



Microbes and Infectious Diseases

Journal homepage: <https://mid.journals.ekb.eg/>

Original Article

Estimation of the burden of tsutsugamushi disease in central part of Nepal with high resource settings

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ARTICLE INFO

Article history:

Received: 21 May 2023

Received in revised form:

Accepted: 10 June 2023

Keywords:

Rickettsia

Scrub typhus

Multorgan failure

ABSTRACT

Background: Tsutsugamushi disease is an endemic disease and acute febrile illness caused by bacteria known as rickettsia. It is a serious public health issue that has threatened the billion of people around the globe. It can lead to multiorgan failure and the disease manifests as flu like symptoms such as myalgia, cough, shortness of breath, fever, eschars at the bitten site, petechial rashes throughout the body, generalized lymphadenopathy, abdominal pains, nausea and vomiting. **Aim and objectives:** The purpose of this study was to illustrate the frequency of patients affected by this bacteria in different age groups, gender, and geographical areas. **Material and methods:** The bacteria was identified from the samples collected from the various clinical departments of Chitwan Medical College and Teaching Hospital. **Results:** The study illustrates that cases of AFI was highly prevalent in housewives followed by the students and also predominant in the people of urban area than in comparison to those of rural area. The study also suggests that people of age group 31-60 had more positive cases of acute febrile illness. 90 of the cases had positive status of scrub typhus among all the patients admitted with AFI. This study shows that various symptoms like fever, headache, myalgia, cough, eschar, petechiae and low platelet count were observed in the patients of scrub typhus. **Conclusions:** Scrub typhus might cause multiorgan and multisystem failure. It is an under diagnosed and grossly neglected disease around the whole world.

Introduction

Scrub typhus is an acute febrile illness caused by gram negative bacteria known as rickettsia, Orientia tsutsugamushi or Rickettsia tsutsugamushi. The disease is also known as tsutsugamushi disease which is transmitted by the bite of chiggers, a larva of trombiculid mites [1].

Scrub typhus is an endemic disease and a serious public health issue that has threatened to the billion of people around the globe. It can lead to multiorgan failure because it is a neglected and grossly underdiagnosed disease around the different corners of the world. The disease manifests as non-specific

DOI: **10.21608/MID.2023.212325.1525**

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flu like symptoms such as myalgia, cough, shortness of breath, fever, eschars at the bitten site, petechial rashes throughout the body, generalized lymphadenopathy, abdominal pains, diarrhea, nausea and vomiting [2]. The World Health Organization (WHO) has described Tsutsugamushi disease as one of the most underreported and underdiagnosed disease that requires hospitalization. WHO has strongly emphasized a surveillance demonstrating a high case fatality rate in higher percentage of untreated patients [3].

There are various systemic complications that defines Tsutsugamushi disease. These complications include disseminated intravascular coagulation (DIC), acute kidney injury (AKI), pneumonitis, acute respiratory distress syndrome (ARDS), septic shock, acute hepatitis, multiple organ dysfunction syndrome (MODS), meningitis and pancreatitis [4].

The burden of scrub typhus has been reported from many parts of Asia including Nepal and India. The disease has become endemic in Japan, India, Pakistan, Korea, and eastern asia. A huge population are being affected by this disease every year [5].

The vectors of scrub typhus prefer to survive in scrub vegetations, grassy areas, forests and riversides. The terai belts of Nepal provides a favourable environment for Scrub typhus[6]. The earthquake in 2072 B.S in Nepal has altered the epidemiology and environmental conditions that has supported the growth of chiggers in Terai. There has been a close relation between the rodents and humans [7]. The Epidemiology Disease Control Division of Nepal states that this disease is prevalent in various cities and rural areas of Chitwan, Sankhuwasabha, Bhojpur, Nuwakot, Baglung, Gorkha, Dhading, Nawalparasi, Sindhupalchowk, Kailali, Parsa, Bara, Dhankuta, Ilam, Sindhuli, Sarlahi, Morang, Makwanpur and Rukum[8]. Some of the evidences suggest that the combination of human expansion in previously inhabited areas and the changes in climate conditions might increase the burden of scrub typhus and reemerge the infections [9]. Because of the limited or patchy survey on geographical mite distributions, insufficient researches related to the characteristics of vectors, the burden of scrub typhus is still neglected or underdiagnosed in many parts of the world [9].

The present study aims to determine the prevalence of scrub typhus among different age

groups, male and female, in rural and urban area and occupation wise.

Rationale for the study

Despite of the lack of awareness, Scrub typhus has become the leading cause of undifferentiated treatable febrile illness in Asia. The burden of this disease appears to be highly significant across the different areas of the globe.

So, the present study estimates the burden of scrub typhus in the central region of Nepal. The present study also summarizes the literature related to the incidence of burden of scrub typhus in various regions of the globe.

Methods

Study design and participants

The recent study is a laboratory based prospective study that was conducted in ISO certified Central Laboratory of CMCTH, a tertiary care centre with high resources which lies in Chitwan district of Nepal. The ISO accreditation to the laboratory of CMCTH is a great achievement in the health sector of Nepal especially in the central region of the country. The study was conducted during 2022-september 2022 to February 2023. This study was ethically permitted to be conducted by the Institutional Review Committee of CMCTH with a reference number CMC-IRC/079/080-057.

Study population

This study was conducted in 300 patients having acute febrile illness. The informed consent was taken from the patients. The demographic information and health status of the patients were documented by using the questionnaires.

Inclusion criteria

The patients willing to participate in the study were only enrolled in the study. All the patients admitted with acute febrile illness were included in the study.

Exclusion criteria

Patients with acute febrile illness diagnosed with other diseases such as typhoid, malaria, leptospirosis, brucellosis and dengue were not included in this study.

Sample collection, handling and transportation

A total of 300 blood samples were collected aseptically by veinpuncture in vacutainer.

The blood samples were aseptically transported to the clinical laboratory of CMCTH.

Processing of the samples

The antibody against *O.tsutsugamushi* was detected. ELISA, a serological method was applied to detect IgM against *O.tsutsugamushi* using the instructions in the kit by manufacturing company. Diagnosis of Scrub typhus was done on the basis of clinical symptoms and serological tests.

Strengths and limitations of the study

The clinical and paraclinical profiles of the positive patients were not documented in this study. The confirm cases of the positive patients were only noted in the study. Comparison of commonly used method that is weil felix test was not done in this study. The indirect fluorescent assay that gives better sensitivity and specificity was not used in this test.

Results

The present study illustrates that cases of AFI were highly prevalent in housewives followed by the students. AFI was also present in the cases of farmers, businessman, poultry workers and other group of people. Besides, the present study also illustrates that AFI was predominant in the people of urban area than in comparison to those of rural area.

The incidences from (table 2) suggests that people of age group 31-60 had more positive cases of acute febrile illness followed by the age group of 0-30 whereas the people of age group above 60 had also acute febrile illness.

The evidences in table (3) illustrates that 90 of the cases had positive status of scrub typhus among all the patients admitted with AFI whereas 210 of them were scrub typhus negative.

Table 1: Occupations and geographical distribution pattern of acute febrile illness (AFI) in patients attending CMCTH

Variable	Category	Frequency(Percentage)
Occupation	Student	40 (13.33)
	Farmer	70 (6.7)
	Housewife	80 (26.7)
	Businessman	38 (12.7)
	Poultry	20 (6.7)
	Others	52 (17.3)
Residency	Rural	190 (63.3)
	Urban	110 (36.6)

Table (4) states that among the total cases of AFI, scrub typhus was highly predominant in the age group 31-60 followed by the age group above 60. Moreover, the female patients were more likely to be infected by scrub typhus than in comparison to the male patients admitted at CMCTH with AFI.

Table (5) illustrates that various symptoms like fever, headache, myalgia,diarrhea, cough, eschar presence, petechial rashes and low platelet counts were observed in the patients with positive status of scrub typhus. Petechial rashes and thrombocytopenia were observed in all the positive cases of scrub typhus. Almost all of the positive patients were presented with the symptoms of myalgia, diarrhoea and cough.

The results in **table (6)** shows that the morphology of RBC, WBC and Platelets were not altered in the positive cases of Scrub typhus. The level of haemoglobin and platelets was reduced in majority of the positive cases. Leukopenia and Leukocytosis were also observed in most of the patients. Microcytic anaemia was also found to be present in few of the cases.

The ALT,AST and ALP level was found to be elevated in majority of the patients. The total bilirubin level was also found to be altered in almost half of the positive cases.

The level of creatinine greater was also found to be elevated in few positive cases.

The systemic examinations of the positive cases revealed that the breath sounds was normal in 97.7% of the positive cases whereas none of the positive cases had altered sensorium state and organomegaly.

Table 2: Distribution pattern of patients with acute febrile illness in various age groups

Age group	Male (%)	Female (%)	Total
0-30	70 (38.8)	30 (25)	100
31-60	75 (41.7)	70 (58.3)	145
Above 60	35 (19.4)	20(16.7)	55
Total	180	120	300

Table 3: Presence of scrub typhus among patients with acute febrile illness attending CMCTH

AFI	Number of cases	Percentage
ST positive	90	30
ST negative	210	70
Total	300	100

Table 4: Age wise burden of scrub typhus positive in patients with AFI

Variables	scrub typhus status	
	Positive	Negative
Age group		
0-30	15	85
31-60	40	105
Above 60	35	20
sex		
Male	50	130
Female	60	60

Table 5: Clinical features of positive cases of scrub typhus tested by ELISA

Variables	Scrub typhus status	
	Present	Absent
Fever	75	15
Headache	65	25
Myalgia	88	2
Diarrhoea	86	4
Cough	85	5
Escher presence	50	40
Petechial rashes	90	0
Thrombocytopaenia	90	0

Table 6: Clinical examinations in scrub typhus positive cases (n=90)

Haematological examinations	Number (%)
Morphology of RBC (normal)	90 (100)
Morphology of WBC (normal)	90 (100)
Morphology of platelets (normal)	90 (100)
Haemoglobin (g/dl) [< 11-18gm]	85 (94.4)
Platelet count (<1,50,000) or Thrombocytopenia	90 (100)
TLC count (<4000-11,000 cells per cubic mm) or Leukopenia	40 (44.4)
TLC count (>11,000 cells per cubic mm) or Leukocytosis	50 (55.5)
Microcytic anaemia	25 (27.7)
Liver function tests	
Bilirubin (total) [<0.2-1.0mg/dl]	40 (44.4)
SGPT/GPT/ALT [IU/L] [>36]	55 (61.1)
SGOT /AST [IU/L] [>48]	60 (66.6)
Alkaline phosphate (ALP) [>136 IU/L]	61 (67.7)
Renal function tests	
Creatinine (>1.4 mg/dl)	25 (27.7)
Systemic examinations	
Vesicular breath sounds (normal)	88 (97.7)
Altered sensorium	Nil (0)
Organomegaly	Nil (0)

RBC: Red Blood cells, WBC: White Blood Cells, TLC=Total Leukocyte Count, ALT :alanine aminotransferase, AST=Aspartate aminotransferase, SGPT :Serum Glutamic-Pyruvic Transaminase, GPT :Glutamic-Pyruvic Transaminase , SGOT: serum glutamic-oxaloacetic transaminase , ALP: Alkaline Phosphate

Discussion

Although the scrub typhus disease has remained a threat to the health of Nepalese, the geographical distribution of the vectors is still unclear. The disease has remained as neglected, underreported and grossly underdiagnosed in most parts of the globe including Nepal because of the lack of medical resources, awareness and proper economical status.

The table 1 in the present study illustrates that majority of the housewives had acute febrile illness followed by farmers which is also similar to the study carried out by Gautam et.al in 2019 . This could be because housewives are usually involved in the garden works and household works in the Nepalese community. Farmers are usually involved in the grasslands, vegetable fields where they are at high risk of getting contact with the rodents. This might be the possibility why the farmers in Nepalese community are also at a higher risk of endemic diseases [10]. The surveillance carried out by Devasagayam E et.al in 2021 also states that 53.3%, i.e. higher percentage of agricultural workers are

infected with scrub typhus with acute febrile illness which is somewhat similar to the present study [11].

The present study also demonstrates that the people of rural areas are at a high risk of endemic diseases. This finding is similar to the research carried out by Gautam et.al in 2019 [10]. The study carried out by Devasagayam E et.al in 2021 also states that majority of the cases with acute febrile illness was present in people of rural area residing close to the grassy areas, bushes and shrubs [11]. The rodents perhaps could get a shelter in these bushy area because of which they might act as a transmitting agent of this zoonotic disease. Rodents population in these area might be responsible to transmit such diseases in human beings. Preventive measures such as rodenticides might be used to reduce this huge mass of rodents so as to avoid the endemic zoonotic diseases.

The present study also demonstrates that males had a greater ratio than females in having acute febrile illness which is similar to the surveys of Jyothi et.al in 2015 [12]. The study by Bonnell A et.al in 2017 states that females were most

commonly affected with acute febrile illness than in comparison to males which is different to the present study [13]. The sociodemographic informations illustrated in the study carried out by Mansor et.al 2021 also states that AFI caused by rickettsia is predominant in females which could be because of the ladies working in paddy fields during the harvesting season [14]. Moreover, Mansor et.al 2021 also states that rural populations and populations with poor socioeconomic conditions are highly affected with scrub typhus since they are much engaged in plantation and agricultural activities, and they have a high probability of contact with animals and rodents in the grassy areas[14].

The study carried out by Roopa et.al [15]demonstrates that 41.3% of patients with scrub typhus had fever whereas the study by Borkakoty [16] shows that 96.9% of the patients with scrub typhus had fever.

The prominent haematological abnormalities included in this study were leukopaenia, thrombocytopaenia, microcytic anaemia and leucocytosis.

Inspite of the several hindrance on the quality and the number of accessibility of the reports, we found that Scrub typhus is largely underdiagnosed and underappreciated tropical disease affecting the people of various age groups, both the sexes and in different geographical aspects including both the rural and urban areas as well.

Conclusions

In conclusion, Scrub typhus might be an important cause of multiorgan and multisystem involvement leading to failure of several organs. This study strongly suggests that the protocols in identifying the scrub typhus must include PCR. Despite the availability and limitations of the data, make a positive case for scrub typhus a truly neglected and underdiagnosed disease in various tropical regions. No licensed vaccines and unsystematic efforts of vector eradication has lead to the increasing rate of scrub typhus in different parts of the globe. Despite the awareness and health education , the burden of the scrub typhus has remained grossly unknown in most of the tropical states. Unfortunately, there are too many limitations for economical and mapping approaches for the symptomatic treatment of scrub typhus.

Acknowledgements:

Authors are so grateful to all those who have been directly or indirectly involved in carrying out the research. The authors highly appreciate the Faculty members and Post graduate residents of Department of Microbiology of CMCTH for their constant support during the study. We always remain thankful to the management team, laboratory team, Principal, academic director, hospital director and laboratory director for their valuable supports in carrying out this research. The authors always remain thankful to the Chairman of CMCTH who always provided a beautiful premises of research and highly motivated us to be present in the field of research.

Conflicts of interest:None.

Financial disclosure: None

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