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### RESEARCH ARTICLE

#### SEROPREVALENCE OF SCRUB TYPHUS AND LEPTOSPIROSIS IN PATIENTS WITH ACUTE FEBRILE ILLNESS IN A TERTIARY CARE HOSPITAL, VIJAYAWADA, A.P

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#### Abstract

Two significant causes of acute febrile illness are Scrub typhus and Leptospirosis, these zoonotic illnesses are primarily transmitted by rodents. Both illnesses present with similar and non-specific clinical symptoms, have a similar seasonal trend and can be identified by IgM ELISA. This study aims at identifying the presence of antibodies to scrub typhus and leptospirosis and their co-infection in patients of all age groups by IgM ELISA. Data was collected retrospectively over a period of four years, from January 2019 to September 2023 and analysis was done. A total number of 320 samples were received at the laboratory during the study period and IgM ELISA was performed for both scrub typhus and leptospirosis for all the samples received. Of the 320 samples tested, IgM ELISA for Scrub typhus was positive in 72(22.5%), Leptospirosis in 23(7.18%) and 6(1.87%) for both Scrub typhus and Leptospirosis were seen. Seroprevalence of Scrub typhus was more in Male population whereas Female predominance was observed in Leptospirosis. Age group in our study ranged from 0-60 years and most of the infected individuals are from Rural areas. As both leptospirosis and scrub typhus present with similar clinical features, co-infection of these two diseases may occur and require early diagnosis which helps the physician in treating the cases. IgM is a cost effective method of diagnosis of these zoonotic infections and plays a major role in early diagnosis thereby reducing the morbidity and mortality in health care settings.

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#### Introduction:-

Acute febrile illness is the commonest clinical presentation to healthcare workers where patients attend the Out-patient departments with non-specific signs and symptoms. Acute febrile illness can be due to various pathogenic microbial agents like bacteria, viruses, fungi and parasites. Zoonotic infections can be defined as diseases originating from animals and humans acquiring the disease either naturally or by vectors. The spread of zoonotic

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infections can be due to changing ecology leading to increase in infections by bacterial agents causing Scrub typhus and Leptospirosis.

The larval mites (chiggers) of the *Leptotrombidium deliense* group are the source of scrub typhus, an acute zoonotic sickness. When a person walks onto the "mite islands," which are regions where mites are prevalent, they unintentionally become infected. However, the illness can appear in a variety of environments, including semi-desert areas, rice fields and seashores [12]. The aggressive intracellular bacteria that causes scrub typhus, *Orientia tsutsugamushi*, is indigenous to a specific geographic area known as the "tsutsugamushi triangle" which consists of China, Taiwan, South Korea and Japan [4]. Scrub typhus is often diagnosed based on the clinical presentation and medical history of the patient. However, due to their striking similarities in clinical signs and symptoms, it can be challenging to distinguish scrub typhus from other acute tropical febrile disorders like leptospirosis, murine typhus, malaria, dengue fever and viral hemorrhagic fevers [23].

Leptospirosis is a zoonosis caused by a pathogenic strain of Spirochaete *Leptospira interrogans* that is found all over the world [17]. Numerous domestic and wild animals excrete pathogenic spirochetes of the species *Leptospira* in their urine, which is the source of the disease. Direct contact with infected animals can spread the spirochete to humans, as can exposure to freshwater or soil tainted by the urine of sick animals. Many nations, including Thailand, are experiencing an increase in the yearly number of reported cases of leptospirosis since 1908 [7]. While there are well-described classical presentations of leptospirosis and scrub typhus, the majority of patients arrive at hospitals exhibiting vague signs and symptoms. The most typical clinical manifestation of both scrub typhus and leptospirosis is acute undifferentiated fever or acute fever without a clear centre of infection [18].

Due to water stagnation and blockage, leptospirosis incidence rises during and after monsoon [28,30]. During the post-monsoon season, scrub typhus is more common due to the proliferation of scrubs, which provide an ideal environment for mite growth. Leptospirosis and scrub typhus are two underappreciated tropical illnesses that share similar clinical characteristics, making it challenging to differentiate between them based solely on symptoms. Although eschar is a diagnostic tool for scrub typhus, few cases are typically discovered. Both of these illnesses are associated with symptoms such as headache, rash and myalgia [3]. IgM ELISA is widely used in low- and middle-income nations with limited resources to diagnose leptospirosis and scrub typhus. The monsoon and post-monsoon seasons pose the greatest risk of typhoid, dengue and scrub typhus transmission. Due to the involvement of several etiological agents and/or vectors, co-infections among the organisms are rare, although the probability cannot be ignored. One of the main problems with ELISA has been the potential for cross reactivity.

In order to identify the possibility of dual infection and make coinfection diagnosis easier, the current study compared the clinical symptoms and routine service-based laboratory data of patients with leptospirosis, scrub typhus and coinfections.

### **Methodology:-**

This retrospective study was conducted in the Virology research and diagnostic laboratory, Department of Microbiology, Siddhartha Medical College, Vijayawada. A total of 320 patients, both adults and children of different age groups with features suggestive of acute febrile illness tested for both Scrub typhus and *Leptospira* were included in the study. Details of the patients with fever and other clinical features for whom IgM ELISA for Scrub typhus and *Leptospira* were performed were collected and the details were tabulated.

The study composed of villagers with comparable symptoms from the impacted villages, as well as admitted and out-of-hospital cases of pyrexia ( $>38^{\circ}$  C) at the Government General Hospital (GGH) in Vijayawada and surrounding Primary Health Care Centres. The retrospective study involved hospitalised children and adults who had fever for at least five days without a discernible infection or fever for at least five days with any two clinical features strongly suggestive such as rash, oedema, mylagia and an eschar, with or without a history of tick exposure. The study was carried out between January 2019 and September 2023. Venous blood was collected from 320 suspected cases and tested for the presence of IgM antibodies to Scrub typhus by ELISA method following standard kit protocol (InBios International, Inc.) A value of IgM units greater than 0.500 was considered positive for scrub typhus IgM antibodies (as per kit instructions). Similarly, IgM antibodies to leptospirosis by ELISA method following standard kit protocol (Abbott Diagnostics Medical Pvt. Ltd.) and a cut-off of 0.5 of optical density (OD) was taken as positive. The laboratory parameters and other data were entered in the excel spreadsheet (Microsoft Office, Redmond, Washington, USA) and analysis was done by using SPSS version 16.

### Results and Discussion:-

Scrub typhus and leptospirosis are diseases that nearly a million people encounter each year. Scrub typhus is most common in populations that come into regular or occupational contact with scrub vegetation. The disease, which was previously thought to be endemic in the southern region of India, has slipped the scientific community's notice until recently [13]. This was most likely caused by changes in lifestyle, the widespread use of pesticides, and the empirical use of tetracycline and chloramphenicol for acute febrile diseases [19]. Leptospirosis is also endemic in the country's coastal and southern regions. Contact with animals, contaminated environments, agricultural areas, stagnant water sources and seasonal variations like floods and severe rains are risk factors commonly linked to both diseases [22,29].

The current study emphasises the discovery that fevers, especially scrub typhus and leptospirosis, are a significant contributor to the high degree of complications and various clinical presentations that go undetected. We have demonstrated that it is possible to do a precise serological diagnosis of this infection using ELISA-based technology, which can help with the early detection and management of infections. There are reports of rickettsial illnesses throughout Southeast Asia [1]. Infections with rickettsiales, including Indian tick typhus and scrub typhus, are a newly recognised category of zoonosis in India [5]. As described in the Indian literature [25,16], we saw a post-monsoon rise in Rickettsial cases in the current study. Even though the secondary scrub vegetation increases during the post-monsoon season, only 10% of the cases in this study showed evidence of a clear exposure to scrub vegetation. This suggests that more research is necessary to ascertain how the environment affects the life cycle and dissemination of the trombiculid mite, which is the scrub typhus vector.

Since many instances remain undetected because of a lack of knowledge about the illness and a dearth of specialised laboratory facilities in high-burden areas, these reports probably underestimate the full incidence of the disease. In the absence of a precise diagnosis, families frequently have to bear the disproportionate financial burden of lengthy examinations and a variety of incorrect antibiotic uses [19]. It has been noted that there is variation in the clinical manifestations of rickettsial infection. Only a small percentage of the individuals in our study had the traditionally

linked rash and eschar (Figs. 1&2).



**Figure 1&2:-** Eschar.

During the study period of four years a total number of 320 serum samples were received for serological testing of Scrub typhus and leptospirosis. Out of these samples 72 were positive for IgM antibodies to Scrub typhus as detected by ELISA with a serological prevalence of 22.5% among patients with acute febrile illness. This correlates with study by R P Thakur et al <sup>[26]</sup>, with a prevalence rate of 22.8% and Sinha et al <sup>[24]</sup>, with a prevalence rate of 24.7%.

Of these patients, 38 (52.77%) were male and 34 (47.22%) were female. In our study, more men were affected than women. B Kanwar et al <sup>[18]</sup>, reported similar incidence of male preponderance of 52.04% and George M Varghese et al <sup>[27]</sup>, 54%.

There were 28 (38.89%) patients of 0 – 15 years age, 13 (18.05%) of 16-30 years, 14 (19.44%) of 31-45 years, 14 (19.44%) of 46-60 years and 3 (4.16%) of  $\geq 60$  years of age. Incidence ranged from age group 0-60 years in our study. R P Thakur et al<sup>[26]</sup>, reported age range between 3-78 years and E Mathai et al<sup>[14]</sup>, as 16-65 years.

The value of Scrub typhus positive samples mean is 14.40, SD = 8.90.

**Table 1:-** The demographic detail of test result against scrub typhus, leptospirosis and both.

Infections	Male	Female
Scrub Typhus	38	34
Leptospirosis	10	13
Both	3	3

Out of these samples 23 were detected to be having IgM antibodies to leptospira by ELISA with a serological prevalence of 7.18% among patients with acute febrile illness. B Kanwar et al<sup>[8]</sup>, reported an incidence of 8.89% and Satyakamala et al<sup>[20]</sup>, over a study period of 10 years, noted an overall prevalence of 9.14% whereas S Surabhi et al<sup>[25]</sup>, have reported a positivity of 22% with IgM ELISA.

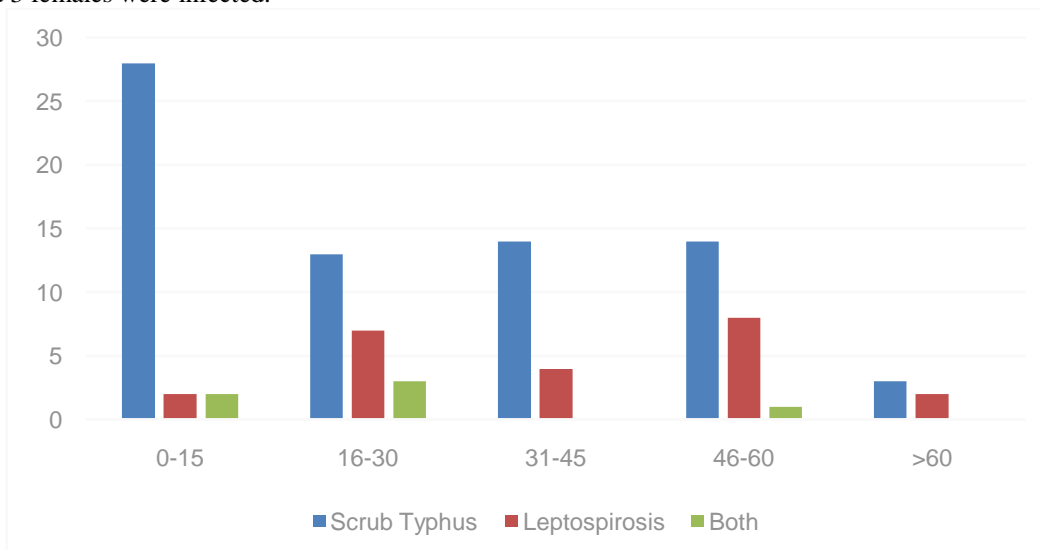
Of these patients, 10 (43.47%) were male and 13 (56.52%) were female with a female preponderance in our study. Studies by P kaur et al<sup>[9]</sup>, and Satyakamala et al<sup>[20]</sup>, reported male prevalence. Satyakamala et al<sup>[20]</sup>, has reported in their 10 year study an increased positivity in female positives during Covid-19 pandemic which includes our study period.

There were 1 (4.34%) patient of 0 – 15 years age, 4 (17.39%) of 16-30 years, 4 (17.39%) of 31-45 years and 1 (4.34%) of  $\geq 60$  years of age. As reported by P kaur et.al<sup>[9]</sup>, and Satyakamala et.al<sup>[20]</sup>, incidence is common in the age group of 21- 40 years and this correlates with our study.

The value of leptospirosis positive samples mean is 4.60, SD = 2.79.

Six serum samples in this analysis exhibited dual positive, suggesting a high likelihood of cross-reactivity. It is debatable whether people with both IgM ELISA scrub typhus and leptospirosis positivity actually have co-infection of scrub typhus and leptospirosis, or whether antibodies cross-react in these cases. While leptospirosis and scrub typhus can co-exist and have similar clinical presentations, separate techniques are needed to confirm co infection.

Incidence of dual positivity is 1.8% in our study whereas others has reported the incidence of 7.36% [8] and 25% [3] in their studies. Male predominance is noted in their studies whereas in our study there is equal incidence where 3 male and 3 females were infected.



**Fig 3:-** Demonstrates various age groups affected by leptospirosis, scrub typhus, and both.

Meningoencephalitis, shock, lung damage, and other potentially fatal consequences are possible manifestations of scrub typhus. Additionally, there is growing evidence from India that scrub typhus is linked to serious side effects like multi-organ failure [11]. According to Sedhain A et al [21] shock, renal failure and CNS involvement are frequently linked to death. A 13-year-old girl in our study passed away after being diagnosed with scrub typhus. While mortality has been declining recently, earlier Indian research have showed a range of deaths between 2 to 17.2% [21].

According to G Watt et al [29] majority of the patients were agricultural laborers who worked in rice fields from rural areas. In our study, 53 of the 72 patients tested positive for Scrub typhus, 17 of the 23 leptospirosis positive and 4 of the 6 dual positive cases are from rural areas. Very few patients reported coming into contact with flooded rice fields or roadways in the month prior to hospital admission. Huge number of patients in our study had fevers that lasted longer than seven days and the majority of them had nonspecific symptoms when they first arrived.

**Table 2:-** Demonstrates number of patients effected from Urban and Rural areas.

Infections	Urban	Rural
Scrub Typhus	19	53
Leptospirosis	6	17
Both	2	4

Symptoms in the laboratory or clinical domain can be useful in differentiating between scrub typhus and leptospirosis. For instance, leptospirosis is strongly suggested by the combination of jaundice and acute renal failure in an otherwise healthy patient with an appropriate exposure history; scrub typhus is suggested by an eschar [10]. However, because leptospirosis and scrub typhus share risk factors for acquisition, medical professionals should be aware of the possibility of coinfection with other illnesses if leptospirosis or scrub typhus is diagnosed. Both the current study and other publications revealed a significant percentage of patients with likely coinfections [15]. When developing novel diagnostic tests and treating feverish tourists returning from endemic areas, it is important to consider mixed infections. Scrub typhus is limited to Asia, the South Pacific, and northern Australia, while leptospirosis is present around the world.

Because there is typically a favourable response to treatment, early detection is crucial. Individual diagnosis is necessary because both infections have unique treatment protocols. Careful supportive therapy is necessary to avoid problems, and prompt antimicrobial medication may also help avoid difficulties. In addition, animals who consume cooked water and harbour leptospire can be protected against exposure.

### Conclusion:-

Leptospirosis and scrub typhus can co-infect each other since their clinical presentations are similar. To verify these circumstances, various methods are required. Leptospirosis and scrub typhus molecular confirmation are required in addition to ELISA for the identification of IgG antibodies in order to further corroborate our findings. However, the present report will assist in the future with thorough surveillance, patient management, developing effective public health responses, and increasing public knowledge of scrub typhus and leptospirosis. Timely initiation of efficacious antimicrobial therapy is facilitated by early diagnosis. Medication that treats both disorders must be a part of the empirical treatment. In order to close this gap, future research should concentrate on creating improved, more sensitive, and more focused serological test(s). Health education campaigns are essential for educating the general public and medical professionals about zoonotic diseases.

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