



Case Series

Scrub typhus in a primary health care center of Nepal: A case series

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ABSTRACT

Introduction: Scrub typhus is endemic in most parts of Southeast Asia including Nepal. Fever, rash, headache, myalgia, eschar are the common clinical features. Though endemic, scrub typhus is grossly underdiagnosed in our country due to the lack of diagnostic tools and non-specific presentation of the disease. Here we present a series of 23 cases of scrub typhus from a primary healthcare center of Nepal.

Method: This is a retrospective case series done among 23 patients diagnosed with scrub typhus and admitted to Aaruchanaute Primary health care center between August 15, 2021 to September 14, 2021. Epidemiological, clinical features and clinical outcomes of all the patients are described.

Results: Among 23 patients admitted to the primary health care center, 78% were of age group 20–60 with 47% male patients. Fever was reported by all patients followed by headache (65%), cough (43%) and eschar (8%). All patients were diagnosed by rapid diagnostic kit. 95% of patients had complete recovery whereas 1 patient was referred to a higher center due to complications he developed during the period of hospital stay.

Conclusion: We conclude that when a patient presents with fever and eschar, there should be a high index of suspicion for scrub typhus, though eschar may not be present in many of the cases. Early diagnosis and prompt treatment with antibiotics is the key as the disease entity shows a good response to treatment while preventing potentially fatal complications.

1. Introduction

Scrub typhus, a mite-borne disease is caused by a gram-negative, obligate intracellular organism *Orientia tsutsugamushi* and is transmitted by the bite of the larva of trombiculid mites (chiggers). The bacteria multiply at the site of the bite with formation of eschar, a characteristic necrotic skin lesion. Fever, rash, headache, myalgia is the usual presentation with signs of organ damage sometimes [1].

Scrub typhus is one of the emerging infectious causes of acute febrile illness in the Southeast Asia and Pacific region including Nepal [2–4]. Outbreaks of scrub typhus have been reported from different parts of Nepal following the devastating earthquake of April 2015 with the most recent outbreak on monsoon of 2021 in the far-western district of Baitadi [5,6]. Here we report 23 cases of scrub typhus from a primary health care center of Nepal with a brief literature review.

2. Methodology

This is a retrospective case series that describes the epidemiological, clinical features and outcomes among 23 patients who were admitted to Aaruchanaute Primary health care center between August 15, 2021 to September 14, 2021. Since all the cases were managed as per the prevailing and standard management tools and medications, ethical approval was not requested. The manuscript has been registered at Research Registry with unique identifying number [researchregistry7594](https://www.researchregistry.com/record/y7594). It has been reported in line with PROCESS 2020 guidelines [7].

All patients were asked for their presenting complaints. Detail physical examination was done and lab investigations comprising of complete blood count, renal function test, urine and stool routine microscopy, serology for dengue and optiMAL test for malarial parasite were done in all patients. Similarly, the diagnosis was done analyzing eschar and by using RDT (Scrub typhus IgG/IgM Rapid Test Kit manufactured by Athenese-Dx Pvt. Ltd, Tramani, Chennai). Complications that developed in each patient were recorded along with the duration of

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hospital stay.

In our study, we have defined different symptoms like headache, cough, pain abdomen etc. as per patients' subjective complaints. Similarly, anemia was defined when Hb < 10 g/dl, leukocytosis when WBC counts >12,000, and thrombocytopenia if platelet count is < 150,000 cells/mm³.

3. Results

Among different patients admitted to Aaruchanaute Primary health care center between August 15, 2021 to September 14, 2021, 23 patients were found to have scrub typhus detected by rapid diagnostic kit (Table 5). 78% of the population group were adults of age 20–60 years with 13% below 20 years and remaining above 60 years. 47.8% of them were males (Table 1).

All admitted patients had fever, with headache being the second most common subjective complaint reported by 65%. Cough was reported by 43% of the population. 21% of the population had abdominal pain and the same number of populations had diarrhoea (Table 2).

The average haemoglobin level of the cases was 13.41 with 8045 and 260238 the average WBC and platelet counts respectively (Table 3). 17% of the cases had abnormal findings in urine routine microscopy whereas 8% had abnormal stool examination (Table 4). None of the patients had positive dengue or malaria simultaneously (Table 4).

All of the patients were diagnosed positive by RDT kit and among them, 8.6% had Eschar as well (Table 5). All patients received tablet doxycycline 100 mg twice daily for 7 days along with symptomatic management.

The majority of patients were admitted for 3–7 days and 95% of the cases recovered uneventfully (Table 6). One patient developed septic shock and required further management so was referred to a higher center and there was no mortality.

4. Discussion

Scrub typhus, a zoonotic disease caused by *Orientia tsutsugamushi* is endemic in the Asia-Pacific rim. The causative organism has a high tendency for antigenic variation and thus there has been no development regarding vaccines against this disease [8]. Following a bite by vector *Leptotrombidium* mite, the infected individual can show a myriad of features like fever, headache, cough, abdominal pain and generalized lymphadenopathy [9]. Of note, the presence of eschar is an important examination finding which is painless and often missed both by the patient and the examiner [10]. The eschar is a progressive dermatological finding that starts with a papule that grows and the central portion undergoes necrosis and becomes covered by a black crust with surrounding erythema, which is often described as cigarette burn appearance [11]. The prevalence of eschar in scrub typhus patients is variable from 20 to 87% [10] and our study had 8.7% of patients with eschar.

Serology has remained the mainstay of diagnosis for scrub typhus. It can be diagnosed by inexpensive tests like the Weil-Felix test which has low sensitivity and specificity [12]. Micro-immunofluorescence assay, M-IFA is the gold standard diagnostic test for rickettsial disease currently [13]. However, immunofluorescence assays are not widely used attributable to the higher cost of its consumables as well as the

Table 1
Demographic of patients.

| Age (in years) | Number (%) |
|----------------|------------|
| <20 years | 13.04 |
| 20–60 years | 78.26 |
| >60 years | 8.69 |
| Sex | |
| Male | 47.8 |
| Female | 52.2 |

Table 2
Clinical presentation.

| Clinical features | Numbers (%) |
|---------------------|-------------|
| Subjective fever | 100 |
| Headache | 65.2 |
| Cough | 43.5 |
| Shortness of breath | 0 |
| Nausea/Vomiting | 4.3 |
| Pain abdomen | 21.7 |
| Diarrhoea | 21.7 |
| Others | 47.8 |

Table 3
Complete Blood count.

| Parameters | Mean | SD |
|-------------|-----------|-----------|
| Haemoglobin | 13.41 | 1.24 |
| WBC | 8045.24 | 1305.17 |
| Platelets | 260238.10 | 49084.524 |

Table 4
Laboratory parameters.

| Laboratory Parameters | Frequency (%) |
|---------------------------|---------------|
| Dengue | 0 |
| Mp OptiMAL | 0 |
| Abnormal Urine Microscopy | 17.39 |
| Abnormal Stool Microscopy | 8.69 |
| Enteric Fever | 17.39 |

Table 5
Criteria for diagnosis of scrub typhus.

| Criteria | Number (%) |
|--------------|------------|
| Eschar alone | 0 |
| Eschar + RDT | 8.6 |
| RDT alone | 100 |

Table 6
Outcome and complications.

| Outcomes | Number (%) |
|-------------------------|------------|
| Length of hospital stay | |
| <3 days | 4.34 |
| 3–7 days | 95.65 |
| >7 days | 0 |
| Complete recovery | 95.65 |
| Death | 0 |
| Complications | 4.34 |

technical expertise it demands to be used efficiently [14]. Culture of the organism is tough and requires skilled and dedicated labs while molecular tests like PCR, though can detect disease in the earlier timeframe of disease, its usefulness declines with treatment [13]. For our study, we used commercially available Scrub typhus IgG/IgM Rapid Test, a lateral flow immunoassay that aided in simultaneous detection along with differentiation among IgM and IgG antibodies for *Orientia tsutsugamushi* in human plasma or serum or even whole blood specimens.

As for treatment, earlier trials by Sheehy et al. demonstrated tetracycline was superior to chloramphenicol [15], one of the pioneer antibiotics for scrub typhus [16]. Another trial by Song et al. showed the effectiveness of doxycycline which was comparable to that of conventional tetracycline [17]. Trials by Phimda et al. highlighted azithromycin to be equally effective as doxycycline with fewer gastrointestinal side effects [18]. A trial by Watt et al. has pointed out rifampicin to be superior to doxycycline [19]. A recent analysis by Tsai

et al. have highlighted levofloxacin with equal efficacy compared to tetracycline, however with a cost of higher mortality if used for severe diseases [20]. Thus, different trials highlight how the antibiotics have been changing in terms of efficacy, safety and suitability for patients with time for scrub typhus. In our study, a week course of Doxycycline was used and 22 patients showed complete recovery whereas one patient developed complication for which he was referred to a higher center for further treatment.

Common complications following infection with scrub typhus as per Singh et al. are hepatitis among 78.7%, thrombocytopenia among 46.8%, acute renal failure among 31.9% and acute respiratory distress syndrome among 19.2% with mortality among 6.4% [21]. Another study by Jamil et al. pointed out multiorgan dysfunction syndrome to be the most common complication seen among 16.94% [22]. Similarly, Chauhan et al. pointed out that the presence of eschar is associated with poor prognosis in scrub typhus compared to those without eschars [23]. In our study, one patient developed septic shock during the course of treatment and was referred to a higher center for further treatment as he required ventilator support.

The main strength of our study is our capacity to provide a level of care in a resource-limited setting during the local outbreak of scrub typhus. The small sample size is the limitation of our study. Similarly, the clinical presentation of the patients are incompletely described.

5. Conclusion

From this study, we conclude that scrub typhus is endemic in many places of Nepal. When a patient presents with fever and eschar, there should be a high index of suspicion for scrub typhus. However, eschar may not be present in many of the cases and absence of eschar doesn't rule out the disease. Scrub typhus, an important zoonotic disease, can be easily missed while trying to exclude COVID-19 during this pandemic. So, early diagnosis and prompt treatment with antibiotics is the key as the disease entity shows a good response to treatment while preventing potentially fatal complications.

Ethical approval

Ethical approval is not required because we describe our clinical practice.

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Consent

Informed verbal consent from all the patients was taken during their admission and management at the health care center.

Author contributions

Shekhar Gurung: study concept, data collection, writing the paper. Saurab Karki, Subashchandra Pokharel, Kishor Bhatta: data collection, writing the paper.

Registration of research studies

1. Name of the registry: Research Registry (<http://www.researchregistry.com>)
2. Unique Identifying number or registration ID: researchregistry7594
3. Hyperlink to your specific registration: [researchregistry7594](http://www.researchregistry.com)

Guarantor

The Guarantor is the one or more people who accept full

responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Declaration of competing interest

There is no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2022.103490>.

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