

## Study of Scrub Typhus - Clinical Profile, Laboratory Profile, Complications and Outcome

Dr. Garuda Rama, MD, MRCPCH (London)

Associate Professor, Paediatrics Department, Konaseema Institute of Medical Sciences, Amalapuram, Andhra Pradesh, India, Pin-533021.

---

**Abstract:** Objectives: To study the diverse clinical features, laboratory manifestations, complications and outcome in children with scrub typhus.

**Materials and Methods:** Children below 15 yrs of age, presenting with fever, during June '13 to-Dec '14. Scrub typhus was suspected when fever continued for more than 5 days, with 1) an eschar and 2) one or more of the following clinical features - rash, edema, hepato-splenomegaly, lymphadenopathy, capillary leak, tick bite or 3) positive IgM antibodies (rapid test immuno-chromatography).

**Results:** Twenty five cases were seen with age ranging 2-15 years, with male preponderance. The common symptoms were fever, myalgia, edema, headache, gastrointestinal related and cough. Eschar was found in 36% of patients. Common signs were hepatomegaly (72%), splenomegaly (56%), maculopapular rash (40%) and lymphadenopathy (28%). IgM antibody test for scrub typhus was positive in 64% of patients. Thrombocytopenia (56%) and anicteric hepatitis (48%) were commonest complications. There was no mortality.

**Conclusions:** Any child presenting with features of hemorrhagic fever needs exclusion of other infections before scrub typhus is investigated for and once confirmed is treated with Doxycycline, to prevent complications including mortality.

**Keywords:** Hemorrhagic Fever, Scrub Typhus, Immuno-chromatography, Eschar

---

### I. Introduction

Rickettsial infections are acute febrile illnesses caused by intracellular, gram negative bacteria. In the Indian sub-continent scrub typhus is commonly caused by *Orientia tsutsugamushi*[2]. Scrub typhus is spread by tick bite and an eschar is produced at the site, in 45-55% of cases[9]. Scrub typhus is characterized by focal or disseminated vasculitis and perivasculitis involving the liver, spleen, heart, lungs and nervous system and may present as non-specific febrile illness or multi-organ involvement[1]. Scrub Typhus is one of the differential diagnosis of Hemorrhagic fever, hence after exclusion of other infections, prompt treatment is begun to prevent morbidity and mortality[3,4]. Recently epidemics of scrub typhus have been reported from many parts of our country and although it is endemic, it is grossly under-diagnosed due to its non-specific clinical features, lack of awareness among physicians and dearth of diagnostic facilities[2,3,4]. In our area, there is an increasing incidence, hence this study was carried out to assess the clinical profile, complications and outcome of patients.

### II. Material and Methods

The present study was conducted on a series of 25 patients who were diagnosed as scrub typhus over a period of 18 months from June 2013 to December 2014.

Selection of cases: 1. Children upto 15 years who had febrile illness of >5 days duration. 2. Children who had one or more of the following clinical features (after exclusion of other infections) - rash, edema, features of capillary leak, hepatomegaly, splenomegaly, lymphadenopathy and history of tick exposure[10]. 3. Presence of eschar. 4. Positive for IgM antibodies with immuno-chromatography.

Methods: Diagnostic work-up included history taking for tick exposure, general and systemic examination and search for eschar. CBC, platelet count, renal and liver functions tests, serum electrolytes, x-ray chest, ultrasound abdomen were performed. Investigated to exclude other infections that mimic scrub typhus - Peripheral smear and QBC (Malaria), Widal test and IgM (Salmonella tyhoid), Dengue serology, Leptospiral serology, Tuberculin test, HIV Elisa, Urine exam for pus cells and protein, Urine and Blood culture. All patients were tested for rapid IgM based on immune-chromatography which has sensitivity of 43-67% and specificity of 95-98%[6,7,8] and has been shown to be reliable and suitable in developing countries[8]. PT, APTT and INR were done if there was bleeding diathesis. CSF analysis was done if there was suspicion of meningitis. ECG, ECHO and serum CPK were done if myocarditis and congestive heart failure was suspected. All patients were treated with Doxycycline or Azithromycin and complications if any, were taken care of.

**Analysis**

The patients were analyzed for age, sex, seasonal variation, varied clinical features, eschar, complications and response to treatment.

**III. Results**

**Age and Sex distribution**

25 patients with scrub typhus were studied. The age ranged from 2-15 years. There were 7 patients from 0-5yrs (28%), 13 from 6-10yrs (52%) and 5 from 11-15yrs (20%). There were 14 (56%) males and 11 (44%) females. Peak incidence was following rainfall, from September to November, corresponding to some studies[4,5].

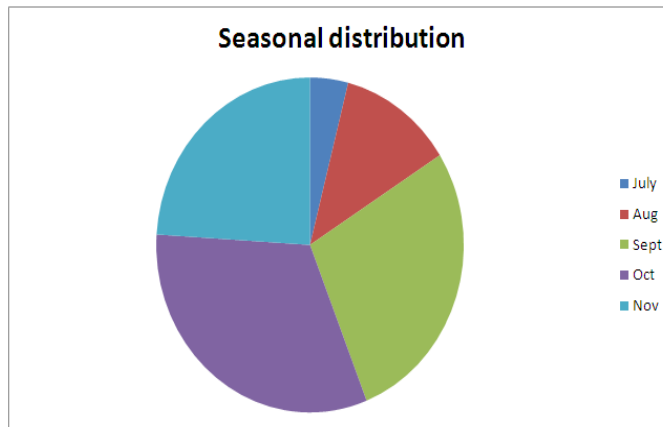
**Table-1. Age and Sex distribution**

Age	no.	%
0-5	7	28
6-10	13	52
11-15	5	20

Sex	no.	%
M	14	56
F	11	44

**Seasonal distribution**

- July 1 (4%)
- Aug 3 (12%)
- Sept 7 (28%)
- Oct 8 (32%)
- Nov 6 (24%)



**Clinical features:** All patients presented with fever. 72% had fever for more than 7days and 68% had high grade (>101<sup>0</sup>F). The common symptoms were headache, myalgia, swelling of body, cough and vomiting. Hypotension was seen in 32% and tachypnoea in 36%. Maculopapular rash was seen in 40% and predominantly on peripheries. Eschar was found in 32%, predominantly in thin moist areas groin, scrotum, axilla and other sites were of neck and thigh. Oedema was present in 40% of which 5 had facial puffiness, 3 anasarca and 2 pedal edema. Liver and spleen were palpable in 72% and 56% of cases. Lymphadenopathy was present in 28% of cases. Features of capillary leak with pleural effusion and ascites were present in 24% of cases, crackles and wheeze were heard on auscultation in 32%. Only one patient had altered sensorium.



Showing Eschar in Right Axilla

**Table-2. Clinical profile**

<u>Symptoms</u>	<u>No.</u>	<u>%</u>	<u>Signs</u>	<u>No.</u>	<u>%</u>
Fever <7days	7	28	Temp>101° F	17	68
Fever>7days	18	72	Temp<101° F	8	32
Headache	9	36	Tachypnoea	9	36
Myalgia	13	52	Hypotension	8	32
Vomiting/nausea	10	40	Maculopapular rash	10	40
Loose motion	3	12	Eschar	8	32
Abdominal pain	7	28	Lymphadenopathy	7	28
Jaundice	2	8	Hepatomegaly	18	72
Cough	14	56	Splenomegaly	14	56
Breathlessness	9	36	Crackles/wheeze	8	32
Swelling	11	44	Oedema	10	40
Seizures	1	4	Altered sensorium	1	4
Oliguria	2	8	Features of capill leak	6	24

Laboratory findings: Leucocytosis was seen in 24% and leucopenia in 32% of patients. Moderate thrombocytopenia was seen in 32% and severe thrombocytopenia in 24% of patients. Most of the patients (48%) had elevated transaminases with only 2 patients having elevated serum bilirubin. Hypoalbuminemia was seen in 32%, mild renal insufficiency in 8% and hyponatremia in one case. IgM antibodies with rapid test using immune-chromatography were elevated in 64% of cases.

**Table 3. Laboratory profile in children with scrub typhus**

<u>Biochemical profile</u>			<u>Hematological profile</u>		<u>Serology</u>	
	<u>No.</u>	<u>%</u>	<u>No.</u>	<u>%</u>	<u>No.</u>	<u>%</u>
ALT/AST	12	48	<u>TLC(mm3)</u>		IgM antibodies	16 64
Alk. phosphatase	10	40	<4000	8	32	
Bilirubin	2	8	4000-11000	11	44	
Hypoalbuminemia	8	32	>11000	6	24	
Creatinine>1.5mg/dl	2	8	<u>Platelets(mm3)</u>			
Hyponatremia	1	4	>1.5 lakh	11	44	
Albuminuria	3	12	< 1.5 lakh	8	32	
			< 1.0 lakh	8	24	

**Complications:** Thrombocytopenia (56%) was the commonest, followed by hepatic dysfunction, pneumonia, renal impairment, encephalopathy and meningitis. None had ARDS and Myocarditis.

**Table-4. Complications**

<u>Complication</u>	<u>No</u>	<u>%</u>
Thrombocytopenia	14	56
Hepatic dysfunction	12	48
Pneumonia	3	12
Renal impairment	2	8
Encephalopathy	1	4
Meningitis	1	4

**Treatment and outcome:** All patients received Doxycycline (6mg/kg/day b.d), Only one patient with encephalopathy received an additional IV Azithromycin. Patients with hypotension received IV bolus Normal saline and only 2 patients needed vasopressors. All responded to treatment. There was no mortality.

#### IV. Discussion

Scrub typhus was diagnosed in children who had one or more of the following clinical features (after exclusion of other infections) rash, edema, hepatomegaly, splenomegaly, lymphadenopathy, features of capillary leak and h/o tick exposure, presence of eschar or presence of IgM antibodies. Children in the age group of 5-10 years were mostly affected[2,13]. More males were affected than females in the ratio of 14:11, may be due to

high exposure to ticks among boys who are likely to play outdoors[2,10,11]. Majority of cases were seen after rainy season during the months of August-November[2,4,5,12]. However a study from Taiwan observed that majority of cases occurred during months of May – August[13].

In the present study most of the children presented with fever (100%), hepatomegaly (70%), splenomegaly (56%), cough (56%), headache with myalgia (52%), swelling of body (44%), which is similar to study by M.kumar et al[2]. A necrotic eschar which was pathognomonic of scrub typhus was seen in 32% of cases[9]. In contrast some authors found eschar in very few patients[2,12] and some studies outside India reported the presence of eschar in 50-80% of cases[13]. Maculo-papular rash was seen in 40% of patients[3]. Lymphadenopathy was seen in 28% patients correlating with study of M.kumar et al[2]. Features of capillary leak with pleural effusion and ascites which was an important finding in scrub typhus were seen in 24% of patients due to vasculitis[3]. Another important finding was predominance of gastrointestinal symptoms in 40% of patients that may be helpful distinguishing scrub typhus from other febrile illnesses like dengue fever or leptospirosis.[3]. Tachypnoea with crackles were seen in 36% of patients due to pleural effusion and pneumonia. Hypotension was observed in 32% of patients and many of them responded to fluids. Only two patients needed vasopressors. Only one patient presented with altered sensorium and seizures due to encephalopathy.

The mainstay of diagnosis in scrub typhus is serology. Immunofluorescence and Immunoperoxidase were the gold standard for diagnosis of scrub typhus with high sensitivity and specificity of >90% but these assays are very expensive, the results are delayed and are not available in our country[3,6,7]. In our country most used test is Weil-Felix, which is highly specific (98%) with low sensitivity (43%). Rapid diagnostic test using immune-chromatography were studied in Korea, Thailand and in India [6,7,8,9] which showed high specificity (95%) and low sensitivity (46-67%). Coleman et al [8] demonstrated that rapid immunographic assays has been shown to be reliable and suitable for use in developing countries. We used immune-chromatography for diagnosis of scrub typhus which showed positive with raised IgM antibodies in 16 patients (64%) corresponding to other studies [6,7,8,9]. The advantage of immune-chromatography is its rapidity, and high specificity for scrub typhus with the only disadvantage of low sensitivity.

In our study thrombocytopenia and hepatic dysfunction were the commonest complications[12,13]. Most of our patients had elevation of serum transaminases with elevated serum bilirubin in 2 patients only and without evidence of multi-organ dysfunction corresponding to other studies[3,4,12,13]. Three of our patients had pneumonia and they responded to antibiotics. 2 patients had mild renal impairment that improved with conservative management. Two patients had CNS complications, 1 patient with encephalopathy and the other with meningitis. Both recovered. In contrast, Myocarditis, AKI and ARDS were commonest complications along with thrombocytopenia and hepatitis in study by Manish et al [2].

**Table-5 Comparison of complications in %**

Complications	Present	Manish [2]	Murali [11]	Digra [5]	Somashekar [12]	Huang [13]
Thrombocytopenia	56	31	-	-	63.4	50
Hepatitis	48	31	-	14.2	70.7	91.3
Renal impairment	8	20	-	4.7	-	-
Pneumonia	12	3	12.2	9.5	12.2	7.1
Encephalopathy	4	17	25	19	14.6	17.9
Meningitis	4	6	12.2	19	12.2	21.4
ARDS	-	9	-	-	-	-
Myocarditis	-	34	-	14.2	-	-

All patients were treated with tab Doxycycline (6mg/kg/day b.d) orally. Only one patient suffering from encephalopathy needed IV Azithromycin. All patients with hypotension received IV Normal saline, only 2 patients required vasopressors in addition to fluids. Patients with pneumonia received antibiotic in addition to doxycycline. Two patients who had mild renal impairment responded to fluids and conservative treatment. All our patients recovered (no mortality) with tab Doxycycline and conservative management.

## V. Conclusion

Any child presenting with features of hemorrhagic fever and found to be negative for other infections, scrub typhus should be considered and investigated for. It should be treated empirically with doxycycline to prevent complications and mortality.

### References

- [1]. Clinical Profile of Scrub Typhus in children and its association with Haemophagocytic lymphocytosis. Indian Pediatrics, vol 51, Aug 15,2014,651-653. Naveen Sankhyan, LG Saptharishi, Kandasamy Saridaran.
- [2]. Scrub Typhus in children at a tertiary hospital in Southern India- Clinical profile and complications. Manish Kumar. Sriram Krishna Murthy, C.G.Delhikumar, Parameswaran Narayanan. Journal of infection and Public Health, 2012, 82-88.
- [3]. Scrub Typhus in patients reporting with acute febrile illness at a tertiary health care institution in Goa. Indian J Med Res 136, Dec 2012, pp 1020-1024. Kedareshvafr P.S, Sario Rodrigura, Ramnath, Lydia Dias, Amit Dias, Marina Vaz and E.Gomes.
- [4]. Outbreak of Scrub typhus in Pondicherry - J API, Jan 2010, vol 58, pp 24-28. M.Vivekanandan, Anna Mani, Yamini Sundara, Ajai Pratap Singh, Samuel Jayakumar, Shashikala Purty.
- [5]. Scrub typhus in children: Jammu experience- Jk science, Vol 12 no.2, April-June 2010,pp 95-97. Sanjeev kumar Digra, Ghan Shyam Saini, Virender Singh, Sunil Dutt Sharma, Rajesh Kaul.
- [6]. Accuracy of rapid IgM based immunochromatographic and immunoblot assays for diagnosis of scrub typhus. Pubmed. gov Ann J Trop med, Aug 2010,pp 365-369. Black Sell SD, Jenjaroen K, Phetsouvanh R, Tanquanu Chitcharchai A.
- [7]. Diagnosis of scrub typhus : Introduction of the immunochromatographic test in Korea. Korean J Intern Med 2014; 29:253-255. Ki Deok Lee, Chisook Moon, Won Supoh, Kyung Mok Solmn.
- [8]. Coleman et al, Comparative evaluation of selected diagnostic assays for the detection of IgG and IgM antibody in Orienta Tsutsugamushi in Thailand. Am J Trop Med hyg. 2002; 67; 497-503.
- [9]. Indian J Paediatrics 2012 no 79(11) 1459-62. Clinical profile of scrub typhus in children. Palanivel S, Nedunchelian K, Poovazhaqi V, Raghuna Dan R, P. Ramchandran.
- [10]. Rickettsial diseases in central India: Proposed clinical scoring system for early detection of spotted fever. Indian pediatr 2011, March 15. Rathi NB, Rathi AN, Goodman MH, Aghai ZH.
- [11]. Rickettsial infection in South India - How to spot the spotted fever. Indian Pediatr 2001;38:1393-6. Murali N, Pillai S, Raghupathy P, Padmini V, Mathai E.
- [12]. Magnitude and features of scrub typhus and spotted fever in children in India, J Trop pediatr 2005;16:228-9. Somashekar HR, Moses PD, Pavithran S, Mathew IG, Agarwal I, Rolain JM, et al.
- [13]. Scrub typhus in children in a teaching hospital in Eastern Taiwan,2000-2005. Southeast Asian J Trop Med Public Health 2009;40:789-94. Huang CT, Chi H, Lee HC, Chiu NC, Huang FY.