Section: General Medicine

Original Research Article

AN OBSERVATIONAL STUDY ON CLINICAL SPECTRUM, DIAGNOSIS, COMPLICATIONS AND THERAPEUTIC OUTCOME OF SCRUB TYPHUS: AN EMERGING RICKETTSIAL INFECTION

Geetika Roat[1], Ravi Singh[2], Sandeep Kumar[3], Laxmikant Tank[4*], Ashok Mosalpuri[5], Anoop Dadhich[6], Subhash Jain[7]

[1,2,3,5]PG Third year, [4,6]Assistant Professor, [7]Senior Professor and HOD, Department of General Medicine, Jhalawar Medical College, Jhalawar, Rajasthan, India.

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Corresponding Author:
Dr. Laxmikant Tank,
Email: doclaxmikanttank21@gmail.com

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Abstract

Introduction: Scrub Typhus is an acute febrile illness caused by Orientia tsutsugamushi, a bacteria from the Rickettsiaceae family. It is important cause of AFI in south eastern belt of Rajasthan. Outbreaks of AFI occur usually in the rainy and post-rainy season in India. Scrub typhus is characterized by fever, which is one of the causes of "fever of unknown origin" in endemic areas usually accompanied by a rash, myalgia, and widespread lymphadenopathy, and it can progress to organ failure and death. Scrub typhus is diagnosed by a necrotic eschar at the mite's inoculating site. Untreated scrub typhus has a median mortality rate of 6.0%. The occurrence of organ failure is high in patients who were diagnosed late and received antibiotics late. **Aim and objective:** To study the clinical spectrum, laboratory parameters, complications and its prognosis in patients with IgM ELISA positive for scrub typhus. **Material and methods:** This Descriptive observational study was conducted in the patients with IgM ELISA positive for scrub typhus admitted in general medicine ward in a tertiary care hospital. A total 132 patients were included and clinical features, lab parameters, and outcomes were evaluated in all patients with scrub typhus. Data analysis was done by using SPSS version 24. **Results:** A statistically significant high mortality was found in the patients from rural area, patients who had rashes, jaundice, decreased urine output, confusion, swelling, shortness of breath, seizures, hepatomegaly, Lymphadenopathy, eschar and fever of >7 days (Table 4). A statistically significant high TLC, blood urea, uric acid, Total billirubin, AST, ALT and ALP were found while a statistically significant low platelets and albumin was found among the patients who died. **Conclusion:** Scrub typhus is an important cause of acute febrile illness with multisystem involvement. A high index of suspicion is needed in patients presenting with fever especially during monsoon and post monsoon season. Though eschar is pathognomic, may not be seen. An early diagnosis with “suspect and treat” strategy with prompt treatment implementation can prevent morbidity and mortality.

INTRODUCTION

Acute febrile illness (AFI) is the most common presenting complaint in the emergency and outpatient clinics in developing countries. Outbreaks of AFI occur usually in the rainy and post-rainy season in India. Malaria, dengue, typhoid, scrub typhus, and several viral infections have been classically responsible for such outbreaks.[1] Scrub typhus is a vector-borne zoonosis caused by the bacterium Orientia tsutsugamushi, endemic in South Asia, Southeast Asia, East Asia, the Pacific Islands, and Northern Australia (the “tsutsugamushi triangle”). Rickettsial diseases are considered as some of the most covert emerging and re-emerging diseases and are being increasingly recognized.[2] Scrub typhus is the most common rickettsial infection from Indian subcontinent.[3]

In India, every year during and after monsoon season, there is sudden rise in cases of acute febrile illness. Viral infections, malaria, dengue, typhoid, leptospirosis and scrub typhus have been classically responsible for such outbreaks.[4] These diseases may presents with overlapping clinical features.[5] This often leads to either misdiagnosis or delay in diagnosis. This study will provide diagnostic clues to the primary care physicians, so that they can diagnose cases of scrub typhus earlier for better outcome of

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patients. This disease can progress to severe complications like acute respiratory distress syndrome (ARDS), hepatitis, acute kidney injury, myocarditis leading to heart failure, and meningoencephalitis in different proportions of the patients. A late presentation, delay in diagnosis and treatment, and varying levels of antibiotic resistance exhibited by the organism are factors responsible for high mortality.[6] An early diagnosis and institution of specific treatment will reduce morbidity and mortality from this infectious disease.[7] This study was designed to carry out and document the clinical presentation and outcomes of adult patients with scrub typhus attended hospital.

MATERIALS AND METHODS

Current study was Descriptive observational study conducted at the Department of Medicine in Shri Rajendra general hospital (SRGH), Jhalawar Medical College, Jhalawar, Rajasthan from February 2021 to December 2022. Calculated sample size 132 and a total 140 patients, >18 years of age with IgM ELISA positive for scrub typhus were included in the study and Acute febrile illness patients with IgM ELISA negative for scrub typhus, Patients with co-infection with dengue or malaria and Patients having co-morbid condition like chronic renal failure, chronic liver disease and patients with known neoplastic diseases etc were excluded from the study.

All demographic information, thorough clinical history, including age, gender, occupation and presenting complaints were meticulously noted in chronological sequence. All patients underwent a thorough physical examination, with particular emphasis paid to temperature, the existence of skin eschar, icterus, respiratory rate, altered sensorium, lymphadenopathy and hepatosplenomegaly.

Data were analysed in SPSS v- 24. Independent t-test and Chi-square test were applied. p value <0.05 was considered statistically significant.

RESULTS

Mean age of study participants was 38.8±9.8 years and maximum participants were in age group of <30 years. Out of the 140 participants, maximum 75 were female and 104 from rural area. (Table 1)

Most common symptom was fever and present in all the patients followed by headache in 91, rashes in 63 and jaundice in 56 patients and most common findings on examination was hepatomegaly found in 64 patients, pallor in 56 and Eschar was present in 51 patients and 10 patients had B/L heterogeneous infiltrate followed by

5 patients had B/L lower zone infiltration (Table 2). Among the laboratory parameters thrombocytopenia seen and total bilirubin, direct bilirubin, ALT, AST, ALP were increased (Table 3). Mortality was found in 14 (10%) patients (Figure 1). A statistically significant high mortality was found in the patients from rural area, patients who had rashes, jaundice, decreased urine output, confusion, swelling, shortness of breath, seizures, hepatomegaly, Lymphadenopathy, eschar and fever > 7 days (Table 4). A statistically significant high TLC, blood urea, uric acid, Total billirubin, AST, ALT and ALP was found while a statistically significant low platelets and albumin was found among the patients who died (Table 5).

Table 1: Socio-demographic of study participants (N=140):

Variables	Frequency	Percent
Age (Mean±SD)	38.8±9.8 years	
Age:		
<30 years	63	45.0
31-40 years	20	14.3
41-50 years	19	13.6
51-60 years	24	17.1
>60 years	14	10.0
Gender:		
Female	75	53.6
Male	65	46.4
Residence:		
Rural	104	74.3
Urban	36	25.7

Table 2: Distribution of participants according to symptoms

SYMPTOMS	No. of patients	Percent
Fever	140	100.0%
Vomiting	17	12.1%
Headache	91	65.0%
Loose stool	29	20.7%
Pain abdomen	29	20.7%
Cough	44	31.4%
Myalgia	49	35.0%
Swelling	4	2.9%
Burning micturition	14	10.0%
decreased urine output	16	11.4%
Rashes	63	45.0%

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Jaundice	56	40.0%
SOB	13	9.3%
Confusion/Altered sensorium	25	17.9%
Seizure	4	2.9%
GPE:		
Pallor	56	40.0%
Oedema	34	24.3%
Lymphadenopathy	38	27.1%
Hepatomegaly	64	45.7%
Splenomegaly	14	10.0%
Eschar	51	36.4%
Trunk	38	27.1%
Axillary	9	6.4%
Inframammary	7	5.0%
Inguinal	9	6.4%
X-RAY FINDINGS:		
B/L heterogeneous infiltrate	10	7.1%
B/L lower zone infiltration	5	3.6%
Left lower zone consolidation	3	2.1%
Pleural effusion	2	1.4%

Table 3: Distribution of laboratory parameters among the study participants

	Mean	**SD**
Hemoglobin (gm%)	8.97	2.92
Hematocrit (%)	31.87	8.25
Total leukocyte count (103/µL)	4684.14	4063.28
Platelet count (103/µL)	24.99	22.13
Blood glucose level (random) (g/dl)	112.29	25.31
Urea (mg/dl)	56.51	41.24
Creatinine (mg/dl)	1.44	1.13
Uric acid (mg/dl)	5.32	1.65
TB (mg/dl)	1.69	1.6
DB (mg/dl)	1.17	1.41
AST (U/L)	138.01	200.25
ALT (U/L)	93.31	118.35
ALP (U/L)	159.68	119.93
TP (g/dl)	6.31	0.98
Albumin (g/dl)	2.89	1.14
Sodium (meq/L)	136.52	11.06
Potassium (meq/L)	4.52	4.26
Triglycerides	167.87	57.66

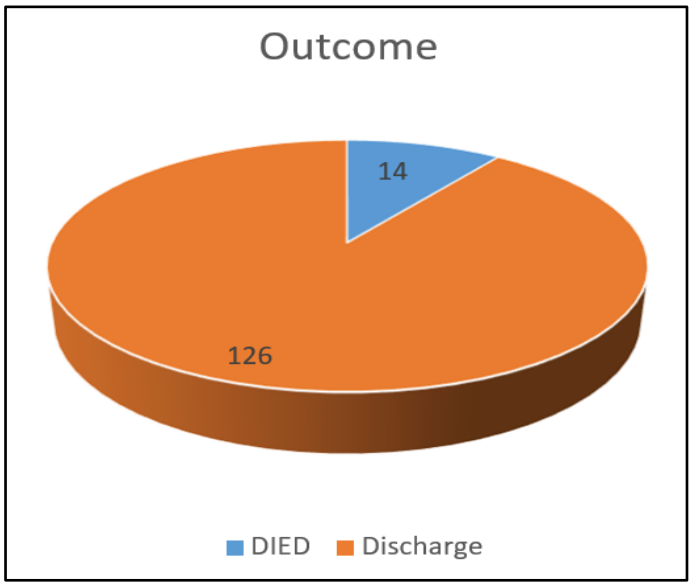

Figure 1: Distribution of participants according to final outcome

Table 4: Comparison of various parameters with final outcome:

RESIDENCE	**DIED**		**Discharge**		**p-value**
	n	**%**	**n**	**%**	
Rural	9	64.3%	111	88.1%	0.016

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Urban	5	35.7%	15	11.9%	
SYMPTOMS:					
Fever	14	100.0%	126	100.0%	1.000
Vomiting	2	14.3%	15	11.9%	0.796
Headache	8	57.1%	83	65.9%	0.516
Loose stool	2	14.3%	19	15.1%	0.937
Pain abdomen	5	35.7%	24	19.0%	0.144
Cough	4	28.6%	40	31.7%	0.808
Myalgia	4	28.6%	45	35.7%	0.595
Swelling	4	28.6%	0	0%	0.001
Burning micturition	8	57.1%	6	4.7%	0.001
decreased urine output	8	57.1%	8	6.3%	0.001
Rashes	14	100.0%	49	37.9%	0.001
Jaundice	8	57.1%	48	38.1%	0.001
SOB	4	28.6%	9	7.1%	0.001
Confusion/Altered sensorium	8	57.1%	17	13.5%	0.001
Seizures	3	21.4%	1	0.7%	0.001
FEVER:					
<7 days	4	28.6%	55	43.7%	0.045
7-14 days	7	50.0%	53	42.1%	
14-21 days	0	0.0%	12	9.5%	
>21 days	3	21.4%	6	4.8%	
GPE:					
Pallor	2	14.3%	26	20.6%	0.573
Oedema	4	28.6%	30	23.8%	0.786
Lymphadenopathy	8	57.1%	30	23.8%	0.001
Hepatomegaly	9	64.3%	55	43.7%	0.141
Splenomegaly	1	7.1%	13	10.3%	0.707
Eschar	9	64.3%	42	33.3%	0.001
ECG					
Tachycardia	14	100.0%	21	16.7%	0.001
WNL	0	0.0%	105	83.3%	
X-RAY FINDINGS					
B/L heterogeneous infiltrate	2	14.3%	8	6.3%	0.001
B/l lower zone infiltration	2	14.3%	3	2.4%	
Left lower zone consolidation	2	14.3%	1	0.7%	
Pleural effusion	2	14.3%	0	0.0%	

Table 5: Comparison of laboratory parameters with final outcome:

OUTCOME	**DIED**		**Discharge**		**p-value**
	Mean	**SD**	**Mean**	**SD**	
Hemoglobin (gm%)	7.97	3.20	8.97	2.90	0.735
Hematocrit (%)	28.70	9.59	31.88	8.13	0.741
Total leukocyte count (103/µL)	6474.36	5629.32	4707.45	3880.49	0.001
Platelet count (103/µL)	14.43	22.01	24.83	22.22	0.001
Blood glucose level (random) (g/dl)	111.07	14.42	112.43	26.29	0.850
Urea (mg/dl)	75.57	32.54	56.62	42.20	0.001
Uric acid (mg/dl)	7.33	1.52	5.32	1.67	0.001
TB (mg/dl)	2.58	1.82	1.30	1.58	0.001
AST (U/L)	177.98	63.48	121.35	209.91	0.001
ALT (U/L)	103.39	42.43	74.41	124.00	0.001
ALP (U/L)	204.86	218.34	154.62	103.70	0.001
Albumin (g/dl)	2.18	1.12	3.86	1.14	0.020
Sodium (Meq/L)	134.86	6.87	136.71	11.44	0.555
Potassium (Meq/L)	3.89	.63	4.59	4.48	0.562
Triglycerides	169.56	67.37	167.69	56.79	0.909
Cholesterol	166.59	49.01	164.31	53.64	0.879
HDL	36.51	8.50	39.98	11.87	0.291
LDL	93.49	42.55	90.83	43.94	0.830

DISCUSSION

In our study of 140 patients, most common symptom was fever and present in all the patients followed by headache in 91 (65%) and rashes in 63 (45%) patients. Other symptoms were myalgia (35%) Jaundice (40%), cough (31.4%), loose stool (20.7%), pain abdomen (20.7%), confusion/altered sensorium (17.9%), vomiting (12.1%), decreased urine output (11.4%), SOB in (9.3%), swelling (2.9%) and seizures in (2.9%) patients, most common findings on examination were hepatomegaly present in 64 (45.7%) patients, pallor was found in 56 (40%) and eschar was present in 51 (36.4%) patients. most common site of Eschar was trunk and present in 38 (27.1%) patients followed by axillary in 9 (6.4%).

A study was conducted by Atri SK et al[8] and the mean duration of fever before presentation to the hospital was 11.1±4.9 days. The most common presenting symptoms were Fever (100%), shortness

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of breath (40%), altered sensorium (22.5%), nausea/vomiting (10%), diarrhea (7.5%). An Eschar was seen in 15% of the patients.

Sharma N et al[9] revealed that High-grade fever associated with chills and rigor was the most common presenting symptom in 85% (median duration of 10 days [IQR = 7–15 days]. Breathlessness was the presenting feature in 42%, jaundice in 32%, abdominal pain in 28%, renal failure in 11%, diarrhea in 10%, rashes in 9%, and seizures in 7% Verma SK et al[10] found that the patients had fever with an average duration of 9.6 ± 2 days. Fever was high grade, continuous in majority of patients. Twenty one (40.3%) and sixteen (30.7%) patients presented as fever with chills and pyrexia of unknown origin respectively. Other associated symptoms were headache (69.2%), followed by nausea and vomiting (59.6%). On examination, icterus was present in fifteen (28.8%) patients. Eschar, a characteristic skin lesion seen in patients of Scrub typhus, was found in eleven patients (21.2%) on abdomen, thighs and arms. Erythematous maculopapular rash was seen in 4 (7.7%) patients. On abdominal examination, hepatomegaly was present in 11 (21.2%) and splenomegaly in 15 (28.8%) patients. Lakshmi RMMV et al[11] also found that majority of the patients (58.6%) presented with 7–14 days of fever and 10.3% of them had prolonged pyrexia beyond 2weeks. Similarly, Jayprakash V et al[12] observed anorexia, nausea, and vomiting in 21.24% of patients, jaundice in 6.22% of patients and eschar in 28.49% of patients. Thigh was commonest location of the eschar, followed by neck and chest, abdomen, perineum, axillae, and the back. Our study is comparable to other studies as described. In the current study, 10 patients had B/L heterogeneous infiltrate followed by 5 patients had B/L lower zone infiltration and high mortality seen among patients having tachycardia and abnormal lung findings and among those who had thrombocytopenia, hypoalbuminemia and total bilirubin, direct bilirubin, ALT, AST, ALP levels were raised.

Sharma N et al[9] revealed that common laboratory findings included thrombocytopenia (85%), raised aminotransferase level (57%), leukocytosis (45%), Hyperbilirubinemia (20.6%) and leucopenia (15%).

Atri SK et al[8] found the most common laboratory finding was a deranged hepatic function in 61% and thrombocytopenia in 90% of patients. Acute kidney injury (32%), ARDS (25%), and DIC (16%) were the commonest complications. Hepatorenal syndrome was seen in 38% and MODS was seen in 20% patients.

Verma SK et al[10] revealed that complete blood count revealed anemia in 31 (59.6%), leucocytosis in 26 (50%) and thrombocytopenia in 40 (76.9%) patients. Liver function test showed elevated transaminases with rise in SGOT and SGPT in thirty-six (69.2%) and thirty (57.7%) patients, respectively and hyperbilirubinemia (bilirubin > 2mg/ dL) in eighteen (34.6%) patients. Rise in SGOT was more than SGPT (SGOT/SGPT > 1).

In our study, out of the 140 participants, mortality was found in 14 (10%) patients. A statistically significant high mortality was found in the patients from rural area, patients who had rashes, jaundice, decreased urine output, confusion, swelling, shortness of breath, seizures, hepatomegaly, Lymphadenopathy, eschar and fever of more than 7 days (Table 4). A statistically significant high TLC, blood urea, uric acid, Total billirubin, AST, ALT and ALP were found while a statistically significant low platelets and albumin was found among the patients who died. A statistically significant tachycardia and a significant bilateral heterogenous infiltration on chest x-ray was found among patients who died.

Sharma N et al[9] reported the case fatality rate was 13.6%. Atri SK et al[8] found the overall mortality was 10%. Data from other Indian studies have shown that the case fatality rate in scrub typhus has ranged from 1.2% to as high as 46.3% depending on the complications. [13-16] From south India, other studies have reported nearly similar fatality rates that the authors attributed to a lack of awareness of this disease.[17]

CONCLUSION

Scrub typhus is an important cause of acute febrile illness with multisystem involvement. A high index of suspicion is needed in patients presenting with fever especially during monsoon and post monsoon season. Though eschar is pathognomic, may not be seen. ARDS, hepatitis, MODS, AKI, meningitis and shock are life – threatening complications that leads to higher case fatality rates. An early diagnosis with "suspect and treat" strategy with prompt treatment implementation can prevent morbidity and mortality.

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