ISSN- O: 2458 - 868X, ISSN –P: 2458 - 8687

International Journal of Medical Science and Innovative Research (IJMSIR)

IJMSIR : A Medical Publication Hub

Available Online at: www.ijmsir.com

Volume – 2, Issue – 4, July - August - 2017, Page No. : 169 – 174

Prevalence of scrub typhus in and around Vishakhapatnam, Andhra Pradesh as a cause of fever of unknown origin (FUO)

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Conflicts of Interest: Nil

Introduction: Scrub typhus is a rickettsial infection which is caused by *Orientia tsutsugamushi*. Diagnosis should be largely based on a high index of suspicion and careful clinical, laboratory and epidemiological evaluation. Delay in diagnosis can be fatal otherwise the treatment is simple, doxycycline being the drug of choice.

Materials And Methods : Fever of unknown origin (FUO) of two consequent year 2013 & 2014 for period of 5 months (August to December) were screened for scrub typhus by Rapid method immune chromatographic assay (SD Bioline Tsutsugamushi, one step developed using major surface protein 56 kDa antigen of representation *O . tsutsugamushi*).

Results : Total 200 cases in year 2013 and 240 cases in year 2014, suspected FUO cases admitted in hospital, Scrub typhus antibodies were detected in 50/200 (25% in year 2013), 59/240 (24.4% in year 2014). Patients present with most common symptom fever (100%) with chills and rigors, Eschar finding is almost zero in all cases. Laboratory parameters showed, thrombocytopenia (72% in 2013, 68% in 2014), deranged liver function, Creatinine (52% in 2013, 48% in 2014), hypoalbuminemia (52% in 2013, 37% in 2014). Complications leading to death (4%) are seen in year 2013 but zero in year 2014. Dramatic response to doxycycline seen in nearly all patients.

Conclusion: The present study emphasises the importance of scrub typhus among cases of FUO especially after rainy season and during early cooler months. Early detection and treatment leads to reduce in morbidity and mortality.

Keywords: Fever of unknown origin, Orientia tsutsugamushi, Scrub typhus.

Introduction

Scrub typhus infections are re-emerging with increased reports from different parts of the India. Scrub typhus is an acute febrile illness and delay in diagnosis is associated with considerable morbidity and mortality. Although it is a neglected disease in India, but in recent years there are reports from Maharashtra, Tamil Nadu, Karnataka, Kerala, Jammu and Kashmir, Uttaranchal, Himachal Pradesh, Rajasthan, Assam and West Bengal indicating the resurgence of the disease in this part India also. [1-6]

Scrub typhus or Bush typhus is a rickettsial infection which is caused by *Orientia tsutsugamushi* and transmitted by some species of trombiculid mites ("chiggers", particularly a *Leptotrombidium deliense*). [3] The name is derived from the prevalence of the mites in areas of heavy scrub vegetation. The disease is endemic in the geographical region known as "tsutsugamushi triangle" which extends from northern Japan and far-eastern Russia in the north, to the territories around the Solomon Sea into northern Australia in the south, and to Pakistan and Afghanistan in the west. The bite of this mite leaves a characteristic black eschar that is useful to the doctor for making the diagnosis. [2, 7]

Although there are multiple causes of FUO but infections such as enteric fever, malaria, dengue, tuberculosis, brucellosis are among most common causes. [8] Scrub typhus (ST), a rickettsial disease caused by *Orientia tsutsugamushi*, is a very less-known cause of FUO. It is underdiagnosed in India due to its non-specific clinical presentations, low index of suspicion amongst clinicians, limited awareness and limited diagnostic facilities. The incidence increase in monsoon and post monsoon seasons (August to December).

Serious complications of scrub typhus are not uncommon and may be fatal; they include pneumonia, myocarditis, meningoencephalitis, acute renal failure and gastrointestinal bleeding. Early diagnosis is important because there is usually an excellent response to treatment and timely anti-microbial therapy may help prevent complications. In developing countries with limited diagnostic facilities, it is prudent to recommend empiric therapy in patients with undifferentiated febrile illness having evidence of multiple system involvement. [9]

Several tests are available with their own advantages and limitations. [10]Among all the serological tests available Weil-Felix test is the cheapest and easily available, but this is notoriously unreliable. Indirect immunofluorescence test, the gold standard is beyond affordability specially in poor countries and needs expertise for interpretation as the choice of cut-off values for positive diagnosis is influenced by several factors such as antibody kinetics, geography, negative seroconversion and seasonality. [11, 12]

IgM ELISA has been evaluated and found to be quite satisfactory in comparison to the gold standard, but samples need to be pooled for ELISA which can lead to delayed diagnosis thus influencing the overall outcome. [13]

Rapid tests have come which are economic and single tests can be carried out. Rapid Flow Assay Using recombinant Major Outer Membrane Protein Antigen (r56) of *Orientia tsutsugamushi*.[14,15]

Aim of study

The aim of this study is to determine the prevalence of Scrub typhus cases as one of the causes of fever of unknown origin (FUO), for two consecutive years of 2013 and 2014.

Objectives

1. Identifying the cases of Scrub typhus from cases admitted for Fever of Unknown Origin (FUO) in Private Hospital, Visakhapatnam for two consecutive years, 2013 & 2014.
2. Laboratory investigations (Serological, Biochemical & Haematological parameters) are determined & correlated with the clinical presentations.
3. Comparing the Laboratory investigations, Complications & Mortality rates for two consecutive years, 2013 & 2014.

Materials and Methods

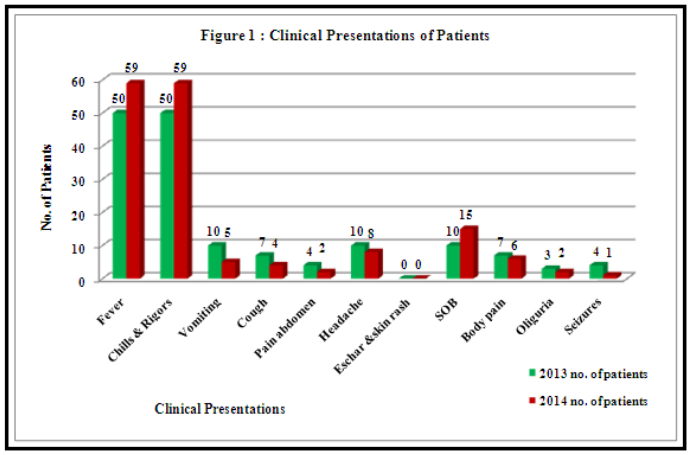
A study of total 200 and 240 clinically suspected cases of fever of unknown origin (FUO), for two consecutive years of 2013 and 2014 were examined and investigated for scrub typhus, in Private Hospital, Visakhapatnam, Andhra Pradesh, over a period of 5 months (August to December). Basic laboratory tests, complete blood count, peripheral smear, creatinine, liver function test, and serology test for dengue, malaria, typhoid, and tuberculosis were done. Detection of scrub typhus IgM antibodies by Rapid method was done using SD Bioline Tsutsugamushi, one step scrub typhus antibody test developed using major surface protein 56kDa antigen of representation O.tsutsugamushi . Clinical features of the patients were retrieved from hospital medical records. Statistical analysis was done.

Results

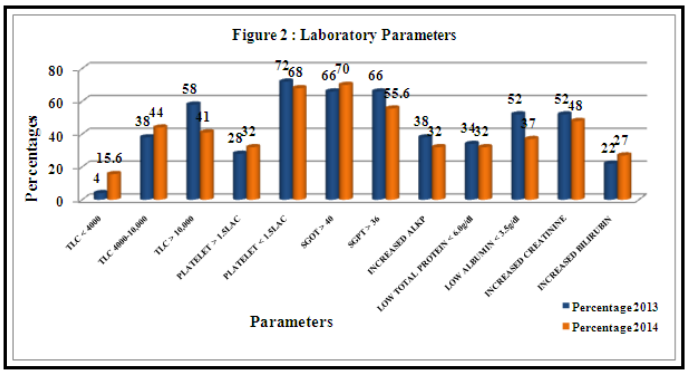
Of the total 200 cases in year 2013 and 240 cases in year 2014, suspected FUO cases admitted in hospital, Scrub typhus IgM antibodies were detected in 50/200 (25% in year 2013), 59/240 (24.4% in year 2014) patients by Rapid test.

Most of the patients were from rural area belonging to place Vijayanagaram of Visakhapatnam district and Ganjam district of Orissa & maximum numbers of cases were seen after rainy season and in early cooler months (i.e. August to December).

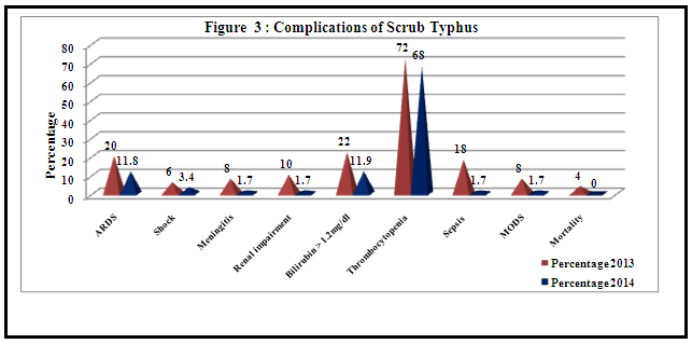
Patients present with most common symptom fever (100%) with chills and rigors and other symptoms as shown in Figure 1. Eschar finding in almost zero in all cases.



The laboratory parameters showed thrombocytopenia, deranged liver function test, increased creatinine, raised total leukocyte count as shown in Figure 2.



Complications due to scrub typhus as of late detection and treatment in year 2013, accordingly the percentage of complications and deaths (2 cases) are more & no deaths in 2014 as shown in Figure 3



Discussion

Scrub typhus is a rickettsial disease caused by *O. tsutsugamushi*. It is transmitted by the bite of mite belonging to the genus Leptotrombidium (*L. delienis*) in India. [16]

Originally scrub typhus, has also been found in a variety of habitats like sandy beaches, rice fields, mountain deserts, equatorial rain forests and even in semi desert.[17] Previous studies, showed reports of ST from Himachal Pradesh (2003) belonging to hilly areas and Pondicherry (2006) belonging to sandy beaches of India.[18,19]. In the present study the majority of cases are from semi forest areas of Visakhapatnam (Costal area), Orissa states of India & were from rural background.

Seasonal distribution showed maximum number of cases between the months of August & December. This is

because the mites are more active during or at the end of rainy season which coincides with the months of August to September in India. Earlier reports from India indicate similar period of disease occurrence. [18, 19]

The diagnosis of scrub typhus poses a problem due to low index of suspicion, non-specific signs and symptoms, absence of specific presentation of eschar and lack of latest diagnostic facilities in India. [13]

In present study diagnosis of scrub typhus is done by using one step rapid scrub typhus antibodies test (SD Bioline) similar method used by Kammili e tal, W.M Ching etal [13,14,20]

Fever with chills and rigor was the most common presentation in our study which is similar to a hospital-based study in Taiwan and a study by Dass *et al.*, from the state of Meghalaya, India. [13, 21]

A study from Chennai reported seizures, signs of consolidation, thrombocytopenia, elevated serum alkaline phosphates and renal failure in 25%, 40%, 37.5%, 52%and 33% patients, respectively & 6.25% of patients died of multiorgan failure. [23]

In our study thrombocytopenia (72% in 2013, 68% in 2014), increased levels of Total bilirubin (22% in 2013, 27% in 2014), SGOT (66% in 2013, 70% in 2014) SGPT (66% in 2013, 55.6% in 2014), Creatinine (52% in 2013, 48% in 2014), hypoalbuminameia (52% in 2013, 37% in 2014). Complications leading to death (4%) are seen in year 2013 but no deaths were seen in year 2014

10 % (5/50) of our patients in 2013, 3.3% in 2014 had multisystem involvement [Table 1]. 3 out of 5 patients presented with significant breathlessness & had evidence of ARDS with diffuse infiltrates in the chest X- ray. Two of these patients required ventilator support and one of them expired due to multi-organ failure. Case presented with shock and renal failure treated initially in rural centre has expired due to multi-organ failure.

Table 1 : Salient features of patients with multisystem involvement

Sl.no	ARDS	Shock	Renal impairment	Sepsis	MODS	Bilirubin >1.2mg/dl	Thrombocytopenia	Death
2013 Data								
1.	-	P	P	P	P	P	P	1
2.	-	P	P	P	P	P	P	
3.	P	-	P	P	P	-	-	
4.	P	P		P		P	P	1
5.	P	-	-	P	P	-	P	
2014 Data								
1.	-	-	-	-	-	P	P	
2.	-	-	P	P	-	P	-	

Doxycycline 200 mg/day is the treatment of choice for scrub typhus. Other useful antibiotics are chloramphenicol, azithromycin and rifampicin. Rapid resolution of fever following doxycycline is so characteristic that it can be used as a therapeutic test.[17] Nearly all our cases responded dramatically to doxycycline, with resolution of symptoms within 3-4 days.

Case recognizing ,diagnosing, treatment and follow up was started in 2013 which showed more morbidity and mortality than our consequent study in year 2014 .This decrease is due to awareness by doctors about Scrub typhus infection and its seasonal occurrence.

This study report emphasizes the need for increased awareness of scrub typhus infections to health care professionals treating a case of febrile illness during post monsoon season especially patients coming from rural areas, other vegetation area where mites possibilities are high in India. Because of current circumstances in India, we suggest that the diagnosis of scrub typhus should be largely based on a high index of suspicion and careful clinical, laboratory and epidemiological evaluation. Use of empiric treatment should also be considered to reduce the high mortality observed with the disease.

The government and Health care board dealing with communicable disease should make the health care professionals and people get aware of scrub typhus infection as one of the case of acute febrile illness as

dengue, malaria etc, as the presentation of patients are similar and mortality due this infection are also high.

Conclusion

Scrub typhus is prevalent but an under diagnosed disease in India. It should be considered in the differential diagnosis of patients suffering from acute febrile illness (FUO) especially with pneumonitis, thrombocytopenia, elevation of liver enzyme, serum urea and serum creatinine. Scrub typhus screening should be included during post monsoon season people from rural back ground mainly. A thorough and probing search for an eschar, particularly in the hidden areas is very useful for diagnosis. However, the eschar may not be present in a large number of cases. Rapid and specific diagnostic methods using ELISA can be carried out timely for early diagnosis of scrub typhus in patients with FUO in developing countries like India. But in comparison to ELISA, Rapid tests are more feasible, cost-effective & moreover results can be obtained very quickly so that treatment can be started without delay to avoid complications. Empirical therapy with doxycycline may be life saving when clinical suspicion is high. Recommending the government to take part in awareness programs on Scrub typhus, so morbidity and mortality can be controlled by early diagnosis & treatment.

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