

CLINICAL PROFILE AND OUTCOME OF SCRUB TYPHUS PATIENTS ADMITTED IN BANKURA SAMMILANI MEDICAL COLLEGE & HOSPITAL

1st - Dr Subhrajyoti Mitra (Associate Professor, Dept Of General Medicine, Bankura Sammilani Medical College & Hospital, Bankura.

2nd- Dr Sudipta Pal (Assistant Professor, Dept Of General Medicine, Bankura Sammilani Medical College & Hospital, Bankura.) Corresponding Author*

3rd- Dr Suvamoy Pandit (Post Graduate Trainee, Dept Of General Medicine, Bankura Sammilani Medical College & Hospital, Bankura.)

ABSTRACT

Introduction: The World Health Organization has dubbed scrub typhus as one of the world's most underdiagnosed/underreported diseases that often requires hospitalization. Scrub typhus is a zoonotic, acute febrile illness that is endemic in the regional population, caused by *Orientia tsutsugamushi*, an obligate intercellular anaerobic bacterium, which was previously categorized in the *Rickettsia* genus, is naturally maintained in the mites of *Leptotrombidium* genus, belonging to the family Trombiculidae, by trans-ovarian transmission.

Aims: In this cross sectional, observational, descriptive study, an attempt has been made to document and review the clinical profile and complications in diagnosed cases of scrub typhus in this regional population, thus helping to create a better clinical and laboratory profile of this re-emerging disease for clinicians to work with.

Materials and Methods: It is a descriptive, cross-sectional and analytical study. This Study was conducted from 18 months at Department of General Medicine, BSMCH.

Result: Headache was present in 41(77.4%) patients, myalgia/arthritis were complained by 46(86.8%) patients. 13(24.5%) patients had Platelet count of $<1.5 \times 10^9/\text{cmm}$. Incidence of significantly raised (3 fold) SGPT ($>100 \text{U/L}$) was found in 10(18.9%) patients, and that of SGOT was found in 11(20.7%) patients. Among respiratory symptoms, cough was present in 17(32.1%) patients, shortness of breath was in 16(30.2%) . On respiratory system examination, 15(28.3%) patients had bilateral decreased VBS (subsequently found to have either B/L plural effusion or ARDS or pneumonitis). 6(11.3%) patients had B/L Infiltrates in chest X Ray, 10(18.9%) patients had B/L pleural effusion . In our study, 2(3.8%) patients had Oliguria. On neurological examination, 5(9.4%) patients had clinical features suggestive of Meningitis, 3(5.7%) patients had features suggestive of Meningoencephalitis. 1(1.9%) patient was found to have focal neurodeficit in form of left lateral rectus palsy. Only 1(1.9%) patient presented with Eschar in left thigh and associated left inguinal lymphadenopathy

Conclusion: We found that, in patients presenting with fever and respiratory symptoms having B/L infiltrate and/or B/L pleural effusion, suspicion of scrub typhus should be kept in mind.

INTRODUCTION

The World Health Organization has dubbed scrub typhus as one of the world's most underdiagnosed/underreported diseases that often requires hospitalization¹. Scrub typhus is a zoonotic, acute febrile illness that is endemic in the regional population, it is caused by *Orientia tsutsugamushi*, an obligate intercellular anaerobic bacterium, is naturally maintained in the mites of Trombiculidae, by trans-ovarian transmission^{2,3}. This disease is grossly under-reported and under-diagnosed owing to the misconception that scrub typhus is only a concern in heavily forested areas⁴. After an incubation period of about 6-21 days, the first sign of scrub typhus is a vesicular lesion at the site of mite feeding, which later becomes an eschar or an ulcer with or

without regional lymphadenopathy. A thorough and probing search for an eschar is very useful for diagnosis **3,4**. The clinical spectrum of scrub typhus varies from mild to moderate severity. Acute fever is the most common manifestation later accompanied by headache, myalgia and cough. Severe complications include prominent encephalitis, interstitial pneumonia, ARDS and circulatory collapse with haemorrhagic features.**5** Diagnostic tests such as the Weil–Felix test are very insensitive and non-specific. The current choice for the serologic diagnosis is IgM ELISA testing or immunofluorescence assay (IFA), which is considered the gold standard, although it is less frequently available. Empirical therapy with doxycycline, in cases having high index of suspicion, especially in endemic areas, may be life saving.**6**

AIM AND OBJECTIVE OF THE STUDY:

In this cross sectional, observational, descriptive study, an attempt has been made to document and review the clinical profile and complications in diagnosed cases of scrub typhus in this regional population, thus helping to create a better clinical and laboratory profile of this re-emerging disease for clinicians to work with.

METHODOLOGY

It is a descriptive, cross sectional and analytical study done in Indoor medicine wards of department of General Medicine, BSMCH from January 2020 to June 2021. All diagnosed cases of scrub typhus IgM ELISA Reactive patients aged between 18 years to 60 years and screened negative for COVID 19 infection by Rapid Antigen Kit admitted in the indoor wards of department of Medicine, BSMCH were included in this study.

All patients diagnosed to have scrub typhus or those with strong clinical suspicion of scrub typhus were treated with doxycycline in the dose of 100 mg twice daily PO for 10 days. In those patients who presented with features suggestive of meningitis, injection ceftriaxone was started empirically but later stopped when scrub typhus IgM ELISA report came positive. In one patient who was intubated, he received injection meropenem and IV doxycycline as antibiotic therapy.

Data collected from admitted patients by structured interview (history taking) and clinical examination (general survey and systemic examination). Laboratory investigation, parameters and procedure- Routine haematological and biochemical tests, and radiological investigations were studied. The data compiled and codified in Micro Soft Excel spread sheet. Analysis done by appropriate statistical method.

RESULT AND ANALYSIS

Distribution of age group

Age group	Frequency	Percent
18-30	24	45.3%
31-40	11	20.8%
41-50	9	17.0%
51-60	9	17.0%
Total	53	100.0%

Distribution of Sex group

sex	Frequency	Percent
Female	33	62.3%
Male	20	37.7%
Total	53	100.0%

Distribution of fever duration

Fever duration in days	Frequency	Percent
1-5	27	50.9%
6-10	25	47.2%
>10	1	1.9%
Total	53	100.0%

Distribution of clinical features

	Frequency	Percent
Headache	41	77.4%
Arthralgia / Myalgia	46	86.8%
Cough	17	32.1%
Shortness of breath	16	30.2%
Vomiting	10	18.9%
Icterus	8	15.1%
Pain abdomen	11	20.8%
Malena	1	1.9%
Altered sensorium	8	15.1%
Convulsion	3	5.7%
Focal neurodeficit , Left lateral rectus palsy	1	1.9%

Neck rigidity	8	15.1%
Eschar	1	1.9%
Rash	8	15.1%
Lymphadenopathy	1	1.9%
Oliguria	2	3.8%
Puffiness/generalized swelling	7	13.2%
Suggestive of Meningitis	5	9.4%
Suggestive of Meningoencephalitis	3	5.7%

Distribution of Total leucocyte count(TLC) and platelet

TLC<4000	12	22.6%
TLC 4000-10000	19	35.8%
TLC >10000	22	41.5%
PLT< 1.5 Lac	13	24.5%
PLT>1.5 Lac	40	75.5%
P time >16.5 secs	8	15.1%

Distribution of Gastro Intestinal Features

Gastro Intestinal System	Frequency	Percent
Ascites	3	5.7%
Hepatomegaly	1	1.9%
Tenderness in umbilical region	12	22.6%
Total	53	100.0%

Distribution of USG WHOLE ABDOMEN and CXR

	Frequency	Percent
Ascites	2	3.8%
Hepatomegaly	7	13.2%
B/L Infiltrate	6	11.3%
B/L Plural effusion	10	18.9%

Distribution of Ascitic fluid cell type

Ascitic fluid cell type	Frequency	Percent
≥ 80% Lymphocyte	3	100.0%
Total	53	100.0%

Distribution of Serum/Ascitic fluid albumin gradient(SAAG):

Serum albumin	Ascitic fluid albumin	SAAG
4gm/dl	1.5gm/dl	2.5
3.2gm/dl	1.8gm/dl	1.4
3.2gm/dl	2gm/dl	1.2

Distribution of NCCT Scan Brain

NCCT Scan Brain	Frequency	Percent
Diffuse cerebral edema	1	1.9%
Not Applicable	45	84.9%
Normal CT Scan	7	13.2%
Total	53	100.0%

CSF Study Properties

CSF study	No	Percentage
Lymphocyte ≥80%	8	15.1%
Cell count 0-5/cmm	0	0%
Cell count 5-10/cmm	0	0%
Cell count >10/cmm	8	15.1%
CSF protein>40mg/dl	8	15.1%

Distribution of MODS

Multi Organ Dysfunction Syndrome	Frequency	Percent
No	42	79.2%
Yes	11	20.8%
Total	53	100.0%

Distribution of final outcome

Final Outcome	Frequency	Percent
Discharged	52	98.1%
Expired after 12 days	1	1.9%
Total	53	100.0

DISCUSSION .**SUMMARY OF RESULT AND ANALYSIS**

In this study, maximum number of patients were in the age group of 18-30 years(45.3%). Mean age was 35 years. Male female ratio ratio was 1.65:1(33:20). All patients presented with fever. Mean duration of fever of patients in our study was 5.98 days, minimum being 3 days and maximum being 12 days. Headache was present in 41(77.4%) patients, myalgia/arthralgia were complained by 46(86.8%) patients. Among respiratory symptoms, cough was present in 17(32.1%) patients, shortness of breath was in 16(30.2%) patients. In our study, 10(18.9%) patients had vomiting, 8(15.1%) patients had Icterus, Only 1(1.9%) patient presented with Eschar in left thigh and associated left inguinal lymphadenopathy. In our study, 2(3.8%) patients had Oliguria and 7(13.2%) patient had puffiness/generalized Swelling. Among CNS findings, 8(15.1%) patients had Altered Sensorium, all of them found to have neck rigidity, 3(5.7%) patients had history of convulsion, and 1(1.9%) patient was found to have focal neurodeficit in form of left lateral rectus palsy. On examination of gastro intestinal system, 3(5.7%) patients had Ascites, 1(1.9%) patients had hepatomegaly, 12(22.6%) patients had tenderness in umbilical region, and 37(69.8%) patients had no abnormal findings. On neurological examination, 5(9.4%) patients had clinical features suggestive of Meningitis, 3(5.7%) patients had features suggestive of Meningoencephalitis. In this study, 12(22.6%) patients had TLC of <4000, 19(35.8%) patients had normal TLC (in range of 4000-10000) and 22(41.5%) patients had TLC of >10000. 13(24.5%) patients had Platelet count of <1.5lac/cmm and 40(75.5%) patients had normal platelet count. 12(22.6%) patients had bilirubin level of >2mg/dl, Incidence of significantly raised (3 fold) SGPT(>100U/L) was found in 10(18.9%) patients, and that of SGOT was found in 11(20.7%) patients. On respiratory system examination, 15(28.3%) patients had bilateral decreased VBS (subsequently found to have either B/L plural effusion or ARDS or pneumonitis). 6(11.3%) patients had B/L Infiltrates in chest X Ray, 10(18.9%) patients had B/L pleural effusion and 37(69.8%) patients had normal Chest X Ray. Pleural fluid aspiration and laboratory examination was not done because all patients had B/L pleural effusion, and it was associated with either ascites or features of ana sarca in most of the cases.

Among USG whole abdomen findings, (3.8%) patients had ascites, 1(1.9%) patients had Ascites with B/L swollen kidney, 4(7.5%) patients had B/L swollen kidney, 7(13.2%) patients had hepatomegaly, 2(3.8%) patients had hepatosplenomegaly and 37(69.8%) patients had normal USG of abdomen. In our study, all 3 patients having ascites had $\geq 80\%$ Lymphocyte count in

ascitic fluid. All 3 patients having ascites had ascitic fluid protein amount of $<3\text{gm /dl}$. All 3 patients who had developed ascites had SAAG value of >1.1 .

NCCT Scan of brain was done for all patients having CNS features (suggestive of meningitis/meningoencephalitis). 1(1.9%) patient had diffuse cerebral edema in NCCT Scan of Brain and 7(13.2%) patients had no abnormality in NCCT Scan Brain.

All 8(15.1%) patients having meningitis/meningoencephalitis had $>10/\text{cmm}$ cell count in CSF. All 8(15.1%) patients having meningitis/meningoencephalitis had $\geq 80\%$ lymphocyte in CSF and CSF protein level of $>40\text{mg/dl}$.

In our study, 7(13.2%) patients received injection Ceftriaxone + Doxycycline, 45(84.9%) patients received only oral Doxycycline and 1(1.9%) patient received Injection Meropenem + Injection Doxycycline as antibiotic therapy.

Premraj SS et al 5(2018) found that the symptoms included fever, abdominal symptoms, headache, dysuria, breathlessness and altered sensorium. Most common findings on physical examination were eschar (58%), crepitations in the chest (36%), hepatomegaly (34%) and lymphadenopathy (30%). 32% had respiratory complications, 4% required mechanical ventilation, 24% had shock, 16% had acute kidney injury, and 6% had dysfunction of ≥ 2 organs. Age of >50 years, longer duration of illness (>7 days), residence in a rural area and the absence of eschar were found to be independent risk factors for development of severe illness.

Vivekanandan M et al 7(2010) found that common symptoms were high grade fever of 7-14 days duration, nausea, vomiting, headache, myalgia, cough and breathlessness. Eschar was seen in 23 cases (46%) and the common sites were axilla, breast and groin. Liver enzymes were elevated in nearly all cases (95.9%). Multiple Organ Dysfunction Syndrome (MODS) was present in one third of our patients (34%). Hypotension (16%), renal impairment (12%), ARDS (8%) and meningitis (14%) were some of the important complications.

Ghimire RH et al 8(2020) found that most patients (70.15%) were of above 40 years. Fever 47 (100%), asthenia 40 (85.10%), generalized body-ache 41 (87.23%), anorexia 46 (97.87%) and headache 39 (82.97%) were present in most of their patients at some point during their illness. Respiratory dysfunction was the commonest 37 (78.72%) system dysfunction followed by renal 30 (63.82%) and hepatic 20 (42.55%) impairment.

Varghese GM et al 9(2014) found that the most common presenting symptoms were fever (100%), nausea/vomiting (54%), shortness of breath (49%), headache (46%), cough (38%), and altered sensorium (26%). An eschar was present in 43.5% of patients. Common laboratory findings included elevated transaminases (87%), thrombocytopenia (79%), and leukocytosis (46%). MODS was seen in 34% of patients. The overall case-fatality rate was 9.0%. Features of acute lung injury were observed in 33.7%, and 29.5% required ventilatory support.

Kumar V et al 10(2014) found that mean age of study population was 34.1 ± 14.4 years. Majority were males and a seasonal trend was evident with most cases following the rainy season. Overall, renal abnormalities were seen in 82% patients, 53% of patients had AKI (stage 1, 2 and 3 in 10%, 8% and 35%, respectively). Acute respiratory distress syndrome (ARDS) and shock were seen in 57% and 16% of patients, respectively..

Jamil MD et al 11(2014) found that with males more than females. Most (42.37%) belonged to 18 to 30 years age group. Fever with headache was the commonest presentation (94.91%). Multiorgan dysfunction syndrome was the most common complication (16.94%). The mortality rate was 8.47%.

CONCLUSION

This study shows wide variety of clinical manifestations and complications of scrub typhus, a well-known mite borne disease in India and other south-east Asian countries.

This study also highlights the paucity of eschar in scrub typhus patients in this particular geographic region, also scarcity of features suggestive of cardiac complications like myocarditis, contrast to other studies done in other parts of India and other south eastern countries.

When a patient comes with history of fever and elevated liver enzymes, and malaria/dengue serology is negative, scrub typhus should be considered as differential diagnosis and an empirical therapy with doxycycline should be started if there is high index of suspicion.

In patients presenting with fever and respiratory symptoms having B/L infiltrate and/or B/L pleural effusion, suspicion of scrub typhus should be kept in mind.

In cases of meningitis/meningoencephalitis also, if tubercular or bacterial aetiology is ruled out, scrub typhus should be considered as differential diagnosis and an empirical therapy with doxycycline should be started if there is high index of suspicion.

Due to the varied presentation and complications, a high index of suspicion is much required.

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