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# SCRUB TYPHUS IN CHILDREN: A RETROSPECTIVE STUDY IN A TERTIARY CARE HOSPITAL OF RURAL WEST BENGAL, INDIA

Pediatrics

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## ABSTRACT

Scrub typhus is an emerging acute undifferentiated febrile illness (AUFI) among children, particularly in rural West Bengal. Due to the lack of gold standard diagnostic tests, and lack of awareness among healthcare personnel, it leads to delay in diagnosis and specific treatment which leads to several complications and even death. In this perspective, with the hope to know better, this study was done to evaluate clinical features, complications, laboratory profiles and outcome of scrub typhus in the paediatric population.

**AIMS AND OBJECTIVES:** To study clinical features, complications, laboratory profiles and outcomes of scrub typhus in children.

**MATERIAL AND METHODS:** This retrospective study was conducted in the Department of Paediatrics of Bankura Sammilani Medical College and Hospital (BSMCH), Bankura, India. Data of 75 children who were found to be IgM positive to *Orientia tsutsugamushi*, aged one month to 12 years were collected from the case register maintained in our unit from June 2020 to August 2021 and were analysed by Epi Info, version 3.5.1, software.

**RESULTS:** Fever was the most common presenting symptoms seen in 100% (n=75) of cases. Other common signs and symptoms were vomiting (n=22,29.3%), pain abdomen (n=15,20%), cough(n=22,29.3%), myalgia (n=12,16%), headache (n=12,16%), convulsions (n=8,10.7%), pallor (n=25,33.3%), facial puffiness (n=28,37.3%), oedema (n=12,16%), eschar (n=20,26.7%), hepatomegaly (n=45,60%) and splenomegaly (n=42,56%). Among laboratory parameters, anaemia (n=72,96%), leucocytosis (n=31,41.3%), thrombocytopenia (n=43,57.3%), raised alanine aminotransferase (n=49,65.3%), aspartate aminotransferase (n=46,61.3%) and hypoalbuminemia (n=31,41.3%) were observed. Meningoencephalitis was present in 10.7% (n=8) of cases.

**CONCLUSION:** A high index of suspicion and abnormal laboratory findings will help physicians in the timely diagnosis of scrub typhus and initiate anti-scrub treatment early, thereby preventing complications and minimising fatality.

## KEYWORDS

Scrub typhus, children, undifferentiated, complication.

## INTRODUCTION:

Scrub typhus is an emerging acute undifferentiated febrile illness (AUFI) with high morbidity and mortality reported from different parts of India including West Bengal [1,2,3,4]. There are a handful of studies on scrub typhus from West Bengal, most of which are on the adult population residing in the northern and southernmost part of Bengal. No such literature on scrub typhus either in adults or in children was found from the western region of West Bengal. It was also observed that a large number of children with scrub typhus and its several complications had been admitted to the Department of Paediatrics, BSMCH, Bankura, West Bengal, India over the last 3 – 4 years.

Scrub typhus is caused by *Orientia* (formerly Rickettsia) *tsutsugamushi*, an obligate intracellular, gram-negative Cocco-bacilli belonging to family Rickettsiae [5,6]. It was first described in Japan in 1899 [7]. Now it is endemic in a zone depicted by a triangle bounded by Japan to the north, Northern Australia to the south and the Arabian Peninsula to the west [8]. Scrub typhus is a zoonotic disease and human is the accidental host. It is transmitted to humans by the bite of an infected "chigger" larval stages of trombiculide mites [9]. Following the bite, the bacteria multiply at the site of inoculation with the formation of papules that ulcerate and become necrotic evolving into an eschar which is commonly found on the groin, axilla and neck where skin folds meet [7,10]. Following the entry into the bloodstream, the bacteria invade the endothelial cell leading to perivascular inflammatory lesions and disseminated vasculitis which in turn leads to micro vascular leakage, tissue hypoperfusion, oedema and ensuing end-organ ischemic injury [11,12] and associated with haematological and biochemical changes [13].

After an incubation period of 10-12 days [13], the clinical features such as fever, malaise, headache and eschar may develop [12,14]. The most common clinical features in children are fever, headache and vomiting, abdominal pain, shortness of breath, hepatosplenomegaly, generalised swelling, maculopapular rash and lymphadenopathy [2,15]Although eschar is considered to be the pathognomic sign of scrub typhus, it is found only in 8- 41% of cases [11,15] and is frequently missed if not looked into carefully. The absence of specific signs and symptoms makes it very difficult to diagnose early but if not diagnosed in time and treated quickly, the bacteria can spread systemically and cause several complications like interstitial pneumonia, myocardial damage, hepatitis, meningoencephalitis, ARDS and multi-organ failure and even death [14,16].

In presence of diverse clinical features of scrub typhus mimicking signs and symptoms of typhoid fever, malaria, dengue and leptospirosis [17] and lack of gold standard Immunofluorescence (IFA) test, the diagnosis is usually confirmed by ELISA test which captures IgM antibody of O. tsutsugamushi. Though there is a plentiful supply of antibiotics against O. tsutsugamushi in our country, due to the non-availability of ELISA tests in all health care facilities and lack of awareness among primary care physicians (PCP) and even paediatricians, it leads to delay in diagnosis and specific treatment which in turn leads to fatal complications. In all resource-limited countries like India, a high index of suspicion and some routine investigations such as complete blood count, liver and renal function test and serum electrolytes; will definitely help PCP and paediatricians working in rural as well as urban areas to arrive at a diagnosis early and to administer anti-scrub treatment in time. In this perspective, with the hope to know better, we intended to do this retrospective study to evaluate clinical features, complications, laboratory profiles and outcome of scrub typhus in children.

## AIMS AND OBJECTIVES:

To study clinical features, complications laboratory profiles and outcome of Scrub typhus in children.

## MATERIAL AND METHODS:

This retrospective observational study was conducted in the Department of Paediatrics, BSMCH, Bankura, West Bengal, India. All relevant data about patient's age, gender, residency, clinical features, laboratory parameters, complications and outcome of seventy-five (75) children aged one month to twelve (12) years who

were found to be IgM positive for O. tsutsugamushi and were admitted in our unit in both general paediatrics ward and paediatric intensive care unit (PICU) during the period from June 2020 to August 2021, were collected from the case-based register using predesigned proforma. Apart from ELISA for scrub typhus, complete blood count (CBC), C-reactive protein (CRP), liver function test (LFT), renal function test (RFT), serum electrolytes and urinalysis were done. To rule out malaria, dengue and typhoid fever; malaria parasite double antigen (MPDA), ELISA and Widal test were done respectively. Other investigations such as tests for cardiac evaluation, cerebrospinal fluid analysis, and test for coagulation profiles were performed when indicated. Imaging studies like chest X-ray, ultrasonography (USG), computed tomography (CT) and magnetic resonance imaging (MRI) were also done when indicated. Epi Info (version 3.5.1) software was used for statistical analysis. Numerical data were calculated as mean and standard deviation and categorical data as a percentage, ratio and proportion. A comparative study between laboratory parameters and duration of fever has been made by one away ANOVA statistical method. P-value of 0.05 was set as statistically significant.

## RESULTS:

Demography (Table -1): Data from 75 children aged one month to 12 years were analysed. Out of 75, forty-four (44) children were male and the rest thirty-one (31) were female. The male-female ratio was 1.42:1. The mean age of presentation was 4.82±3.72 years with a minimum of 45 days and a maximum of 11.92 years of age. 94.7% (n=71) of our study sample had come from rural areas and the rest 5.3% (n=4] were from urban. In our study, Scrub typhus showed seasonal variation occurring between June to December.

**Table – 1: Shows age, gender and residential characters**

| Demography | Male | Female | Total (%) |
|---|---|---|---|
| **Age** | | | |
| **1 month – 12 years** | **44** | **31** | **75 (100)** |
| 1 month -1 year | 6 | 8 | 14 (18.7) |
| >1 year – 5 years | 15 | 9 | 24 (32) |
| >5 years – 10 years | 16 | 6 | 22 (29.3 |
| >10 years | 6 | 9 | 15 (20) |
| **Residency** | | | |
| Rural | 42 | 29 | 71(94.7) |
| Urban | 3 | 1 | 4 (5.3) |

**Clinical symptoms (Table-2):** Most common presenting symptom was fever observed in 100% (n-75) of cases. Vomiting (n=20, 26.7%), pain abdomen (n=15, 20%), cough, headache and myalgia (n=12, 16% each), shortness of breath (n=7, 9.3%) and convulsions (n=8, 10.7%) were others common presenting symptoms. History of bleeding manifestations like haematuria (n=2, 2.7%), hematemesis and melena (n=1, 1.3% each) were also observed.

**Table – 2: Shows clinical symptoms at the time of presentation**

| Symptoms | Number | Percentages (%) |
|---|---|---|
| **Fever** | **75** | **100** |
| ≤ 7 days | 27 | 36 |
| 7-14 days | 42 | 56 |
| 15-21 days | 6 | 8 |
| **Gastrointestinal system** | **41** | **54.7** |
| Vomiting | 22 | 29.3 |
| Pain abdomen | 15 | 20 |
| Loose stool | 4 | 5.3 |
| Hematemesis | 1 | 1.3 |
| Melena | 1 | 1.3 |
| **Respiratory system** | **29** | **38.7** |
| Cough | 22 | 29.3 |
| Shortness of breath | 7 | 9.3 |
| **Central nervous system** | **26** | **34.7** |
| Headache | 12 | 16 |
| Altered sensorium | 6 | 8 |
| Convulsion | 8 | 10.7 |
| **Renal system** | | |
| Decrease urine | 3 | 4 |
| Haematuria | 2 | 2.7 |
| **Musculoskeletal symptoms** | | |
| Myalgia | 12 | 16 |
| **Ophthalmological symptom** | | |
| Photophobia | 3 | 4 |

Clinical signs (Table-3): Upon clinical examination hepatomegaly, splenomegaly and hepatosplenomegaly were found to be present in 60% (n=45), 56% (n=42) and 48% (n=36) of cases respectively. In our present study, pallor and lymphadenopathy were seen in 33.3% (n=25) and 8% (n=6) of children respectively. Third spacing such as facial puffiness, oedema, ascites, pleural and pericardial effusion were also present in 37.3% (n=28), 16% (n=12), 5.3% (n=4), 2.7% (n=2) and 1.3% (n=1) of cases respectively. Eschar, the diagnostic clinical sign of scrub typhus was present in 26.7% (n=25) of cases only. Conjunctival congestion and meningeal signs were present in 5.3% (n=4) and 4% (n=3) of the children respectively. Signs of bleeding manifestations such as petechial and ecchymotic skin lesions (n=1, 1.3% each) were also observed in our study.

**Table – 3: Shows clinical signs at the time of presentation**

| Clinical signs | Number | Percentages (%) |
|---|---|---|
| Pallor | 25 | 33.3 |
| Lymphadenopathy | 6 | 8 |
| **Third spacing** | 43 | 57.3 |
| Facial puffiness | 28 | 37.3 |
| Oedema (pedal) | 12 | 16 |
| Ascites | 4 | 5.3 |
| Pleural effusion | 2 | 2.7 |
| Pericardial effusion | 1 | 1.3 |
| Skin lesion | | |
| Eschar | 20 | 26.7 |
| Maculopapular rash | 12 | 16 |
| Petechiae | 1 | 1.3 |
| Ecchymosis | 1 | 1.3 |
| Organomegaly | | |
| Hepatomegaly | 45 | 60 |
| Splenomegaly | 42 | 56 |
| Hepatosplenomegaly | 36 | 48 |
| Meningeal sign | 3 | 4 |
| Conjunctival congestion | 4 | 5.3 |

**Laboratory profiles (Table-4):**

Anaemia ( 11gm/dl) was found in 92% (n=72) of cases, of which, 12% (n=9) patients had haemoglobin level less than 7 gm% . Microcytosis ( 70 fl.) was seen in 16% (n=12) of cases. Leucocytosis was found to be present in 41.3% (n=31) of children. 57.3% (n=43) children had thrombocytopenia (platelets count 1.5×105/mm3). Of which, 2.7% (n=2) children had platelets count 50000/mm3. Erythrocyte sedimentation rate in 1st hour was raised ( 20mm) in 18.7% (n=14) of cases and CRP was found to be positive in 73.3% (n=22) child. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were raised (>45 U/L) in 65.3 % (n=49) and 61.3% (n=46) of cases respectively. No bilirubin level was found to be high above 1mg/dl in any cases of our study sample. Hypoproteinaemia (<5gm/dl) and hypoalbuminemia (<3.5gm/dl) were found in 26.3% (n=20) and 43.3% (n=31) of cases respectively. Renal parameters such as urea and creatinine level were within normal limits (urea - <40mg/l, creatinine – 1mg/dl) in all cases

**Table- 4: Shows changes in haematological and biochemical parameter**

| Laboratory parameter | Total number†(n/N) | Percentages |
|---|---|---|
| Anaemia (<11gm/dl) | **72/75** | **96.0** |
| 9-<11(mild) | 19/75 | 25.3 |
| 7-<9 (moderate) | 44/75 | 58.7 |
| <7 (severe) | 9/75 | 12.0 |
| Leucocytosis (>11× $10^3$/$mm^3$) | 31/75 | 41.3 |
| Thrombocytopenia ( <1.5×$10^5$/$mm^3$) | **43/75** | **57.3** |
| ≥1.0 - <1.5 | 20/75 | 26.7 |
| ≥0.5 - <1.0 | 21/75 | 28.0 |
| <0.5 | 2/75 | 2.7 |
| MCV*(<70 fl.) | 12/75 | 16.0 |
| CRP* (>6mg/L) | 22/30 | 73.3 |
| ESR* (>20mm in 1st hour) | 14/26 | 18.7 |
| ALT* (**>45**U/L) | **49/75** | **65.3** |
| AST* (**>45**U/L) | **46/75** | **61.3** |
| Hypoproteinemia ( <5 gram/dl) | 20/75 | 26.7 |
| Hypoalbuminemia (<3.5 gram/dl) | **31/75** | **41.3** |

*MCV- mean corpuscular volume, ESR- erythrocyte sedimentation rate, CRP- c-reactive protein, ALT – alanine aminotransferase and AST- aspartate aminotransferase. †n= number of the sample shows abnormal findings, N= number of sample tested.

A comparative analysis between laboratory parameters and duration of fever (Table-5) was done and anaemia, thrombocytopenia and hypoalbuminemia were found to be significant statistically ((P<0.05).

**Table – 5: Shows a comparative analysis between duration fever and different haematological and biochemical parameters.**

| Laboratory parameter/Fever | <7 days | 7-14 days | >14 days | F value | P-value |
|---|---|---|---|---|---|
| Hb% (gm/dl), mean | 9.79 | 8.66 | 8.40 | 6.467 | 0.003 |
| *RBC ($\times10^6$/mm$^3$), mean | 4.23 | 3.98 | 3.64 | 3.024 | 0.054 |
| *WBC ($\times10^3$/mm$^3$), mean | 10.94 | 12.00 | 13.23 | 0.575 | 0.475 |
| Platelets ($\times10^5$/mm$^3$), mean | 1.95 | 1.29 | 0.93 | 5.665 | 0.005 |
| *ALT(U/L), mean | 66.03 | 69.69 | 79.88 | 0.203 | 0.817 |
| *AST(U/L), mean | 56.22 | 63.83 | 72.50 | 0.816 | 0.446 |
| Total protein (gm/dl), mean | 5.72 | 5.69 | 5.15 | 0.833 | 0.439 |
| Albumin (gm/dl), mean | 3.77 | 3.28 | 3.10 | 7.190 | 0.014 |

*RBC- red blood corpuscles, WBC- white blood corpuscles, ALT – alanine aminotransferase and AST- aspartate aminotransferase.

**Complications (Table -6):** Anicteric hepatitis was the most common (n=49, 65.3%) complication observed in our present study. Others were severe anaemia (Hb %< 7gm%/dl) (n=7, 9.3%), thrombocytopenia (n=43, 57.3%), hypoalbuminemia (n=41, 54.7%), pneumonia (n=8,10.7%), meningoencephalitis (n=8,10.7%), bleeding manifestation (n=3,4.0%) and shock (n=1, 1.3%).

**Table – 6: Shows complications of scrub typhus.**

| Complications | Number | Percentages |
|---|---|---|
| **Laboratory parameters** | 7 | 9.3 |
| Anaemia(severe,<7gm/dl) | 31 | 41.3 |
| Leucocytosis | 43 | 57.3 |
| Thrombocytopenia | 31 | 41.3 |
| Hypoalbuminemia | | |
| **Clinical parameters** | | |
| Anicteric hepatitis | 49 | 65.3 |
| Pneumonia | 8 | 10.7 |
| Meningoencephalitis | 8 | 10.7 |
| Myocarditis | 2 | 2.7 |
| Ascites | 4 | 5.3 |
| Pleural effusion | 2 | 2.7 |
| Pericardial effusion | 1 | 1.3 |
| Bleeding manifestation | 3 | 4.0 |
| Fluid refractory shock | 1 | 1.3. |

Fifteen patients of our study population were admitted to PICU for special care. Of which, eight were for meningoencephalitis, three for bleeding manifestation, two for myocarditis, one each for pericardial effusion and shock.

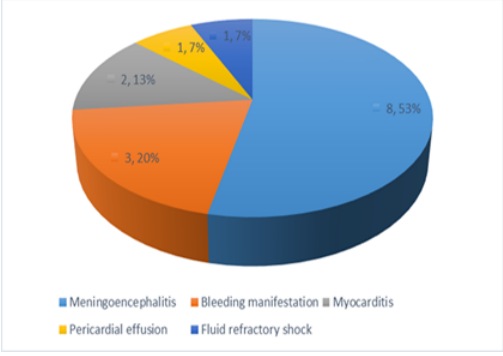


**Figure – 1: Pie chart shows the relative proportion of patients with complications needing PICU admission.**

All patients received anti-scrub treatment either Doxycycline (4.5mg/kg of body weight in two divided doses) or Azithromycin (10mg/kg of body weight as a single daily dose) plus 3rd generation cephalosporin as per our unit protocol. 3rd generation cephalosporin had been withdrawn upon confirmation of scrub typhus serologically. Other supportive measures like antipyretics, anti-seizure drugs, decongestants for congestive cardiac failure, pressure agents for fluid refractory shock and parenteral fluid and oxygen were administered whenever necessary. Fever defervescence occurred within forty-eight (48) hours in all cases. No casualty has occurred in our unit so far.

## DISCUSSION:

There have been several studies regarding scrub typhus from different parts of India but hardly any study was found describing demography, clinical features, complications, laboratory profiles and outcomes particularly in children from the western regions of West Bengal. In this study, we have analysed retrospectively the laboratory parameters along with the patient's characteristics, clinical features, complications and outcome of 75 children with scrub typhus admitted in our unit of Department of Paediatrics, BSMCH, Bankura, West Bengal from June 2020 to August 2021.

In our study, it was found that 58.7% (n=44) of children were male and the rest 41.3% (n=31) were female. A similar observation was reported by Das et al and Bhat et al. [18, 19]. This gender preference may be due to a child's social behaviour, and gender inequity in the community. The age of 50.7% (n=38) of children in our study were ≤ 5 years which is like other studies conducted by different authors [14,20]. However, contrary to our study, Bajracharya L reported only 16.7% of children were less than 5 years of age [21]. In our present study, the age of 49.3% (n=37) of children was more than 5 years which is less than the study conducted by Lakshmanan S et al which showed 58% of children were school going [22]. This difference is probably due to the ongoing closure of schools during the nCovid-19 pandemic ruling since March 2020 in India. However, a substantial proportion (n=14, 18.7%] of cases were found among the children of ≤1 year of age who stay predominantly indoors probably due to adaptation to the indoor habitat of the chiggers during monsoon [23]. The youngest child of our study was 45 days old female and the eldest one was 11 years 11 months old male. In one study, it was found that the youngest age of presentation was 53 days [24]. The mean age of presentation was 4.82±3.72 years in our present study and it is comparable to the study conducted by Das P et al [18].

Scrub typhus shows seasonal variation in our country. In our study, the cases increased from June to December with a peak incidence between August and November. Scrub typhus cases were reported by authors from the different regions of India with a varying peak incidence from June to January [18,22,25].

In our study, it was found that 94.7% (n=71) of children were from rural areas supporting the natural place of habitat of the chiggers. Other attributable factors could be the practice of open field defecation [22] and urination with squatting position, growing of shrubs in the premises of the house during monsoon season and children playing around it. In Lakshmanan S et al study, 87% of children hailed from rural areas [22].

Scrub typhus usually presents with prolonged fever without any specific symptoms and signs except eschar which has diagnostic importance. In our present study, all children had a fever (n=75,100%). A similar observation was reported by other researchers [20,26]. Our study showed that 64% (n=48) of children had a fever for ≥7 days which is comparable to a study conducted by other researchers [10,22]. In our study, it was found that 54.7% (n=41) of cases had gastrointestinal symptoms which are comparable to the study conducted by Narayanasamy et al [27]. Hepatomegaly (n=45, 60.0%), splenomegaly (n=42, 56.0%), hepatosplenomegaly (n=36, 48.0%) and ascites (n=4, 5.3%) were the gastrointestinal findings of what we had observed. The presence of splenomegaly is significant as it distinguishes it from dengue where splenomegaly is unusual [28].

Headache (n=12,16%), altered sensorium (n=6, 8%) and convulsions (n=8, 10.7%) were the most common symptoms of the central nervous system observed in our study and is comparable to the study conducted by Bajracharya L [21]. Decreased urine output (n=3, 4%), haematuria (n=3,2.7%) and photophobia (n=3,4%) were the other symptoms that we had observed. It was also found that 16% (n=12) of children had myalgia which is comparable to the study conducted by other authors [22]. Eschar, a pathognomic sign of scrub typhus, was present in 26.7% (n=20) of cases in our present study and is comparable to the study conducted by Das et.al and Basu et al [18, 29]. There is a wide variation in the finding of eschar ranging from 25% to 90% [30]. This variation is probably due to ignorance of patients to eschar and a detailed physical examination targeted to look for it, is rarely done.

In children with scrub typhus, lymphadenopathy is a common finding. Only 8% (n=6) of children presented with localised lymphadenitis which is comparable to a study conducted by Lakhsmanan S et al [22].

Lymphadenopathy can be a differentiating clinical feature that distinguishes it from other causes of fever like malaria and dengue [31].

In our study, the maculopapular rash was found in 16 % (n=12) of cases and is comparable to the other studies conducted by Bhat et al. and Das et al [18,19]. Low incidence of rash in our study may be due to varied skin complexion of patients and failure in detailed clinical examination.

Our present study showed third spacing of fluid (n=43, 57.3%) in the form of facial puffiness (n=28, 37.3), oedema (n=12, 16%), ascites (n=4, 5.3%), pleural (n=2, 2.7%) and pericardial effusion (n=1, 1.3%). It was also reported by Das et al. though it is lower (39.6%) than our study [18]. This disparity could be due to geographical variation of nutritional status of the study sample and prolonged duration of illness which leads to nutritional deprivation arising out of poor appetite.

Scrub typhus in children is associated with significant haematological and biochemical changes which have been reported by different authors [10]. In our present study, haematological parameters such as anaemia (n=72, 96%), leucocytosis (n=31, 41.3%), and thrombocytopenia (n=43, 57.3%) were inconceivable findings. Microcytic anaemia (MCV <70 fl.) and raised erythrocyte sedimentation rate (ESR) in 1st hour were found to be present in 16% (n=12) and 18.7% (n=14) of children respectively. Our study showed anaemia (n=72, 96%) which is higher than other studies conducted by different authors which showed anaemia ranging from 74% to 84% [10,24,32]. A higher incidence of anaemia in our study is likely due to variation in nutritional status among the study population, socioeconomic status and variation in adherence to the ongoing nutritional program. In our present study, the mean haemoglobin level (gm/dl) was inversely related to the duration of illness, and it is statistically significant (P- value=0.003). There was no such study that showed this unique characteristic in the haematological parameter of scrub typhus in children. Leucocytosis was present in 41.3% (n=31) of children and it is comparable to other studies reported by different authors, and it is ranging from 21% to 47% [10,28,31]. In our study, mean leucocyte counts (×103/mm3) were 10.9, 12.5 and 13.3 when the fever was <7 days, 7-14 days and > 14 days respectively. It means that mean leukocyte counts are directly proportional to the duration of fever but not significant statistically (P-value = 0.475). Our present study showed that thrombocytopenia (<1.5 lakhs/mm3) was present in 57.3% (n=43) cases. It is comparable to a study conducted by Bajracharya L which showed 52% [21]. Thrombocytopenia in children with scrub typhus is ranging from 20% to 88% reported by different authors [20,28,31]. Our study showed that mean platelets count was inversely related to the duration of fever. Lower mean platelets count (mean = 0.93) was found when the duration of fever was more than two weeks at the time of admission and the presence of thrombocytopenia is statistically significant (P-value = 0.005). We have documented that 16 %(n=12) of children among the study population had microcytic anaemia which can be due to nutritional deficiency and chronic blood loss due to hookworm infestation. Association between scrub typhus in children and microcytic anaemia requires further in-depth investigation. Hence, from the diagnostic point of view, anaemia, leucocytosis and thrombocytopenia along with other clinical characteristics will help us to start empirical anti-scrub treatment pending serological confirmation which is time-consuming.

Scrub typhus is associated with different biochemical changes reported by several authors [18,22,33]. Of which, the elevation of liver enzymes is worthy of remark. In our present study, it was found that ALT and AST (> 45 U/L) were raised in 65.3% (n=49) and 61.3% (n=46) of children respectively. Elevation of liver enzymes was also reported by different authors, and it is ranging from 21% to 95.31% [18, 22, 32, 34]. Hypoalbuminemia, another biochemical parameter, was found to be present in 41.3% (n=31) of cases in our present study. It is also reported by different authors and ranges from 22% to 85.49% [10,14,18]. Hypoalbuminemia in scrub typhus is likely due to capillary leakage. The wide range of variation of hypoalbuminemia in different studies could be due to the prolongation of illness and the presence of protein-energy malnutrition. In our study, it was found that the mean albumin level (gm/dl) in the blood is inversely related to the duration of fever, and it has shown to be significant statistically (P-value = 0.014). The mean values (gm/dl) were 3.77, 3.28 and 3.10 when the duration of fever < 7 days, 7 – 14 days and > 7 days at the time of admission respectively. This singular characteristic of the biochemical parameter that has been analysed in our study, had never been reported previously.

In our present study, complications of scrub typhus were anicteric hepatitis (n=49, 65.3%), pneumonia (n=8, 10.7%), meningoencephalitis (n=8, 10.7%), ascites (n=4, 5.3%), myocarditis (n=1, 1.3%) pericardial effusion (n=2, 2.7%, pleural effusion (n=2, 2.7%), congestive cardiac failure (n=2, 2.7%) and shock (n=1, 1.3%). In our study, 10.7% (n=8) of children had meningoencephalitis which is more or less similar to other studies [18,32]. In our present study, fifteen patients (15) were admitted in PICU with different complications.

In our study, no casualty had occurred so far. This was possible due to heightened perception of the situation among paediatricians about the diverse clinical manifestations of scrub typhus; prompt administration of anti-scrub measures based on clinical features and routine investigations and close monitoring of children who had complications or potential for developing complications. No death from Scrub Typhus was also reported by Das P et al and Lakshmanan S et al [18,22]. Whereas other authors had reported mortality from scrub typhus ranging from 4.8% to 12.7% [10, 28, 31].

**Limitations of our study:**

Being retrospective in nature, our study has some limitations. First, it is a hospital-based study, so the actual burden of scrub typhus in terms of morbidity and mortality in the community is not estimated. Second, CRP, ESR and serum electrolytes reports had not been done in all cases which may lead to bias in data analysis. Third, children below five years of age do not accurately articulate the symptoms like myalgia, headache which were not recorded in their medical records. Forth, as no gold diagnostic (IFA) test is available in our set-up, we had relied upon the ELISA test for confirmation of scrub typhus fever. Despite these limitations, we hope that this study will help PCP and paediatricians working even in remote areas in arriving at the diagnosis of scrub typhus early and initiate treatment in due time.

## CONCLUSION:

In a country like India, particularly in the light of rural settings, scrub typhus should be suspected in any child presenting with prolonged fever ≥ 5 days in rainy, autumn and late autumn season (June to December) with any one of the following clinical features - vomiting, abdominal pain, headache, cough, shortness of breath, altered sensorium, convulsion, bleeding manifestation and clinical findings suggestive of multiorgan involvement such as hepatomegaly, splenomegaly, third spacing, pneumonia, meningoencephalitis, myocarditis and shock. Abnormal laboratory parameters like anaemia, leucocytosis, thrombocytopenia, increased liver enzymes, hypoalbuminemia, raised CRP will also definitely guide PCP and paediatricians in clinching the diagnosis early pending ELISA report and administering anti-scrub treatment in due time.

## RECOMMENDATIONS:

We recommend following measures to reduce morbidity and mortality from scrub typhus. At primary level of care: Upon high index of suspicion, administration of doxycycline (4.5mg/kg) in two divided doses for 5 days in a child when he/she will come to the health care facility with fever for 5 days or more particularly in monsoon season. Administration of 1st dose of doxycycline should be administered before referring the patient with serious illness to higher levels of care. At secondary and tertiary level of care – investigations are to be performed to confirm the diagnosis and rule out end organ damage. Along with anti-scrub measurement, all supportive care depending on the patient's condition should be administered accordingly. At community level: Vector control – reduction of the habitat of the chiggers and rodents through environmental modification and application of chemical such as indane or chlordane to the ground intending to kill mites. Personnel protection – impregnating cloths and blanket with benzyl benzoate and application of mite repellent (diethyltoluamide) to exposed skin surfaces. At administrative and researcher level – Investigation should be undertaken at community level to know the actual burden of scrub typhus. Health awareness among people should be increased to the highest possible level through information, education and communication. Keeping in mind the bed side tests like MPDA for malaria, newer diagnostic tools should be invented with highest possible quality in terms of sensitivity and specificity.

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