

Original Research Article

A STUDY OF CLINICAL PROFILE OF IgM ELISA POSITIVE SCRUB TYPHUS CASES IN TERTIARY CARE PAEDIATRIC HOSPITAL

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ABSTRACT

Background: Scrub typhus is an important but frequently underdiagnosed cause of acute febrile illness in children. Its clinical manifestations vary widely, and delayed diagnosis may result in severe multisystem complications.

Materials and Methods: This hospital-based prospective observational study included 100 children aged 2 months to 18 years with IgM ELISA-positive scrub typhus admitted to a tertiary care pediatric hospital from November 2019 to October 2021. Demographic characteristics, clinical manifestations, laboratory parameters, Weil-Felix results, requirement for ICU and respiratory support, and outcomes were evaluated.

Results: The mean age was 7.58 ± 3.81 years; 58% were males and 62% were from rural areas. Fever was present in all children, followed by vomiting (48%), seizures (33%), altered sensorium (30%), abdominal pain (21%), and headache (21%). Hepatomegaly was present in 32%, while eschar was identified in only 1%. Thrombocytopenia (72%), hyponatremia (60%), hypoalbuminemia (43%), transaminitis (84%), and elevated CRP (87%) were common laboratory abnormalities. Weil-Felix testing was positive in 69% of IgM ELISA-confirmed cases. Twenty-three percent required ICU/respiratory support and 15% required invasive ventilation. Altered sensorium and shock were significantly associated with ICU requirement. Ninety-nine children were discharged, while one child died from MODS/ARDS.

Conclusion: Pediatric scrub typhus has a diverse clinical and laboratory profile, with neurological involvement and shock indicating greater disease severity. A high index of suspicion and IgM ELISA-based confirmation can facilitate early diagnosis and treatment, resulting in favorable outcomes.

Keywords: Scrub typhus; children; *Orientia tsutsugamushi*; IgM ELISA; thrombocytopenia; acute febrile illness; ICU.

INTRODUCTION

Scrub typhus is an acute febrile illness caused by *Orientia tsutsugamushi* and transmitted through the bite of infected larval trombiculid mites. It remains an important but frequently underrecognized cause of acute febrile illness in children, particularly in endemic regions of India. Pediatric scrub typhus may have a variable clinical presentation and can progress from an uncomplicated febrile illness to

severe multisystem disease if diagnosis and treatment are delayed.^[1]

The clinical spectrum in children includes fever, gastrointestinal symptoms, headache, rash, lymphadenopathy, hepatosplenomegaly, respiratory manifestations, and neurological involvement. Severe disease may be associated with shock, meningoencephalitis, acute kidney injury, hepatic dysfunction, myocarditis, and multiorgan dysfunction.^[2] Recent evidence has emphasized considerable geographical variation in the clinical

presentation and severity of pediatric scrub typhus.^[3]

Diagnosis remains challenging because early manifestations often resemble other tropical febrile illnesses. Clinical suspicion supported by appropriate laboratory testing is therefore essential.^[4] Neurological manifestations, particularly altered sensorium and seizures, may indicate severe disease and require early recognition.^[5] Moreover, atypical presentations may further delay diagnosis in children.^[6] Recent Indian pediatric studies continue to demonstrate substantial variation in clinical and laboratory manifestations, reinforcing the need for region-specific data.^[7]

Hence, the present study was undertaken to assess the demographic, clinical, and laboratory profile of IgM ELISA-positive scrub typhus cases in children admitted to a tertiary care pediatric hospital.

MATERIALS AND METHODS

Study Design and Setting

The present study was a **hospital-based prospective observational study** conducted at the **Indira Gandhi Institute of Child Health (IGICH), Bengaluru**, a tertiary care pediatric hospital. The study was carried out over a period of **24 months, from November 2019 to October 2021**.

Study Population

Children aged **2 months to 18 years** who were admitted with clinically suspected scrub typhus and subsequently found to be **positive for scrub typhus IgM by ELISA** were enrolled. A total of **100 children** fulfilling the eligibility criteria were included in the study.

Inclusion Criteria

Children aged 2 months to 18 years admitted with clinically suspected scrub typhus, with **positive scrub typhus IgM ELISA**, and whose parents/guardians provided informed consent were included.

Exclusion Criteria

Children were excluded if they:

1. Were **negative for scrub typhus IgM ELISA**.
2. Had conditions that could interfere with the **kinetics of immunogenicity**.

Sample Size

Based on published literature, the expected IgM ELISA positivity for scrub typhus was taken as **40%**. With a 5% level of significance and an absolute precision of 10%, the sample size was estimated using the formula:

$$n = \frac{Z_{1-\alpha/2}^2 \times p(1-p)}{d^2}$$

where p was the anticipated proportion (0.40), Z was the standard normal deviate at the specified significance level, and d was the absolute precision (0.10). A final sample size of **100 children** was considered for better validation of the study results.

Data Collection and Clinical Assessment

After enrollment, demographic characteristics including **age, sex, and rural/urban residence** were recorded using a predesigned and prestructured proforma. A detailed history was obtained, followed by complete general and systemic examination.

Clinical manifestations including **fever, vomiting, seizures, altered sensorium, abdominal pain, headache, skin lesions, and breathlessness** were documented. Examination findings such as **hepatomegaly, splenomegaly, lymphadenopathy**, and other systemic abnormalities were also recorded.

Laboratory Evaluation

Baseline laboratory investigations included **complete blood count, serum electrolytes, liver function tests, renal function tests, and C-reactive protein (CRP)**. Hematological abnormalities including anemia, leukocytosis and thrombocytopenia and biochemical abnormalities such as hypoalbuminemia were assessed.

All clinically suspected cases were investigated using the **Weil-Felix test and scrub typhus IgM ELISA**. Only children with a positive IgM ELISA result were included in the final study cohort. Requirement for intensive care support, complications, duration of hospitalization, and final outcome were recorded.

Statistical Analysis

Data were entered into **Microsoft Excel**, and a master chart was prepared. Statistical analysis was performed using **SPSS software version 20**. Categorical variables were presented as frequencies and percentages, while continuous variables were summarized using appropriate descriptive statistics. **ANOVA, Student's t-test, and Chi-square test** were applied as appropriate to determine associations between study variables. A **p-value <0.05** was considered statistically significant.

RESULTS

A total of 100 children with IgM ELISA-positive scrub typhus were included. The mean age was 7.58 ± 3.81 years, with the largest proportion belonging to the 6–10-year age group (41%). There was a slight male predominance, with 58% males and 42% females. Most children (62%) were from a rural background.

Table 1: Demographic and clinical profile of children with scrub typhus (N=100)

Parameter	n	%
Age group		
<5 years	32	32
6–10 years	41	41
11–15 years	27	27
Sex		

Male	58	58
Female	42	42
Residence		
Rural	62	62
Urban	38	38
Clinical manifestations		
Fever	100	100
Vomiting	48	48
Seizures	33	33
Altered sensorium	30	30
Pain abdomen	21	21
Headache	21	21
Skin lesions	11	11
Difficulty in breathing	7	7
Speech abnormality	5	5
Difficulty in walking	5	5
Bleeding manifestations	3	3
Shock	3	3
Examination findings		
Hepatomegaly	32	32
Splenomegaly	11	11
Lymphadenopathy	10	10

Fever was present in all children. Among other symptoms, vomiting was the most common (48%), followed by seizures (33%) and altered sensorium (30%). Hepatomegaly was found in 32%, while splenomegaly and lymphadenopathy were present in 11% and 10%, respectively.

Regarding duration of fever, 46% presented after 6–10 days of fever, while 44% presented within five days. Skin manifestations were relatively uncommon; petechiae were observed in 10%,

purpura fulminans in 2%, and a characteristic eschar was identified in only 1%.

Neurological involvement was prominent. CNS examination was abnormal in 48 children, including raised intracranial tension in 26%, cerebellar signs in 11%, and encephalopathy signs in 11%. Headache ($p=0.0298$) and seizures ($p=0.016$) were significantly associated with abnormal CNS findings.

Table 2: Laboratory profile of children with scrub typhus

Laboratory parameter	Mean $\pm$ SD	Median (IQR)	Important abnormality
Hemoglobin (g/dL)	9.782 $\pm$ 1.49	9.9 (2.0)	Anemia: 24%*
Total leukocyte count (/mm ³)	11,419.6 $\pm$ 5,575.76	11,000 (6,000)	Leukocytosis: 22%
Neutrophils (%)	57.44 $\pm$ 15.49	60 (20.5)	—
Lymphocytes (%)	36.05 $\pm$ 15.38	30 (20.5)	—
Platelet count (/mm ³)	118,422 $\pm$ 15,356.38	114,411 (42,211)	Thrombocytopenia: 72%
Serum sodium (mEq/L)	133.75 $\pm$ 2.81	134 (4)	Hyponatremia: 60%
Serum potassium (mEq/L)	4.37 $\pm$ 0.64	4.375 (1.05)	—
Serum chloride (mEq/L)	100.39 $\pm$ 5.96	100.3 (6.1)	—
Serum albumin (g/dL)	2.735 $\pm$ 0.39	2.8 (0.4)	Hypoalbuminemia: 43%
SGOT (U/L)	148.21 $\pm$ 193.97	82.5 (144)	—
SGPT (U/L)	89.07 $\pm$ 89.13	58 (75.55)	—
CRP (mg/L)	58.21 $\pm$ 32.80	60 (55.5)	Elevated: 87%
Transaminitis	—	—	84%

*The thesis reports 24% with hemoglobin <11 g/dL in its categorical table; this has been retained as reported.

The laboratory profile was characterized predominantly by thrombocytopenia (72%), hyponatremia (60%), hypoalbuminemia (43%), transaminitis (84%), and elevated CRP (87%). The mean CRP was 58.21 $\pm$ 32.80 mg/L.

Thrombocytopenia showed a significant association with CNS involvement ($p=0.0016$), whereas albumin, sodium, liver enzymes, bilirubin, CRP, and transaminitis did not demonstrate significant associations with CNS manifestations.

Table 3: Weil-Felix testing, ICU/respiratory support and outcome

Parameter	n	%
Weil-Felix test		
Positive	69	69
Negative	31	31
Titres among Weil-Felix-positive cases (n=69)		
1:160	16	23.19
1:320	41	59.42
1:640	12	17.39
Respiratory support		
No respiratory support	77	77
Oxygen by mask/prongs	4	4
CPAP	4	4

Invasive ventilation	15	15
ICU support		
Required	23	23
Not required	77	77
Outcome		
Discharged	99	99
Death	1	1

Although all children were IgM ELISA positive, the Weil-Felix test was positive in only 69%. Among Weil-Felix-positive cases, a titre of 1:320 was the most frequent (59.42%), followed by 1:160 (23.19%) and 1:640 (17.39%).

Twenty-three children (23%) required respiratory and ICU support; invasive ventilation was required in 15%, while CPAP and oxygen by mask/prongs were required in 4% each. Overall outcome was favorable, with 99% discharged and one death (1%), which was attributed to MODS/ARDS.

Table 4: Factors significantly associated with CNS involvement and ICU/respiratory support

Predictor/association	Comparison	χ^2	p-value
Headache	CNS involvement	4.72	0.0298
Seizures	CNS involvement	5.80	0.0160
Thrombocytopenia	CNS involvement	9.91	0.0016
Altered sensorium	ICU support	5.69	0.0171
Shock	ICU support	6.36	0.0117
Altered sensorium	Respiratory support	5.69	0.0171
Shock	Respiratory support	6.36	0.0117
CNS involvement	ICU support	29.71	<0.0001
Respiratory support	ICU support	94.43	<0.0001
Hospital stay duration	CNS involvement	25.63	<0.0001
Hospital stay duration	ICU support	25.12	<0.0001

CNS involvement was strongly associated with the requirement for ICU care ($p<0.0001$). Altered sensorium and shock were significantly associated with both ICU and respiratory support, suggesting that these clinical features identified children with more severe disease. The duration of hospital stay was also significantly associated with CNS involvement, respiratory support, and ICU requirement (all $p<0.0001$).

Overall, the study demonstrated that pediatric scrub typhus commonly presented with fever, gastrointestinal and neurological symptoms, thrombocytopenia, hyponatremia, hypoalbuminemia, transaminitis, and elevated inflammatory markers. Despite 23% of children requiring ICU support, the overall mortality was low at 1%.

DISCUSSION

Scrub typhus is an important cause of acute febrile illness in children, with considerable variation in clinical presentation and severity. In the present study, the mean age was 7.58 ± 3.81 years, with the largest proportion of children belonging to the 6–10-year age group. Males constituted 58% of the cohort, and 62% of children were from rural areas. Similar pediatric studies from India have demonstrated a substantial burden of scrub typhus, particularly in children from rural and endemic regions.^[7] A recent systematic review also highlighted the considerable contribution of scrub typhus to acute febrile illness across India.^[8]

Fever was present in all patients, while vomiting (48%), seizures (33%), altered sensorium (30%),

abdominal pain (21%), and headache (21%) were common presenting manifestations. Hepatomegaly was observed in 32%, followed by splenomegaly and lymphadenopathy. Eschar, although considered a characteristic clinical finding, was identified in only 1% of patients. This low prevalence is important because absence of an eschar should not exclude scrub typhus. Gupta et al. similarly demonstrated substantial variability in the frequency and anatomical distribution of eschar among Indian patients.^[9]

Laboratory abnormalities were frequent, particularly thrombocytopenia (72%), hyponatremia (60%), hypoalbuminemia (43%), transaminitis (84%), and elevated CRP (87%). The mean SGOT and SGPT levels were 148.21 and 89.07 U/L, respectively. Hepatic involvement is well recognized in pediatric scrub typhus, and Narayanasamy et al. also reported significant clinical and laboratory abnormalities among children with scrub typhus-associated elevation of hepatic transaminases.^[10] Early recognition is important because effective antimicrobial therapy generally produces a rapid clinical response; evidence also supports the effectiveness of macrolides as therapeutic options in pediatric scrub typhus.^[11]

Neurological involvement represented an important marker of disease severity in our cohort. Headache and seizures were significantly associated with abnormal CNS findings, while thrombocytopenia was also significantly associated with CNS involvement ($p=0.0016$). Altered sensorium and shock were significantly associated with ICU and respiratory support requirements. These findings are consistent with reports showing that pediatric scrub

typhus can produce severe neurological and multisystem complications.^[12]

Overall, 23% of children required ICU and respiratory support, including 15% who required invasive ventilation. Despite this considerable burden of severe illness, mortality was only 1%, with one child dying due to MODS/ARDS. Systematic evidence has shown that complications and mortality remain important concerns in pediatric scrub typhus, particularly in children with severe organ dysfunction.^[13] Similarly, large pediatric cohorts have demonstrated that timely diagnosis and appropriate antimicrobial treatment are associated with generally favorable outcomes.^[14]

An important diagnostic finding was that although all 100 children were IgM ELISA positive, the Weil-Felix test was positive in only 69%. Thus, nearly one-third of confirmed cases would have been missed if Weil-Felix testing alone had been relied upon. These findings reinforce the importance of maintaining a high index of clinical suspicion and using IgM ELISA where available.

CONCLUSION

Scrub typhus should be considered in children presenting with acute febrile illness, particularly when associated with gastrointestinal, neurological, hematological, or hepatic abnormalities. Thrombocytopenia, hyponatremia, transaminitis, and elevated CRP were common, while altered sensorium and shock were associated with greater requirement for ICU support. IgM ELISA was more useful for confirmation than the Weil-Felix test, and early diagnosis with appropriate treatment resulted in a favorable outcome with only 1% mortality.

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