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RESEARCH ARTICLE

SCRUB TYPHUS - A RE-EMERGING DISEASE: ESTIMATING THE BURDEN AND OUTCOME OF SCRUB TYPHUS IN A TERTIARY CARE CENTRE

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Abstract

Background: Scrub typhus is regarded as an important cause of acute febrile illness. If not diagnosed early, it is often tends to be fatal.
Methods: A Prospective Observational study was carried out among patients reporting with fever in a tertiary care hospital at Delhi. Weil Felix test and rapid test for scrub typhus was performed on the patient samples.
Results: A total of 265 cases were screened for typhus group of fever, of these 26 (9.1%) patients (18 males and 8 females) were diagnosed having rickettsial fever. Out of these, 24 (92.3%) were diagnosed having scrub typhus fever.
Conclusions: In present study, we observed 9.1% seropositivity in acute febrile illness. We conclude that a simple Weil Felix test should be included in routine workup of fever cases and a strong suspicion should be there where other laboratory tests remain inconclusive in endemic areas like Delhi-NCR.

Introduction:-

Scrub typhus fever is one of the important causes of Acute Undifferentiated Febrile Illness (AUFI). Recently published reports suggest that it is re-emerging as a serious threat to public health. Scrub typhus is a chigger born disease caused by intracellular obligate weak gram negative bacterium Orientia tsutsugamushi. Chigger is a larval stage of leptotrombiculid mite that feed on rodents once in life time. Man is an accidental host in this zoonotic disease. Endemic typhus by Rickettsia typhi vector rat flea and Rickettsia conori vector tick of rodents[1].

Scrub typhus is commonly seen in famous tsutsugamushi triangle which is formed by Japan in the east, going through China, tropical Australia in the south, and west encompassing India, Pakistan through Afghanistan and southern parts of the Soviet Union [2]. Shavlik ranges, Kashmir, Assam, Eastern and Western Ghats, and the Vindhyachal and Satpura ranges are affected areas in India[3]. Grassy regions, forest clearings areas and riverbanks provide optimal conditions for the infected mites to thrive. These small geographic regions are called scrub typhus islands. The natural hosts of leptotrombiculide mites are vertebrates which cohabit the mite islands [4].

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A billion people are at risk and nearly a million cases are reported every year in Asia Pacific region. Mortality rates for scrub typhus range from less than 1% to 50% where antibiotic choice has been shown to play a role, health status of the individual affected, and the type of strain of *O.tsutsugamushi* encountered [5]. The first case of scrub typhus was reported in 2009 from Kerala[6]. Most of the time typhus fever remains undiagnosed due to low index of suspicion existing among clinicians and at times non-availability of serological tests. When infection becomes serious and not properly managed it often leads to increased morbidity and mortality [5,7].

Among other typhus fever, scrub typhus is showing a recent resurgence in our country as evidenced by various reports published from different parts of India in the last two decades. Many outbreaks have occurred since the beginning of century in India. Tamil Nadu in 2001–2002 had 28 cases, Himachal Pradesh in 2011 had 200 cases of which 13 were fatal, Nagaland in 2011 had 9 cases, 3 were fatal, Meghalaya in 2010 had 80 cases, 5 were fatal [7,8].

Incubation period is 6 to 21 days, and its manifestation may be prolonged (5-36 days). Rickettsial infection present with fever as predominant symptom, Fever is often associated with eschar, suffused conjunctiva, severe headache, drowsiness, apathy, pain in the shins and other muscles, and more characteristically lymphadenopathy and hepatosplenomegaly. Systemic symptoms ensue mostly involving the central nervous system, cardiovascular system, renal, respiratory, and gastrointestinal systems [9].

To carry out diagnosis and surveillance of diseases caused by rickettsia are challenging in the absence of advanced laboratory techniques. Rickettsia can be identified in clinical samples; however, serological tests remainthe main tool for diagnosis [10,11]. Weil Felix test detects both IgM and IgG antibody which are detectable 5-14 days after the onset of symptoms. The test is simple,economical, and highly specific when clinically correlated, but has less sensitivity. A fourfold rise in titre is usually confirmative but most of the time repeat sample is almost not available. Immunofluorescence assay (IFA) is the “gold standard” [8]. Recently published reports indicated that typhus like outbreak or illness can be expected anywhere and everywhere in the world and we need to be alert for its early diagnosis and treatment [12,13]. It is a serious acute febrile illness associated with significant morbidity and mortality if diagnosed late [14]. The current study was planned with the aim to estimate the burden of scrub typhus and its outcome in a tertiary care hospital. The hospital being a tertiary care hospital is not involved in primary care of febrile patients. However, cases form local population are being referred as PUO or as fever with complication.

Methods:-

A prospective observational study was carried out in a tertiary care centre at Delhi. The hospital catered to patients reporting/ referred from Delhi and NCR which included patients from both urban and rural area. Sample population included of all the patients with an acute febrile illness reported to various OPDs in hospital. The study was carried out for 6 months, all patients fulfilling inclusion criteria were recruited into the study and therefore, sample size was not calculated. Patients already diagnosed/ confirmed of the cause of febrile illness were excluded from study. A detailed history was noted, clinical examination carried out. All patients were subjected to routine investigations for common causes of fever. This included malaria, typhoid, dengue, leptospira, leishmaniasis, viral fever, respiratory and urinary and tract infections etc. Patients found negative for the above tests were subjected to Weil Felix test. Weil Felix agglutination test (Mfd - Tulip Diagnostics, India) was performed using protocol provided by manufacturer with dilution from 1: 20 to 1: 160 for carrying out initial screening. It was followed by further dilution to achieve end titre and titre of more than 1:80 was taken as cut off and interpreted accordingly with clinical and other laboratory test results.Thosefound positive for OXK, suggestive of scrub typhus, a Scrub Rapid IgM &IgG Card (ICT) (SD Bioline& Immune med) was used as second serological test. Whenever second sample was available after 10 -12 days the Weil Felix test was repeated for increasing titre. Sample positive for OX2 suggestive for spotted fever and OX19 were suggestive for endemic typhus and OX2 +OX19 for tick typhus.

Results:-

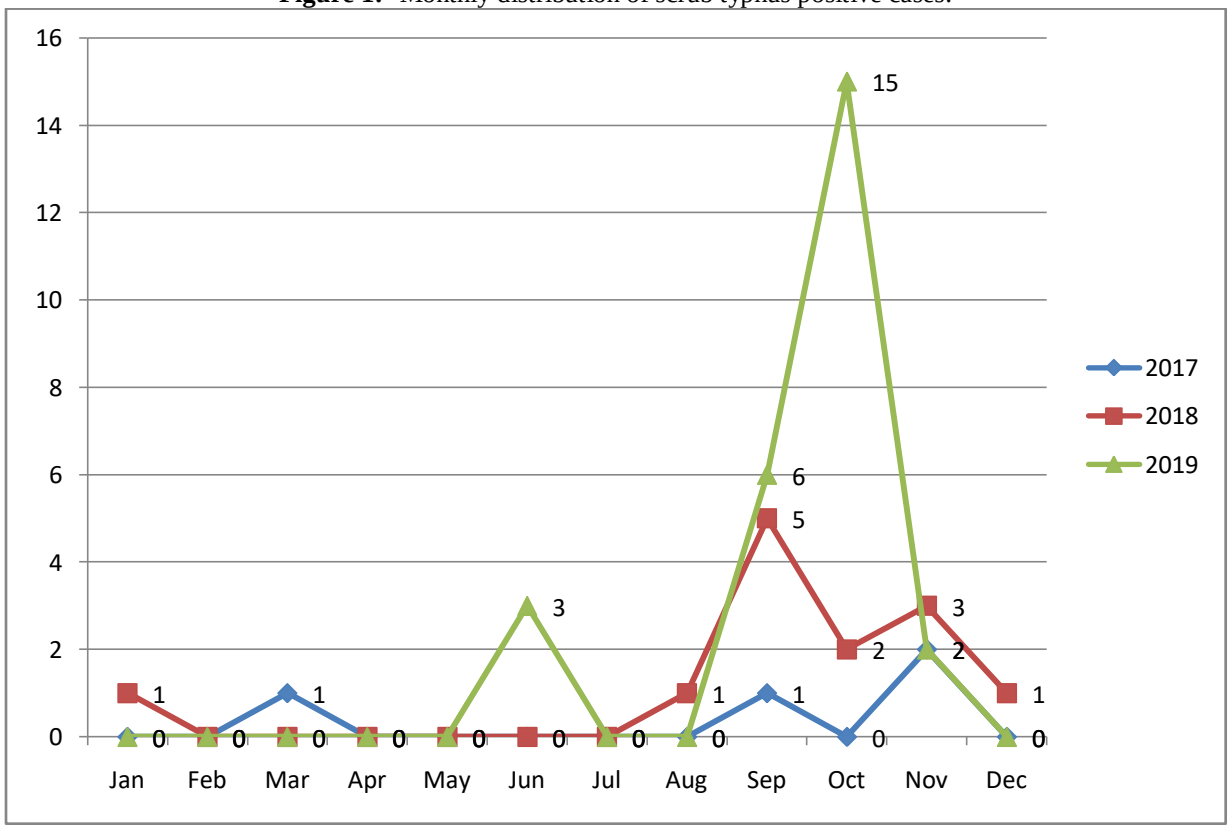
A total 3800 cases of fever reported to OPDs during study period among them 265 cases were screened for typhus group of fever once other routine causes of fever were excluded during the study period. Of these 26 (9.1%) patients (18 males and 8 females) were diagnosed having rickettsial fever. 24 (92.3%) were diagnosed having scrub typhus fever. One case was positive for epidemic and one for tick typhus as per serological results. Predominant symptomatology and clinical findings are presented in Table 1.

Table 1:- Clinical Findings of Rickettsial diseases in Delhi.

1. Total Number of cases screened: 265	
2. Total Number positive: 26 (9.1%)	
3. (i) Scrub Typhus: 24 (ii) Tick typhus : 01 (iii) Epidemic typhus : 01	
4. Average Duration of illness before diagnosis : 8 days	
5. Age :	
<10 years	01
10-60 years	24
>60 years	01
6. Important Findings :	
Fever with Chills	26 (100 %)
Eschar	02 (7.6%)
Sepsis with multiorgan failure	02 (7.6%)
Total leucocytes count >10,000/mm	04 (15.3%)
Thrombocytopenia	02 (7.6%)

The titre of OXK for scrub typhus fever was more than 1:320 in all cases. There was no correlation established between titre of Weil Felix test and severity of disease. Fever with chills and rigors was the predominant symptoms in 100% of cases and duration of fever ranged from 7 to 15 days. In majority of the cases total leucocytes were within normal limits. 04(15%) cases showed increased leucocytosis. Abnormal renal functions and low platelets counts were observed in 02(7%) cases. Two cases had severe respiratory dysfunction and needed ventilatory support. Adequate clinical response was obtained in all the cases after the initiation of treatment with doxycycline or azithromycin within 2-3 days. Antibiotics were continued for 14 days. Overall mortality was zero in our study. Monthly distribution of cases is listed (Figure-1). Only two cases reported back for follow up and were retested after 12 days. Titre remained high (>1:160) till follow up for one month. All 26 cases met the Indian criteria for diagnosis of scrub typhus.

Figure 1:- Monthly distribution of scrub typhus positive cases.



Discussion:-

Scrub typhus fever is potentially fatal infection if not diagnosed and treated properly. One million people are affected every year. Rickettsial infections have been reported from various states of India [5]. Sporadic cases do occur in eastern and southern Indian states. In our study we observed 9.1% serpositivity in acute febrile illness for Rickettsial fever and scrub typhus seems to be the commonest. Study conducted during the 1999-2004 at Delhi by the Zoonosis Division of the NCDC Delhi showed similar positivity (8.2%) with titre 1: 80 or above [6]. Recently conducted observational study revealed 22.8% and 24.7% serpositivity in patients with acute febrile illness in Rajasthan [7,8]. Being a referral hospital, patients from local and adjoining area of NCR area were admitted for treatment. Age and gender and occupation are known to influence the occurrence of typhus fever more so scrub typhus. People working in fields/ thick vegetation are at risk of getting infected more. Most of our patients were in age group of 10-60 years. In our study males were affected more as compared to females. Different studies showed variation in affected genders [5,6]. Distribution of cases was spread all over the years but increase in monsoon was observed in our study also indicating thick vegetation growth and working in fields during monsoons [7]. Fever was the first symptom in all the cases. Nearly all the patients were diagnosed in second week after onset of symptom when all other suspected causes of fever were ruled out. Only two patients had eschar (7.6%) in our study. Its presence has been low (4%-12%) in most of the Indian studies [7].Escharis a blackish necrotic lesion resembling a cigarette burn at the site of attachment of the chigger/ mite larva where skin is thin. Its presence is pathognomic of typhus fever but its absence does not exclude. Study from Vietnam, Taiwan, and Korea reported slightly higher incidences of eschar probably due to fair skinned population of these countries [8,9,10]. In our study two cases developed respiratory difficulty and thrombocytopenia. Both required ventilator support during hospital stay. Mild cases having scrub typhus fever do not develop much abnormality in blood cells counts, but few cases can do so and develop thrombocytopenia with increased total leucocytes counts. Two cases had thrombocytopenia in our study. No patient had meningitis or encephalitis at our centre while many other studies have shown variable results (9.5%-23.3%)[11]. Multi organ failure is also very high in scrub typhus cases. It may reach upto 48.5% as shown by Rajender Prasad Takhar etal in their study [12]. Late diagnosis has been the main cause for increased mortality [13]. The recommended treatment regimen for scrub typhus is doxycycline for 7–15 days). A single dose of 200 mg may be taken as for prophylaxis for scrub typhus. However, occurrence of natural resistance often makes choice of appropriate antibiotic difficult. Prophylaxis for scrub typhus with doxycycline has shown promising results when started before the exposure to infection.

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