Scrub Typhus in Children

Zainab M[1], Gupta AK[2], Guha S[3]

Abstract

Introduction: Scrub typhus is an acute febrile illness caused by infection with rickettsial bacilli *Orientia tsutsugamushi*. This was a retrospective observational study to study the clinical profile of paediatric scrub typhus, its associated complications and response to treatment **Material and Methods:** Record files of all patients diagnosed with positive Weil felix (OXK>1:80) and Scrub IgM positive over a period of one year were analysed. Total of 10 cases were diagnosed as scrub with median age of presentation 4.1 years. **Results:** Fever was present in all followed by pain abdomen (50%), rash. Anaemia (90%), lymphadenopathy (70%) hepatomegaly (100%), Leukopenia was present in those cases with fever <1 week while leucocytosis was found thereafter. Most common complication were hepatitis (100%) shock (50%), acute kidney injury (AKI) 30%, DIC in 20% cases. Secondary HLH was found in 20% and pancarditis in one case. All the cases showed dramatic response to doxycycline. **Conclusion:** So a high index of suspicion is required to diagnose scrub and early initiation of treatment is essential to prevent mortality from the disease.

Key words: rickettsia, re-emerging infection, multisystem involvement

Introduction

Scrub typhus is a re-emerging infection in the India. It is caused by intracellular gram negative bacilli *Orientia tsutsugamushi* and transmitted by bite of trombiculid mite. It should be considered as a differential in children presenting with acute febrile illness with rash, oedema, hepatosplenomgaly and lymphadenopathy It is characterised by focal or disseminated vasculitis and perivasculitis involving the heart, lung, liver, kidney and central nervous system[1]. Various case reports have been published from North and South India and in the hilly terrains of north and north east.[2,3,4] However the disease is not restricted to these regions now as increased cases being detected in the cities of eastern India as well. Rickettsial infections are grossly under diagnosed in India because of their non-specific clinical presentation, a limited awareness about the disease, a low index of suspicion among clinicians and a lack of diagnostic facilities.

[1]Dr. Madiha Zainab, MBBS, Post graduate trainee, [2]Prof. Dr. Atul Kumar Gupta, MBBS, DCH, MD, Head of Department, [3]Dr. Suparna Guha, Associate Professor, MBBS, MD. All from the department of Paediatrics, Vivekananda Institute of Medical Sciences, Kolkata

Address for correspondence
Dr. Madiha Zainab.
P-67, C.I.T.Road. Sch -52,
Kolkata 700014, West Bengal.
Tel No; +919903655132.
E-mail: madiha_zainab@ymail.com

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The objectives of the study were to study the clinical profile of paediatric scrub typhus, its associated complications and response to treatment.

Material and Methods

This was a retrospective observational study carried out in the paediatric department of Vivekananda Institute of Medical Sciences from Jan 2015- Jan 2016 after taking due clearance from the ethical committee of the institute.

All record files of patients with positive Weil Felix (OX K titre >1:80) and Scrub IgM positive by ELISA were selected for study purpose. The presenting complaints of the patients, their course during hospital stay, investigations done, complications developed if any, treatment received and the response to treatment were analysed from the case files. Initially common infections like malaria, enteric fever, dengue, UTI, septicaemia, tuberculosis were ruled out by relevant investigations and clinical examination. Lumbar puncture done if suspected meningitis. In suspected cases of scrub typhus, scrub typhus IgM by ELISA was sent. In those cases of scrub typhus, complete blood counts, liver function test, kidney function test were analysed. Echocardiography, and ECG were done if suspected myocarditis and in cases complicated with congestive cardiac failure.

Results

A total of ten cases were diagnosed as scrub typhus with positive scrub typhus IgM by ELISA. Males (4) and females (6). Three cases were from Kolkata, four from districts of south 24 parganas and Two from Hooghly district and one case from Contai. No history of travel to endemic region was obtained from any of the cases. Seven cases presented in the period from June-November. Median age of presentation was 4.1 year. Median duration of fever was 12 days (5-24 days). Other important presenting features were pain abdomen (5), cough (5), rash (3), oedema (2), convulsion (2), jaundice (2) and haematuria (1).

On examination, pallor was present in 90% cases. Other significant findings were lymphadenopathy (7), hepatomegaly (10), splenomegaly (8), and ascites (5). Wheeze was present in five cases and S3 gallop in four of the cases. Only two cases had characteristic eschar.

Leukopenia was observed if fever duration < 6 days and neutrophilic leucocytosis if fever> 6 days. Thrombocytopenia was present in 30% cases. Hypalbuminaemia, elevated transaminase present in all the cases. INR was however deranged in three cases which presented with DIC and shock. CSF analysis were done in two cases who had convulsion during hospital stay which showed pleocytosis with lymphocyte predominance.

Most common complication was hepatitis present in all the cases (Table 2), four cases had features of myocarditis, shock and acute kidney injury (AKI). Two of which were also complicated with features of disseminated intravascular coagulation (DIC) and needed blood products as part of supportive treatment. HLH has previously been reported with scrub typhus. In our study we had two cases with secondary HLH which responded to doxycycline.one case had pancarditis with Left ventricular ejection fraction 50% along with

Table 1: Clinical features and laboratory findings in scrub typhus patients.

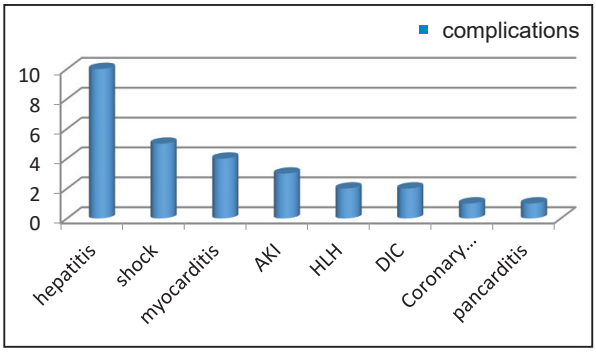
Sign And Symptom	Number (%)	Laboratory Findings	Number (%)
Fever	10 (100%)	Anaemia	9 (90%)
Pain abdomen	5 (50%)	Leucopenia<5000/cmm	4 (40%)
Rash	3 (30%)	Leucocytosis>15000/cmm	6 (60%)
Oedema	2 (20%)	Platelets< 1.5lc/cmm	3 (30%)
Convulsion	2 (20%)	Albumin< 3g/dl	10 (100%)
Jaundice	2 (20%)	AST> 40U/L	10 (100%)
Cough	5 (50%)	Creatinine> 1mg/dl	3 (30%)
Haematuria	1 (10%)	Urine RBC>5/HPF	1 (10%)
Eschar	2 (20%)	CSF pleocytosis	2 (20%)
Lymphadenopathy	7 (70%)	ALT> 40U/L	10 (100%)
Hepatomegaly	10 (100%)		
Splenomegaly	8 (80%)		
Ascites	5 (50%)		
Wheeze/crepts	5 (50%)		
S3 gallop	4 (40%)		

pericardial effusion, DIC and septic shock which responded to doxycycline. Coronary dilatation, which is rare association of scrub typhus, was found in one case in this study.

All the cases initially were empirically started on ceftriaxone after sending the relevant investigations. However there was no improvement. In five of the cases azithromycin was added later on. Only one of the case responded to azithromycin and did not need doxycycline. In the rest of the cases doxycycline had to be given @5mg/kg for 7 days. Minimum time for deffervescence of fever was 15 hour and the maximum time was 72 hour. No mortality was however reported in this study.

Table 2: Complications associated with scrub typhus

Complications	Number (%)
Hepatitis	10 (100%)
Shock (Septic, Cardiogenic)	5 (3, 2) (50%, 30%, 20%)
Myocarditis	4 (40%)
AKI	3 (30%)
DIC	2 (20%)
HLH	2 (20%)
Coronary Dilatation	1 (10%)
Pancarditis	1 (10%)



Discussion

In this study we describe the clinical profile of paediatric scrub typhus and its complications in a tertiary care centre in West Bengal. There is paucity of data from this part of India. Various case series and sporadic case reports have been published from North India and South India[3,4]. However scrub is equally prevalent in this part of subcontinent as well.

In most of the studies there has been male predominance[3,4], however our study shows female predominance. Majority of the cases presented in the months of June-November which is similar to the study in North India[3]. Similar seasonal variation has been observed in studies from South East Asian countries like Taiwan[6]. Mean age of presentation in our study was 4.1 years. Previous lowest age reported in case series is 6.3 years[7].

Fever was the universal finding with mean duration of 12 days in our study. Other presenting features being pain abdomen and cough. Oedema was present in 60% case from study in Pondicherry[8] while another from Vellore reported to be 37%[9].While in our study 20% had oedema on presentation while 50% developed ascites in due course. Eschar was present in 20% cases similar to most studies[3] from North India. In contrast, some studies outside India report eschar in 50-80% cases while other authors did not find an eschar in any of the cases. Rash has been reported to be 20% in cases from south while from north as high as 90% may be found[3,4]. In our study it was present in 30% cases.

Naveen et al report hepatosplenomegaly in nearly all children with scrub[3]. Hepatic dysfunction being present in 77% cases, however we found hepatomegaly along with raised liver enzymes in all the patients. Liver involvement is a marker of scrub infection. An important finding was leukopenia in the first week of illness while leucocytosis thereafter. Thrombocytopenia and hypalbuminaemia are associated with severe scrub as evident from our study, however these findings needs to be validated on a larger sample. Similar findings were present case series reported from previously[3].

The definitive diagnosis of scrub is by serology. Gold standard serological tests are immunofluorescence antibody test or indirect immune-peroxidase assay[5] but are not readily available and very costly. Weil Felix is however readily available in our country. It is highly specific but lacks sensitivity[10]. In the present study we used ELISA testing for IgM antibody for diagnosis. This test has shown good sensitivity and specificity and has been adequately validated[11].

An important outcome of the study was to show the high relation of myocarditis (40%), cardiogenic and septic shock associated with scrub typhus needing vasopressors for support and showing dramatic response to doxycycline. Such high prevalence previously reported 34% only by Kumar M et.al[4]. Sporadic case reports show incidence to be 1-14%[12]. have been published but case series is lacking. One rare association was found with coronary dilatation in a young infant who was initially diagnosed as Incomplete Kawasaki Disease and treated with IVIG. However it was only after giving doxycycline that fever and hepatosplenomegaly subsided. This shows that scrub can be a mimicker of Kawasaki disease in infants and young children.

Acute kidney injury (AKI) was found in 40% of the cases, 50% of which were associated with myocarditis and 20% associated with DIC. Other studies[4] report AKI to be 20% while some report 2-4.7%[12]. A study in adult scrub from Goa[16] reported AKI to be as high as 33%. Severe haematuria is an uncommon presentation of scrub which was found in one of our case, who responded dramatically to doxycycline after confirmation of the diagnosis. T say et al[17] from Taiwan reported eight cases with ARDS, three cases with ARF, one myocarditis, one septic shock.

CSF abnormalities is similar to viral meningitis. Two cases had aseptic meningitis. A study done in Vellore suggests that scrub typhus should be considered in the differential diagnosis of subacute meningitis especially when associated with renal failure and jaundice[13,14].

20% case developed secondary HLH. Previously a study North India reported three out of 1fifteen with secondary HLH[3]. This suggests that HLH may not be uncommon in children with severe scrub. For patients with reactive HLH, supportive care and treatment of underlying infection is associated with recovery in 60-70%[15].

All the cases in our study responded to doxycycline except one which responded to azithromycin. There was however no response to ceftriaxone as almost all cases in our study was started on ceftriaxone initially for a broad spectrum coverage against multiple pathogens which affects children with the mentioned symptoms. Minimum time for defervescence was 15hr and maximum 72 hr in those cases who developed pancarditis and shock. No mortality was however reported in our study in spite of the severe complications.

Conclusion

Scrub typhus is readily prevalent in eastern India and is grossly under diagnosed and under reported. The diagnosis requires a high index of suspicion by the clinician. It can present in all age groups and is associated with grave complications like myocarditis, AKI, DIC and may even mimic Kawasaki disease in infants. Dramatic response is seen if treatment initiated on time.

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