

# A Prospective Study of Clinical Profile and Laboratory Diagnosis Which Predicts the Severity of Scrub Typhus in Children

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## Abstract

**Background:** Scrub typhus is an acute febrile illness caused by the obligate intracellular Rickettsial organism, *Orientia tsutsugamushi*. It is transmitted by the bite of larval forms of trombiculid mites, *Leptotrombium* mite (Chiggers). Approx one million adults and children are affected worldwide annually. Once an uncommon disease, this potentially fatal zoonosis is re-emerging in many parts of India such as Maharashtra, Karnataka, Tamil Nadu, Pondicherry, and Kerala in the past decade. Here, we tried to find out the predictors of severity of scrub typhus and evaluate clinical profile and laboratory diagnosis and complications which predict the severity of scrub typhus.

**Materials and Methods:** This Descriptive Observational longitudinal hospital-based study was conducted in the Department of Pediatric Medicine, R G Kar Medical College and Hospital prospectively from Dec 2018-Nov 2019. Children below 12 years of age with scrub typhus were admitted in the Department of Pediatric Medicine, R G Kar Medical College, and Hospital. A total of 60 participants was taken in this study.

**Result and Analysis:** In non-severe scrub typhus, no children had AKI. In severe scrub typhus, 4(16.7%) children had AKI. Association of AKI versus scrub typhus group was statistically significant ( $P = 0.0112$ ). In non-severe scrub typhus, 36 (100.0%) children were discharged. In severe scrub typhus, 3 (12.5%) children died and 21 (87.5%) children were discharged. Association of outcome versus scrub typhus group was statistically significant ( $P = 0.0295$ ).

**Conclusion:** Symptoms of scrub typhus are quite non-specific. The presence of these factors should alert the physician about the impending life-threatening complications and should warrant intensive care monitoring, treatment or referral to the tertiary care center. Early recognition of the disease is very important as any delay in treatment can lead to severe morbidity and high mortality.

**Key words:** Clinical profile, Laboratory diagnosis, Predictors, Scrub typhus, Severity

## BACKGROUND

Scrub typhus is an acute febrile illness caused by the obligate intracellular Rickettsial organism, *Orientia tsutsugamushi*. It is transmitted by the bite of larval forms of trombiculid mites, *Leptotrombium* mite (Chiggers).<sup>[1]</sup> Approx

one million adults and children are affected worldwide annually. Once an uncommon disease, this potentially fatal zoonosis is re-emerging in many parts of India like Maharashtra, Karnataka, Tamil Nadu, Pondicherry, and Kerala in the past decade.<sup>[1]</sup> Now a days many cases are reported from West Bengal. Pediatric scrub typhus is a very common clinical syndrome encountered in the last few years. The first phase of the illness is parallel to any other undifferentiated fever making early diagnosis complicated. Moreover, serological diagnosis cannot be made before 7 days of onset of fever, further negating the chance of early diagnosis. Scrub typhus is essentially a focal or perivasculitis that can involve any organ system leading to widespread complications. Meningoencephalitis,

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septic shock, acute kidney injury, severe thrombocytopenia, myocarditis, acute respiratory distress syndrome, and multi-organ dysfunction syndrome are some of the clinically significant complications seen in pediatric scrub typhus.<sup>[2]</sup> Most of these complications are life-threatening and have to be picked up early in the course of illness and treated for full recovery.

Orientalsutsugamushi and Rickettsia species are important causes of non-malarial febrile illness in Southeast Asia preceded only by dengue. Among rickettsioses, scrub typhus is most common followed by Indian tick typhus. The incubation period for symptoms ranges between 6 and 21 days from exposure. Patients may present with sudden fever, chills, headache, backache, profuse sweating, vomiting, and enlarged lymph nodes. A macular or maculopapular rash may appear on the trunk, and later it may extend to the arms and the legs. An eschar at the wound site is the single most useful diagnostic clue. The Indirect Immuno fluorescence Assay test is currently the reference standard for the diagnosis of scrub typhus.<sup>[3]</sup>

Treatment with doxycycline is associated with a rapid abatement of fever and this effect has even been considered almost diagnostic. Azithromycin is also effective and is easier to administer, given its shorter treatment duration, and less gastrointestinal side effects. It is suitable for use in pregnancy and for children. The symptoms of scrub typhus are usually mild and its clinical course is uneventful. However, some patients experience severe or fatal events. Serious complications include pneumonitis, acute respiratory distress syndrome, acute renal failure, myocarditis, and septic shock. Mortality rates in untreated patients range from 0 to 30%.<sup>[4]</sup>

The infection often causes vasculitis and multiple-organ failure. Patients with such complications usually have poor prognosis that may end with death, especially those with delayed diagnosis and treatment. Systemic complications commonly reported as causes of death include respiratory involvement (15–36%), cardiovascular involvement (2–34%) renal involvement (9–20%), hepatic involvement (4–31%) central nervous system involvement (4–23%) or multiple-organ involvement (11.9%). Mortality is reported in up to 30% of cases.

Clinical individuality for prognostication of scrub typhus severity and death has been the subject of many studies. These characters may include any combination of the following systems: respiratory system-dyspnea, crepitation, and abnormal chest film; cardiovascular structure-septic shock; hepatobiliary system-serum albumin  $\leq 3$  g/dl, bilirubin  $>1.5$  mg/dl, and more than twofold increase in aspartate aminotransferase; and kidney system-serum

creatinine  $>1.4$  mg/dl and positive urine albumin.<sup>[5]</sup> Early detection of these characteristics might be used to assist clinical guidelines for patient management.

Information about common presentations and complications along with timely analysis and intervention are central in limiting the morbidity and mortality. Though there are studies on clinical profile of severe scrub typhus in Indian children, very few looked into predictors of severity in those cases. Most of our understandings about the predictors of severity in scrub typhus are from adult studies, which cannot be extrapolated to children for obvious reasons.<sup>[6,7]</sup> Former information of factors predicting severity would help in anticipation, timely intervention, or referral in these children.

We tried to find out the predictors of severity of scrub typhus and evaluate clinical profile and laboratory diagnosis and complications which predict the severity of scrub typhus.

## MATERIALS AND METHODS

### Study Area and Study Population

Department of Pediatric Medicine, R G Kar Medical College, and Hospital, Kolkata. Children below 12 years of age with scrub typhus were admitted in R G Kar Medical College and Hospital, Kolkata from December 2019 to November 2020.

### Inclusion Criteria

All children below 12 years of age admitted in R G Kar Medical College and Hospital, Kolkata with acute febrile illness during the study period, with positive scrub typhus IgM serology were included in the study.

### Exclusion Criteria

- Patients diagnosed to have febrile illness due to a underlying specific disease (e.g. Dengue fever, Malaria, Typhoid, UTI, Tuberculosis) and other comorbid conditions like chronic lung disease, chronic hepatitis, and immune-deficient children.
- Those patients who were unwilling to give their consent for the study.

### Method of Data Collection

Data were collected in a preformed proforma from the patient who fulfilled the inclusion criteria after obtaining informed consent from the parents to include their children in the study.

### Statistical Analysis

For statistical analysis, data were entered into a Microsoft excel spreadsheet and then analyzed by SPSS 24.0. and

GraphPad Prism version 5. A chi-squared test ( $\chi^2$  test) was any statistical hypothesis test wherein the sampling distribution of the test statistic is a Chi-squared distribution when the null hypothesis is true. Without other qualification, “Chi-squared test” often is used as short for Pearson’s chi-squared test. Unpaired proportions were compared by Chi-square test or Fischer’s exact test, as appropriate.  $P \leq 0.05$  was considered for statistically significant.

## RESULT AND ANALYSIS

We showed in our study 36 (60.0%) children’s had non-severe scrub typhus and 24 (40.0%) children’s had severe scrub typhus.

Our study showed 3 (5.0%) children died and 57 (95.0%) children were discharged. In non-severe scrub typhus, 17 (47.2%) children were female and 19 (52.9%) children were male. In severe scrub typhus, 11 (45.8%) children were female and 13 (54.2%) children were male. Association of sex versus. scrub typhus group was not statistically significant ( $P = 0.9158$ ). In non-severe scrub typhus, 4 (11.1%) children had >14 days of fever and 32 (88.9%) children had 7–14 days of fever. In severe scrub typhus, 4 (16.7%) children had >14 days of fever and 20 (83.3%) children had 7–14 days of fever. Association of duration of fever versus. scrub typhus group was not statistically significant ( $P = 0.5351$ ).

We found in non-severe scrub typhus, 4 (11.1%) children had maculopapular rash. In severe scrub typhus, 5 (20.8%) children had maculopapular rash. Association of maculopapular rash versus. scrub typhus group was not statistically significant ( $P = 0.3015$ ). In non-severe scrub typhus, 8 (22.2%) children had headache. In severe scrub typhus, 6 (25.0%) children had headache. Association of headache versus. scrub typhus group was not statistically significant ( $P = 0.8031$ ). In non-severe scrub typhus, 8 (22.2%) children had tachypnoea. In severe scrub typhus, 2 (8.3%) children had tachypnoea. Association of tachypnoea versus. scrub typhus group was not statistically significant ( $P = 0.1573$ ).

We showed in non-severe scrub typhus, 1 (2.8%) child had breathlessness. In severe scrub typhus, 10 (41.7%) children had breathlessness. Association of breathlessness versus. scrub typhus group was statistically significant ( $P = 0.0001$ ). In non-severe scrub typhus, 12 (33.3%) children had coughed. In severe scrub typhus, 10 (41.7%) children had coughed. Association of cough versus. scrub typhus group was not statistically significant ( $P = 0.5116$ ). In non-severe scrub typhus, 16 (44.4%) children had myalgia. In severe scrub typhus, 14 (58.3%) children had myalgia. Association

of myalgia versus. scrub typhus group was not statistically significant ( $P = 0.2918$ ). In non-severe scrub typhus, 6 (16.7%) children had abdominal pain. In severe scrub typhus, 5 (20.8%) children had abdominal pain. Association of abdominal pain versus. scrub typhus group was not statistically significant ( $P = 0.6828$ ). In non-severe scrub typhus, 2 (5.6%) children had altered sensorium. In severe scrub typhus, 12 (50.0%) children had altered sensorium. Association of altered sensorium versus. scrub typhus group was statistically significant ( $P < 0.0001$ ).

Our study showed that in non-severe scrub typhus, 4 (11.1%) children had hepatomegaly. In severe scrub typhus, 5 (20.8%) children had hepatomegaly. Association of hepatomegaly versus. scrub typhus group was not statistically significant ( $P = 0.3015$ ). In non-severe scrub typhus, 4 (11.1%) children had splenomegaly. In severe scrub typhus, 5 (20.8%) children had splenomegaly. Association of splenomegaly versus. scrub typhus group was not statistically significant ( $P = 0.3015$ ). In non-severe scrub typhus, 3 (8.3%) children had hypoalbuminemia. In severe scrub typhus, 15 (62.5%) children had hypoalbuminemia. Association of hypoalbuminemia versus. scrub typhus group was statistically significant ( $P < 0.0001$ ). In non-severe scrub typhus, 8 (22.2%) children had hyponatremia. In severe scrub typhus, 20 (83.3%) children had hyponatremia. Association of hyponatremia versus. scrub typhus group was statistically significant ( $P < 0.0001$ ).

We found in non-severe scrub typhus, 3 (8.3%) children had hyperbilirubinemia. In severe scrub typhus, 11 (45.8%) children had hyperbilirubinemia. Association of hyperbilirubinemia versus. scrub typhus group was statistically significant ( $P = 0.00076$ ). In non-severe scrub typhus, no children had ARDS. In severe scrub typhus, 2 (8.3%) children had ARDS. Association of ARDS versus. scrub typhus group was not statistically significant ( $P = 0.0781$ ). In non-severe scrub typhus, no children had pneumonia. In severe scrub typhus, 5 (20.8%) children had pneumonia. Association of pneumonia versus. scrub typhus group was statistically significant ( $P = 0.0042$ ). In non-severe scrub typhus, no children had shock. In severe scrub typhus, 9 (37.5%) children had shock. Association of shock versus. scrub typhus group was statistically significant ( $P < 0.0001$ ).

Our study showed in non-severe scrub typhus, no children had severe thrombocytopenia. In severe scrub typhus, 3 (12.5%) children had severe thrombocytopenia. Association of severe thrombocytopenia versus. scrub typhus group was statistically significant ( $P = 0.0295$ ). In non-severe scrub typhus, no children had AKI. In severe scrub typhus, 4 (16.7%) children had AKI. Association of AKI versus. scrub typhus group was statistically significant

( $P = 0.0112$ ). In non-severe scrub typhus, 36 (100.0%) children were discharged. In severe scrub typhus, 3 (12.5%) children died and 21 (87.5%) children were discharged. Association of outcome versus scrub typhus group was statistically significant ( $P = 0.0295$ ) [Table 1].

## DISCUSSION

We found that 36 (60.0%) children's had non-severe scrub typhus and 24 (40.0%) children's had severe scrub typhus.

Sankhyan *et al.*<sup>[8]</sup> found that 15 children (9 boys) tested positive for scrub typhus. Thrombocytopenia, hypoalbuminemia. Roy *et al.*<sup>[9]</sup> found that the mean age of the children was 5.5 years, 61% were male, 91% had rural habitats and admissions peaked between August and December. Mean duration of fever before the presentation was 10.3 days.

In non-severe scrub typhus, 17 (47.2%) children were female and 19 (52.9%) children were male. In severe scrub typhus, 11 (45.8%) children were female and 13 (54.2%) children were male. Association of sex versus scrub typhus group was not statistically significant ( $P = 0.9158$ ).

Narayanasamy *et al.*<sup>[10]</sup> found that Clinical (symptoms and signs) and laboratory factors were analyzed between severe and non-severe groups. Other factors such as age group, sex of the child, headache, vomiting, abdomen pain, epatomegaly, splenomegaly, hemoglobin level, absolute eosinophil count, and absolute monocyte count showed no significant difference ( $P > 0.05$ ) between these groups. The mean duration for the fever to touch the baseline and mean duration of hospital stay was 36 h and 6.5 d, respectively, in non-severe scrub typhus cases. The time for fever defervescence was 47 h and mean duration of hospital stay was 7.5 d in severe scrub typhus group. There was no mortality seen during the study period.

We found that 8 (13.3%) children's had >14 days of fever and 52 (86.7%) children's had 7–14 days of fever. 13 (21.7%) children's had eschar. 9 (15.0%) children's had maculopapular rash. 18 (30.0%) children's had generalized lymphadenopathy. 16 (26.7%) children's had edema. 14 (23.3%) children's had headache. 10 (16.7%) children's had tachypnoea. 11 (18.3%) children's were breathlessness. Twenty-two (36.7%) children's had cough. 30 (50.0%) children's had myalgia. Eleven (18.3%) children's had abdominal pain. 14 (23.3%) children's had altered sesorium. Nine (15.0%) children's had hepatomegaly. Nine (15.0%) children's had splenomegaly.

Bal *et al.*<sup>[11]</sup> found that Eschar was found in 17.9% of cases.

It was found that 20 (33.3%) children's had leucocytosis. Eighteen (30.0%) children's had hypoalbuminemia.

**Table 1: Association between Sex, Duration of fever, Maculopapular rash, Edema, Headache, Tachypnoea, Breathlessness, Cough, Myalgia, Abdominal pain, Altered sensorium, Hepatomegaly, Splenomegaly, Hypoalbuminemia, Hyponatremia, Hyperbilirubinemia, Ards, Pneumonia, Shock, Severe thrombocytopenia, Aki and Outcome: group**

Variables	Non severe scrub typhus	Severe scrub typhus	Total	Chi-square value	P-value
Sex					
Female	17	11	28	0.0112	0.9158
Male	19	13	32		
Duration of fever					
>14 days	4	4	8	0.3846	0.5351
7–14 days	32	20	52		
Maculopapular rash					
Absent	32	19	51	1.0675	0.3015
Present	4	5	9		
Edema					
Absent	23	21	44	4.1051	0.0427
Present	13	3	16		
Headache					
Absent	28	18	46	0.0621	0.8031
Present	8	6	14		
Tachypnoea					
Absent	28	22	50	2.0000	0.1573
Present	8	2	10		
Breathlessness					
Absent	35	14	49	14.5455	<0.0001
Present	1	10	11		
Cough					
Absent	24	14	38	0.4306	0.5116
Present	12	10	22		
Myalgia					
Absent	20	10	30	1.1111	0.2918
Present	16	14	30		
Abdominal pain					
Absent	30	19	49	0.1670	0.6828
Present	6	5	11		
Altered sensorium					
Absent	34	12	46	15.9006	<0.0001
Present	2	12	14		
Hepatomegaly					
Absent	32	19	51	1.0675	0.3015
Present	4	5	9		
Splenomegaly					
Absent	32	19	51	1.0675	0.3015
Present	4	5	9		
Hypoalbuminemia					
Absent	33	9	42	20.1190	<0.0001
Present	3	15	18		
Hyponatremia					
Absent	28	4	32	21.6071	<0.0001
Present	8	20	28		
Hyperbilirubinemia					
Absent	33	13	46	11.3199	0.00076
Present	3	11	14		
Ards					
Absent	36	22	58	3.1034	0.0781
Present	0	2	2		
Pneumonia					
Absent	36	19	55	8.1818	0.0042
Present	0	5	5		

(Contd...)

**Table 1: (Continued)**

Variables	Non severe scrub typhus	Severe scrub typhus	Total	Chi-square value	P-value
Shock					
Absent	36	15	51	15.8824	<0.0001
Present	0	9	9		
Severe thrombocytopenia					
Absent	36	21	57	4.7368	0.0295
Present	0	3	3		
AKI					
Absent	36	20	56	6.4286	0.0112
Present	0	4	4		
Outcome					
Death	0	3	3	4.7368	0.0295
Discharged	36	21	57		

Twenty-eight (46.7%) children's had hyponatremia. Fourteen (23.3%) children's had hyperbilirubinemia. Two (3.3%) children's had ARDS. Five (8.3%) children's had pneumonia. Four (6.7%) children's had myocarditis. Nine (15.0%) children were shocked. Three (5.0%) children's had severe thrombocytopenia. Four (6.7%) children's had AKI. Two (3.3%) children's had hepatic dysfunction. Two (3.3%) children's had meningoencephalitis. Three (5.0%) children were death and 57 (95.0%) children were discharged.

Bhat *et al.*<sup>[12]</sup> found that all children presented with fever. Other common symptoms were vomiting (56%), facial swelling (52%), cough (35%), abdominal pain (33%), breathlessness (29%), and decreased urine output (29%). High-grade fever (>101 oF) was recorded in 91% of children. Other common signs were hepatomegaly, splenomegaly, edema, tender lymphadenopathy, and hypotension, observed in 82%, 59%, 39%, 38%, and 36% of cases, respectively.

We found that in non-severe scrub typhus, 10 (27.8%) children's had eschar. In severe scrub typhus, 3 (12.5%) children's had eschar. Association of eschar versus scrub typhus group was not statistically significant ( $P = 0.1593$ ). Association of maculopapular rash versus scrub typhus group was not statistically significant ( $P = 0.3015$ ).

Khandelwal *et al.*<sup>[13]</sup> found that common clinical features were fever in 52 (100%), hepatomegaly in 34 (65.3%), nausea/vomiting in 23 (44.2%), lymphadenopathy in 22 (42.3%), abdominal pain, and splenomegaly each in 21 (40.3%), generalized swelling in 17 (32%) and headache in 12 (23%) patients. Eschar was seen in one patient only.

Lakshmanan *et al.*<sup>[14]</sup> found that of these 55 were boys and 28 were girls. Prolonged fever (100%), gastrointestinal symptoms (76%) such as vomiting, diarrhea, and abdominal

pain, lymphadenopathy (96%), and hepatosplenomegaly (61%) were common signs and symptoms of pediatric scrub typhus. Only six patients had severe illnesses. Out of these 83 patients, eschar was seen in 50 (60%) patients.

Our study found that in non-severe scrub typhus, 8 (22.2%) children had headache. In severe scrub typhus, 6 (25.0%) children's had headache. Association of headache versus scrub typhus group was not statistically significant ( $P = 0.8031$ ). In non-severe scrub typhus, 8 (22.2%) children's had tachypnoea. In severe scrub typhus, 2 (8.3%) children's had tachypnoea. Association of tachypnoea versus scrub typhus group was not statistically significant ( $P = 0.1573$ ).

It was found that in non-severe scrub typhus, 1 (2.8%) child was breathlessness. In severe scrub typhus, 10 (41.7%) children were breathlessness. Association of breathlessness versus scrub typhus group was statistically significant ( $P = 0.0001$ ). Our study found that in non-severe scrub typhus, 12 (33.3%) children's had coughed. In severe scrub typhus, 10 (41.7%) children's had coughed. Association of cough versus scrub typhus group was not statistically significant ( $P = 0.5116$ ). In non-severe scrub typhus, 16 (44.4%) children's had myalgia. In severe scrub typhus, 14 (58.3%) children's had myalgia. Association of myalgia versus scrub typhus group was not statistically significant ( $P = 0.2918$ ). It was found that in non-severe scrub typhus, 6 (16.7%) children's had abdominal pain. In severe scrub typhus, 5 (20.8%) children's had abdominal pain. Association of abdominal pain versus scrub typhus group was not statistically significant ( $P = 0.6828$ ). Our study found that in non-severe scrub typhus, two (5.6%) children's had altered sensorium. In severe scrub typhus, 12 (50.0%) children's had altered sensorium. Association of altered sensorium versus scrub typhus group was statistically significant ( $P < 0.0001$ ). Our study found that in non-severe scrub typhus, 4 (11.1%) children's had hepatomegaly. In severe scrub typhus, 5 (20.8%) children's had hepatomegaly. Association of hepatomegaly versus scrub typhus group was not statistically significant ( $P = 0.3015$ ). It was found that in non-severe scrub typhus, 4 (11.1%) children's had splenomegaly. In severe scrub typhus, 5 (20.8%) children's had splenomegaly. Association of splenomegaly versus scrub typhus group was not statistically significant ( $P = 0.3015$ ). It was found that in non-severe scrub typhus, 3 (8.3%) children's had hypoalbuminemia. In severe scrub typhus, 15 (62.5%) children's had hypoalbuminemia. Association of hypoalbuminemia versus scrub typhus group was statistically significant ( $P < 0.0001$ ).

Khandelwal *et al.*<sup>[13]</sup> found that among the laboratory parameters raised SGOT was seen in 49 (94.2%), raised SGPT in 41 (78.8%), thrombocytopenia in 46 (88.4%),

leucopenia in 12 (23%) and leukocytosis in 11 (21.1%) patients.

It was found that in non-severe scrub typhus, 8 (22.2%) children's had hyponatremia. In severe scrub typhus, 20 (83.3%) children's had hyponatremia. Association of hyponatremia versus scrub typhus group was statistically significant ( $P < 0.0001$ ). It was found that in non-severe scrub typhus, 3 (8.3%) children's had hyperbilirubinemia. In severe scrub typhus, 11 (45.8%) children's had hyperbilirubinemia. Association of hyperbilirubinemia versus scrub typhus group was statistically significant ( $P = 0.00076$ ).

Our study found that association of ARDS versus scrub typhus group was not statistically significant ( $P = 0.0781$ ).

Zhao *et al.*<sup>[15]</sup> found that early recognition of the patients at risk of MODS would be helpful in providing timely management and reducing mortality. The patients were classified into MODS present (64 cases, 14.3%) or MODS absent (385 cases, 85.7%). Multivariate logistic regression analyses revealed that the prognostic factors for MODS included skin rash.

In non-severe scrub typhus, 36 (100.0%) children's were discharged. In severe scrub typhus, 3 (12.5%) children were death and 21 (87.5%) children were discharged. Association of outcome versus scrub typhus group was statistically significant ( $P = 0.0295$ ).

## CONCLUSION

We found that duration of fever was higher in severe scrub typhus than non severe scrub typhus disease in children. It was found that the presence of breathlessness was significantly associated with severe scrub typhus than non-severe scrub typhus. The present study showed that altered sensorium was significantly higher with severe scrub typhus than non-severe scrub typhus. We also found that leukocytosis, hypoalbuminemia, hyponatremia, and hyperbilirubinemia were significantly related with severe scrub typhus than non-severe scrub typhus disease in children. It was found that morbidity and mortality were higher with severe scrub typhus disease in children.

Scrub typhus should be considered in the differential diagnosis of acute febrile illness associated with

gastrointestinal symptoms, hepatosplenomegaly, and lymphadenopathy including those with organ dysfunctions such as hepatitis, thrombocytopenia, MODS, meningitis, or ARDS. Empirical treatment for scrub typhus may be given in cases with strong clinical suspicion.

Symptoms of scrub typhus are quite non-specific. The presence of these factors should alert the physician about the impending life-threatening complications and should warrant intensive care monitoring, treatment, or referral to tertiary care center. Early recognition of the disease is a very important as any delay in treatment can lead to severe morbidity and high mortality.

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