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Original Research Article

Complication profile of scrub typhus and its association with total leucocyte count

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ABSTRACT

Background: Recent reports from several parts of India indicate that there is a resurgence of scrub typhus. There have been a few studies analysing the association of various complications of scrub typhus with leukocyte count. The objective of this study was to study the association of various complications of scrub typhus with leukocyte count in children.
Methods: A prospective study done at SPMCHI, SMS Medical College, Jaipur from August 2014 to November 2014. 75 Scrub typhus positive children were included in the study group. A detailed history of signs, symptoms, complications, demographic background was taken and relevant laboratory investigations done. The association between the complications of scrub and the total leukocyte count was studied, statistical analysis was done using Chi Square test.
Results: Meningoencephalitis was most commonly seen complication in 14.7% followed by ARDS (9.3%), hepatitis (8%), AKI (6.7%), shock (6.7%) and myocarditis (1.3%). Meningoencephalitis and acute renal failure were more frequent among Scrub Typhus cases with leucopenia ($p = 0.006$, $P = 0.011$ respectively). It was observed that hepatitis was more frequent with leukocytosis, but was not statistically significant.
Conclusions: Our study revealed that leukopenia has a significant association with meningoencephalitis and acute kidney injury.

Keywords: Children, Leukopenia, Meningoencephalitis, Orientia tsutsugamushi, Scrub typhus

INTRODUCTION

Scrub typhus is an important cause of acute febrile illness in South East Asia. The causative agent of scrub typhus is Orientia tsusugamushi which is transmitted by the bite of chiggers (larva) of trombiculid mite (leptotrombidium). Like other vascular rickettsiae, O. tsutsugamushi infects endothelial cells and causes vasculitis, the predominant clinico- pathologic feature of the disease. However, the organism also infects cardiac myocytes and macrophages.[1] Clinical manifestations include headache, vomiting, abdominal pain, myalgia, arthalgia, swelling, altered sensorium, seizures, rash, lymphadenopathy, hepatomegaly, splenomegaly, bleeding mainifestations, icterus, and eschar.[2] Eschar is a black necrotic lesion usually found in areas where skin is thin, moist or wrinkled and where the clothing is tight like axilla, genitalia and inguinal area. Serious complications occur during the second week of illness if not treated appropriately. Common complications are meningo-encephalitis, myocarditis, acute kidney injury (AKI), acute respiratory distress syndrome (ARDS), shock, hepatitis.[3,4]

There is a paucity of studies regarding clinico-laboratory profile of scrub typhus in children as majority of studies

done on the adult population in India. Hence, we planned this study with the objective to study the association of total leucocyte count and various complications of scrub typhus.

METHODS

This study was done at the Sir Padampat Mother and Child Health Institute, Jaipur, the largest tertiary care referral hospital serving Jaipur and surrounding districts of Rajasthan. All 281 patients reported to our hospital during post monsoon months (August to November 2014) with febrile illness were tested for scrub IgM ELISA. Rapid antigen test for malaria parasite, dengue serology (IgM and IgG), Widal test were also done to exclude alternative diagnosis. A detailed history of signs, symptoms, and demographic, geographic, social background was taken and complete physical examination was done. 75 patients which were Scrub typhus IgM positive were included in the study group. They were evaluated further with laboratory tests i.e. complete blood count, peripheral blood smear, liver function tests (LFT) renal function tests (RFT), Ultrasonography abdomen (USG) and CSF examination where indicated.

Meningo-encephalitis was defined as presence of fever and/or altered sensorium and/or seizures and/or signs of meningeal irritation associated with elevated proteins and >5 cells on CSF analysis. ARDS is defined as bilateral alveolar or interstitial infiltrates on chest radiograph and PaO2/FIO2 <300 mm Hg on arterial blood gas analysis.[5] Acute kidney injury (AKI) was diagnosed if there was an abrupt (within 48 hour) reduction of kidney function, defined as an absolute increase in serum creatinine of either >0.3mg/dl or percentage increase of >50% or reduction in urine output (documented urine output of <0.5 ml/kg/hr).[6] Patients who had elevated serum transaminases (>10 times normal) were labelled to have deranged liver function tests. Myocarditis was defined as presence of left ventricular systolic dysfunction (EF<55%) on echocardiography. Shock was defined when despite administration of isotonic intravenous fluid bolus >60 ml/kg in 1 hour, blood pressure (BP) was <5th percentile for age or patient required vasoactive drug to maintain BP. Demographic data, history, examination and investigations were noted and stored in an Excel spread sheet for analysis. Chi square test (or Fischer's exact test) was performed for categorical data. Statistical significance was defined as p value < 0.05.

RESULTS

A total 75 children with scrub typhus were analyzed. Majority 49/75 (65.3%) of patients were > 5 years of age. There were 38 (50.7%) males and 37 (49.3%) females, mostly 64/75 (85.3%) were from rural areas.

Vomiting 30 (42.8%) was the most common presenting symptom followed by abdominal pain 28 (38.8%), swelling 25 (32.6%), headache 14 (18.4%), myalgia/arthralgia 12 (16%), seizures 12 (16%), altered sensorium 8 (10.6%), rash 7 (9.3%), cough 6 (8%) and diarrhoea 4 (5.3%) (Figure 1).

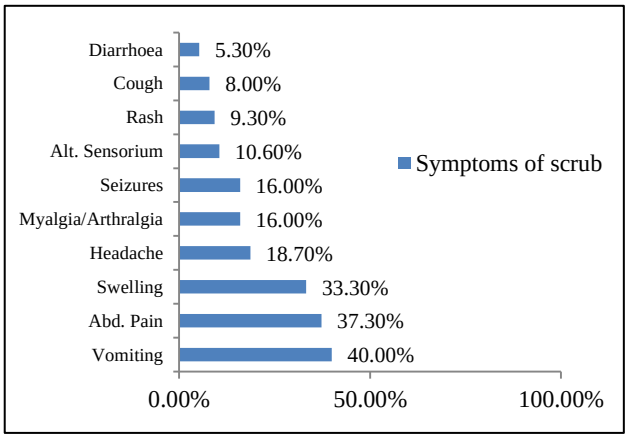

Figure 1: Common presenting symptoms of scrub typhus.

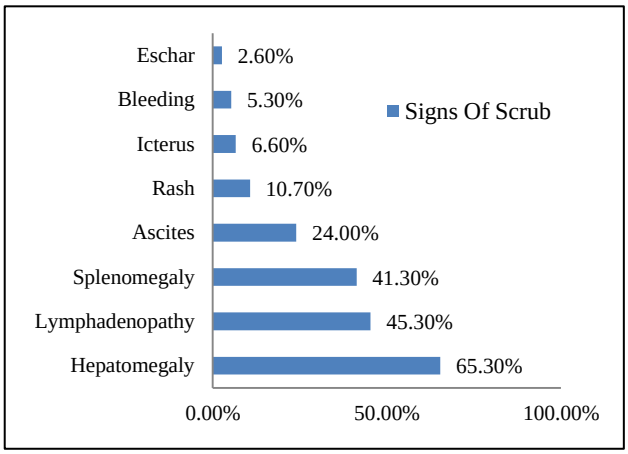

Figure 2: Common presenting signs of scrub typhus.

Hepatomegaly 49 (65.3%) was commonest sign observed, followed by lymphadenopathy 34 (45.3%), splenomegaly 31 (41.3%), ascites 18 (22.4%), rash 8 (10.7%), icterus 5 (6.6%), bleeding 4 (5.3%), eschar 2 (2.6%) (Figure 2).

Table 1: Deranged laboratory parameters in scrub typhus cases.

Lab parameters	Scrub (n = 75)
Anaemia (Hb<11g/dl)	65 (86.7%)
Thrombocytopenia (<1 lakh/cu.mm)	30 (40.0%)
Fluid leakage on USG (ascites±pleural effusion)	29 (38.7%)
Leukocytosis (>11000/cu.mm)	21 (28.0%)
Leucopenia (<4000/cu.mm)	11 (14.7%)
Deranged Liver Function Tests	6 (8.0%)
Deranged Renal Function Tests	5 (6.7%)

Anaemia was a prominent laboratory finding seen in 65 (85.7%) cases. Thrombocytopenia 30 (40%), Fluid leakage on USG 29 (38.7%), deranged LFT'S 6 (8.0%), deranged RFT'S 5 (6.7%). Leukocytosis 21 (28.6%) was more common finding than leucopenia 11 (14.7%) (Table 1). Among the complications (Table 2) meningoencephalitis was most commonly seen in 11/75 (14.7%) followed by ARDS 7/75 (9.3%), hepatitis 6/75 (8%), AKI 5/75 (6.7%), shock 5/75 (6.7%) and myocarditis 1/49(1.30%). It was observed that meningoencephalitis and acute renal failure were significantly higher in cases of scrub typhus with leucopenia ($p = 0.006$ and $p = 0.011$ respectively) than in cases with leukocytosis and normal leukocyte count. There was no significant difference in other complications.

Table 2: Association of TLC with complications of scrub typhus.

Complications (n = 75)	Normal TLC (n = 43)	Leucopenia (n = 11)	Leukocytosis (n = 21)	Level of significance p value
Meningoencephalitis (n = 11)	5 (11.6%)	5 (45.4%)	1 (4.8%)	0.006
ARDS (n = 7)	2 (4.7%)	3 (27.2%)	2 (9.5%)	0.011
Hepatitis (n = 6)	1 (2.3%)	1 (9.1%)	4 (19.0%)	0.071
Shock (n = 5)	1 (2.3%)	2 (18.2%)	2 (9.5%)	0.141
Acute kidney injury (n = 5)	1 (2.3%)	3 (27.3%)	1 (4.8%)	0.713
Myocarditis (n = 1)	1 (2.3%)	0	1 (4.8%)	0.068

DISCUSSION

Scrub typhus is a vector borne febrile illness with varied presentations. In this study there were almost equal no of male and female cases with scrub as compared to other studies where males were more common.[7-10] Most of the children diagnosed with scrub typhus were >5 years of age, which is similar to that by Huang et al.[7] This may be explained by the fact that children above 5 years tend to engage more in outdoor activities.

Common symptoms in this study were vomiting (40%), abdominal pain (37.30%), swelling (33.30%), seizures (16%), altered sensorium (10.6%) and cough (8%). Kumar et al reported puffiness of face and pedal edema in 63% and 60%.[11] Nowneet et al reported Vomiting (56%), cough (35%), abdominal pain (33%), breathlessness (29%) and seizures (20%) as the chief presenting symptoms.[10] Huang et al reported cough in 50% and vomiting in 29% of cases.[7] Cough and breathlessness were not frequently seen in the present study as respiratory system was less involved in our cases.

Hepatomegaly and Splenomegaly was observed in 65.30% and 41.30% cases respectively which is similar to other authors who have reported hepatomegaly in 59% to 98% and splenomegaly in 18% to 88%.[10-12] Lymphadenopathy, an important sign in scrub typhus that helps to distinguish it from dengue was seen in 45.30%, which was in the range of 18% to 62% as recorded by other authors.[11-13] Rash was seen in 8 (10.7%) patients while in previous studies it is reported in 20% cases.[10,11] Eschar, a valuable clinical clue in the diagnosis of scrub typhus as reported by Kumar et al and Somashekar et al was seen in 2 (2.6%) cases.[11,14] This is in accordance with the authors who suggest that the absence of an eschar does not rule out the diagnosis of scrub.[15-17]

Thrombocytopenia as reported by other studies was a common laboratory feature seen in 40% cases and was within the reported frequency of 22% to 78%.[10-12] The most common laboratory parameter seen was anemia (86.7%). This might be attributed to the poor nutritional status of the Indian children. In the present study, at the time of presentation normal leucocyte count was 57.3%, leucocytosis (28.0%) was a more common finding than leucopenia (14.7%).

Scrub typhus has life threatening complications like meningoencephalitis, which was the most common complication and seen in 14.7% cases in the present study and is quite similar to others who have reported it between 5% to 19%.[2,11,12] ARDS was seen in 7 (9.3%) cases, as compared to a study by Raman et al [18] in which 24 (19.2%) developed ARDS; 17 of which required assisted ventilation. Hepatitis was seen in 8% in the present study while Kumar et al reports hepatitis in 31%.[11]

The lower incidence of hepatitis may be due to the higher cut off of the level of transaminases (>10 times) taken in the present study to label it as hepatitis. In the present study AKI was seen in 6.7 % of the cases as compared to two previous Indian studies based on pediatric data which have reported incidences of AKI in rickettsial infections from 2 to 4.7%.[16,17] Kumar et al report a higher incidence of AKI (20%).[11] Hypotension was observed in 6.7% of cases against 25.8% reported in a previous study that required inotropes.[10] Myocarditis was a less common but a serious complication seen in 1.3% of the cases which is

lower than two previous studies from India which reported myocarditis in 10-14.2% of their study subjects.[19,20] Manish et al report a high incidence of myocarditis (34%)in their study subjects.[21]

In the present study an attempt to study the association between complications of scrub typhus and total leukocyte count was made. The frequency of all complications except hepatitis was high in patients with leucopenia as compared to patients with leukocytosis and normal counts. The occurrence of meningoencephalitis and ARDS amongst the cases with leucopenia was found to be statistically significant (p = 0.006, P = 0.011 respectively) when compared with normal and raised leukocyte counts. Hepatitis was more frequently seen with leukocytosis, but was not statistically significant. However, to find the association between other complications and total leukocyte count we need more cases.

CONCLUSION

The common complications of scrub typhus were meningo-encephalitis, ARDS, hepatitis, ARF, shock, myocarditis. Meningoencephalitis and acute renal failure were more frequent among scrub typhus cases with leucopenia (p = 0.006, P = 0.011 respectively) than with leukocytosis and normal counts. Therefore, our study revealed leucopenia as a significant risk factor for meningoencephalitis and ARDS. The small sample size of the study is a limiting factor for generalizing the observations. A larger study is needed to confirm the findings.

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