

A Cross Sectional Study of Clinico-Pathological Profile of Scrub Typhus in Children

Dr.M.Bhuvaneshwari^{1*}, Dr. G.B.Meghana², Dr. G. Sudeep³

¹Senior Consultant, Professor and HOD, Department of Pediatrics, GVR Children Hospital, Kurnool.

²Consultant Dermatologist, GVR Children Hospital, Kurnool.

³GVR Children Hospital, Kurnool.

Corresponding Author: Dr.M.Bhuvaneshwari

Abstract

Introduction: Scrub typhus is a Rickettsial infection caused by *Orientia tsutsugamushi*, mainly transmitted by the bite of larvae of a trombiculid mite. The symptoms of scrub typhus are indistinguishable from other illnesses like leptospirosis, malaria, and dengue fever. Epidemics of scrub typhus have been documented worldwide.

Materials and methods: The study design was a prospective cross-sectional study. The study was conducted from January 2020 to December 2020. Diagnosed patients of scrub typhus between 1 month to 12 years of age admitted in the Department of Pediatrics, GVR Children Hospital, Kurnool were the study population.

Results: There were total 164 patients with serologically diagnosed scrub typhus (OD value >0.5 on IgM ELISA for *O. tsutsugamushi*). Table 1 shows the age distribution and clinical characteristics of these patients. In this study pallor (89%) was the commonest finding followed by hepato-splenomegaly (73.2%), pneumonia (65.9%), rash in 43.9% and ascitis in 24.4% of cases. Eschar was found in 32.9% whereas serious complication like shock and meningoencephalitis was found in 9.8% of the cases (Table 1).

Conclusion: This study emphasizes the need for routine echocardiographic screening of all patients of scrub typhus which can depict coronary artery dilatation and pericardial effusion, which can have prognostic and therapeutic implications. In our study, although response was achieved with both doxycycline and azithromycin, we found doxycycline to be superior to azithromycin in terms of therapeutic response.

Key Words: Scrub typhus, doxycycline, azithromycin, doxycycline, leptospirosis, malaria, and dengue fever.

Date of Submission: 20-12-2021

Date of Acceptance: 04-01-2022

I. Introduction

Scrub typhus is a Rickettsial infection caused by *Orientia tsutsugamushi*, mainly transmitted by the bite of larvae of a trombiculid mite.¹ The symptoms of scrub typhus are indistinguishable from other illnesses like leptospirosis, malaria, and dengue fever. Epidemics of scrub typhus have been documented worldwide.²

In India, Goa, North eastern states and south India have reported the disease. It is wide spread in Japan, Taiwan, China, South Korea, Nepal, Australia and Indonesia.³ The common symptoms and signs seen in scrub typhus cases is fever, chills with rigors, myalgia, headache and rash with dysfunction of organs such as kidney (acute renal failure), liver (hepatitis), lungs (acute respiratory distress syndrome, central nervous system (meningitis), GIT (vomiting and diarrhea) or circulatory collapse with haemorrhagic features.⁴

Eschar is a characteristic features of scrub typhus. Although it is characteristic, many studies have reported scrub typhus without eschar. Puducherry is a small coastal town surrounded by many villages from Tamil Nadu.⁵ Presently there is an increase in number of cases of scrub typhus presenting with fever, rash and hepatorenal involvement. In the present study, the clinical profile and laboratory findings of these patients were studied.

II. Materials And Methods

The study design was a prospective cross-sectional study. The study was conducted from January 2020 to December 2020. Diagnosed patients of scrub typhus between 1 month to 12 years of age admitted in the Department of Pediatrics, GVR Children Hospital, Kurnool were the study population.

Method of collection of data

All children between 1 month and 12 years of age, admitted with fever for more than 5 days and positive IgM ELISA for scrub typhus were included in the study. These children were followed up during the hospital stay and their laboratory results, response to treatment and complications were documented. Initial

investigation for malaria, dengue, UTI, pneumonia and enteric fever was negative. This study population was randomly divided into 2 groups of 41 patients each, into doxycycline and azithromycin group. They were then evaluated for therapeutic response in terms of defervescence of fever, resolution of symptoms as well as improvement of relevant echocardiographic findings. All patients were followed up for a period of 1 month to detect any residual disease.

Inclusion criteria

Children between 1 month to 12 years of age with persistent fever >5 days with OD value >0.5 for *O. tsutsugamushi* on IgM ELISA and Eschar (irrespective of duration of fever) were included in the study.

Exclusion criteria

Other causes of acute febrile illness such as malaria, dengue, leptospira, UTI, pneumonia and skin/soft tissue infections were excluded from the study.

Statistical analysis

Clinical and laboratory parameters of the patients and the significant factors were demonstrated using frequency table and appropriate chart/graphs. The vital and demographic factors of patient were evaluated using Chi square test or Fisher’s exact test. Comparison between azithromycin or doxycycline for their performance was done using t test or Mann Whitney test, based on the nature of the dataset and subsequent results were tabulated with statistic value or p value. Any p value <0.05 was taken as significant. The statistical software used was SPSS v21.0.

III. Results

There were total 164 patients with serologically diagnosed scrub typhus (OD value >0.5 on IgM ELISA for *O. tsutsugamushi*). Table 1 shows the age distribution and clinical characteristics of these patients.

In this study pallor (89%) was the commonest finding followed by hepato-splenomegaly (73.2%), pneumonia (65.9%), rash in 43.9% and ascitis in 24.4% of cases. Eschar was found in 32.9% whereas serious complication like shock and meningoencephalitis was found in 9.8% of the cases (Table 1).

Table 1: Age distribution and clinical characteristics of patients (N=144)

Clinical characteristics	Number	Percentage
Age distribution		
1 month to 2 years	28	34
3 years to 5 years	70	42.6
6 years to 12 years	66	40.2
Eschar		
Present	54	32.9
Absent	110	67.1
Rash		
Present	72	43.9
Absent	92	56.1
Pallor		
Present	146	89
Absent	18	11
Edema		
Present	44	26.8
Absent	120	73.2
Lymphadenopathy		
Present	104	63.4
Absent	60	36.6
Hepatosplenomegaly		
Present	120	73.2
Absent	44	26.8
Ascitis		
Present	40	24.4
Absent	124	75.6
Shock		
Present	16	9.8
Absent	148	90.2
Pneumonia		
Present	108	65.9
Absent	56	34.1
Meningoencephalitis		
Present	16	9.8
Absent	148	90

Table 2: Laboratory parameters.

Laboratory parameters	Number	Percentage
Hb <11 gm/dl		
Present	148	90
Absent	16	10
Leucocytosis (WBC >15000 /mm³)		
Present	64	39
Absent	100	61
Thrombocytopenia (platelet <100,000 /mm³)		
Present	18	11
Absent	146	89
Raised CRP (>6 mg/l)		
Present	164	100
Hypoalbuminemia (alb <2.5 gm/dl)		
Present	46	28
Absent	118	72
Hyponatremia (Na <135 meq/l)		
Present	56	34.1
Absent	108	65.9
Transaminitis (raised AST, ALT)		
Present	112	68.3
Absent	52	31.7
Raised PT/INR		
Present	6	3.7
Absent	158	96.3
Azotemia (raised urea/creatinine)		
Present	22	13.4
Absent	142	86.6
Echo showing (pericardial effusion)		
Present	38	23.2
Absent	126	76.8
Echo showing coronary artery dilation		
Present	18	11
Absent	146	89
Echo showing (both effusion and CAD)		
Present	4	2.4
Absent	160	97.6

Table 3: Association between drug response and therapy.

Drug response	Azithromycin	Doxycycline	Total
No	22	6	28
Row (%)	78.6	21.4	100.0
Col (%)	26.8	7.3	17.1
Yes	60	76	136
Row (%)	44.1	55.9	100.0
Col (%)	73.2	92.7	82.9
Total	82	82	164
Row (%)	50.0	50.0	100.0
Col (%)	100.0	100.0	100.0

Table 4: Repeat echocardiogram

Repeat echo after 2 weeks	Frequency	Percent
Normal	56	100
Total	56	100

Among the laboratory parameters, CRP was raised in all patients followed by anaemia in 90% of patients, raised transaminases in 68.3%, leucocytosis in 39%, hypoalbuminemia in 28% and hyponatremia in 34% of children. Thrombocytopenia was found in 11% of patients and altered PT/INR in 3.7% of cases. Renal failure was detected in 13.4% (Table 2).

IV. Discussion

Fever of more than 5 days duration was the inclusion criteria for enrolling the patients and the mean duration of fever in our study population was approximately 9 days. There were total 82 patients with serologically diagnosed scrub typhus (OD value >0.5 on IgM ELISA for *O. tsutsugamushi*). In a study by Kannan et al found that detecting *O. tsutsugamushi* specific IgM antibodies by ELISA have excellent sensitivity and specificity for the diagnosis of scrub typhus. But a four-fold rise in the antibody level between the acute and

convalescent sera is confirmatory. We found that 156 out of 164 patients demonstrated significant rise in the titre of antibodies by scrub IgM ELISA between acute and convalescent sera which is statistically significant ($p < 0.05$).

There was a diversity of clinical manifestations such as Eschar (32.9%), rash (43.9%), pallor (89%), edema (26.3%), lymphadenopathy (63.4%), hepatosplenomegaly (73.2%), ascites (24.4%), shock (10%), pneumonia (65.9%), meningoencephalitis (10%) in our study population. Lakshmanan et al (2018) found that scrub typhus is a common aetiology for an acute undifferentiated fever among children.¹³ In their study in 83 patients, gastrointestinal symptoms (76%) such as vomiting, diarrhoea and abdominal pain, lymph-adenopathy (96%) and hepatosplenomegaly (61%) were common signs and symptoms and only six patients had severe illnesses. Out of these 83 patients, Eschar was seen in 50 (60%) patients.

In our study, we documented spectrum of laboratory abnormalities which were anaemia (90%), leucocytosis (39%), thrombocytopenia (11%), hyponatraemia (34%), hypoalbuminaemia (28%), raised transaminases (68.3%), altered coagulation profile (3.7%), renal failure in 13.4%, and CSF lymphocytic pleocytosis in 10%. Anaemia was the most common laboratory abnormality seen in 90% of patients, while CRP was raised in all the patients.

In a study by Khandelwal et al in 52 patients with scrub typhus, 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.¹⁴ Common complication were hepatitis in 49 (94.2%), multi-organ dysfunction syndrome (MODS) in 12 (23.1%), ARDS and hypotension each in 10 (19.2%), meningoencephalitis in 5 (9.6%), acute kidney injury (AKI) in 3 (5.8%), hemophagocytic lymphohistiocytosis (HLH) and myocarditis in 1 (1.9%) patient each.

In a study by Narayanasamy et al 2018, in 230 children with scrub typhus, multivariate analysis identified 5 factors, breathlessness (OR: 6.85, 95%CI: 2.69 to 9.87), altered sensorium (OR: 11.48, 95% CI: 3.43 to 10.19), leucocytosis (OR: 3.38, 95% CI: 1.12 to 10.16), hypoalbuminemia (OR: 10.78, 95% CI: 2.66 to 48.76), and hyponatremia (OR: 10.08, 95% CI: 2.11 to 23.42) to be significantly associated with the severe scrub typhus cases.

V. Conclusion

There can be a huge diversity in the range of clinical presentations of scrub typhus involving almost every organ system ranging from pneumonia, cardiac involvement, shock, meningoencephalitis or renal failure. This study emphasizes the need for routine echocardiographic screening of all patients of scrub typhus which can depict coronary artery dilatation and pericardial effusion, which can have prognostic and therapeutic implications. In our study, although response was achieved with both doxycycline and azithromycin, we found doxycycline to be superior to azithromycin in terms of therapeutic response.

References

- [1]. Kothari VM, Karnad DR, Bichile LS. Tropical infections in the ICU J Assoc Physicians India 2006; 54 : 291-8.
- [2]. Chogle AR. Diagnosis and treatment of scrub typhus - the Indian scenario. J Assoc Physicians India 2010; 58 : 11-2.
- [3]. Kedareshwar PS, Rodrigues S, Nevrekar RP, Dias L, Dias A, Vaz M and Gomes E. Scrub typhus in patients reporting with acute febrile illness at a tertiary health care institution in Goa Indian J Med Res, 2012 Dec;136: 1020-24.
- [4]. Sharma A, Mahajan S, Gupta ML, Kanga A, Sharma V. Investigation of an outbreak of scrub typhus in the himalayan region of India Jpn J Infect Dis 2005; 58 : 208-10.
- [5]. Batra HV. Spotted fevers and typhus fever in Tamil Nadu. Indian J Med Res 2007; 126 : 101-3.
- [6]. Mathai E, Lloyd G, Cherian T, Abraham OC, Cherian AM. 4. Serological evidence for the continued presence of human rickettsioses in southern India. Ann Trop Med Parasitol 2001; 95 : 395-8.
- [7]. Ittyachen AM. Emerging infections in Kerala: a case of scrub typhus Natl Med J India 2009; 22 : 333-4.
- [8]. Varghese GM, Abraham OC, Mathai D, Thomas K, Aaron R, 5. Kavitha ML, et al. Scrub typhus among hospitalised patients with febrile illness in South India: magnitude and clinical predictors J Infect 2006; 52: 56-60.
- [9]. Lee YS, Wang PH, Tseng SJ, Ko CF, Teng HJ, 2006. Epidemiology of scrub typhus in eastern Taiwan Jpn J Infect Dis 2004; 59: 235-238.
- [10]. Nagano I, Kasuya S, Noda N, Yamashita T. Virulence in mice of *O. tsutsugamushi* isolated from patients in a new endemic area in Japan. Microbiol Immunol 1996 ; 40: 743- 47.