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### RESEARCH ARTICLE

## OUTBREAK OF SCRUB TYPHUS IN PYREXIA OF UNKNOWN ORIGIN DURING COOLER MONTHS IN GUNTUR DISTRICT, ANDHRA PRADESH, SOUTH INDIA.

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### Abstract

Scrub typhus is a Rickettsial infection caused by *Orientia tsutsugamushi* and transmitted by bite of the chigger of a mite *Trombidium deliense*. It is an acute febrile illness and Zoonotic disease endemic in the South East Asian countries and Western Pacific region but less common known cause of PUO in India. Treatment is simple with Doxycycline and Azithromycin being drugs of choice and delay in diagnosis can be fatal. A total of 216 patients attending Medical OP with PUO at GGH, Guntur, from September 2013 to February 2014 were considered for the study. Suspected cases with Eschar (58) were screened for IgM antibodies to *Orientia tsutsugamushi* by Weil-Felix and Rapid Immunochromatographic method and positive for either of these tests were further confirmed by ELISA. They were also screened for Malaria, Typhoid, Tuberculosis, HIV and Hepatitis B infections. Scrub typhus IgM antibodies were positive in 26(44.8%) by both Weil-Felix and ELISA, 56(96.5%) cases were positive and 2 negative with Immunochromatographic assay and 57(98.3%) were positive with ELISA. Among 58 screened positive cases, 36(62.69%) were males and 22(37.9%) females. Scrub typhus positivity was higher in males than females. The lesion eschar was present in 56(96.5%) cases. The laboratory parameters were abnormal in most of the patients as evident by thrombocytopenia (82.7%), deranged liver functions 72.4% and renal functions 24.1%. Scrub typhus is prevalent but an under diagnosed disease in India and early diagnosis and administration of antibiotics will prevent the complications and mortality.

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### Introduction:-

Scrub typhus is an acute febrile illness caused by *Orientia tsutsugamushi* which is a gram negative obligate intracellular bacteria transmitted by the bite of infected larva (chigger) of a mite *Leptotrombidium deliense* in India. Scrub typhus is a zoonotic disease in which humans are the accidental hosts. Scrub typhus or bush typhus is named from the type of vegetation that harbors the vector *Leptotrombidium deliense* i.e., secondary vegetation in transitional terrain between woods and clearings. Scrub typhus is an important military disease and thousands of cases occurred during the Second World War.

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PUO can be defined as temperature above 38.3°C for more than one week duration and there are multiple causes like Malaria, Dengue, Flu, Enteric fever and Tuberculosis. Scrub typhus is a very less known cause of PUO always under diagnosed in India due to its non specific clinical presentations, low level of suspicion amongst clinicians, lack of awareness and limited diagnostic facilities. The disease is endemic in East Asia from Korea to Indonesia and in Pacific Islands including Australia and was first observed in Japan.

An outbreak of PUO was observed in Guntur district, Andhra Pradesh during cooler months from September 2013 to February 2014. A total of 216 cases were recorded in medical OP at GGH, Guntur. Only suspected cases of PUO with presence of characteristic eschar were tested for IgM antibodies by Weil-Felix and rapid ICT test. The positive tests were further confirmed by IgM ELISA. The present study was undertaken to estimate the prevalence of the disease in clinically suspected patients to compare rapid ICT which is simple and IgM ELISA method. There was 96.5% and 98.3% positivity in rapid ICT and ELISA respectively than Weil-Felix test which is neither sensitive nor specific for diagnosis of these diseases.

### Materials And Methods:-

A total of 216 patients attended the medical OP in GGH Guntur with PUO from September 2013 to February 2014 and a number of 58 suspected cases were screened for scrub typhus by Weil-Felix agglutination test containing *Proteus vulgaris* antigen suspension OX19, OX2 and *Proteus mirabilis* antigen suspension OXK (Tulip diagnostic Pvt Ltd Goa, India) and Rapid Immunochromatographic assay or ICT (standard diagnostics, Bioline, Inc, Korea) containing a major surface protein 56KDa antigen representative of *Orientia tsutsugamushi* (Karp, Kato, Gilliam). Weil-Felix test with a titre of >1:160 and ICT positive were considered positive. All 58 positive for IgM antibodies of scrub typhus were further confirmed by IgM ELISA (Bio International Seattle, WA, USA) that used recombinant antigens to detect IgM antibodies for *O. tsutsugamushi*.

The data was statistically analysed on SPSS 17.0 software by using chi-square ( $\chi^2$ ) test. The probability value (P value) was calculated and P-value of less than 0.00001 was considered significant.

### Results:-

A total of 216 patients with PUO reported to Medical OP, GGH, Guntur from September 2013 to February 2014. Among 216, only suspected cases with fever >38.3°C for more than one week with eschar were screened for IgM antibodies for Scrub typhus and 58 cases were Seropositive. More number of cases were reported in the months of September and October in 2013 (Figure 1).

Among these 58 positive cases 36 (62.9%) were male and 22 (37.9%) were female. Males were more affected than females. Age-wise and sex-wise distribution and their seropositivity are shown in figure 2. Age group of the patients ranged between 2 to 80 years. The seropositivity for IgM antibodies was highest in 41-60 yrs (56.8%) age group followed by 21-40 yrs (32.7%) in both sexes.

Weil-Felix test was positive in 26 cases (44.8%) and negative in 32 (55.1%). Rapid Immunochromatographic assay (Fig. III) positive in 56 (96.5%) and negative in two cases (3.5%). ELISA was positive in 57 (98.3%) and negative in one patient (1.07%). The correlation between rapid ICT and ELISA was 96.5% and 98.3% respectively (Table I).

Fever >38.3°C for one week with chills and rigors was the most common manifestation (100%) including nausea and vomiting. Presence of characteristic eschar was observed in 56 (96.5%) patients. Other presentations like Hypotension, Myalgia (86.2%), Hepatosplenomegaly (62%), Abdominal pain 34%, Cough with dyspnoea 25.8%, Oliguria 34.4% and Skin rash in 5 (8.6%) patients. There was no eschar in 2 patients. Among these 58 cases, 1 (1.7%) death was reported due to Acute respiratory failure (Table II).

The laboratory parameters thrombocytopenia, deranged liver function tests and renal function tests were seen in 48 (82.7%), 42 (72.4%) and 14 (24.1%). Total Leucocyte count was raised in 44 (75.8%) (Table III). Most of the patients were from rural areas belonging to Guntur, Prakasam and Krishna districts of Andhra Pradesh. Number of cases reported during cooler months between September and October were high. All 58 cases were negative for common causes of fever such as typhoid, tuberculosis, malaria, dengue, HIV and Hepatitis B. All cases diagnosed as scrub typhus were followed up and one death was reported and it was not significant.

**Discussion:-**

Rickettsial infections are reemerging with increasing reports from India and other countries with considerable morbidity and mortality. Scrub typhus is a rickettsial infection caused by *Orientia tsutsugamushi*. Incidence of scrub typhus varies from 0.8% to 60% in different countries.

Among 216 recorded cases with PUO, a total of 58 cases reported with fever  $>38.3^{\circ}\text{C}$  with chills and rigors, were tested for the presence of antibodies and were found to be positive. Among these 36 were males and 22 were females. Incidence was more among males than females and this correlates with studies by S Gurung *et al.* who reported 204 patients with PUO and 63 were confirmed positive of which 42 were males and 21 females, A Ramyasree *et al.* tested 100 patients among which 39 were positive and of these 23 were males and 16 were females. Highest seropositivity was observed in 41-60years age group which correlates with the study of A Ramyasree *et al.* and R Bithu *et al.*

The prevalence of Fever with chills and rigors with vomiting (100%) and presence of characteristic eschar (96.5%) were the most common presentations in our study which is similar to a study by S Gurung *et al.*, A Ramyasree *et al.* and others. S Gurung *et al.* have reported eschar in 12 patients and studies in Korea reported a high incidence of eschar. This may be due to variation in serotypes among the regions and also the eschar is usually painless and does not itch, so remains undetected.

In the present study most of the patients were from rural background. The number of cases reported in the months of September and October were high. This is because of the increased activity of mites during or at the end of rainy season (Figure I) which correlates with study by R Bithu *et al.*, Sharma A *et al.* and Vivekanandan M *et al.*

Several studies have reported eschar and skin rash in different populations from different parts of the world. The prevalence of the rash has been reported varying from 8.9% to 90% by different authors and in our study, it was 8.6%. S Gurung *et al.* reported eschar in 12 cases and rash in 14(34.4%). Hypotension (86.2%) was another abnormal parameter in our study and Vivekanandan M reported 16% incidence in his study. The most important abnormal laboratory parameter noticed in the present study was thrombocytopenia 48(82.7%). Other laboratory findings include elevation of liver enzymes, serum urea and serum creatinine. Similar abnormalities have been observed by R Bithu *et al.* and Vivekanandan M *et al.* and other studies.

In this study, one death 1.7% has been reported due to acute respiratory failure with fever, cough and dyspnoea. R. Bithu *et al.* reported a mortality of 9.7% in their study of 133 cases with common cause of death as acute respiratory failure presenting with fever, cough and dyspnoea.

The diagnosis of scrub typhus is a problem due to low index of suspicion and lack of diagnostic facilities in India. Weil-Felix test is widely used in diagnosis of rickettsial diseases but this test is neither sensitive nor specific. The test result may be negative during early stages of disease, the antibodies are detectable only during second week of the onset of the disease. It has been replaced by more accurate and sensitive immunological tests. Among these, specific immunological tests, indirect immunofluorescence test and PCR which provide accurate and specific diagnosis, either not available or are too expensive. There is need for a rapid technically simple and economic test. ELISA is an easy and comparatively economic test. In the present study suspected cases (58) were screened with W-F test and rapid immunochromatographic assay and positive cases were further confirmed by IgM ELISA. Gurung *et al.*, reported positive test with W-F 51, ICT in 64 and IgM ELISA in 63 patients. In our study 2 samples were negative by rapid method but positive by ELISA and one sample positive by rapid method (ICT) was negative for ELISA which correlated with the study of Gurung *et al.*, with one patient's sample positive for Weil-Felix and ICT and negative for IgM ELISA. By using rapid test and ELISA for detection of antibodies of scrub typhus the positivity was 96.5% and 98.2% in our study. The difference was statistically significant. Sharma *et al.* tested 150 samples from patients with PUO of which 52 were found to be positive for OXK antibodies by Weil-Felix test. Therefore it can be concluded that both rapid test and ELISA are equally good. In the high work load centres, ELISA should be used but with less number of samples rapid method may be used for early diagnosis of scrub typhus.

FIGURE-I

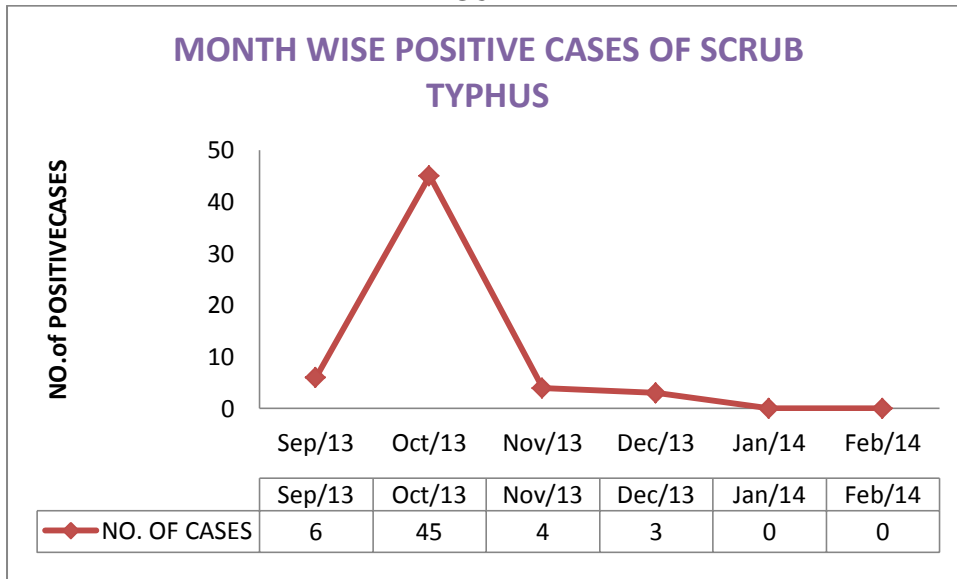


FIGURE - II

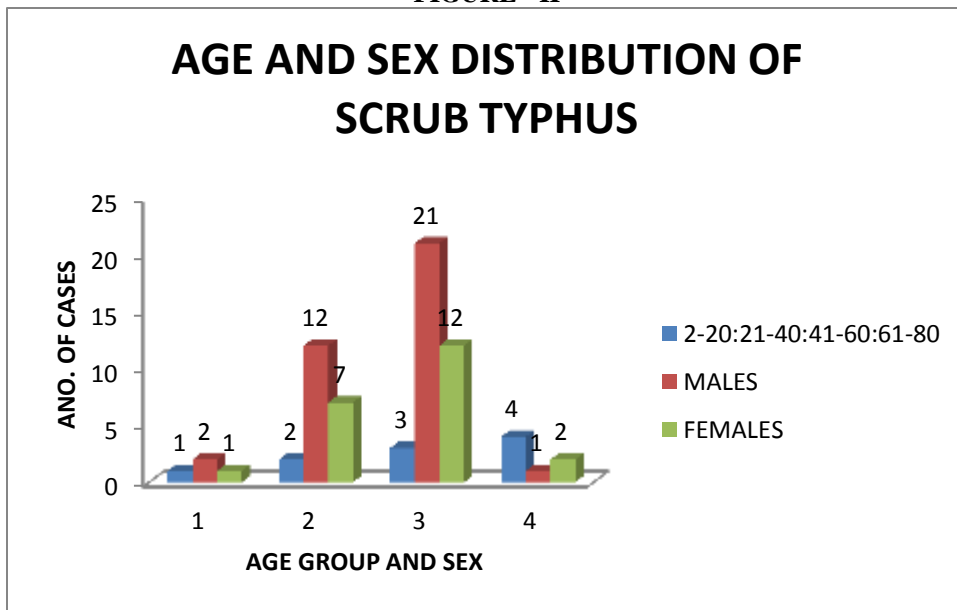


Figure:-Iii Immunochromatography



Figure Iv:-Eschar

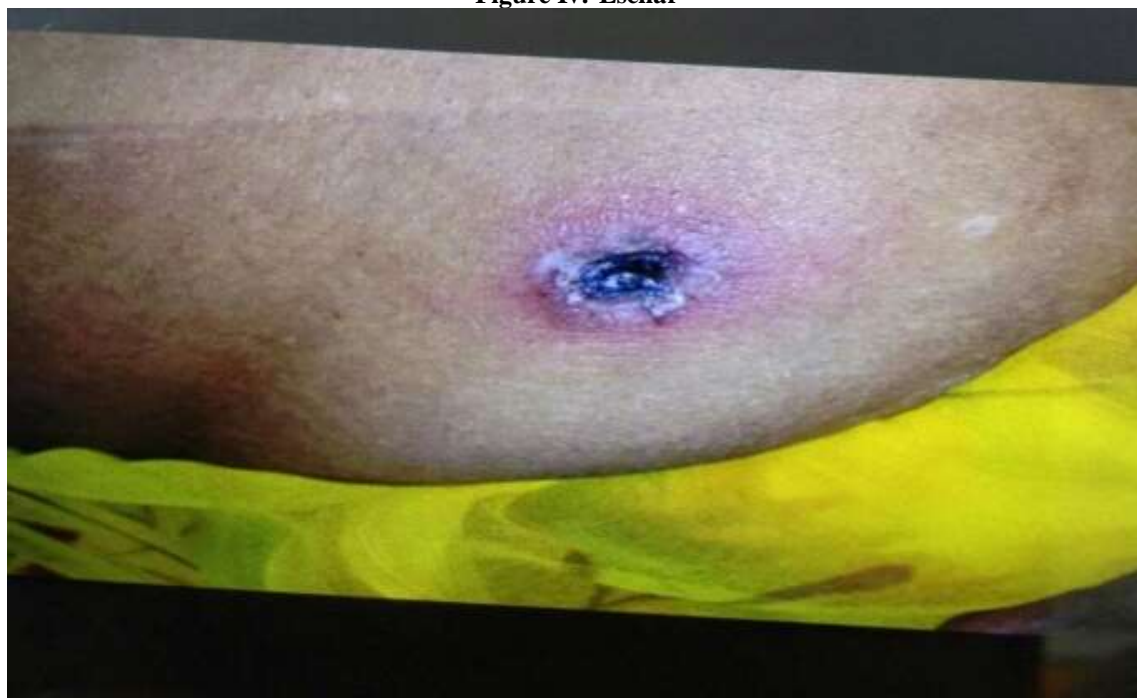


Table-I: Laboratory Tests For Diagnosis Of Scrub Typhus

NAME OF THE TEST	POSITIVE	NEGATIVE	TOTAL
WEIL-FELIX	26	32	58
ICT	56	2	58
ELISA	57	1	58
WEIL-FELIX & ICT	1	1 (ELISA)	2
WEIL-FELIX & ELISA	2	2 (ICT)	4
TOTAL	142	38	180

$X^2=67.3648$ ,  $df = 4$ ,  $p < 0.00001$ , significant

**Table: II** Clinical Features

Sl. No.	Clinical features	Number of patients	Percentage
1.	Fever >38.3 <sup>0</sup> C >1 week, chills & rigors	58	100
2.	Headache	30	51.7
3.	Nausea & Vomitting	58	100
4.	Presence of Eschar	56	96.5
5.	Abdominal pain	20	34.4
6.	Cough with dyspnea	15	25.8
7.	Myalgia	50	86.2
8.	Hepatosplenomegaly	26	62
9.	Skin rash	05	8.6
10.	Oliguria	20	34.4
11.	Hypotension	50	86.2
12.	Mortality	01	1.7

**Table:-Iii** Other Laboratory Parameters In Scrub Typhus Cases

Sl. No.	Name of the investigation	Number of patients	Percentage
1.	Total leucocyte count -less than 4.3 x 10 <sup>3</sup> /mm <sup>3</sup> -Between 4.3 x 10 <sup>3</sup> /mm <sup>3</sup> -more than 4.3 x 10 <sup>3</sup> /mm <sup>3</sup>	6 8 44	13.4 13.8 75.8
2.	Platelet count below 1.4 lakhs/mm <sup>3</sup>	48	82.7
3.	Liver function tests - Raised SGOT (>40u/L) - Raised SGPT (>36u/L) - Raised serum alkaline phosphatase (>150IU/L) - Raised total Bilirubin (>1gm/dl)	42 16 32 26	72.4 27.6 55.1 44.8
4.	Renal function tests - Raised blood urea (>45mg/dl) - Raised serum creatinine (>1.5mg/dl)	14 06	24.1 13.4

**Conclusion:-**

Scrub typhus is prevalent but an under diagnosed disease in India. Scrub typhus cases have been reported from neighbouring states like Tamil Nadu, Pondicherry, Kerala, Karnataka and Orissa. The climatic conditions in Andhra Pradesh are more or less similar to these states. Therefore it is recommended that scrub typhus should be included in the differential diagnosis of Pyrexia of Unknown Origin along with other endemic diseases during cooler months between September and October in this region. Rapid ICT and specific diagnostic methods using ELISA can be carried out timely for early diagnosis of scrub typhus. An early empiric therapy with Doxycycline and Azithromycin can be given to reduce serious complications which are associated with high mortality.

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**References:-**

1. Ahmad S, Srivastava S, Verma S.K., Puri P, Shriazi N. scrub typhus in Uttarakhand, India: A common rickettsial disease in an uncommon geographical region. Trop Doct. 2010 July;40(3):188- 90 : doi :10.1258/td.2010.090447.
2. Baily & Scott diagnostic microbiology – 10<sup>th</sup> edition. Betty A Forbes Daniel F, Sahn, Alice S. Weiss Field.
3. Biswajyothi Borkatoty, Aniruddha Jakharia, Dipankar Biswas, Jagadish mahanta. Co-infection of scrub typhus and leptospirosis in patients with Pyrexia unknown origin in Longding district of Arunachal Pradesh in 2013. Indian journal of medical microbiology, (2016) 34(1):88-91.

4. Boorugu H, Dinaker M, Roy ND, Jude JA. Reporting a case of scrub typhus from Andhra Pradesh. *J Assoc Physicians India* 2010;42:209-13.
5. Chang WH. Current status of Tsutsugamushi disease in Korea. *J Korean Med Sci* 1995;10:227-38.
6. Dass R, Deka NM, Guwarah GS, Barman H, Hoque R, Mili D, *et al.* Characteristics of pediatric scrub typhus during an outbreak in the North Eastern region of India: Peculiarities in clinical presentation, laboratory findings and complications. *Indian J Pediatr* 2011;78:1365-70.
7. *District Laboratory Practice in Tropical Countries South Asian Edition, 2006, Part I* by Monika Cheesbrough.
8. Jang W, Huh M, Park K, Choi M, Kim IS. Evaluation of immunoglobulin M capture Enzyme linked immunosorbent assay for diagnosis of *Orientia tsutsugamushi* infection. *Clin Diagn Lab Immunol* 2003;10:394-8.
9. Kammili N, Swathi A, Devara SM, Anuradha PR. Prevalence of scrub typhus among acute undifferentiated febrile illness cases provisionally diagnosed as Dengue fever. *J Evol Med Dent Sci* 2013;2:2661-64.
10. Kim DM, Won KJ, Park CY, Yu KD, Kim HS, Yang TY, *et al.* distribution of Eschars on the body of Scrub Typhus patients: A prospective study. *Am J Trop Med Hyg* 2007;76:806-9.
11. Kim DM, Kim SW, Choi SH, Yun NR. Clinical and laboratory findings associated with scrub typhus. *BMC Infect Dis* 2010;10:108.
12. Koh GC, Maude RJ, Paris DH, Newton PN, Blacksell SD. Diagnosis of Scrub typhus. *Am J Trop Med Hyg*, 2010 Mar;82(3):368-70. Doi:10.4269/ajtmh.2010.09-0233.
13. *Mansons Tropical Diseases* by Jeremy Farrar, Peter Hotez, Thomas Junghanss, Gagandeep Kang, David Lalloo, Nicholas White, 23<sup>rd</sup> edition.
14. Mathai E, Rolain JM, Verghese GM, Abraham OC, Mathai D, Mathai M, *et al.* Outbreak of scrub typhus in southern India during the cooler months. *Ann NY Acad Sci* 2003;990:359-64.
15. R Bithu, V Kanodia, RK Maheswari – possibility of Scrub typhus in fever of unknown origin (FUO) cases: An experience from Rajasthan: *Indian Journal of Medical Microbiology* – (2014) 32(4):387-390.
16. *Medical Microbiology: A Guide to Microbial Infections: Pathogenesis, Immunity, Laboratory Diagnosis and Control* by David Greenwood, Richard C.B. BLACK, John F. Peutherer, Michael R. Barer. 17<sup>th</sup> Revised edition.
17. *Park's text book of preventive and social medicine* by K. Park, 23<sup>rd</sup> edition 2015.
18. Razak A, Satyanarayanan V, Prabhu M, Sangar M Balasubramanian R. scrub typhus in southern India: are we doing enough? *Trop Doct*-2010. Jul;40(3):149-51, doi:10.1258/td.2010.090508.
19. S Gurung, J Pradhan, PY Bhutis. Outbreak of scrub typhus in North east Himalayan region-sikkim. An emerging threat. *Indian journal of medical microbiology*, (2013) 31(1):72-74.
20. Sharma A, Mahajan S, Gupta ML, Kanga A, Sharma V. investigation of an outbreak of scrub typhus in the Himalayan region of India. *Jpn J Infect Dis* 2005;58:208-10.
21. Tsay RW, Chang FY. Serious complications in scrub typhus. *J Microbiol Immunol Infect* 1998;31:240-4.
22. Vivekanandan M, Mani A, Priya YS, Singh A, Jayakumar S, Purthy S. outbreak of scrub typhus in Pondicherry: *J Associ Physicians India*, 2010. Jan;58:24-8.