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Eschar as a Sensitive Marker for Scrub Typhus Diagnosis at the Primary Healthcare Level

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Abstract

Background and aim of study: Scrub typhus, a potentially fatal rickettsial disease, is reported from many Indian states, but mostly from tertiary care centers. This study is distinct as it was undertaken in a primary care center in a rural area. Aim was to observe the age, gender and occupational profile of patients diagnosed with scrub typhus at our center during the period from January 2017-19; to find out about the site and day of appearance of eschar with respect to duration of fever and to note the clinical features and complications of scrub typhus.

Methods: Study sample consisted of patients presenting with fever who developed an eschar and positive serology for Ig M on the 10th day.

Conclusion: A total of 31cases were seen, of which four were children and eighteen were adult females. The "eschar" was picked up within 5 days of onset of fever in 26(84%) cases. There was no mortality. This study is unique also in the large size of the cases from a rural center and short latency to effective treatment. The study emphasizes the necessity of picking up the eschar by detailed examination in all cases of pyrexia and instituting early specific treatment.

Keywords: eschar, fever, primary health care, scrub typhus

Introduction

Scrub typhus is a mite-borne febrile illness is caused by rickettsia Orientia tsutsugamushi .In the endemic Asia-Pacific region, one billion people are estimated to be at risk of infection and one million cases of scrub typhus occur every year.[1] It is an important re-emerging infection in India, affecting multiple organ systems and ranging from a mild disease to one with a mortality rate of up to 70 percent, especially in untreated cases.[2]

Orientia tsutsugamushi is inoculated by the bite of the larval stage 'chigger' of the trombiculid mite. A black area of necrosis called eschar maybe seen at the site of bite and may provide key to the diagnosis.[3]

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Chigger activity is determined by temperature and humidity hence seen in the tropics throughout the year.[4] Human infection of scrub typhus is acquired by outdoor occupation or activity in areas of scrub growth teeming with mites, hence the name.[5] Deforestation, urbanization, climate change and natural calamities may enable migration of rodents carrying infected mites to more urban and non-endemic areas.[1]

Scrub typhus, for many years, was thought to be confined to areas of the tsutsugamushi triangle.6Evidence from recent serological and molecular studies confirm the presence of scrub typhus beyond the endemic triangle.[6,7] Case reports and outbreaks have been reported from Africa, South America and UAE.[7,8] Cases in Europe and America have been traced to Asia and acquired by 'eco-tourism'.[9,10]

In India, the disease was first seen among troops during World War II in Assam and West Bengal, and during Indo-Pak war in 1965.[11] However it was only in 1990 that the illness resurfaced at Pakistan border of India.[12] Maybe empirical treatment of fever with tetracyclines, extensive use of insecticides and better protective clothing led to reduced incidence.[13] Case reports have since been made from many Indian states. Scrub typhus is under-diagnosed and under-reported, even though field epidemiology studies show prevalence of infection almost all over India.[1]

Symptoms of Scrub typhus appear in 5-14 days (even up to 21 days) and include fever, rash, myalgia, lymphadenopathy, nausea, vomiting, eschar (a painless punched out ulcer up to 1 cm wide with a black necrotic centre), abdominal pain, and non-specific flu-like symptoms.

The mortality due to scrub typhus depends on various factors like geographical location, pathogenic strain involved and various host factors such as age, immune status, co-morbidities and are due to complications like acute renal failure, and disseminated intravascular coagulation (DIC), acute respiratory distress syndrome, myocarditis, and meningoencephalitis.[1,14]

Inflammatory host response to invasion of skin by Orientia tsutsugamushi through chigger bites results in an eschar. With serological diagnosis being unavailable, costly and sensitive only after days of symptom onset, eschar is the key diagnostic feature specific to scrub typhus. It starts as a central vesicle surrounded by erythema which progresses to form a black crust with surrounding erythema and as the scale on the crust mounts, a typical eschar forms at 6-8 days of onset.[15] Being painless, they should be diligently looked for in case of clinical suspicion and patient followed up as they may erupt during the course of illness. Though presence of eschar at mite biting site is a specific (98.9%) marker and clinches the diagnosis, however, the presence of eschar varies extensively in patients from 7 to 97%[16,17], maybe even uncommon in Asian population18 .When present, groin, axilla,genitalia, abdomen and chest are common sites.[19]

We have studied 31 patients who presented with febrile illness and were treated on the lines of scrub typhus solely on the basis of appearance of eschar and confirmed by serology later.

Aim and Objectives

To observe the age, gender and occupational profile of patients diagnosed with scrub typhus at our center during the period from January 2017-19

To find out about the site and day of appearance of eschar with respect to duration of fever

To note the clinical features and complications of scrub typhus

Materials and Methods

The setting for this study was a primary health care set-up with in-patient facility, located in a hilly rural place 35 Km from the Trivandrum city. It caters to the needs of a population which is composed mostly of laborers and farmers. There was an epidemic of Scrub typhus in the region as early as 2004 which prompted this study from Jan 2017-2019. All patients who presented with fever, who developed an eschar and confirmed to be scrub typhus by IgM ELISA serology test performed on the 10th day after onset of fever formed our study sample. A written informed consent to participate in the study as well as for photographs was taken from all patients.

In all patients with high grade fever in whom

scrub typhus was one of the differential diagnoses, a thorough inspection of whole of the body including perineum, axilla and genitalia was done after undressing the patient and in proper lighting and this was repeated every day. The emergence of eschar with respect to time of onset of fever was noted and photographs taken. Relevant routine blood investigations to investigate fever were done like complete blood count, erythrocyte sedimentation rate, Blood sugar levels, Liver function tests, Serum creatinine, C-reactive protein and Lactate Dehydrogenase. X ray chest, ECG were done when indicated. On the 10th day of fever, serological test namely IgM antibody for scrub typhus was sent in patients who developed an eschar. As a part of routine evaluation of pyrexia, antibodies for Dengue, Leptospirosis and Mycoplasma were done.

When eschar was observed, patient was started on Azithromycin 500 mg OD for 7 days empirically even before getting the IgM antibody result. Supportive treatment in the form of parenteral fluids, control of diabetes, hypoproteinemia and anticoagulants in case of venous thrombosis etc. were given when necessary.

Results and Discussion

Evaluation of pyrexia often requires the expertise of a tertiary care centre, as different causes like Enteric fever, Dengue, Leptospirosis, Scrub typhus, Mycoplasma and recently Covid-19 have to be ruled out. There are only a few prospective studies on scrub typhus in India from a rural care centre as ours, like the one in Rajasthan which has similarity to the current study. However, this too was in a tertiary care hospital.[20,21]Similar reports from Kerala state are few especially concerning pediatric age group and are from tertiary care centres.[22,23,24,25]

Female preponderance was seen among adults with a ratio of 2.2. Maximum number of cases (8,25%) was between 30 to 40 years of age. Similar findings were noted in other studies[26,27] The youngest patient was 3 years of age. The four pediatric patients were in the range of 2 to 4 years, three being females. The adults were daily wage laborers involved in outdoor work among scrubs and bushes.

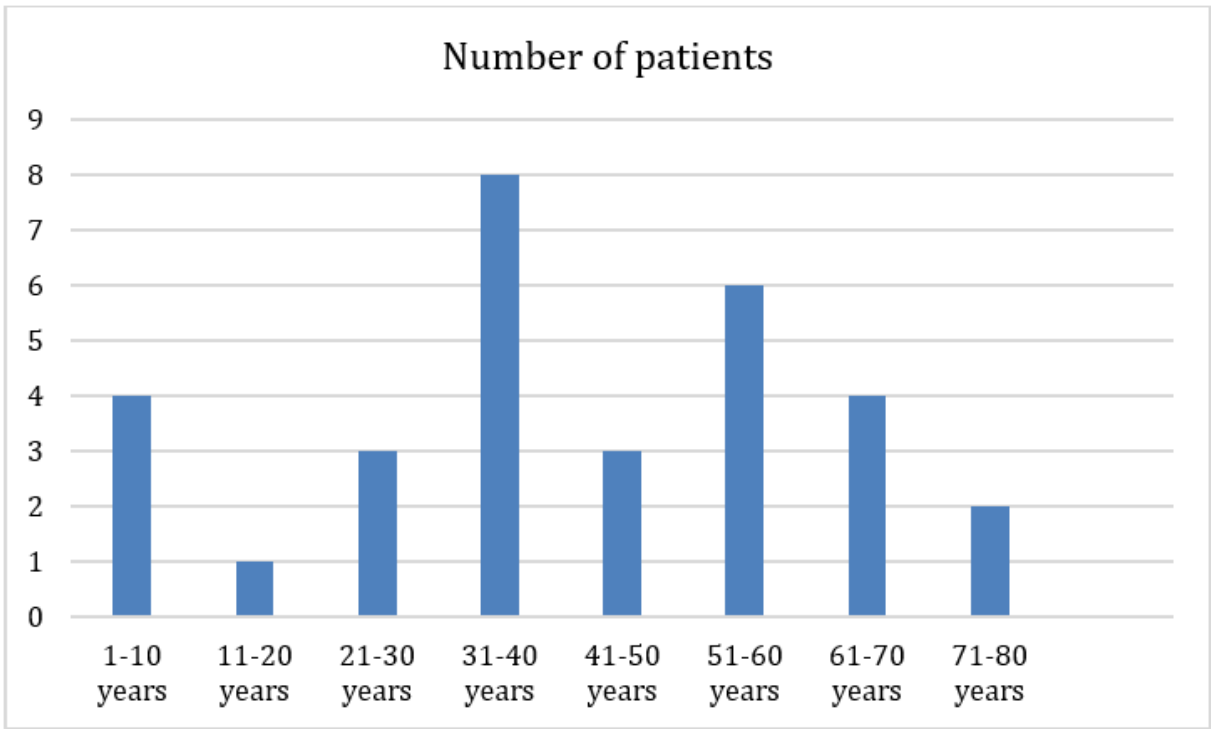

Chart 1: Chart showing age-distribution of patients

Among adults, mean duration of fever at presentation was 3.6 days and ranged from 2 days to up to 10 days. Only six adult patients had fever of 5 days or more. Among children, the mean duration of fever was 4.6 days with a range of 2 to 7 days. Temperature at presentation was in the range of

101 ° F- 103°.None of these patients had taken any specific treatment other than paracetamol for their fever before presenting to us. The duration of fever at presentation varies from mean 8 to 10 or more days in most of these studies conducted at tertiary care centres.[28] Cases have reported with as early as 2 days of fever in this study which will be the case in most of the rural health care centers in India.

Table 1: Table showing the clinical features of the pediatric cases of scrub typhus

Case no	Age	Sex	Clinical features	Signs	Eschar characteristic
1	4 1/2yrs	F	Fever, Abd pain, diarrhea, vomiting	Dehydrated Abdominal distension	Perineum 6th day
2	2yrs	F	Fever, crying, lethargy	–	Lt flank
3	3yrs	M	Fever, body pain	–	Multiple eschars on front and back of chest
3	3	F	Fever, Loose motion	Dehydration	Left side back

In 26 patients (84%), eschar appeared within 5 days of fever. Of which, it appeared on the 3rd day in 11 patients and on 2nd day in 6 patients. Multiple eschars were seen in three patients. In case of multiple eschars, the eruption was not simultaneous.

Table 2: Day of eschar eruption with respect to duration of fever

Day of eschar eruption with respect to duration of fever	Number of patients
3rd day	10 adults,1 pediatric
2nd day	6,2 pediatric
4th day	4
5th day	3
6th day	1,1 pediatric
8th day	1
10th day	1
7th day	1

Location of Eschar in adults

Table 3: Table showing distribution of eschar with respect to site among the patients

Region	Number	Percent	Males	Females
Chest and upper back	9	30	3,1 child*	5
Abdomen and Lower back	10	30	2	6,2 child
Upper limb	4	14.5	1	3
Lower limb	3	11	1	2
Perineum/genitals	5	14.5	2	2*,1 child

* had multiple lesions at the same site

Figure 1: Single ulcer like cigarette-burn type lesion

Figure 2: Figure showing multiple eschars in front and back of chest

Clinical diagnosis can be made even prior to serological diagnosis as was done in this study and prompt treatment instituted. The presence of eschar in a patient with scrub typhus varies widely in different studies, from 9.5% to 86%, with lesser incidence reported from the Oriental countries.[29,30,31] This difference is perhaps related to the skin complexion as erythematous eschar is easily visible and identified in fair-skinned individuals. Studies from Vellore in Tamil Nadu showed eschar pick up rates of 45%–56%[31,32] while Inamdar et al. reported a high incidence of eschar at 75.6%.[33] Another reason for the low incidence of eschars in scrub typhus has also been attributed to the retrospective nature of the studies. The asymptomatic nature, without itching or tenderness and its location in regions like the private parts, loin, back etc. (which cannot be identified by the patient himself) add to the low rates of picking up the eschar. The clothing pattern, previous exposure to pathogen, vasculitis and cutaneous immunity may influence the development of eschar[34]. The eschar resembles a cigarette burn type of shallow ulcer with undermined edges.

Rashes were seen in 6% (2 patients) in this series. Rash becomes apparent after 3-5 days of onset of symptoms Initially rash is in the form of pink, blanching, discrete maculae which becomes maculopapular, petechial or hemorrhagic, may be seen over the trunk and spread to the extremities involving the palm and soles- sparing the face. The chance of picking this up in our population is remote. Rashes and eschar have been picked up as early as 2nd day.[35]

While the indirect immunofluorescence assay (IFA) has been the reference test, this technique is expensive and often unavailable.[36] Hence, ELISA-based estimation of IgM antibodies is now preferred[37]. A limitation of serological tests for the diagnosis of scrub typhus is the insufficient formation of antibodies in the early or acute phases of infection, which could lead to false-negative results. Hence the IgM antibody test was done in suspected cases by 10th day only and showed 100 percent concordance with presence of eschar in our study, stressing on the specificity of eschar in early diagnosis of scrub typhus.

Features associated with Scrub typhus	**Number of patients**
Hepatosplenomegaly +/- abnormal LFT	9 (1 patient had icterus)
Hearing loss	3
Photophobia	2
Chorea due to hypocalcemia	1
Hypoalbuminemia	3(one of whom was in 1st trimester of pregnancy)
Hematuria with casts	1
ARDS	2
Thrombocytopenia with ecchymosis	1

Except in three adults, all the rest were treated with Azithromycin at our centre and all of them recovered and there was no relapse. Notably, none of our patients showed generalized lymphadenopathy. There was no mortality.

O.tsutsugamushi infects the endothelium of the small blood vessels causing disseminated immune-mediated lympho-histiocytic vasculitic illness,

resulting in severe complications such as acute respiratory distress syndrome (ARDS), hepatitis, renal failure, meningoencephalitis, and myocarditis with shock in a varying proportion of patients.[34] TableMyocarditis has been reported to be common among children.[25,38]

The latency for the development of such complications has been observed to be as late as second week or later. But it has been observed that patients with a history of fever of 2 -3 days present with ARDS, develop hypoalbuminemia, gastroenteritis going for shock with short history of fever as in this study. This underlines the importance of early diagnosis.

The one case of scrub typhus complicating pregnancy made a complete recovery despite developing hypoalbuminemia. Scrub typhus complicating pregnancy is associated with high fetal and maternal mortality.[39]

The mortality rate in scrub typhus is reported as 14%–20%.[40] With a, strong awareness of the disease, early detection of eschar assures diagnosis of scrub typhus as evidenced by this study.

Tetracycline, doxycycline, azithromycin, and rifampicin are effective treatment options for scrub typhus and have resulted in few treatment failures.[40]

Conclusion

Early diagnosis and detection of scrub typhus can be done at the primary healthcare centre itself, with high clinical index of suspicion and diligent and daily search for eschar in patients of pyrexia. This can prevent complications and reduce mortality and reduce the expenditure involved in treatment. Aptly stated by WHO in 1999, "Scrub typhus is probably one of the most underdiagnosed and under reported febrile illnesses requiring hospitalization. Scrub typhus is probably the single most prevalent, under-recognized, neglected, and severe but easily treatable disease in the world".

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Conflict of Interest - Nil

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