ORIGINAL RESEARCH PAPER

General Medicine

SCRUB TYPHUS: A PROSPECTIVE OBSERVATIONAL STUDY IN A TERTIARY CARE HOSPITAL DURING AN OUTBREAK IN EASTERN RAJASTHAN

KEY WORDS: Scrub Typhus,eschar, Ards, Polyserositis

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ABSTRACT

OBJECTIVE : To study the clinical profile, epidemiology, complications, and outcome of scrub typhus in eastern Rajasthan.

METHOD: This prospective study was conducted in indoor patients of Government Medical College, Kota from August 2018 to November 2018. 50 cases of scrub typhus IgM was included in the study with the age group between 10 year and 80 years.

RESULTS: Among 50 patients, majority of the patients were females in the age group 30-50 yrs. Most common symptoms were fever, cough with shortness of breath, gastrointestinal symptoms, altered sensorium and bleeding manifestation. Eschar, bilateral pulmonary infiltrates, splenomegaly, and polyserositis were noticed. Some atypical manifestations like hypertriglyceridemia, T inversion V2, V3, reversible pancytopenia, acute cerebellitis and one patient with macroamylasemia with normal pancreas were noticed. Out of 50 patients 13 died due to the complications of septicemia, fulminant hepatic failure, ARDS, encephalitis, sub arachnoid haemorrhage and perforation peritonitis. Rest of them respond to treatment with Doxycycline and azithromycin and recovered well without any residual impairement.

Conclusion : Eastern Rajasthan witnessed an outbreak of scrub typhus. High index of suspicion based on clinical features with or without eschar and prompt therapy with specific antibiotic will result in complete recovery from scrub typhus and favourable outcome.

INTRODUCTION

Scrub typhus also known as chigger borne typhus is one of the most common cause of prolonged fever in south east Asia affecting almost 1 million people annually word wide out of 1 billion exposed[1]. Scrub typhus caused by organism orientia tsutsugamushi which is an obligatory intracellular gram negative coccobacillus through the bite of infected vector *Trombiculidae* family (*Leptotrombidium deliense* and *L. akamushi*) whose larva known as chigger, which is the actual reservoir of the organism. Chigger mites are infected in nature by feeding on the body fluids of rodents. Scrub typhus is endemic to a part of the world known as the tsutsugamushi triangle (13 million km^2) and southern parts of Asia.[1,2]

O. tsutsugamushi are transmitted trans ovarially in mites and maintain their infectivity over long period of time. Humans are accidental host. The target cells in humans are endothelial cells and monocytes. It lacks both lipopolysaccharide and peptidoglycan in its cell wall. There are 3 strains of O. tsutsugamushi (Karp, Gilliam, and Kato). Scrub typhus is generally seen in people whose occupational or recreational activities bring them in to contact with ecotypes favourable with vector chiggers. The incubation period ranges from 7-10 days (range 6-19 days)[2]

The disease was 1st described by the Chinese in the 3rd century (313 A.D). There is no licensed vaccine available till now.

There have been outbreaks in the area located in the sub-Himalayan belt and southern India during the summer and autumn (july to November) after growth of scrub vegetation particularly after rain[3].

Mortality rates for scrub typhus range from < 1% to 50% depending on proper antibiotic treatment, status of the individual infected, and the strain of *O. tsutsugamushi* encountered[4].

Most prominent clinical manifestation is vasculitis and perivasculitis. Illness varies from mild and self -limiting to fatal. The onset is acute with chills and fever, headache, myalgia, cough and gastro intestinal symptoms. The classic case description includes an eschar where the chigger (mite larvae) has fed, regional lymphadenopathy and maculop apular rash.

More virulent strains can cause haemorrhage and disseminated Intravascular coagulation. Other complications like interstitial pneumonia, pulmonary edema, myocarditis, congestive heart failure, circulatory collapse, CNS dysfunctions (delirium, confusion and seizures), scrub cerebellitis, meningo encephalitis, Acute disseminated encephalomyelitis (ADEM), Transverse myelitis, opisthotonus and tetanic spasms, reversible pancytopenia, hepatitis , or multi organ failure.

MATERIALS AND METHODS

STUDY PLACE AND DESIGN

A hospital based prospective, descriptive study was conducted at Government Medical college Hospital, Kota, India. The study protocol was approved by institutional Ethical Committee of Government Medical college, Kota.

STUDY POPULATION

The study was conducted between August 2018 to November 2018 in clinically suspected cases of scrub typhus who present with acute febrile illness, myalgia, body ache, cough, vomiting, abdominal pain, maculopapular rashes, eschar with or without regional lymphadenopathy.

INCLUSION CRITERIA AND EXCLUSION CRITERIA

Patients admitted in medicine ward of Government Medical college Hospital, Kota, who were positive for scrub typhus antibody card test were included after taking informed and written consent from the patient/ attendant and negative card test were excluded from this study. Positive cases were subjected to detailed history, clinical examination, routine

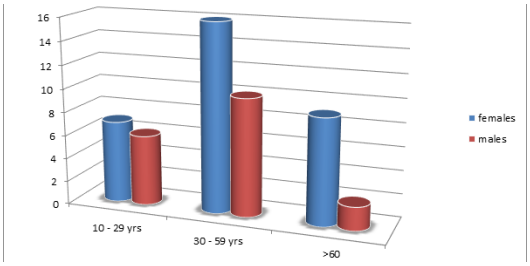
investigations and other supportive laboratory tests

RESULTS

50 cases in the age group 10 to 80 years were studied during this scrub epidemics August 2018 to November 2018.

AGE AND SEX DISTRIBUTION:

The study group was composed of 32(64%) females and 18 (36%) males. Majority of them were in the age group 30 – 60 years (male v/s female - 20% v/s 32%) (**Graph.1 ;Table.1)**



GRAPH.1

TABLE.1

	10- 29yr	30- 59yr	>60yr
Males	6	10	2
Females	7	16	9

FEVER AND OTHER CONSTITUTIONAL SYMPTOMS

48 (96%) patients present with fever: of which 32 (64%) had high grade and associated with chills; The mean duration of fever was 8 days .

DERMATOLOGICAL MANIFESTATION

Eschar were seen in 3(6%)out of which 2 on the nape of the neck and one on the axilla(**figure.1)** 3(6%) patients presented with maculopapular rash; out of which 2 on the trunk and one on the extremity but spares palm and soles. They were found on the 5th day of illness. And disappeared by itself as the patient improves

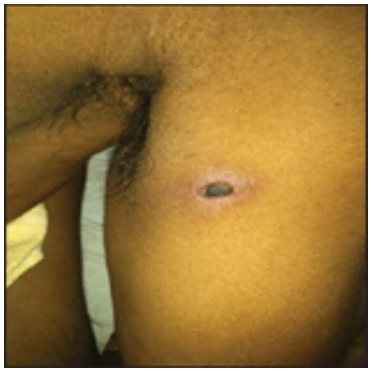


Figure.1

NEUROLOGICAL SIGNS AND SYMPTOMS

About 7 (14%) patients present with fever with altered behaviour, out of which 5 present with generalized tonic clonic seizure and 2 present with loss of consciousness. Neurological symptoms develops towards the end of 1st week. CT of 6 patients were normal and 1 person CT suggestive of sub arachnoid hemorrhage. CSF of 3 person showed lymphocytic predominant with raised proteins and normal sugar. ADA of one case were raised and started on ATT3 (6%) Cases diagnosed to have encephalitis and started on I.V azithromycin and capsule doxycycline 100 mg B.D; out of which one expired with aspiration pneumonitis.

RESPIRATORY SYMPTOMS

Out of 50 , 20 (40%)cases present with cough along with shortness of breath. Out of 20 , 11 (22%) cases X- RAY chest shows bilateral lower lobe infiltrates and the same 11 cases were diagnosed as ARDS out of which 6 were on ventilator and 5 were on non-invasive ventilation . And 5 case expired due to ARDS. 3 patients x-ray shows consolidation in the lower zone; 24 (48%) patients shows USG evidence of pleural effusion, out of which 17 (34%) shows bilateral pleural effusion (**Graph.2)**

CARDIOVASCULAR MANIFESTATION

4 patient developed pericardial effusion as a part of polyserositis which was detected by screening 2D echo and one patient shows massive pericardial effusion and patient expired the next day following pericardiocentesis.

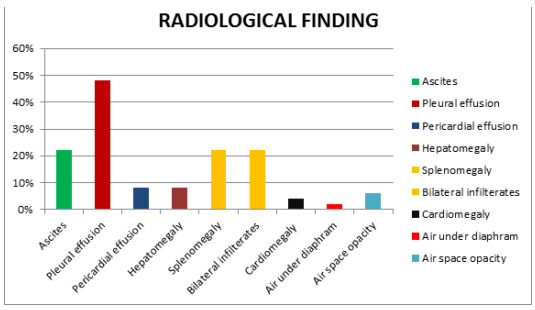
GASTRO INTESTINAL MANIFESTATION

31(62%) patients present with Gastro intestinal manifestation. Of which 10(20%) present with acute diarrhea and 1 present with symptoms of gastro enteritis ; 17(34%) present with abdominal pain and 19 with nausea and vomiting; 16 (32%) patients present with raised bilirubin(34%) patients present with raised SGOT/SGPT ; 12(24%) have raised alkaline phosphatase level and LDH was raised in 15(30%) patients.

2 were HBsAg positive and one patient expired due to fulminant hepatic failure.

Abdominal sonography in 11(22%) patients showed ascitis and edematous gall bladder; 4 (8%) patients have hepatomegaly and 11 (22%) shows splenomegaly and 4 (8%) shows both hepatosplenomegaly.

One patient x ray Flat plain abdomen showed gas under diaphragm and abdominal sonography shows perforation peritonitis and patient expired following surgery.One patient present with macro amylasemia with normal lipase with normal pancrease on sonography(**Graph.2)**



GRAPH.2

GENITO URINARY SYSTEM

- Renal function test were deranged in 16 (32%)patients with normal urine output. None of them went for dialysis and respond with doxycycline and I.V Azithromycin; 9 cases RFT deranged as a part of Septicemia
- Urine microbiological examination showed no abnormality in the form of absence of RBC, protein, WBC, or any crystals
- Sonography pelvis of 3 cases showed left ovarian haemorrhagic cyst and 2 showed left sided renal cyst

BLEEDING MANIFESTATION

4 (8%)Patients present with bleeding manifestation out of which 2 present with black coloured stool and one with hematuria and one with epistaxis; both have platelet count less than 50,000. Sanjay K Mahajan et al [23] in a case report showed that 2 patients present with fever and melena , one required blood transfusion and both were managed conservatively. The microangiopathy involving gastroi ntestinal tract can lead to gastrointestinal bleeding .Another 2 cases present with deranged PT/INR as a part of MODS. One patient present with conjunctival redness and later showed

Dengue IgM positive

HEMODYNAMICS

13 (26%) patients present with hemodynamic instability in the form of hypotension and all of them required ionotropic support.

E.C.G CHANGES

E.C.G abnormalities were seen in 13(26%) patients. E.C.G shows T wave inversion in V2 and V3 in 7 (14%) cases and 2 shows low voltage QRS complex both of them shows pericardial effusion in screening echo and another 2 (4%) shows poor progression of R wave. Arrhythmias in the form of Multi focal Atrial Tachycardia and Ventricular premature contraction is seen in each separate cases.

ROUTINE INVESTIGATIONS

29 (58%) patients present with anemia, of which 6 patients have Hb < 7gm/dl, 15 have Hb in the range of 7-9gm/dl and 8 patients Hb between 9-11 gm/dl . Majority of them were microcytic hypochromic. 30 (60%) patients present with thrombocytopenia, of which 8 patients have platelet in the range between 1 lakh to 1.5 lakh, 50,000 to 1 lakh platelet were seen in 14 patients and 8 patients have < 50,000 platelet. Pancytopenia in 8 patients which was reversible with in 10-14 days in 6 patients and 2 requires transfusion due to bleeding manifestation : lymphocytopenia in 18 (36%) hyponatremia is seen in 5 and hypernatremia in 4 and hypokalemia in 8 patients none of them were had deranged renal function.

SERUM LIPID PROFILE

Hyper triglyceridemia is seen in 16 cases irrespective of the age and none of them were having metabolic syndrome .Out of which 2 patients shows triglyceride level greater than 700 mg/dl. One case shows increased total cholesterol level.

OTHER INFECTIOUS DISEASES

Concurrent Dengue IgM is positive in 2 cases and 6 cases shows malarial parasite positive. 2 cases are HBsAg positive. Mortality rate among them was zero.

COMPLICATIONS

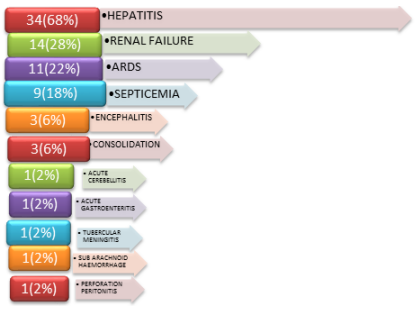
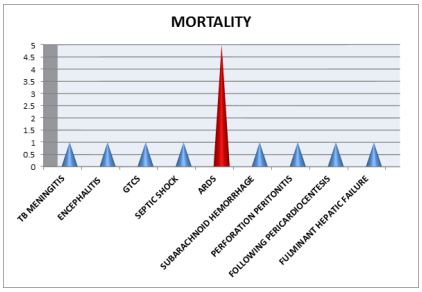


FIGURE.2

MORTALITY

Out of 50 cases 13 cases expired and majority of them (5) expired due to ARDS. Details of the mortality is shown in the figure



GRAPH.3

DISCUSSION

In our study persistent high grade fever was present in majority of the cases. The mean duration of fever 8 days is comparable to the usual mean duration of presentation in most studies[6]. 17(34%) patients present with constitutional symptoms like fatiguability, arthralgia, myalgia and low back ache. Ming-Luen Hu et al[7]in his study showed that main symptoms and signs were fever(100%), chills (37%), headache (30%). KPP Abhilash et al [8]showed that fever (100%), generalized myalgia (83%), headache (65%). Eschar were seen in 3 (6%) patients and another 3 (6%) patients present with maculopapular rash Skin rash were seen in 40% and eschars were found in 67% patients in a study conducted by Ming-Luen Hu et al[7] . KPP Abhilash et al [8] in there study showed that eschar rate was 58.8%. Shirish inamdar et al [9] showed that eschar rate was 57.7% with male predominant.

Neurological manifestation were seen in only minority of cases7(14%).CSF shows raised ADA in one patient and started on ATT 3(6%) were diagnosed to have encephalitis. Jithendra kumar meena et al[10] in a study of Forty nine cases of scrub typhus ,7 (~15%) had meningitis.Cerebrospinal fluid profile show changes similar to viral or tuberculous meningitis. It should be included in differential diagnosis of aseptic meningitis and encephalitis in patients exposed to endemic areas[11,12,13] One patient expired due to sub arachnoid haemorrhage.But Jong-Hoon Chung et al [14] in there case report showed that 1 patient present with subdural haemorrhage and one with Right MCA infarct .

20 (40%)cases present with cough with shortness of breath and 11 cases were diagnosed as ARDS and 5 case expired due to ARDS. 3 patients xray shows consolidation in the lower zone; 24 (48%) patients shows USG evidence of pleural effusion,out of which 17 (34%) shows bilateral pleural effusion KPP Abhilash et al [8] in there study showed that pleural effusion (14.6%), acute respiratory distress syndrome (14%), airspace opacity (10.5%), reticulonodular opacities (10.3%), peribronchial thickening (5.8%), and pulmonary edema (2%) were noticed

Although no myocarditis Joydeep was detected Das et al [15] in their study showed that 11 out of 43 cases showed features of myocarditis requiring vasopressor and Karthik G et al [16] showed that incidence of myocarditis was 21% and pericardial involvement was seen in 51% in the form of mild to moderate pericardial effusion.

Bleeding manifestation in the form of melena and epistaxis were noticed. E.C.G showed T wave inversion in V2 and V3 in 7(14%) cases, multifocal atrial tachycardia and premature ventricular contractions were noticed Dong-Min Kim et al[24] showed that poor R progression (26 cases, 14.8%); AF [16 cases, 9.1%], APC [5 cases, 2.8%] and VPC [1 case, 0.6%]). Although we didn't found any QT prolongation, Joydeep Das et al [15] in their study of 40 paediatric patients showed that five cases showed long QT without progress to ventricular tachycardia.

Bilirubin, SGOT/SGPT, ALP, LDH were deranged in 32%, 68%, 24% and 30% respectively. This was similar to Yang CH et al[17] showed in his study that hepatic dysfunction occurred in 77% (36/47) of patients. Polyserositis is seen in 11 (22%), cases 4 (8%) patients have hepatomegaly, 11 (22%) shows splenomegaly and 4 (8%) shows both hepatosplenomegaly. But study conducted by Shirish inamdar et al [9]showed that hepatomegaly was present in 57% patients (n= 200).One patient diagnosed to have perforation peritonitis and patient expired following surgery. Chang-Hu Lee et al [18] in his case report shows 2 patients present with perforation peritonitis both were recovered after surgery

Alok Bhatt [19] et al in a case report showed a 48 year old female

with acute pancreatitis with pseudocyst and Mona Dhakal et al [20] showed acute pancreatitis in a 22 year male.

Hypertriglyceridemia is seen in 16 cases irrespective of the age and none of them fit into the category of metabolic syndrome . 29 patients present with microcytic hypochromic anemia , 30 patients present with thrombocytopenia, pancytopenia were seen in 8 (16%) patients out of which 6 were reversible. Yu mi wi et al [22] in there study of 57 patients Leukopenia 18, lymphocytopenia 43, anemia 4 and thrombocytopenia 13 were observed.

Renal function test were deranged in 16 (32%)patients and none of them went for dialysis and they respond well with doxycycline and I.V azithromycin. Yen TH et al [21] in a case report of 3 patients showed that with varying degrees of acute renal deterioration, the patients responded very well to doxycycline therapy and recovered completely

Co- infection with malaria and dengue were noticed 6%and 4% respectively both groups had good prognosis.

Mortality seen in 13 cases and majority of them (5) expired due to ARDS, 1 patient expired due to sub arachnoid haemorrhage and 1 due to perforation peritonitis.

Most of the patient responded well and showed marked improvement with a 15 days course od Doxycycline 100 mg BD . Macrolide antibiotics Azithromycin 500 mg od is given for those with respiratory symptoms . And those with features of encephalitis were given both azithromycin injectable and doxycycline.

CONCLUSION

Any person coming from endemic region during the season of july to November with high grade fever and constitutional symptoms along with cough, shortness of breath, vomiting and pain abdomen one can suspect scrub typhus. Although it can affect any system majority of the mortality were due to respiratory problem ARDS. Early recognition of symptoms and thereby institution of antibiotics can prevent these complications. Education of society regarding the symptoms of scrub typhus and the importance of personal hygene especially those who are living in rural areas are important. Since no vaccination is available for scrub typhus protective measures like avoiding contact with chiggers, avoiding travel to endemic areas and use of insect repellent are important.

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