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Clinical Profile of Adult Patients Suffering from Scrub Typhus in Kasturba Hospital Wardha, Central India: A Study of 125 Patients

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Abstract

Background: Scrub Typhus is among the commonest causes of Acute Undifferentiated Fever during the monsoon in central India but there is a gap in knowledge regarding the data of the clinical profile in tropical rural area.

Objective: To study the clinical profile of adult patients admitted with scrub typhus during the monsoon in rural central India.

Material and methods: A Hospital based retrospective study was carried out in the 125 patients admitted to Medicine department of MGIMS during the monsoon period of June to September 2017. The History, clinical features, Lab profile, Treatment, complications and outcomes were studied closely. The data was retrieved from the Hospital Information System. The Outcome was studied in association with the severity of presentation, complications and treatment given. Diagnosis depended on recognizing the syndrome of non-specific symptoms of fever and cough, while diagnosis was confirmed using the IgM Scrub Typhus Rapid Chromatographic Test, which was considered as a Gold Standard in our study. Statistical analysis was done by descriptive and inferential statistics using chi-square test and software SPSS 22.0 version, EPI Info version 7 and Graph Pad Prism 6.0 version.

Results: The clinical illness was characterized by Fever with chills (60.8%) and Cough (68.8%). The Disease was mostly acute (97%) presenting with a history of less than 10 days. The most characteristic physical sign was fever which was present in almost 60 percent of cases and the traditionally mentioned rash called Eschar was found in only 38 percent of patients. ARDS, nephropathy, Liver failure and Multi organ dysfunction occurred in 16%, 20%, 20% and 13.6% respectively. Though Scrub typhus occurs secondary to a chigger bite, only 6 patients out of 125 gave the actual history of insect bite. 9 patients out of 125 (7.2%) succumbed to death. Early treatment with Doxycycline shortened the duration of illness. No relapses

occurred in those patients who received Doxycycline or Azithromycin for at least 7 days.

Conclusion: Serious complications can occur if Scrub typhus is not recognized promptly. Early institution of Doxycycline can save lives in the patients of acute undifferentiated fever pending investigations. General physicians should be Scrub typhus minded to suspect and accurately treat the patients of fever.

Keywords: Scrub typhus; Clinical illness

Introduction

Our present study is an attempt to focus the impact of scrub typhus infection on the clinical features, laboratory variables, complications, response to treatment and ultimately the fate among the patients affected by the disease and thereby to anticipate the severe outcome and intervene timely. Scrub typhus is an emerging zoonotic rickettsial infection caused by *Orientia tsutsugamushi*, characterized by focal or disseminated vasculitis that may involve almost all the organs of the body including lungs, liver, spleen, hematopoietic system and central nervous system. Clinical features may range from a trivial self-limiting illness to a life threatening disease if left untreated or remains undiagnosed.

One million cases of scrub typhus occur each year all over the world with an estimated 10% case fatality rate unless treated appropriately, very likely resulting in more deaths than dengue. Scrub Typhus is known to occur all over India, however, the reported number of cases of Scrub typhus from different parts of the country particularly from large tertiary care hospitals do not give a true picture of prevalence of scrub typhus in the country. The burden of disease in rural areas of Asia is large. Only a few studies have occurred and that shows that scrub typhus contribute up to 20% of all febrile hospital admissions.

In 1999, the World Health Organization (WHO) stated, "Scrub typhus is probably one of the most underdiagnosed and underreported febrile illnesses requiring hospitalization in the region". This opinion remains valid today and could justifiably be adjusted to scrub typhus is probably the single

most prevalent, under-recognized, neglected, and severe but easily treatable disease in the world.

Scrub Typhus leads to serious complications [1] like Pneumonitis, thrombocytopenia and even full blown ARDS. It can also lead to delirium and neuropsychiatric manifestations. Even Multiorgan Failure and deaths have occurred due to this trivial considered disease [2]. It is apparent that scrub typhus has been recognized to occur frequently now in places where the illness was nearly forgotten, including India, Sri Lanka, the Maldives, and Micronesia. It had gained a notoriety to cause ARDS in tropical countries during the monsoon seasons and has contributed to the chunk of mortalities during this season if not diagnosed and treated promptly. As yet, there are not many community based studies in our country.

Hence we have undertaken our study with an objective to explore the effects of Scrub Typhus in a rural area during the monsoon season and add to our knowledge regarding its clinical profile. It will help us to be 'Scrub Typhus Minded', suspect the disease and treat it in infancy to prevent the untimely deaths in otherwise healthy population.

Materials and Methods

This was a prospective observational study conducted in a 150 bedded department of Medicine of Kasturba Hospital Sevagram, situated in the district of Wardha, north eastern Maharashtra in Central India, from June 2017 to September 2017. Out of 146 patients diagnosed to have Scrub typhus, 21 Patients were excluded in view of insufficient hospital information system (HIS) data.

All Patients within an age group of 14 to 85 years who were diagnosed positive to scrub typhus IgM Rapid Chromatographic Test were included in the study. A retrospective comprehensive data collection was performed using Hospital Information System under the headings of demographic variables like age, sex, onset, duration of stay, Clinical symptoms and signs, CXR findings, Laboratory variables like Serum creatinine, Liver enzymes, heamogram, Development of Multi-organ failure and ARDS, treatment given and the outcome. The data was entered in Google Sheets, analyzed and presented.

Results

Out of 1300 patients admitted to our Kasturba Hospital Sevagram during the period of June to September 2017, 146 patients were diagnosed to have Scrub Typhus confirmed with Scrub Typhus IgM Rapid Chromatographic Test. Out of these 21 were excluded due to insufficient HIS Data. 125 patients were included with confirmed serological diagnosis of Scrub Typhus.

Tables 1-4 depict the comprehensive characteristics of the patients, including the demographic profile, clinical features, laboratory considerations, treatment, complications and outcome. The total in hospital mortality observed was 7.2%.

Demography

Table 1 Age and Gender wise distribution of patients.

	No of patients	Percentage (%)
Age Group (years)		
Up to 20 years	11	8.8
21-30 years	19	15.2
31-40 years	38	30.4
41-50 years	14	11.2
51-60 years	19	15.2
>60 years	24	19.2
Total	125	100
Mean \pm SD	43.36 \pm 16.81	
Range	14-85 years	
Gender groups		
Male	47	37.6
Female	78	62.4
Total	125	100

Clinical findings

Table 2 Summary of Clinical Features.

Sr.No	Clinical Parameter	Number	Percentage (%)
1	Fever with chills	76	60.8
2	Cough	86	68.8
3	Lymphadenopathy	8	6.4
4	Conjunctival Injection	7	5.6
5	Rash	5	4
6	Insect bite	6	4.8
7	Eschar	48	38.4
8	Splenomegaly	10	8
9	Delirium	12	9.6
10	Full Blown ARDS	20	16
11	Multiorgan Failure	17	13.6
12	Outcome (Death)	9	7.2

Laboratory findings

Table 3 Summary of Lab Results.

Sr.No	Lab Parameter	Number	Percentage (%)
1	Lymphopenia <5%	7	5.6
2	Lymphocytosis >40%	55	44
3	Thrombocytopenia <1.5 Lakh	45	36
4	Alanine Transaminase (ALT) >120 IU/L	27	21.6
5	Hypoalbuminemia <3 g	21	16.8
6	Serum creatinine >1.4 mg/dl	27	21.6
7	CXR (Pneumonitis)	31	24.8

Treatment

Table 4 Distribution of patients according to Doxycycline (Days).

Doxycycline (Days)	No of patients	Percentage (%)
0-2 days	11	8.80
3-4 days	75	60.0
5-6 days	24	19.2
7-8 days	15	12.0
Total	125	100.0
Mean \pm SD	4.05 \pm 1.42 (2 to 7 days)	

Discussion

Scrub typhus has recently emerged as a killer disease where disseminated vasculitis and peri-vasculitis result in end-organ injury among febrile patients.

Very few studies have tried to study the overall clinical profile of this dreadful but potentially treatable disease. The study was carried out to study the clinical profile, lab characteristics, complications, treatment response and ultimately the outcome from our institution, which is a tertiary care hospital that caters the referred cases from the peripheral primary health centers. We retrospectively studied 125 patients positive for Scrub typhus IGM Chromatographic test. Considering the past records, the temporal profile of the disease suggested that Scrub Typhus concentrates during the monsoon and winter seasons of the year, though it continued to occur with varying frequency all-round the year. Out of 125 patients, 30.4% were young (31 y to 40 y) while 19.2% were over the age of 60 years. It was interesting to note that out of 125, 78 (62.4%) were females. This ratio was approximately similar in other studies from India and Korea [1]. In our study clinical findings and symptomatology and complications were similar to other studies with fever and cough being the most common symptom present in 76 and 86 patients respectively.

The illnesses began acutely in 97 percent of the people with a prodrome of headache, chilliness, anorexia and most importantly fever. An average of 5 days elapsed between onset of illness and hospitalization, at which time most of the patients had already reached maximum fever, usually 40°C [104°F]. Eschar was present in 48 patients (38.4%), in these sites: calf 13 patients; scrotum,4; abdomen, 17; axilla 4; ankle 4; thorax 3; thigh 3; which was similar to 41.7%, 46% from studies done by Dass et al. at Meghalaya [3] and Vivekanandan et al. study at Pondicherry [4]. Tsay et al. [5] from Taiwan and Liu et al [6] from Northern China found eschar 60% and 88.5% of patients in their studies which was quite high from present study.

A maculopapular eruption occurred in 5 patients (4%); it appeared from the third to the eighth day of fever and persisted for an average of 4.2 days. No patient developed a rash once therapy was initiated. The diagnosis of scrub typhus was most often considered in patients with a rash and eschar. Apart from these clinical features, Conjunctival injection was present in 7 patients (5.6%). It was notifiable that the history of insect bite was given by only 6 patients. The Conjunctival injection and Splenomegaly were the rare findings with (5.6%) out 125 having the conjunctival injection and 10 (8%) had splenomegaly. Generalized lymphadenopathy was actually a rare finding in our study which comprised only 6.4% of our patients. This was in contradiction to other studies where Lymphadenopathy was a prominent feature. While it was notable that 12 (9.6%) patients developed delirium during their course of disease, out of which 3 had altered sensorium at the time of admission [7]. Dyspnoea didn't develop frequently and cough predominated among the respiratory complaints of the people diagnosed to have the scrub typhus. But once developed, Dyspnoea was a good clinical indicator of the worse outcome and ARDS. Out of 125 patients,20 (16%) developed Full blown ARDS, out of which 18 patients presented with dysnoea and Cough and rest 2 developed dyspnoea within 2 days of their hospital stay. 17 (13.6%) patients developed Multiorgan failure of which of which 8 patients recovered and 9 (7.2%) succumbed to death.

1/5th of the patients, 27 patients out of 125 (21.6%) had deranged liver enzymes, ALT>120IU to be precise. Renal Functions were deranged in 1/5th of the patients (21.6%) to be exact, with 27 patients having serum creatinine >1.4 mg/dl, Thrombocytopenia was a predominant feature while 45 patients (36%) had Platelet count <1.5 lakh, Lymphocytes tend to increase and Lymphopenia was rare finding with lymphocytosis occurring in 55 patients (44%) having >40% Lymphocytes in their DLC. CXRs of all patients were done, of which 31 patients (24.8%) had Pneumonitis.

Azithromycin, Doxycycline, Fluoroquinolones, (Levofloxacin being the commonest) and Cephalosporins, (Ceftriaxone being the commonest) were the antibiotics used to treat patients in the study group. Almost all patients received Doxycycline for varying number of days, while Azithromycin, Fluoroquinolones and Cephalosporins were given to 19, 10 and 13 patients respectively. Of these patients 25 patients received all the three including Doxycycline, Fluoroquinolones and

Cephalosporins, while 18 patients received Doxycycline and Cephalosporins. It was observed that patients who got a combination of the antibiotics were correlated to the patients having ARDS and Multi-organ Failure. It was also evident from the data that only those patients who were sick to have a prolonged ICU stay required a combination of antibiotics and went on to develop ARDS and the patients who were shifted out from ICU and subsequently discharged were treated with a single drug, mostly Doxycycline signifying the clear success of Doxycycline in treating the Disease. Of all the patients with Scrub typhus admitted to the ICU9 expired (7.2%) while rest went home happily within maximum of 20 days. We found that only 27 patients had received anti scrub antibiotics (doxycycline and azithromycin) prior to hospital admission and rest either received other antibiotics not covering scrub typhus or no treatment at all. We observed that those patients who did not receive any treatment had more rates of mortality and MODS. Those who received treatment had fewer and less severe rates of complications and mortality. Those who died in this group had received the drugs quite late in disease course. This study showed that doxycycline is an effective drug against scrub typhus and maximum patients became afebrile within 48 hours. This is in accordance to other studies [5,8].

Various independent predictors of mortality were duration of fever >7 days, delay in start of treatment >7 days, duration of hospital stay >14 days, shortness of breath, pain abdomen, delirium, hypotension, tachypnea, icterus, increased leukocyte counts, thrombocytopenia, hepatic dysfunction, raised creatinine, ARDS, septic shock, MODS and ventilator support requirement. Altered sensorium, low serum albumin, hepatic dysfunction, renal dysfunction, septic shock, Multi-organ dysfunction, ARDS, duration of fever more than 7 days, were significantly associated with high in-hospital mortality. Identification of these risk factors leading to fatal outcome may help physicians to start early intensive management of complicated scrub typhus. Hypotension, tachypnoea, icterus, raised leukocyte counts, thrombocytopenia, hepatic dysfunction, renal dysfunction, ARDS, septic shock and MODS were independent predictors of mortality after univariate analysis. A longer hospital stay, leukocytosis, thrombocytopenia, azotemia, hypoalbuminemia, hepatic dysfunction and the complications of ARDS, encephalopathy,

need for ICU supports were the factors associated with mortality.

Conclusion

Serious complications can occur if Scrub typhus is not recognized promptly. Early institution of Doxycycline can save lives in the patients of acute undifferentiated fever pending investigations. General physicians should be Scrub typhus minded to suspect and accurately treat the patients of fever.

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