International Journal of Contemporary Pediatrics
Yadav SP et al. Int J Contemp Pediatr. 2018 Sep;5(5):1715-1718
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: http://dx.doi.org/10.18203/2349-3291.ijcp20183504

Original Research Article

Scrub typhus an emerging public health threat in Eastern Nepal: an analysis from a tertiary centre during two years outbreak

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Received: 19 May 2018
Accepted: 26 June 2018

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ABSTRACT

Background: Scrub typhus is an emerging disease in the eastern part of Nepal. Varied clinical presentation and lack of laboratory resources make diagnosis difficult. Epidemic outbreaks have been reported from different parts of Nepal. The objective of this study was to describe the clinical presentation, complications, laboratory profile and outcome of admitted cases with scrub typhus.
Methods: The cases (1 month to 15 years) admitted in paediatric ward or intensive care with confirmed serological diagnosis of scrub typhus over a period of two years 2015 and 2016, were retrospectively evaluated from the maintained records. All the clinical and laboratory parameters along with intervention and outcome were analysed by descriptive statistics.
Results: There were 52 cases of scrub typhus of which 30 were female and 22 males. The youngest case was 2.5 months old and the median age was 3.6 years, mode being 14 years (7 cases). Majority (>71%) of cases were from the hilly districts. Mean duration of illness at presentation was 7.8±2.7 days and ≥94% of the cases had temperature of ≥102°F. More than half of the cases had hepatomegaly (78%), splenomegaly (53.8%), respiratory symptoms (53.8%) and the classical eschar (55.8%). The mean haemoglobin of the cases was below 10 g/dl and the mean platelet count was below 70,000/cu mm, along with hyponatremia, hypoalbuminemia and elevated liver enzymes. X-rays showing variable infiltrates were seen in 59.6%. Respiratory complications like pneumonia and acute respiratory distress syndrome (ARDS) were seen in 46%, encephalopathy in 12%, myocarditis in 40.2%and acute kidney injury in 7.6%. Twenty percent of the cases required intensive care management. There was 15.4% mortality, and all the cases who succumbed had ARDS and myocarditis.
Conclusions: In this study the main clinical features were hepatomegaly, splenomegaly, respiratory symptoms and the classical eschar. Mortality was 15.4%. ARDS and myocarditis were present in all cases who died.

Keywords: Children, Complications, Diagnosis, Scrub typhus

INTRODUCTION

Scrub typhus is a mite borne acute, febrile illness caused by a gram negative intracellular coccobacillus *Orienta tsutsugamushi*.[1] The disease is distributed throughout the Asia Pacific rim and is endemic in Korea, China, Taiwan, Japan, Pakistan, India, Thailand, Malaysia, and Queensland, Australia.[2] In Nepal, a few cases have been found in southern plain region and a study from Patan Hospital found 3.2% of 876 febrile cases serologically positive for scrub typhus.[3] Recently, an outbreak of scrub typhus has occurred in 2015 and 2016 from different

parts of Nepal.[4] Aftermath of a massive earthquake in Nepal in April 2015, the transmission cycle of this mite borne disease is considered to have been favourable, particularly in the monsoon season.[5]

Scrub typhus presents with a variety of clinical features with varying degree of complications, particularly in the second week of illness.[6] Owing to the lack of skilled health workers and diagnostic facilities in the poor communities where the disease is thought to be more concentrated, early diagnosis and initiation of appropriate antibiotics is not always possible, thus increasing the chances of complications and death from this seemingly treatable condition. There was no previous known outbreak reported from the Eastern region of Nepal. We conducted this study to describe the clinical presentation, complications, laboratory profile and outcome of admitted cases with scrub typhus.

METHODS

B. P. Koirala Institute of Health Sciences (BPKIHS) is a tertiary level teaching hospital designated from its inception to be the referral hospital for Eastern region of Nepal. It is also considered to be the centre of excellence for tropical and infectious diseases in the country. Department of Pediatrics, BPKIHS first reported the outbreak of scrub typhus in the country in 2015, when several children brought with undifferentiated febrile illness from eastern hills succumbed while under care in the paediatric intensive care unit (PICU). The diagnosis of scrub typhus was made by serological confirmation of *Orientia tsutsugumushi* in the blood sample sent to National Public Health Laboratory (NPHL), Teku, Kathmandu. The cases of scrub typhus occurred throughout the country in 2016. However, eastern hilly areas remained the hotspot for the infection and BPKIHS remained the centre of referral for paediatric patients in this region.

Hence, in order to analyse the clinical spectrum of the disease, this study was conducted. It constitutes the retrospective chart review of children below 16 years admitted in paediatric ward or PICU from January 2015 to December 2016, with a diagnosis of scrub typhus. The diagnostic test used in the year 2015 was IgM Elisa and PCR, and in 2016 the diagnosis was made by rapid diagnosis test. The diagnosis was made with assistance of NPHL. A well designed proforma was used to collect the records regarding demographic profile, clinical presentation, complication, laboratory investigations, need of intensive care, day of defervescence, duration of hospital admission and outcome. Consent for conducting study was taken from Institutional Review Board. Data was analysed with MS Excel 2007 and StataIC 14.

RESULTS

We managed 52 cases of scrub typhus from January 2015 to December 2016, from age 1 month to 15 years. Out of them there were 30 female and 22 males with ratio of 1:4, showing female preponderance. The youngest case was of 2.5 months old and the median age was 3.6 years, mode being 14 years (7 cases). About 71% of cases were from three hilly districts Sankhuwashava (14 cases), Dhankutta (13 cases) and Bhojpur (10 cases).

Mean duration of illness at presentation to the referral centre was 7.8±2.7 days and ≥94% of the cases had temperatures of ≥102^{0}F. The major clinical findings of the cases presented to our centre are summarized in Table 1.

Table 1: Clinical findings at presentation to hospital (n = 52).

Clinical finding	Number (%)
Fever	52 (100.0)
Hepatomegaly	41 (78.8)
Chills	30 (57.7)
Eschar	29 (55.8)
Splenomegaly	28 (53.8)
Respiratory symptoms	28 (53.8)
Shock	21 (40.4)
Pallor	21 (40.4)
Pain in abdomen	21 (40.4)
Oedema	21 (40.4)
Swelling	20 (38.5)
Rashes	19 (36.5)
Headache	15 (28.8)
Vomiting	11 (21.2)
Altered sensorium	09 (17.3)
Lymphadenopathy	08 (15.4)
Diarrhoea	06 (11.5)
Seizures	04 (07.7)
Decreased urine output	03 (05.8)

More than half of the cases had hepatomegaly (78%), splenomegaly (53.8%), respiratory symptoms like cough, shortness of breath (53.8%) and the classical eschar (55.8%). The classical eschar is depicted in Figure 1.

Figure 1: Classical eschar.

Table 2: Laboratory parameters of cases with scrub typhus.

Lab parameter	Mean (SD)
Haemoglobin (gm/dl)	9.3(1.7)
Hematocrit (%)	27 (05)
Total leucocyte count (counts/cu.mm.)	10,335 (5997)
Platelet count (counts/cu.mm.)	67,143 (40,908)
Sodium (Meq/L)	133.6(05.4)
Potassium (Meq/L)	3.7 (0.5)
Ionized Calcium (mmol/L)	1.1 (0.1)
Urea (mg/dl)	34.4 (17.1)
Creatinine (mg/dl)	0.4 (0.2)
Albumin (gm/dl)	2.7(0.5)
Alanine transaminase (IU/L)	212.6 (133.4)
Aspartate transaminase (IU/L)	240.8(183.7)
Alkaline phosphatase (IU/L)	335.7(278.5)
Total bilirubin (mg/dl)	1.1(0.9)
Direct bilirubin (mg/dl)	0.6(0.6)
Lactic dehydrogenase (IU/L)	609.3(142.5)
Prothrombin time (sec)	18.0(4.6)
International normalised ratio	1.4(0.4)

There are some important laboratory parameters which support the diagnosis of scrub typhus. The mean haemoglobin of the cases was below 10 g/dl, along with hyponatraemia, hypoalbuminaemia and elevated liver enzymes alanine transaminase (ALT), aspartate transaminase (AST) and lactic dehydrogenase (LDH). The average platelet count was also below 70,000/cu mm.However, the total leucocyte usually was in the normal range. X-rays showing variable infiltrates were seen in 59.6%. The mean and the standard deviation of the important laboratory parameters of these cases are depicted in the Table 2.

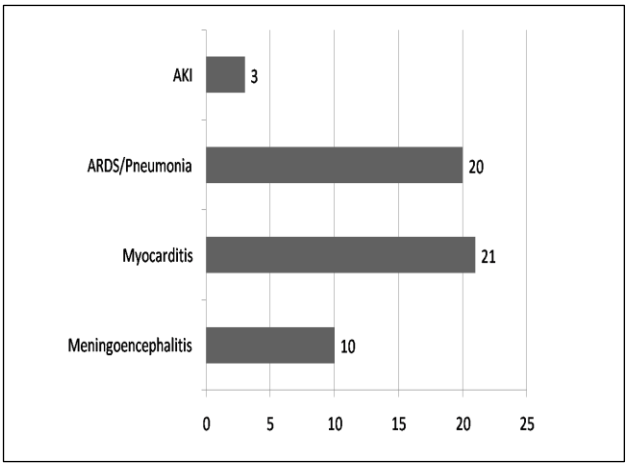

Figure 2: Frequency of complications (n = 52).

There were a few complications in these cases such as pneumonia, acute respiratory distress syndrome (ARDS), myocarditis, meningoencephalitis and acute kidney injury (AKI). The frequency of complications is shown in Figure 2.

Due to severity at presentation, 20% of the cases required intensive care management. The cases were treated with doxycycline (4 cases), azithromycin (4 cases), chloramphenicol (7 cases) and combined chloramphenicol and azithromycin (37 cases). The average duration of defervescence was 2 days. There was 15.4% mortality, and all the cases who succumbed had acute respiratory distress syndrome (ARDS) and myocarditis.

DISCUSSION

Scrub typhus is an emerging disease in Nepal. Up to date there have only been 2 outbreaks reported, the first one in the year 2015 in the Eastern part of Nepal and subsequently in 2016 from different parts of Nepal. The diagnostic tests for the disease were available only in the National Public Health Laboratory, where we got our cases confirmed. However, our centre has recently been equipped with rapid diagnostic kits. The disease presents as an acute illness with non-specific signs and symptoms. In the absence of the characteristic eschar and unavailability of investigation modalities even at tertiary hospitals, diagnosis and management are challenging.[7,8]

There is a preponderance of females getting the disease more frequently, which has also been mentioned in previous reports.[9] All the cases had high grade fever, and 58% had the characteristics eschar. Hepatomegaly and splenomegaly were present in more than half of the cases, while lymphadenopathy was quite uncommon. In different studies the presence of eschar has been reported from 20-87%.[10] Vivekanandan et al reported eschar as a rare finding in South East Asia, whereas lymphadenopathy was common.[11,12] However, Kedareshwar et al reported fever with myalgia in 80%, rash in 54%, hepatomegaly in 60%, and splenomegaly in 26% with rare lymphadenopathy.[13]

On analysis of our laboratory profile, we found that in cases of scrub typhus there is low haemoglobin, platelets and albumin with elevated liver enzymes ALT, AST and LDH. Lung infiltration in chest x-ray is also frequently encountered. There are other studies supporting the same findings of elevated liver enzymes, thrombocytopenia and low serum albumin with leukocytosis.[11,14] However, we infrequently encountered leucocytosis.

We encountered complications like hepatitis, pneumonia and ARDS, myocarditis, meningoencephalitis and AKI in cases of scrub typhus. Studies from southern India and Japan have reported myocarditis in about 35%.[15,16] In the present study it was seen in 40%. A prospective study from India has reported respiratory complications like pneumonia and ARDS in 46%, encephalopathy in 12% and AKI in 7.6% in comparison to 38%, 19%, and 6% in the present study.[17] In the present study, the severe cases

were treated with injectable chloramphenicol and those who had mild to moderate presentation were treated with either chloramphenicol, azithromycin, doxycycline or in combination form. This was because the treatment was based on a high index of suspicion and the confirmatory results were obtained only retrospectively, after the cases were either discharged or had succumbed. We got a very good response with intravenous chloramphenicol in our clinical setting. Due to late presentation and established complications like myocarditis and ARDS we had 15% mortality. The mortality in south east Asia has been reported to be 14-30%.[18,19] ARDS is more frequent in scrub typhus patients diagnosed late and treated late. Patients with ARDS had more deranged liver parameters and raised serum creatinine, LDH, creatinine phosphokinase (CPK), and serum lactate.[20,21] It is essential to make the rapid diagnostic kit available to all the district level hospitals. It is also important to conduct large prospective studies to validate our findings, so that clinicians can manage the cases more effectively.

CONCLUSION

In this study the main clinical features noted in the scrub typhus were hepatomegaly, splenomegaly, respiratory symptoms and the classical eschar. Mortality was 15.4%. ARDS and myocarditis were present in all cases who died.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Yadav SP, Dharel D, Shah GS, Bhattarai NR, Khanal B. Scrub typhus an emerging public health threat in Eastern Nepal: an analysis from a tertiary centre during two years outbreak. Int J Contemp Pediatr 2018;5:1715-8.