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Original Research Article

Increasing trend in pediatric scrub typhus admissions in a tertiary care hospital, South India: Clinical profile and outcomes of cases over four years, 2011-2014.

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ABSTRACT

Background: In developing countries, clinical profile based empirical treatment is practiced for treating pediatric scrub typhus cases. Knowledge on pattern of symptoms and signs will help in early initiation of specific treatment. This study was aimed to describe clinical profile and trends in admissions of pediatric scrub typhus cases in a tertiary teaching hospital.
Methods: A record based cross sectional descriptive study was conducted among all clinically diagnosed scrub typhus pediatric (<13 years of age) cases admitted between 1st January 2011 and 31st December 2014 in a tertiary teaching hospital, South India. Data on symptoms, signs, laboratory findings, treatment and outcome were extracted from clinical case records. Data were entered and analyzed using Epi Data software.
Results: Of the total 228 cases, 124 (54.4%) were males, 131 (57.4%) were less than five years of age and 88% were from rural areas. Fever (100%), vomiting (61.2%) and cough (54.8%) were the most common symptoms. Hepatomegaly (88.6%), splenomegaly (64.5%), lymphadenopathy (48.7%), edema (43.4%) and eschar (38.6%) were the common signs observed. Anemia was present in 122 (59.8%) and thrombocytopenia in 75 (33.3%) children. Only one child (0.4%) died. There was an increasing trend in proportion of scrub typhus cases to overall admissions from 1% to 2.2% over four-year period (2011-2014). More cases were admitted between the months of September and January.
Conclusions: Scrub typhus contributed to significant pediatric admissions in the tertiary care centre with an increase in cases over years. Treatment with doxycycline or azithromycin showed good response and mortality was very low.

Keywords: Clinical Profile, Rickettsia, Scrub Typhus, Seasonal Trends, Zoonoses

INTRODUCTION

Rickettsial diseases are one of the neglected zoonotic diseases of public health importance.[1] With an increase in number of cases over the recent years, WHO has recognized rickettsial diseases as re-emerging diseases.[2] Scrub typhus is the most common rickettsial infection reported from many parts of Asia and the Pacific islands.[3] It is endemic in Asia-Pacific region which is called "tsutsugamushi triangle" bounded by Siberian Russia in the north, South Pacific islands to the east, Northern Australia to the south and central Asia to West.[4] In these endemic areas, around one billion are at risk of acquiring the disease and an estimated one million are affected by scrub typhus every year.[5] An important concern is the high case fatality rate, which may range up to 30-40% of

untreated cases.[6,7] Evidence from serologically confirmed studies suggests that the scrub typhus infection is common among children. Also, community survey from a rural Thai region reported that more than half of scrub typhus cases were children.[8] In India, scrub typhus has been reported from several states.[9-14]

The diagnosis of scrub typhus is quite difficult due to undifferentiated signs and symptoms, lack of disease awareness and low index of suspicion among clinicians and lack of diagnostic facilities.[15] With constraints in diagnosing scrub typhus serologically, WHO has given case definition for clinically suspecting scrub typhus that is mainly based on exclusion of the main causes of PUO in children.[16]

Profiling the clinical symptoms and signs will help in capturing the spectrum of clinical presentation, which will help in evolving regional diagnostic guidelines. Available literature on scrub typhus from India mainly focuses on clinical features and outcomes in an adult population. Very few studies (with small sample size) from India are available on clinical features and outcome in children, though none of them studied the trends in admissions of scrub typhus cases.[17-22]

There is anecdotal evidence on increase in pediatric scrub typhus cases in south India in recent years. Inpatient admissions related to scrub typhus can be taken as a proxy measure for increasing burden of scrub typhus as community based surveys are not feasible. Hence this study was aimed to describe clinical profile and trends in admissions of pediatric scrub typhus cases in a tertiary teaching hospital, south India.

METHODS

A record based cross sectional descriptive study was conducted among children admitted and treated for scrub typhus under Department of Pediatrics at a tertiary care teaching hospital in Puducherry, South India. Both outpatient and inpatient care are provided at free of cost for all patients. On an average, 200 children attend the OPD daily. There are 227 beds for pediatric inpatients and the bed occupancy rate is more than 95% throughout the year. All pediatric scrub typhus patients during January 2011 and 31st December 2014 were included.

In each of the pediatric wards "inpatient registers" were maintained with name of the child, hospital inpatient number, date of admission and diagnosis. All the in-patient case records were maintained in Medical Record Department (MRD) of the tertiary hospital. Using information from "inpatient registers" we traced all the case records from MRD. The data extraction proforma was used to collect information on socio-demographic characteristics, symptoms, signs, complications, available laboratory investigations, treatment details and outcomes during discharge from hospital. Data were extracted by a single investigator. The total number of admissions in each month during the reference period (January 2011 to December 2014) was obtained from MRD. The study protocol was approved by the Institute Ethics Committee of the tertiary care teaching hospital.

Data were entered and analyzed using EpiData software. Clinical profile and outcomes were summarized as percentages. Trends in admissions (overall admissions and scrub typhus cases) were explained using a line diagram.

RESULTS

A total of 228 children were hospitalized with scrub typhus during the reference period. Median (IQR) age of children was 5.4 (3.6) years. Of total, 124 (54.4%) children were males, 131 (57.4%) children were aged less than five years of age. Majority of them (88%) were from rural areas.

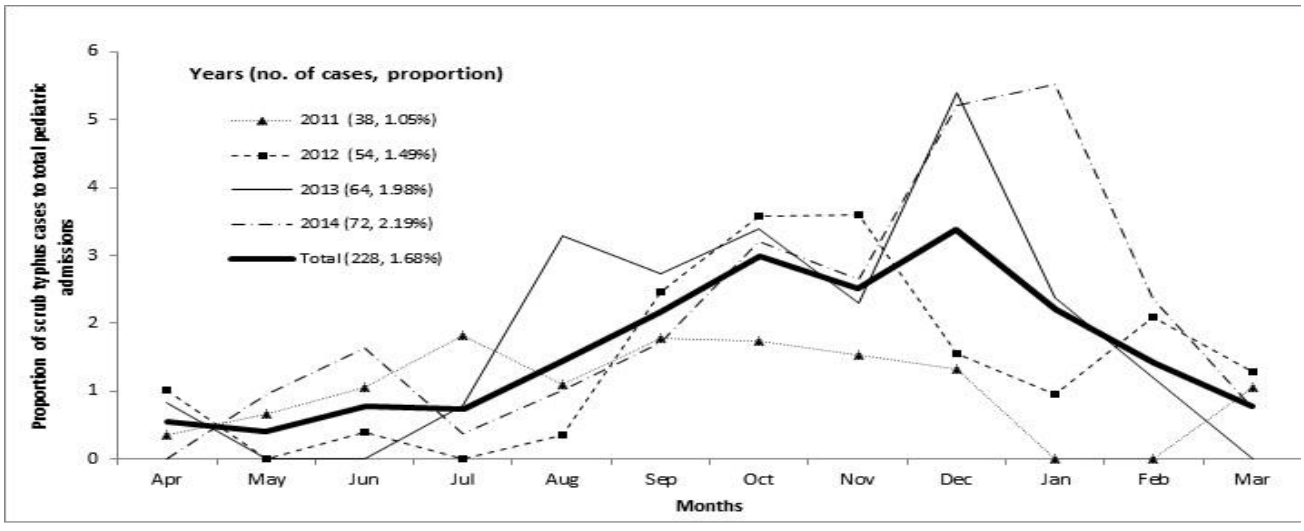

Figure 1: Seasonal trend of proportion of scrub typhus cases to overall admissions in a tertiary care hospital of Puducherry, South India, 2011-2014 (n=228).

Fever was observed in all children (100%), of which (35.1%) had fever with chills. Table 1 shows common symptoms, signs and complications. Few children had symptoms like breathlessness (18%) oliguria (18%), diarrhea (12%) and headache (11%). Commonest signs were hepatomegaly (89%), splenomegaly (65%) and lymphadenopathy (49%). Other findings like pleural effusion (9%), altered sensorium (6%), meningeal signs (5%) and icterus (5%) were found. Anemia was the most common complication noted in 122 (60%) of the cases, followed by thrombocytopenia (33%), capillary leak (26%) and acute respiratory distress syndrome (8%). Ascites (8%), meningoencephalitis (8%), shock (5%) and myocarditis (3%) were the other complications. Pneumonia, hepatitis, leucopenia and acute kidney injury were present in less than two percent of the children.

Majority of the cases were observed during months from September to January (Figure 1).

Table 1: Common symptoms, signs and complications among children with scrub typhus admitted in a tertiary care hospital, Puducherry, South India, 2011-2014 (n=228).

Clinical profile	≤5 years* N=131, n (%)	>5 years* N=97, n (%)	Total N=228, n (%)
Common symptoms			
Fever	131 (100)	97 (100)	228 (100)
Vomiting	70 (53.4)	70 (72.2)	140 (61.2)
Cough	85 (64.9)	40 (41.2)	125 (54.8)
Facial puffiness	67 (51.1)	36 (37.1)	103 (45.2)
Abdominal pain	43 (32.8)	53 (54.6)	96 (42.1)
Abdominal distension	41 (30.6)	11 (11.3)	52 (22.8)
Common signs			
Hepatomegaly	122 (93.1)	80 (82.5)	202 (88.6)
Splenomegaly	89 (67.9)	58 (59.8)	147 (64.5)
Lymphadenopathy	61 (46.6)	50 (51.5)	111 (48.7)
Edema	68 (51.9)	31 (32.0)	99 (43.4)
Eschar	53 (40.5)	35 (36.1)	88 (38.6)
Pallor	20 (15.3)	9 (9.3)	29 (12.7)
Petechiae/Ecchymosis	13 (9.9)	9 (9.3)	22 (9.6)
Maculopapular rash	14 (10.7)	7 (7.2)	21 (9.2)
Common complications			
Anemia (hemoglobin<10g/dl)	84 (71.8)	38 (43.7)	122 (59.8)
Thrombocytopenia (platelets<1 lakh)	45 (34.9)	30 (31.3)	75 (33.3)
Capillary leak	46 (35.1)	14 (14.4)	60 (26.3)
ARDS†	13 (10)	6 (6.2)	19 (8.3)
Ascites	10 (7.6)	7 (7.2)	17 (7.5)
Meningitis/Encephalitis	2 (1.5)	15 (15.5)	17 (7.5)
Shock	6 (4.6)	6 (6.2)	12 (5.3)
Myocarditis	5 (3.8)	2 (2.1)	7 (3.1)

* Column percentage (multiple responses possible). † \ Acute Respiratory Distress Syndrome

Table 2 shows serological and bio-chemical investigations of children included. More than one third of cases were positive for OX K suggestive of scrub typhus. Majority of them had leukocytosis (42.7%) and hyponatremia (45.8%).

Table 3 describes treatment details, duration of hospital stay, and clinical outcomes. Doxycycline (55%) or azithromycin (42%) were the commonly used antibiotics, both drugs were used in 3% of children. Majority of cases (82%) had hospital stay less than a week. Twenty (9%) children were admitted to Intensive Care Unit (ICU), Of the 20 children admitted in ICU, 16 (80%) had ICU stay less than 7 days. Of 228 children, one child (0.4%) died, 3 children (1.3%) left the hospital against medical advice and the remaining 224 children (97.8%) were discharged after recovery. The child who died had complications like myocarditis and ARDS.

There was an increasing trend in proportion of scrub typhus cases to overall admissions over four year period from 1% (2011) to 2.2% (2014) as well as increase in the absolute number of cases during that period (p value for trend <0.001).

Table 2: Laboratory investigations among children with scrub typhus admitted in a tertiary care hospital of Puducherry, South India, 2011-2014.

Laboratory investigations	Number (%)
Weil-Felix test (N=174)	
OX K positive	53 (33.9)
Total leucocytes count (cells/cu.mm) (N=225)	
Leukocytosis (>10000)	96 (42.7)
Sodium in MEq/L (N=212)	
Hyponatremia (<135)	97 (45.8)
Bilirubin in mg/dl (N=196)	
Hyperbilirubinemia (>1.2)	8 (4.1)
Albumin in mg/dl (N=198)	
Hypoalbuminemia (<2.5%)	13 (6.6)
Renal parameters in mg/dl (N=220)	
Elevated Urea (>40)	17 (17.7)
Elevated creatinine (>1)	3 (1.4)

Table 3: Treatment and Clinical outcomes among children admitted with scrub typhus in a tertiary care hospital of Puducherry, South India, 2011-2014 (N=228).

Treatment details	Number (%)
Antibiotic used	
Doxycycline only	125 (54.8)
Azithromycin only	95 (41.7)
Both	8 (3.5)
ICU admission	
Yes	20 (8.8)
No	208 (91.2)
Duration of hospital stay (in days)	
1-7	187 (82)
8-14	32 (14)
≥15	9 (4)
Clinical Outcomes	
Recovered and discharged	224 (98.2)
Discharge against Medical Advice	3 (1.3)
Death	1 (0.4)

DISCUSSION

This hospital based study involving 228 cases over four year period has shown that more than 50% of cases were in less than 5 years age group, almost equally affecting both gender, more from rural areas and an increasing trend in recent years with seasonal variation. Studies from other parts of India and other countries have reported a similar age distribution.[9,10,18-20] Male preponderance among the admitted cases was reported in several studies in contrast to our study finding. Exact reason for this finding is not known. The difference in gender distribution reported in other studies may be due to smaller sample size. Regarding the urban-rural distribution, almost all the studies have reported higher cases from rural areas similar to our study. This may be related to prevailing favorable conditions in rural areas related to source, vector and transmission dynamics of the scrub typhus.[4-6,10,18-22,27-32] Other important finding similar to other studies was the increase in cases during cooler months from September to January. Rainy seasons favors growth of grassy vegetation which helps in increase in vector population and interaction with human host.[6,18-20]

Similar to other studies, fever was the predominant symptom in our study.[1-10,17-32] In the present study facial puffiness was noted in 45.2% of the cases, however higher proportion up to 74.62% have been reported in literature.[9,10.18,19,20] Cough (54.8%), abdominal pain (42.1%), breathlessness (18.4%) and oliguria (17.5%) were other observed symptoms. Previous studies observed presence of cough ranging from 35% to 73.12%, abdominal pain (21-51%), breathlessness (29-37%) and oliguria (29-43%).[1,3-5,8-12,16-22,27-32] Hepatomegaly (88.6%), splenomegaly (64.5%) followed by lymphadenopathy (48.7%) and edema (43.4%) were the common signs found in this study. Other studies reported varied occurrence of hepatomegaly (26%-98%) and splenomegaly (17%-88%).[1,3,9-12,18-22,28-32] Presence of Eschar, a classical sign of the vector bite which varied between 11% and 69% in previous studies, was noted in 38.6% of the cases in the present study. Overall the findings on signs and symptoms in this study population were similar to other studies among children.

Weil-Felix test was used to confirm scrub typhus cases in our study. Though Weil-Felix has low sensitivity and specificity, it remains the only available option to substantiate clinical diagnosis in resource limited developing countries. In the current study, Weil-Felix test was done in only 76.3% cases, mainly due to unavailability of testing kits. Among those who underwent Weil-Felix test (33.9%) children had OX-K titer positive suggestive of Rickettsia tsutsugamushi. Similar positivity rate to Weil-Felix test has been reported in other studies.[8,18,24,28] Anemia (hemoglobin<10g/dl) was seen in 59.8% of the cases similar to previous studies.[10] Thrombocytopenia (platelet count<one lakh/cu.mm) was seen in 33.3% parallel to the reports of previous studies.[1,9,10,18-22] In our study, ARDS and ascites were noted in 8.3% and 7.5% of cases respectively similar to the findings of a previous study.[10] Other studies had reported higher proportion of complications compared to our study. This might be due to late hospitalization in other studies or due to effective management of cases in the present study setting.

Antibiotics like doxycycline or azithromycin were used to treat cases in the study setting. Almost all cases showed a significant response to antibiotics. This is to similar to the findings from other studies.[9,10,18-20,32] The overall mortality observed in the current study was 0.4% and it is very less compared to other studies (ranging from 2.5% to 13%). Possible reasons may be relatively better health seeking behavior, early admission of cases,

effective antibiotic use and availability of advanced care facilities to manage complications at study setting. The case fatality rate may be as high as 30% in untreated cases, low case fatality rate found in this study emphasize the need for early and effective management in preventing mortality due to scrub typhus.

The study has few merits. First the study had larger sample size compared to all published studies on pediatric scrub typhus from India. Hence the estimates from this study are likely to be more precise. Second, we compared the trends over months (seasonal trends) and determined the contribution of scrub typhus cases to overall pediatric admissions. However, there are few limitations. First the true burden of scrub typhus, age and gender distribution and trends of scrub typhus in the community could not be ascertained due to selection of cases only from the hospital. With low burden of scrub typhus and varied and non-specific clinical presentation, carrying out a community based survey is challenging. However, this study setting being one of the largest hospitals with wide catchment area, the findings may be fairly representative for the geographical area. Second, we used clinical diagnosis instead of laboratory confirmed cases which are costly. Hence misclassification of cases cannot be ruled out. This study was conducted in a routine clinical setting where costly diagnostic kits were not available. Hence this study finding gives useful insights regarding the clinical diagnosis and management which can be generalized to similar resource constraint clinical settings in developing countries.

Community based surveys to determine the true burden and also to delineate the endemic areas need to be carried out. Health awareness measures focusing on specific protective measures like wearing protective cloths, insect repellants and avoiding sitting or lying on grassy plains should be carried out in endemic areas. Chemoprophylaxis with chloramphenicol or tetracycline can be considered in the endemic areas. Considering the significant burden of scrub typhus among rural children, any case of fever has to be evaluated for scrub typhus especially in the months between September and January. Establishing sentinel sites at district and medical college hospitals and integrating with the ongoing disease surveillance systems needs to be considered. This will help in monitoring the trends and early identification of outbreaks. Inclusion of scrub typhus or rickettsial diseases into the national vector borne disease control program can be considered.

CONCLUSION

Scrub typhus contributed to significant pediatric admissions in the tertiary care centre with an increase in cases over years. Treatment with doxycycline or azithromycin showed good response and mortality was very low.

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