June	1	2.9
3	July	3	8.8
4	August	1	2.9
5	September	8	23.5
6	October	9	26.5
7	November	8	23.5
8	December	1	2.9
9	Total	34	100.0

Table No.9: Distribution of fever duration before presentation

S.No	Variable	Patients	Percentage	Mean	STD
1	Less than 7 days	03	08.8	10.79	3.59
2	7 to 13 days	20	58.8		
3	>= 14days	11	32.4		
4	Total	34	100.0		

Table No.10: Symptomatology distribution

S.No	Variable	Patients	Percentage
1	Headache	12	35.2
2	Myalgia	18	52.9
3	Cough	12	35.2
4	Breathlessness	13	38.2
5	Vomiting	10	29.4
6	Abdominal pain	08	23.5
7	Loose stools	02	05.8
8	Altered sensorium	02	05.8
9	Seizure	00	00
10	Bleeding	3	8.8
11	Urine output	06	17.6

Table No.11: Distribution of gastrointestinal symptoms

S.No	Variable	Patients	Percentage
1	Vomiting	10	29.4
2	Loose stools	02	05.8
3	Abdominal pain	08	23.5

Table No.12: Signs distribution

S.No	Variable	Patients	Percentage
1	Pallor	12	35.2
2	Icterus	04	11.7
3	Lymph node	01	2.9
4	Eschar	03	8.8

Table No.13: Distribution of hepatomegaly, splenomegaly and hepatosplenomegaly

S.No	Variable	Features	Percentage
1	Hepatomegaly	6	17.6
2	Splenomegaly	04	11.7
3	Hepatosplenomegaly	11	32.3

Table No.14: Distribution of haemoglobin, total leucocyte count and platelets

S.No	Variable	Patients	Percent
1	Haemoglobin (less than 10gm/dl)	13	38.2
2	TC (More than 10000)/mcl	11	32.3
3	Platelets(less than or equal to 1,50,000/cumm)	02	5.8

Table No.15: Distribution of renal abnormalities

S.No	Variable	Patients	Percentage
1	Reduced urine output	06	17.6
2	Urea >40	06	17.6
3	Sr creatinine (> 1.3mg/dl)	10	29.4
4	Haematuria	04	11.76
5	Proteinuria	05	14.7

Table No.16: Distribution of complications

S.No	Variable	Patient	Percentage
1	Hepatitis	11	32.4
2	AKI	07	20.6
3	MODS	08	23.5
4	ARDS	04	11.4
5	Shock	06	17.6
6	Meningoencephalitis	02	5.9
7	Heart Failure	08	23.5

Table No.17: Distribution of X-ray chest findings

S.No	Chest X-ray	Frequency	Percentage
1	Pleural effusion	11	32.3
2	Pneumonitis	05	14.7
3	Pulmonary edema	01	2.9
4	Normal study	17	50.0
5	Total	34	100.0

Table No.18: Distribution of organ support during T/T

S.No	Organ Support	Frequency	Percentage
1	No	24	70.6
2	Yes	10	29.4
3	Total	34	100.0

Table No.19: Distribution of duration of hospital admission

S.No	Hospital stay	Frequency	Percent
1	<=7	16	47.0
2	8-13	18	53
3	>=14	00	00
4	Total	34	100.0



Diagram No.1: Painless eschar: A hallmark of diagnosis of scrub typhus
(Source: Rose, 2017)⁹



Diagram No.2: Maculopapular rash on limbs, soles and trunk
(Source: Saphtharishi and Sankhyan, 2015)¹⁰

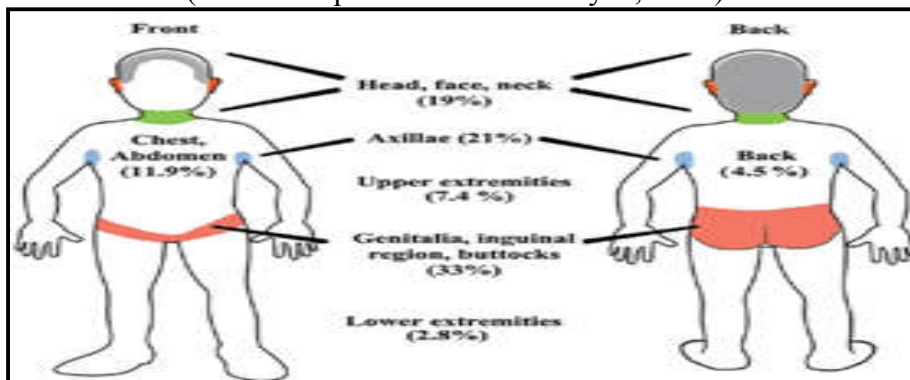


Diagram No.3: Distribution of eschar on a child's body
(Source: Rose, 2017)⁹

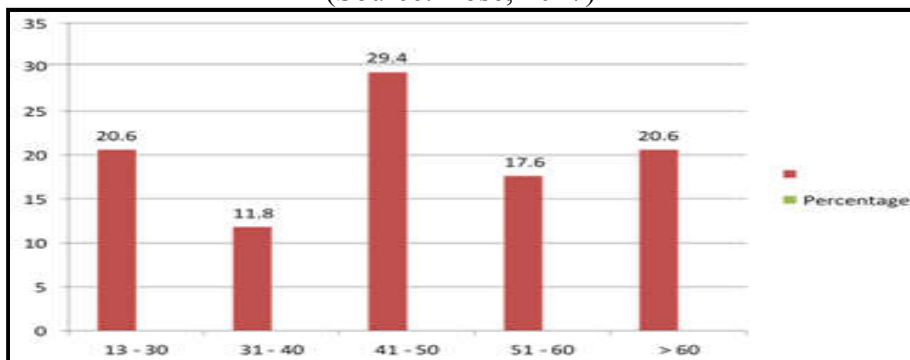


Diagram No.1: Age distribution

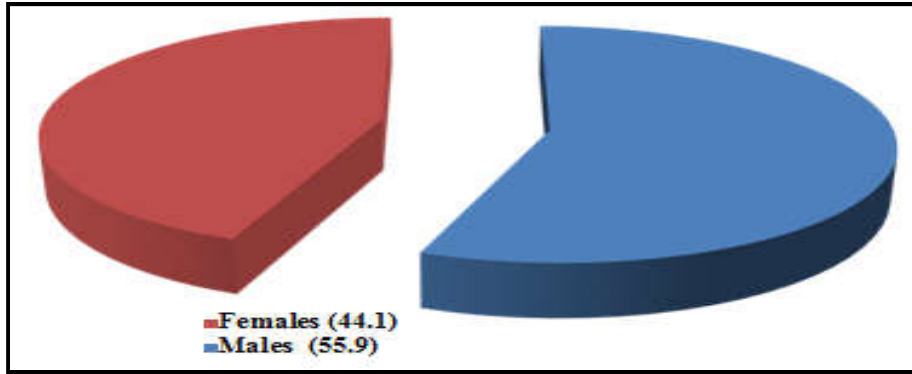


Diagram No.2: Sex distribution

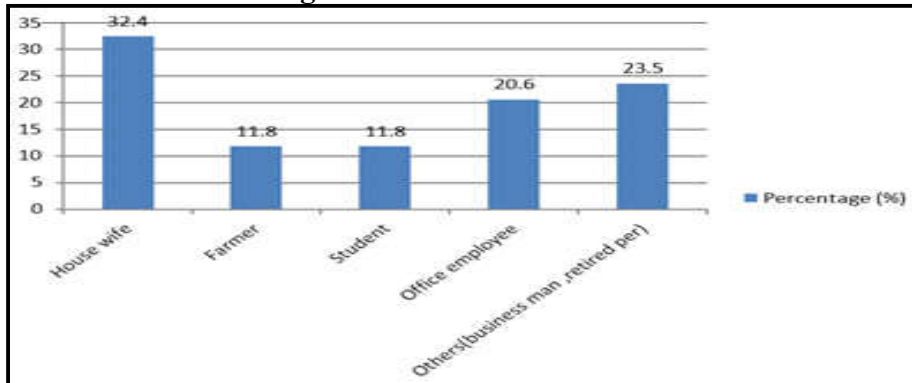


Diagram No.3: Occupational distribution

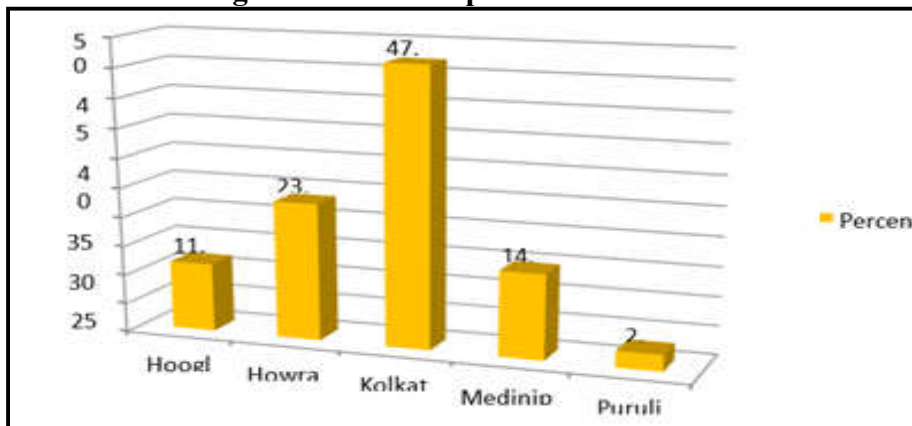


Diagram No.4: District wise distribution

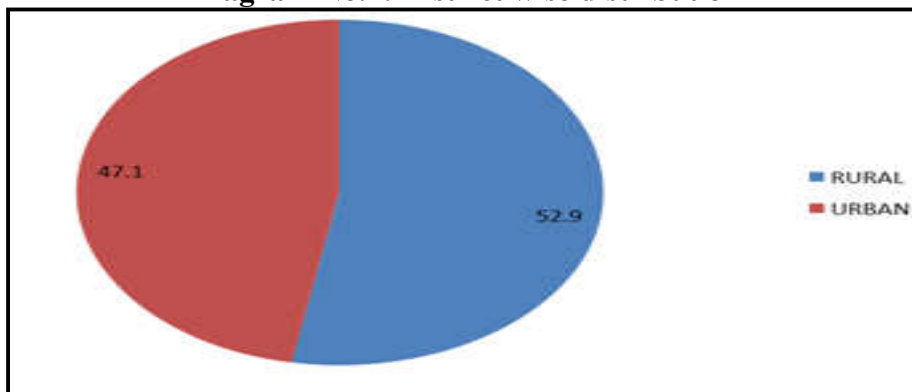


Diagram No.5: Distribution in rural vs urban area

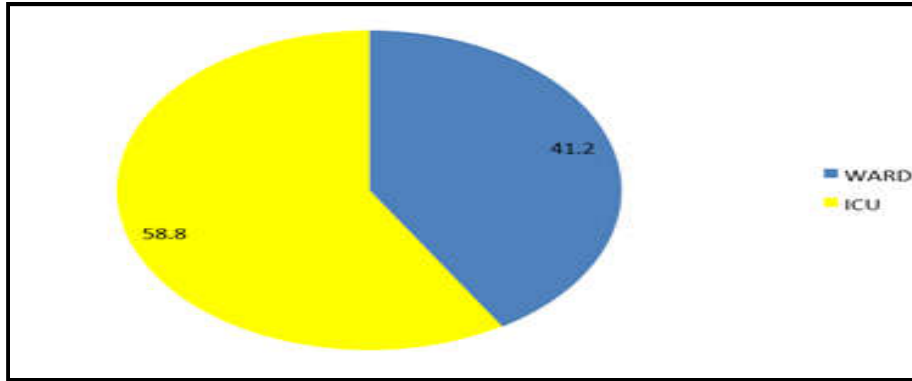


Diagram No.6: Distribution in ward and ICU setting

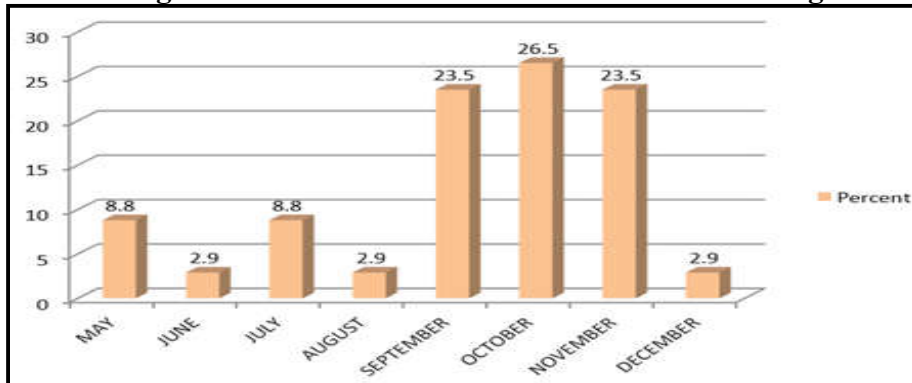


Diagram No.7: Seasonal distribution

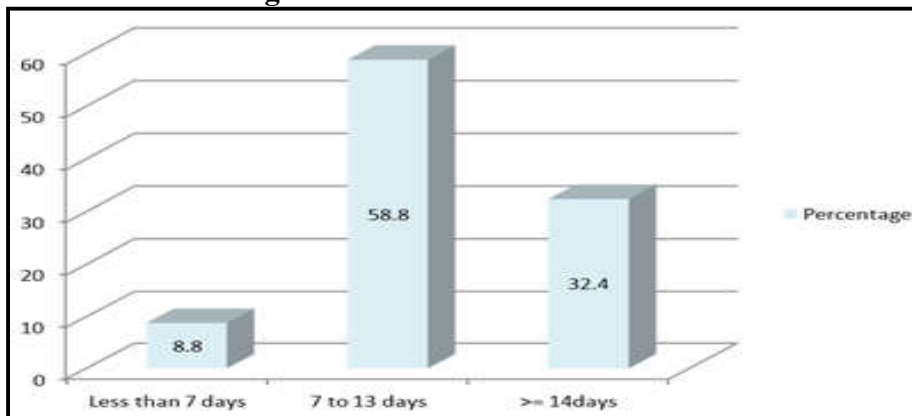


Diagram No.8: Distribution of fever duration before presentation

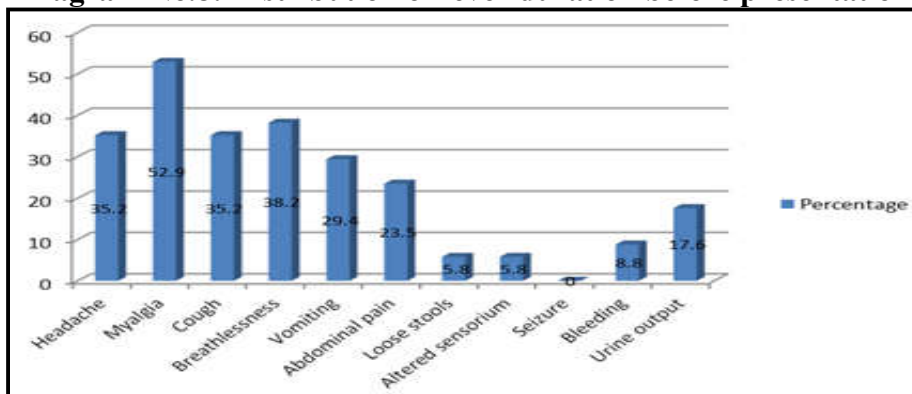


Diagram No.9: Symptomatology distribution

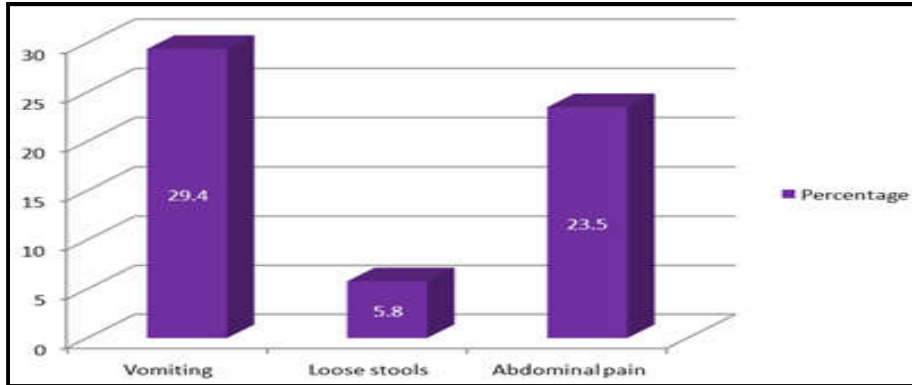


Diagram No.10: Distribution of gastrointestinal symptoms

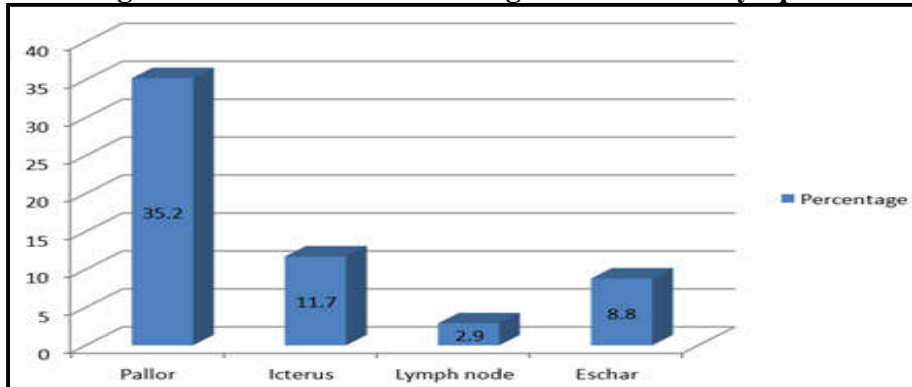


Diagram No.11: Signs distribution

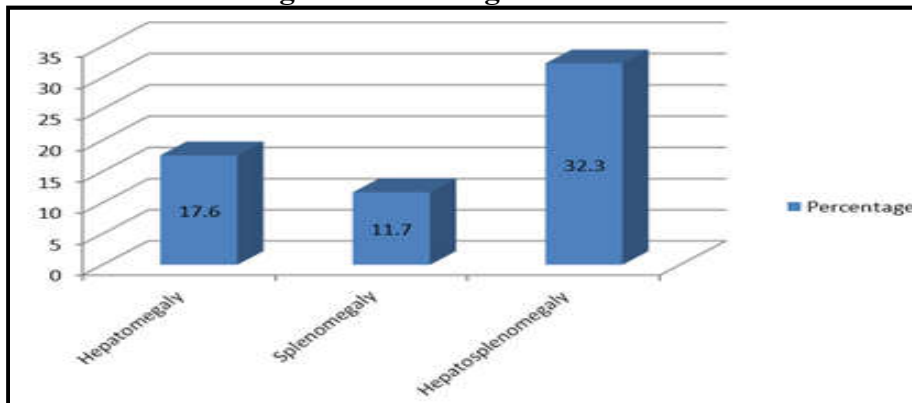


Diagram No.12: Distribution of hepatomegaly, splenomegaly and hepatosplenomegaly

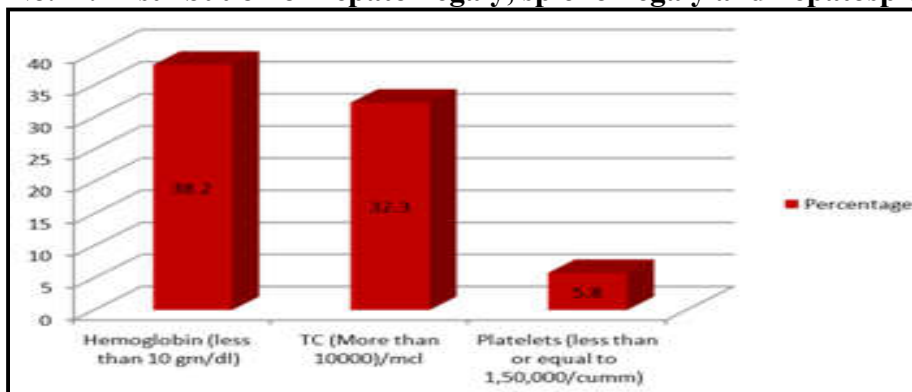


Diagram No.13: Distribution of haemoglobin, total leucocyte count and platelets

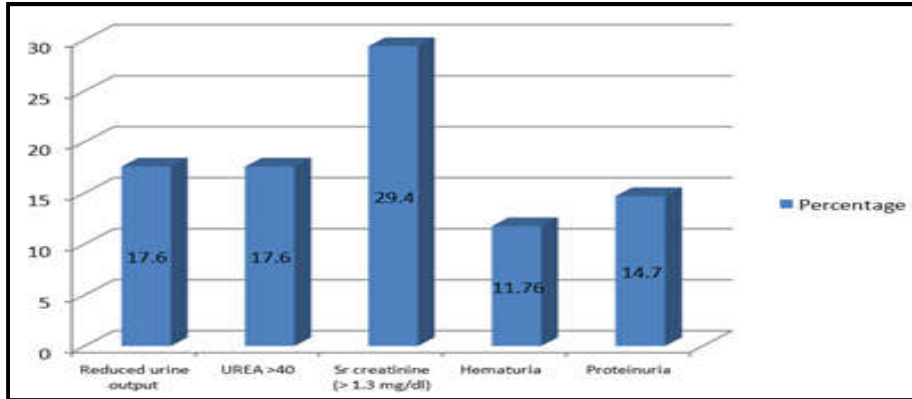


Diagram No.14: Distribution of renal abnormalities

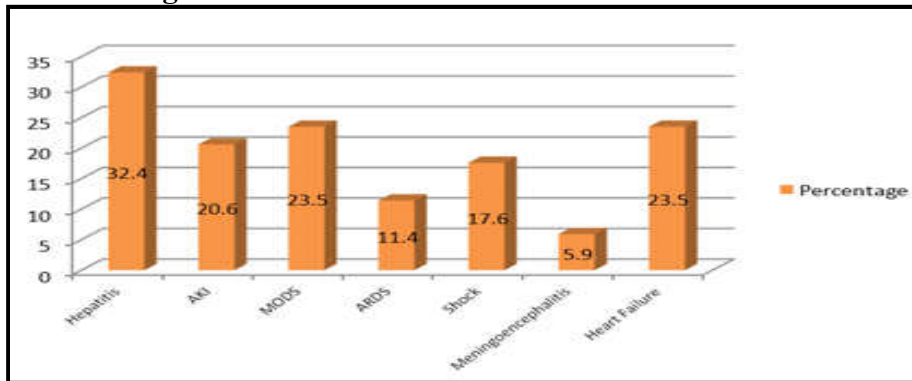


Diagram No.15: Distribution of complications

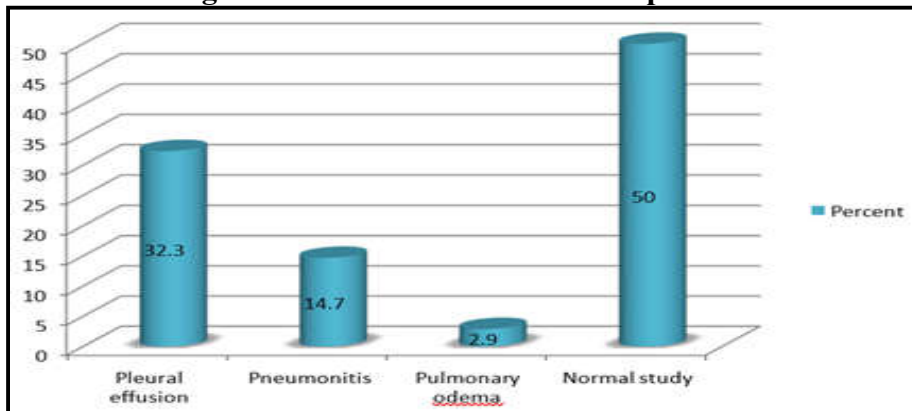


Diagram No.16: Distribution of X-ray chest findings

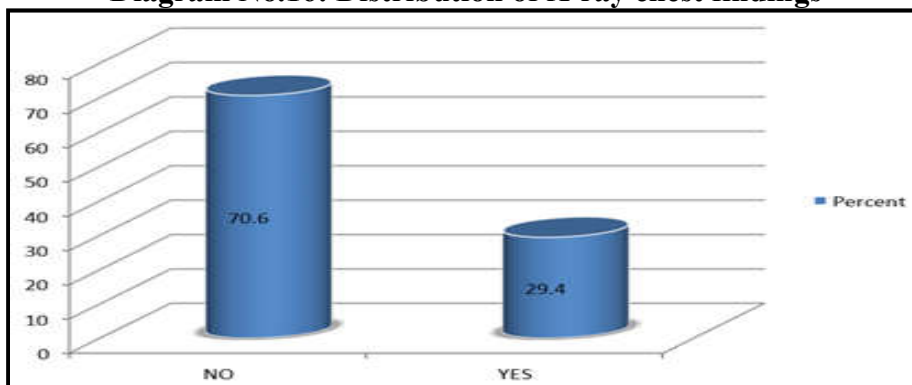


Diagram No.17: Distribution of organ support during T/T

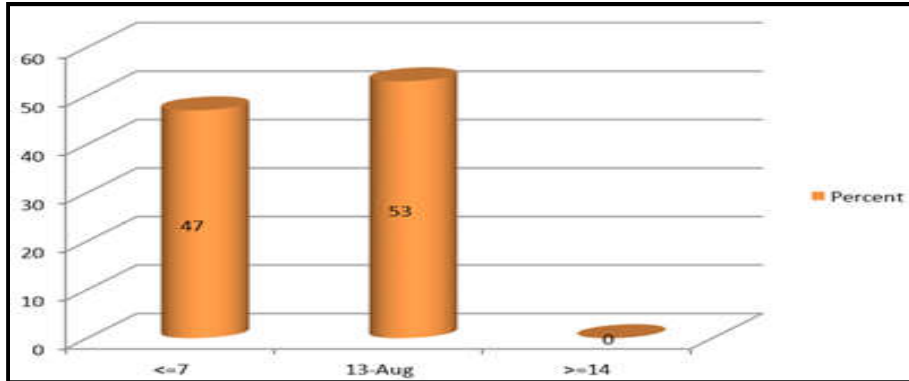


Diagram No.18: Distribution of duration of hospital admission

CONCLUSION

The present study illustrated that scrub typhus is a re-emerging disease whose cases are reported from all regions of India especially in eastern and north-eastern parts of India. West Bengal is an endemic zone where cases have been reported in the last few years with varied presentations. People residing in hilly areas and working in agricultural farms and collecting wood are mostly affected by the scrub typhus disease as they are involved in outdoor activities for most of their time. Children get infected with scrub typhus disease where they get high-grade fever and non-specific symptoms like muscle pain, rash, headache, abdominal pain and lymph node enlargement. The cases clustered were mostly after the monsoon period i.e., post-monsoon period and surge of cases during the cooler months of the year from September to December. Clinically, scrub typhus mimics malaria, dengue fever as they all are presented with fever, thrombocytopenia and mild hepatitis and are also present in locations that are co-endemic with these diseases. Due to overlapping presentations with other diseases and varied presentations, scrub typhus required a high degree of suspicion. In addition, clinical suspicion could also be absent or delayed due to lack of knowledge about the disease and the diagnostic features available. Lack of proper diagnostic procedures and techniques further delays the starting treatment especially in poor-income settings like India. This may be due to the fact that the Weil-Felix test is the only diagnostic test available in the most affected regions of rural India. These deficiencies in diagnostic techniques result in primary care physicians relying solely on

their clinical suspicion in starting the treatment and this increases the burden of the disease in endemic regions especially in India. These factors contribute to the under-diagnosis of scrub typhus in India. Therefore, prompt empirical therapy along with clinical suspicion by primary care physicians may help to prevent the mortality from this disease.

From the above discussion, it can be recommended that a better outlook of the epidemiology and clinical features of scrub typhus would help to prevent as well as control the spread of the disease. Individuals and children presented with fever (acute undifferentiated febrile illness in children) for more than five days should be considered for differential diagnosis especially in cases, if the scrub typhus disease have been reported from that region or endemic in nature. The presence of black painless lesions, eschar present at the chigger entry on the skin should be considered as a distinguishing pointer to the differential diagnosis for scrub typhus. As the disease responds to antibiotics quite well, it is recommended that empirical Azithromycin or Doxycycline should be started as early treatment within 48 hours to prevent morbidity and mortality. It is also recommended that people working in agricultural farms in mite infested areas should use mite repellents and have adequate protective clothing. An eschar should not be missed as it is a pathognomonic sign of scrub typhus disease. Awareness should be created among the people dwelling in hilly areas or involved in farming especially regions endemic to this infection about the scrub typhus disease and its distinguishing clinical symptoms so that proper precautions are taken and

there is no delay in treatment. Timely recognition of symptoms and complications in preventing the adverse outcomes of the scrub typhus disease. IFA should be made available as it is the "gold standard" confirmatory test for this disease. Furthermore, large multi-centred population studies are required to be generalized to other regions.

ACKNOWLEDGEMENT

Special acknowledgement to the doctors and staffs of Critical Care Unit of CK Birla Hospitals, Kolkata, Dr. P.K. Nemani, Academic Advisor, CK Birla Hospitals, Kolkata, and Prof. Dr. Bibhuti Saha, HOD, Tropical Medicine, Kolkata and Consultant, Infectious Diseases, CK Birla Hospitals, Kolkata India for their continuous support and encouragement.

FINANCIAL SUPPORT AND SPONSORSHIP

Sri Sarosij Ray Memorial Research Support Fund.

CONFLICTS OF INTEREST

There are no conflicts of interest.

BIBLIOGRAPHY

1. Peter J V, Sudarsan T I, Varghese G M. Severe scrub typhus infection: Clinical features, diagnostic challenges and management, *World Journal of Critical Care Medicine*, 4(3), 2015, 244-250.
2. Luce-Fedrow A, Lehman M L, Kelly D J, Mullins K, Maina A N, Stewart R L. A review of scrub typhus (*Orientia tsutsugamushi* and related organisms): Then, now, and tomorrow, *Tropical Medicine and Infectious Diseases*, 3(1), 2018, 8.
3. Bonell A, Lubell Y, Newton P N, Crump J A. Estimating the burden of scrub typhus: A systematic review, *PLoS Neglected Tropical Diseases*, 11(9), 2017, e0005838.
4. Nallasamy K, Gupta S, Bansal A. Clinical profile and predictors of intensive care unit admission in pediatric scrub typhus: A retrospective observational study from North India, *Indian Journal of Critical Care Medicine: Peer-reviewed, Official Publication of Indian Society of Critical Care Medicine*, 24(6), 2020, 445-450.
5. Chakraborty S, Sarma N. Scrub typhus: An emerging threat, *Indian Journal of Dermatology*, 62(5), 2017, 478-485.
6. Khan F, Mittal G, Agarwal R K, Ahmad S, Gupta S, Shadab M. Prevalence of scrub typhus-A cause of concern in Uttarakhand Region, India, *Int J Curr Microbiol App Sci*, 1, 2015, 101-109.
7. Saluja M, Vimlani H, Chittora S, Sen P, Suman C, Galav V, Meena D. Scrub typhus: Epidemiology, clinical presentation, diagnostic approach and outcomes, *Journal, Indian Academy of Clinical Medicine*, 20(1), 2019, 15-22.
8. Kundavaram A P, Jonathan A J, Nathaniel S D, Varghese G M. Eschar in scrub typhus: A valuable clue to the diagnosis, *Journal of Postgraduate Medicine*, 59(3), 2013, 177-178.
9. Rose W. Scrub typhus in children, *Current Medical Issues*, 15(2), 2017, 90-94.
10. Saptharishi L G, Sankhyan N. Scrub typhus in children-from hills to plains, *Peepee Publishers and Distributors (P) Ltd*, 2015, 96-101.
11. Sapkota S, Bhandari S, Sapkota S, Hamal R. Dengue and scrub typhus coinfection in a patient presenting with febrile illness, *Case Reports in Infectious Diseases*, 2017, Article ID: 6214083, 2017, 3.
12. Bhat N K, Dhar M, Mittal G, Shirazi N, Rawat A, Kalra B P, Ahmad S. Scrub typhus in children at a tertiary hospital in north India: Clinical profile and complications, *Iranian Journal of Pediatrics*, 24(4), 2014, 387-392.
13. Rapsang A G, Bhattacharyya P. Scrub typhus, *Indian Journal of Anaesthesia*, 57(2), 2013, 127-134.
14. Chunchanur S K. Scrub typhus in India-an impending threat, *Ann Clin Immunol Microbiol*, 1(1), 2018, 1-3.
15. Khan S A, Dutta P, Khan A M, Topno R, Borah J, Chowdhury P, Mahanta J. Re-emergence of scrub typhus in northeast India, *International Journal of Infectious Diseases*, 16(12), 2012, e889-e890.

16. Das P, Singh D, Das M, Nayak R K, Mohakud N K. Epidemiological and clinical features of scrub typhus in Odisha, Eastern India, *Medical Journal of Dr. DY Patil Vidyapeeth*, 12(5), 2019, 419-423.
17. Varghese G M, Raj D, Francis M R, Sarkar R, Trowbridge P, Muliyl J. Epidemiology and risk factors of scrub typhus in south India, *The Indian Journal of Medical Research*, 144(1), 2016, 76-81.
18. Digra S K, Saini G S, Singh V, Sharma S D, Kaul R. Scrub typhus in children: Jammu experience, *Jk Science*, 12(2), 2010, 95-97.
19. Thomas R, Puranik P, Kalal B, Britto C, Kamalesh S, Rego S, Shet A. Five-year analysis of rickettsial fevers in children in South India: Clinical manifestations and complications, *The Journal of Infection in Developing Countries*, 10(06), 2016, 657-661.
20. Mohanty L, Dhanawat A, Gupta P, Maheshwari G. Clinical manifestations and associated complications of scrub typhus in Odisha, India, *Journal of Clinical and Diagnostic Research*, 14(8), 2020, 14-18.
21. Dass R, Deka N M, Duwarah S G, Barman H, Hoque R, Mili D, Barthakur D. Characteristics of pediatric scrub typhus during an outbreak in the North Eastern region of India: peculiarities in clinical presentation, laboratory findings and complications, *The Indian Journal of Pediatrics*, 78(11), 2011, 1365-1370.
22. Kalal B S, Puranik P, Nagaraj S, Rego S, Shet A. Scrub typhus and spotted fever among hospitalised children in South India: Clinical profile and serological epidemiology, *Indian Journal of Medical Microbiology*, 34(3), 2016, 293-298.
23. Balaji J, Punitha P, Babu B R, Kumaravel K S. A study on clinical profile, complications and outcome of scrub typhus in south Indian children, *International Journal of Contemporary Pediatrics*, 4(3), 2017, 848-852.
24. Bhat N K, Pandita N, Saini M, Dhar M, Ahmed S, Shirazi N, Chandar V. Scrub typhus: A clinico-laboratory differentiation of children with and without meningitis, *Journal of Tropical Pediatrics*, 62(3), 2016, 194-199.
25. Williams V, Menon N, Bhatia P, Biswal M, Sreedharanunni S, Jayashree M, Nallasamy K. Hyperferritinemia in children hospitalized with scrub typhus, *Tropical Medicine and Health*, 49(1), 2021, 1-8.
26. Bal M, Mohanta M P, Sahu S, Dwibedi B, Pati S, Ranjit M. Profile of pediatric scrub typhus in Odisha, India, *Indian Pediatrics*, 56(4), 2019, 304-306.
27. Pathak S, Chaudhary N, Dhakal P, Shakya D, Dhungel P, Neupane G, Kurmi O P. Clinical profile, complications and outcome of scrub typhus in children: A hospital based observational study in central Nepal, *PLoS One*, 14(8), 2019, e0220905.
28. Kim D M, Won K J, Park C Y, Yu K D, Kim H S, Yang T Y, Shin H. Distribution of eschars on the body of scrub typhus patients: A prospective study, *The American Journal of Tropical Medicine and Hygiene*, 76(5), 2007, 806-809.
29. Misra U K, Kalita J, Mani V E. Neurological manifestations of scrub typhus, *Journal of Neurology, Neurosurgery and Psychiatry*, 86(7), 2015, 761-766.
30. Vikrant S, Dheer S K, Parashar A, Gupta D, Thakur S, Sharma A, Kanga A. Scrub typhus associated acute kidney injury-a study from a tertiary care hospital from western Himalayan State of India, *Renal Failure*, 35(10), 2013, 1338-1343.
31. Venkategowda P M, Rao S M, Mutkule D P, Rao M V, Taggu A N. Scrub typhus: Clinical spectrum and outcome, *Indian Journal of Critical Care Medicine: Peer-Reviewed, Official Publication of Indian Society of Critical Care Medicine*, 19(4), 2015, 208-213.
32. Wangrangsimakul T, Greer R C, Chanta C, Nedsuwan S, Blacksell S D, Day N P, Paris D H. Clinical characteristics and outcome of children hospitalized with scrub typhus in an area of endemicity, *Journal of the Pediatric Infectious Diseases Society*, 9(2), 2020, 202-209.

33. Jyothi R, Sahira H, Sathyabhama M C, Bai J R. Seroprevalence of scrub typhus among febrile patients in a tertiary care hospital in Thiruvananthapuram, Kerala, *J Acad Ind Res*, 3(11), 2015, 542-545.
34. Subbalaxmi M V, Madisetty M K, Prasad A K, Teja V D, Swaroopa K, Chandra N, Raju Y S. Outbreak of scrub typhus in Andhra Pradesh-experience at a tertiary care hospital, *J Assoc Physicians India*, 62(6), 2014, 490-496.
35. Trowbridge P, Premkumar P S, Varghese G M. Prevalence and risk factors for scrub typhus in South India, *Tropical Medicine and International Health*, 22(5), 2017, 576-582.
36. Sethi S, Prasad A, Biswal M, Hallur V K, Mewara A, Gupta N, Sharma K. Outbreak of scrub typhus in North India: A re-emerging epidemic, *Tropical Doctor*, 44(3), 2014, 156-159.
37. Rungta N. Scrub typhus: Emerging cause of multiorgan dysfunction, *Indian journal of Critical Care Medicine: Peer-Reviewed, Official Publication of Indian Society of Critical Care Medicine*, 18(8), 2014, 489-491.
38. Sivarajan S, Shivalli S, Bhuyan D, Mawlong M, Barman R. Clinical and paraclinical profile, and predictors of outcome in 90 cases of scrub typhus, Meghalaya, India, *Infectious Diseases of Poverty*, 5(1), 2016, 1-10.
39. Narvencar K P, Rodrigues S, Nevrekar R P, Dias L, Dias A, Vaz M, Gomes E. Scrub typhus in patients reporting with acute febrile illness at a tertiary health care institution in Goa, *The Indian Journal of Medical Research*, 136(6), 2012, 1020-1024.
40. Sarkar K, Acharyya A, Ghosh S, Ghosh M, Bhattacharya A, Ghosh K. Clinical manifestation and complications of scrub typhus cases: A hospital-based observational study from rural part of West Bengal, *International Journal of Medicine and Public Heal*, 10(4), 2020, 180-183.
41. Pathania M, Amisha P M, Rathaur V K. Scrub typhus: Overview of demographic variables, clinical profile, and diagnostic issues in the sub-Himalayan region of India and its comparison to other Indian and Asian studies, *Journal of Family Medicine and Primary Care*, 8(3), 2019, 1189-1195.
42. Sariga I, Karthik S S, Ratnam P V J. Clinical and demographic study of scrub typhus in a tertiary care teaching hospital in Puducherry during 2015-2018, *International Journal of Research in Medical Sciences*, 6(11), 2018, 3534-3537.
43. Goswami D, Hing A, Das A, Lyngdoh M. Scrub typhus complicated by acute respiratory distress syndrome and acute liver failure: A case report from Northeast India, *International Journal of Infectious Diseases*, 17(8), 2013, e644-e645.
44. Kumar V, Kumar V, Yadav A K, Iyengar S, Bhalla A, Sharma N, Jha V. Scrub typhus is an under-recognized cause of acute febrile illness with acute kidney injury in India. *PLoS Negl Trop Dis*, 8(1), 2014, e2605.
45. Premraj S S, Mayilanthi K, Krishnan D, Padmanabhan K, Rajasekaran D. Clinical profile and risk factors associated with severe scrub typhus infection among non-ICU patients in semi-urban south India, *Journal of Vector Borne Diseases*, 55(1), 2018, 47-51.

Please cite this article in press as: Sujoy Mukherjee *et al.* Study of clinical characteristics of patients of scrub typhus in multi speciality hospital in eastern India of age group more than 13 yrs: An epidemiological cross-sectional study, *International Journal of Medicine and Health Profession Research*, 8(2), 2021, 141-162.