



“SCRUB TYPHUS MENINGITIS AND MENINGO-ENCEPHALITIS, A DIAGNOSTIC CHALLENGE FOR CLINICIANS: A PROSPECTIVE HOSPITAL BASED STUDY FROM SOUTHERN RAJASTHAN”

General Medicine

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ABSTRACT

Scrub typhus is an acute Zoonotic illness caused by *Orientia (Rickettsia) tsutsugamushi*, transmitted by Mite characterized by fever with headache, lymphadenopathy, eschar, multi-organ involvement.

Aims & objectives: To study the clinical features, laboratory parameters and response to treatment of scrub typhus meningitis/meningoencephalitis

Methodology: A hospital based prospective observational study undertaken in Department of Medicine, RNT Medical College and MB Hospital, Udaipur on 50 clinically & lab diagnosed Scrub typhus positive patients from period June- September 2018

Results: Study shows 54% were males, 98% residing in rural area, 94% having cattle in home, 36% belonging to 31-40 years, 78% with no eschar and with fever in all (100%) and mean GCS score being 11.96 ± 1.46

Conclusion: Majority presented as acute febrile illness with altered sensorium and meningeal sign. Eschar remains absent in majority. Thus a high degree of clinical suspicion and a positive rapid, diagnostic test remains an important point in management of scrub typhus.

KEYWORDS

INTRODUCTION

Scrub typhus is an acute, febrile illness that is caused by *Orientia (formerly Rickettsia) tsutsugamushi* first described from Japan in 1899. Humans are accidental hosts in this zoonotic disease & characterized by fever with headache, suffused face, lymphadenopathy, eschar, multi-organ involvement and rapid response to doxycycline.

Scrub typhus is seen in all terrains of “tsutsugamushi triangle” and is related mostly to agricultural and outdoor activities.¹

Recent reports from several parts of India, including south-west India, indicate that there is a resurgence of scrub typhus.² Horizontal transmission occurs in rodents and humans get accidentally infected following bites of chiggers.³ Infection spreads through both haematogenous and lymphatic routes. Target site for multiplication are the endothelial cells of the various systems.

The classic case description includes an eschar (35-50% cases) where the chigger (mite larva) has fed, regional lymphadenopathy and maculopapular rashes. Eschars are painless and mostly present in concealed sites like axilla, inguinal region, perianal region, scrotum, buttock and thigh.

Central nervous system (CNS) involvement is known complication of scrub typhus which ranges from meningitis to meningoencephalitis. Other neurological complications include seizure, cranial nerve deficits, vasculitic cerebral infarct, brain hemorrhages, polyneuropathy, sensorineural hearing loss, meningitis or meningoencephalitis.^{4,10}

Scrub typhus meningitis/meningoencephalitis remains an unclear entity and diagnosis have to be based on clinical features, especially on the presence of an “eschar” and confirmed by a serum IgM enzyme-linked immunosorbent assay test for scrub typhus. serological tests are still an indispensable tool for diagnosis. Latex agglutination, immunoperoxidase assay, PCR and Weil-Felix test are other tests available.

As scrub typhus is a well-known mite borne disease in the State of Rajasthan with varieties of manifestations, we hereby made an effort to study about CNS manifestations of this disease, which if detected timely and managed appropriately will result in rapid reversal of symptoms without any permanent sequelae.

AIMS & OBJECTIVES

To study the clinical features, laboratory parameters and response to treatment of scrub typhus meningitis/meningo-encephalitis

METHODOLOGY

A hospital based prospective observational study was undertaken in Department of Medicine, RNT Medical College and MB Hospitals, Udaipur was conducted on 50 patients from the period June 2017 to September 2018.

INCLUSION CRITERIA

All patients above 18 years of age were attend and admitted in the various wards of Department of General Medicine with diagnosis of scrub typhus positive from IgM antibody against the 56 kDa protein of *O. tsutsugamushi* by ELISA and having clinical features of meningitis/meningoencephalitis.

Exclusion criteria

1. Patients having associated CNS diseases not related to scrub typhus (i.e., tumor, neurocysticercosis, epilepsy, etc.).
2. Patients diagnosed to have some other associated infections and other causes of acute febrile illness (malaria, dengue, enteric fever, etc.).
3. Patients having co-morbid conditions like chronic renal failure, chronic liver disease, HIV and patients with known neoplastic diseases, etc.
4. Study tool : A semi-structured, valid questionnaire was filled after taking the consent of clinically and lab diagnosed Scrub typhus positive patients.
5. Analysis: The collected data was entered in a master chart in MS Excel and analyzed using simple charts, figures and tables wherever necessary and significance was attributed to $P < 0.05$

RESULTS

Out of 50 Scrub typhus positive meningitis/ meningoencephalitis patients, 54% (27) were male with Male:female ratio 1:1.7. Most of the patients (98%) were from rural areas and Majority of patients (94%) gave history of exposure to Cattle.

In present study maximum number of patients were in 31-40 years age group (36%) followed by 41-50 years age group (26%) with Mean age 42.4 ± 11.24 years. The majority of patients (94%) were admitted in hospital during 7-15 days of illness with Mean duration 8.78 ± 1.61 days. majority of patients (72%) stayed in hospital for ≤ 10 days. (Mean = 10.00 ± 1.73 days). Only 22% of study subjects revealed eschar on examination.

Among 50 cases of scrub typhus prevalence of various manifestations were as fever (100%), altered sensorium (100%), lymphadenopathy (4%), Eschar (22%), neck rigidity (72%) and kerning sign (34%) . (Table 1)

Table 1. showing various Clinical presentation of Scrub Typhus positive patients

Clinical presentation	No. of patients	%
Fever	50	100.00
Vomiting	37	74.00
Headache	41	82.00
Bodyache	25	50.00
Altered sensorium	50	100.00
Jaundice	7	14.00
Lymphadenopathy	2	4.00
Eschar	11	22.00
Hypotension	15	30.00
seizure	5	10.00
Neck rigidity	36	72.00
Kerning sign	17	34.00

In present study majority of patients (68%) were in GCS of 12-14 with mean GCS Score 11.96 ± 1.46 .

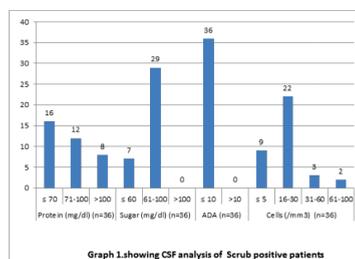
Haemogram shows 76% patients had Haemoglobin level between 7-12gm/dl & Majority(82%) of the patients were found TLC count in normal range ($4000-11000/\text{mm}^3$). 22% patients were found platelet count $<50000/\text{mm}^3$. 74% patients was found between $50000-150000/\text{mm}^3$.

Renal function test (RFT) shows that 44% patients had urea >45 mg/dl and 30% patients had creatinine >1.2 mg/dl.

Liver function test (LFT) shows most of the patients (92%) had SGOT and SGPT >40 IU/L. (Table 2)

Table 2. LFT in scrub typhus patients		
LFT	No. of patients	%
Bilirubin >1.2 mg/dl (1.27 ± 0.80)	17	34.00
SGOT >40 IU/L (102.9 ± 44.08)	46	92.00
SGPT >40 IU/L (85.58 ± 34.85)	45	90.00
ALP >300 IU/L (187.34 ± 74.76)	4	8.00

CSF analysis shows most of the patients (77.77%) were having elevated protein (46-100 mg/dl), 80.55% patients were having elevated sugar level 61-100mg% and majority of patients were having elevated cell count (6-100/mm³). All were lymphocytes. ADA was ≤ 10 in all patients. (Figure 1)



In present study, EEG was done in only 10% (5) patients those who had seizures and found out to be normal.

In present study MRI was done in all patients and detected no significant abnormality.

DISCUSSION

Acute febrile illness with CNS manifestations requires timely diagnosis and treatment to prevent mortality and sequelae. CNS involvement is often a prominent clinical manifestation of scrub typhus.

The results have shown the profile of scrub typhus meningitis from an area already well-known for scrub typhus. The mean duration of fever was 8.78 ± 1.61 days prior to the presentation. This is slightly longer than the mean duration of fever of 7.68 and 8.4 days and its duration is longer than that of viral encephalitis, or acute bacterial meningitis as quoted by Varghese GM *et al*⁷

Most of the affected patients were from rural areas. This may be due to the reason that they are more involved in an outdoor activity like farming, fishing or collecting firewood from the jungle that expose them to mite infested area or vegetation.

Fever and Altered sensorium were present in all patients. Headache is a common symptom in scrub typhus. In the present study, headache was present in 82% cases and was holo-cranial in location in the majority of cases. Other studies like Viswanathan S *et al*⁷, Kim DM *et al*⁶ have reported the occurrence of headache in around 46-77% of patients.^{4,6} In the present study, Neck rigidity and Kernig's sign were present in 72% and 34% patients respectively though other studies shown the presence of neck rigidity in 45.45% and 49% of cases.^{6,7} This may be due to the severity of the cases in our series, or referral bias.

The pathognomic "eschar" that helps in early diagnosis of patients was detected in 22% patients. Eschars are reported from 20% to 86% of patients in different studies.^{4,6,7} Identification of eschar may be difficult in Indian population due to their dark skin and it is also expected to be less in areas endemic for scrub typhus.

Though increase in liver enzymes has been reported in other studies, the disproportionate rise of SGOT over SGPT and raised ALP Levels were detected in our patients. Similar finding has been highlighted in a study Liu YX *et al* from North East India.⁸

The absence of neutrophilic pleocytosis helps in differentiating it from bacterial meningitis but differentiating it from tubercular meningitis remains a challenge. Tubercular meningitis remains the closest differential diagnosis in our setting. With a positive scrub IgM ELISA, other markers like CSF ADA, deranged liver enzymes, thrombocytopenia, no old history of tuberculosis or close contact to patient having pulmonary tuberculosis, short duration of illness and patient improvement after Doxycycline / Azithromycin may be helpful in differentiating scrub meningitis from tubercular meningitis as mentioned in some studies. But, in study CSF ADA was found to be less than 10.

Doxycycline remains the drug of choice. Oral/ Injectable Azithromycin is good alternative for condition.⁹ In the present study as most of the patients were critically ill and injectable Azithromycin 500mg OD for 5 days was used in all patients along with oral Doxycycline 100mg BD for 14 days. Brisk Recovery occurred in 100% patients & usually shows sign of improvement within 48 hour of initiation of specific therapy.

CONCLUSION

Scrub typhus meningitis / meningoencephalitis is not an uncommon complication of scrub typhus. The majority of patients present as acute febrile illness with altered sensorium and meningeal sign. Eschar helps in early diagnosis but in majority it remains absent. CSF analysis shows mild to moderate rise in protein with low to normal glucose. CSF Lymphocytic pleocytosis may be helpful in differentiating it from bacterial meningitis, but tubercular meningitis remains a close differential diagnosis. Thus a high degree of clinical suspicion and positive rapid, diagnostic test remains an important point in management of scrub typhus as timely initiation of specific therapy results in complete recovery and fewer complications.

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