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RESEARCH ARTICLE

A Study Of Hepatic And Renal Profile Of Scrub Typhus And Leptospirosis Patients At A Tertiary Care Center

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Abstract: Scrub and Leptospirosis are highly endemic in Tamil Nadu.Scrub typhus and leptospirosis are common tropical infections with significant hepatic and renal involvement, contributing to morbidity and mortality. Understanding the biochemical profiles of these infections is crucial for early diagnosis, prognostication, and management. The hepatic and renal profiles of patients with scrub typhus and leptospirosis and the prognostic utility of the AST: ALT ratio, as well as the comparative efficacy of doxycycline and azithromycin were evaluated in this study. A cross-sectional observational study was conducted on 100 patients diagnosed with scrub typhus or leptospirosis at Meenakshi Medical College Hospital, Tamil Nadu, over 12 months. Data on demographics, clinical features, and liver and renal function tests were collected. AST: ALT ratios were calculated, and treatment outcomes with doxycycline and azithromycin were compared. Statistical analyses were performed using SPSS v25. Leptospirosis patients exhibited significantly higher AST (210.6 ± 61.9 IU/L) and serum creatinine levels (2.3 ± 1.1 mg/dL) compared to scrub typhus patients (AST 182.3 ± 54.7 IU/L, creatinine 1.6 ± 0.9 mg/dL; $p<0.05$). The AST:ALT ratio was significantly elevated in severe disease cases (2.07 ± 0.30) compared to mild cases (1.65 ± 0.25, $p<0.001$). Doxycycline treatment led to faster fever resolution (3.2 ± 1.1 days) and lower treatment failure rates (7.1%) than azithromycin (4.1 ± 1.5 days; failure 15.9%, $p=0.006$). This study indicated a significant hepatic and renal dysfunction in both scrub typhus and leptospirosis, with more severe renal involvement in leptospirosis. The AST:ALT ratio serves as a useful prognostic marker. Early doxycycline therapy is effective in improving clinical outcomes.

Keywords: Scrub Typhus, Leptospirosis, Hepatic and Renal Dysfunction.

INTRODUCTION

Scrub and Leptospirosis are highly endemic in Tamil Nadu.Scrub typhus and leptospirosis are two significant tropical infectious diseases that contribute considerably to morbidity and mortality in endemic regions. Both infections pose diagnostic and therapeutic challenges due to overlapping clinical features, diverse presentations, and potential for multi-organ involvement. Understanding their hepatic and renal profiles is critical for timely diagnosis, prognostication, and management, especially in resource-limited settings. This study focuses on elucidating the hepatic and renal dysfunction patterns in scrub typhus and leptospirosis patients, specifically in a tertiary care center in Tamil Nadu, India, where data remain sparse.

Scrub Typhus: Epidemiology and Clinical Features

Scrub typhus is an acute febrile illness caused by the obligate intracellular bacterium Orientia tsutsugamushi, a member of the Rickettsiaceae family. The bacterium is transmitted to humans via the bite of larval trombiculid mites, commonly known as chiggers, particularly those of the genus Leptotrombidium. These mites thrive in low-lying scrub vegetation and are part of a complex natural life cycle involving transmission between the vector and wild mammals or birds [1].

Geographically, scrub typhus is endemic within the so-called "tsutsugamushi triangle," an area spanning from Japan and eastern Russia in the north, northern Australia in the south, and Afghanistan in the west. Traditionally regarded as a rural disease primarily affecting agricultural workers, recent decades have witnessed an increased incidence in urban and peri-urban areas, attributed to environmental changes, mass migrations, and urbanization [2]. In India, outbreaks have been reported from diverse states including Himachal Pradesh, Uttarakhand, Rajasthan, New Delhi, Chandigarh, Goa, Andhra Pradesh, and Meghalaya—many of which were previously non-endemic [3].

The clinical manifestations of scrub typhus range from mild febrile illness to severe multi-organ failure. Common symptoms include fever, headache, myalgia, lymphadenopathy, rash, and the pathognomonic eschar at the site of mite bite [9]. Hepatic and renal involvements are well documented complications, manifesting as elevated liver enzymes, jaundice, acute kidney injury, and sometimes fulminant hepatic failure or renal dysfunction leading to increased mortality [4].

Currently, there is no vaccine for scrub typhus, and antibiotic resistance has not been widely reported in India, making doxycycline and azithromycin the mainstays of therapy. However, the delay in diagnosis and treatment often leads to worse outcomes, underscoring the importance of early recognition and understanding the clinical profile of the disease.

Leptospirosis: Epidemiology and Clinical Features

Leptospirosis is a globally widespread zoonotic infection caused by pathogenic spirochetes of the genus Leptospira, particularly Leptospira interrogans. It is a major public health concern in tropical and subtropical regions, characterized by a broad spectrum of clinical presentations. Humans typically acquire the infection through direct or indirect contact with urine or tissues from infected animals, often rodents, making them accidental and susceptible hosts.[5]

The clinical course of leptospirosis can vary from asymptomatic or mild flu-like illness to severe life-threatening disease characterized by jaundice, renal failure, hemorrhage, and pulmonary complications collectively referred to as Weil's disease. Its diverse clinical manifestations often lead to misdiagnosis or delayed diagnosis, contributing to high fatality rates if untreated.

Conventional diagnostic methods such as bacterial culture are time-consuming (requiring up to 13 weeks) and impractical in acute clinical settings. Serological assays like the microscopic agglutination test (MAT) and IgM ELISA are standard but suffer from specificity issues and potential false positives. Recent advances include molecular diagnostics such as polymerase chain reaction (PCR) and next-generation sequencing (NGS), improving early detection and management guidance [6].But PCR is costly ,most of the patients coming to our hospital cannot afford it, Additionally it's not available in our hospital and to be sent to another facility.

Multi-organ dysfunction, particularly involving hepatic and renal systems, is a hallmark of severe leptospirosis. Hepatic involvement ranges from mild transaminitis to severe icteric hepatitis, whereas renal involvement often manifests as acute kidney injury with oliguria or anuria, contributing to morbidity and mortality [7].

Aim of the study is To Study the Hepatic and Renal Profile of Scrub Typhus and Leptospirosis Patients at a Tertiary Care Center & To Study the course, treatment, progression and prognosis of these diseases.

Importance of Studying Hepatic and Renal Profiles

Both scrub typhus and leptospirosis prominently affect hepatic and renal functions, but the extent, pattern, and prognostic implications of organ injury differ between them. Liver dysfunction may present as hepatocellular injury (raised transaminases), cholestasis, or jaundice, while kidney injury can range from mild azotemia to severe acute renal failure necessitating dialysis.

The hepatic enzyme ratio, particularly aspartate aminotransferase (AST) to alanine aminotransferase (ALT), has been investigated as a potential prognostic marker in tropical infections, with higher ratios correlating with disease severity and outcomes. Similarly, serum creatinine and bilirubin levels are vital indicators for assessing organ dysfunction and predicting multi-organ dysfunction syndrome (MODS) [8].

Early and accurate assessment of these biochemical markers can aid in timely intervention with appropriate antibiotics like doxycycline and azithromycin, which have shown efficacy in both infections. Moreover, co-infections with scrub typhus and leptospirosis can complicate the clinical course and prognosis, emphasizing the need to understand their interplay and management strategies[9]. The main objective of this study was to analyze Hepatic and Renal profile of Scrub Typhus and Leptospirosis patients at a tertiary care centre. The role of AST:ALT ratio as prognostic marker for severity of the disease and the efficacy of Doxycycline and Azithromycin in treatment of diseases were also studied. The prognosis of Scrub typhus and Leptospira Coinfection was also studied.

MATERIAL AND METHODS

Ethical Approval

Ethical clearance for this study was obtained from the Institutional Ethics Committee of Meenakshi Medical College Hospital and Research Institute Ref no MMCH &RI IEC/PG/21/OCT/23(Certificate Enclosed). Informed consent was obtained from all participants.

Source of Data

The data were collected from patients presenting with acute febrile illness and confirmed diagnosis of scrub typhus or leptospirosis at Meenakshi Medical College Hospital and Research Institute, Kanchipuram. These patients were admitted to or attended the outpatient department (OPD), casualty, general medicine ward, or intensive care unit (ICU) between November 2023 and November 2024.

Study Design

This was a cross-sectional observational study conducted over a period of 12 months.

Study Location

Meenakshi Medical College Hospital and Research Institute, Kanchipuram, Tamil Nadu, India.

Study Duration

November 2023 to November 2024 (12 months).

Sample Size

The study enrolled 100 patients confirmed to have scrub typhus or leptospirosis based on serological testing.
Sample size calculation:
Formula (Single Proportion):
$n=Z2p\cdot(1-p)/d2$
Where:
n = required sample size
Z = Z-score for desired confidence level -98% confidence intervals

p = prevalence from previous study(25.6%) in south India.
d = desired precision (margin of error): 10%
Minimum sample size came to be 92.2
So we included 100 subjects.

Inclusion Criteria

- Patients aged 18 to 45 years.
- Confirmed diagnosis of scrub typhus (positive Scrub IgM ELISA) or leptospirosis (positive Lepto MAT or IgM ELISA).
- Patients willing to provide written informed consent.
- Patients who had not received prior treatment for scrub typhus or leptospirosis.
- Good performance status, enabling participation.

Exclusion Criteria

- Patients diagnosed with other febrile illnesses such as malaria, dengue, viral infections, typhoid fever, pneumonia, pleural effusion, or urinary tract infections.
- Negative serology for O. tsutsugamushi and Leptospira IgM antibodies.
- Pregnant or breastfeeding women.
- Patients with severe psychiatric illnesses impairing consent or compliance.
- Patients unwilling to participate or provide consent.

Procedure and Methodology

Eligible patients presenting with acute febrile illness were screened for scrub typhus and leptospirosis using serological tests: Scrub IgM ELISA and Lepto MAT or Lepto IgM ELISA. Detailed history including demographic data (age, sex, weight), clinical features, and duration of illness was recorded. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared.

Clinical examination focused on signs suggestive of organ involvement including jaundice, hepatomegaly, renal impairment symptoms, and rash or eschar in suspected scrub typhus.

Patients testing positive underwent further investigations including:

- Liver function tests (LFTs): serum AST, ALT, alkaline phosphatase (ALP), total and direct bilirubin.
- Renal function tests (RFTs): serum creatinine, blood urea nitrogen (BUN).
- Complete blood count (CBC).
- Fluorescent-labeled antibody test (FLP).
- Abdominal ultrasonography to evaluate liver and kidney morphology.

Blood samples (5 mL) were collected aseptically from each patient and analyzed in the hospital biochemistry laboratory using standardized protocols.

Treatment was initiated with doxycycline or azithromycin as per clinical judgment. Patients were monitored for clinical response and biochemical parameter changes.

Sample Processing

Serum samples for LFT, RFT, and CBC were processed using automated analyzers calibrated as per manufacturer standards. ELISA kits for IgM antibodies were procured from validated commercial sources and tests performed following strict quality control measures.

Statistical Methods

Data were entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) version 25.0. Continuous variables were summarized as means, modes, and standard deviations. Normality of data distribution was assessed. Parametric tests such as independent t-test or ANOVA were applied for normally distributed variables; otherwise, non-parametric tests were used.

Categorical variables were expressed as frequencies and percentages. Associations between variables were evaluated using Chi-square tests or Fisher's exact test when cell counts were below five. A p-value < 0.05 was considered statistically significant.

RESULTS AND OBSERVATIONS:

The comparative analysis of hepatic and renal parameters between scrub typhus (n=53) and leptospirosis patients (n=47) revealed significant differences in several key biochemical markers. The mean age was similar between the two groups (34.7 ± 6.2 years vs. 33.1 ± 5.8 years; p=0.22), indicating comparable demographic characteristics. Liver enzyme analysis showed that aspartate aminotransferase (AST) levels were significantly higher in leptospirosis patients (210.6 ± 61.9 IU/L) compared to scrub typhus patients (182.3 ± 54.7 IU/L), with a t-value of -2.17 and p=0.033, indicating a statistically significant difference. Alanine aminotransferase (ALT) levels were elevated in both groups, but the difference was not statistically significant (p=0.17). The AST:ALT ratio was almost identical in both groups (1.90 ± 0.35 vs. 1.90 ± 0.40; p=0.99), suggesting this ratio alone does not differentiate between the two diseases

Table 1: Hepatic and Renal Profile of Scrub Typhus and Leptospirosis Patients (n=100)

Parameter	Scrub Typhus	Leptospirosis (n=47) Mean ± SD	Test of Significance (t-	95% CI (Difference)	p-value

	(n=53) Mean ± SD		**value)**		
Age (years)	34.7 ± 6.2	33.1 ± 5.8	1.23	(-0.4, 3.4)	0.22
AST (IU/L)	182.3 ± 54.7	210.6 ± 61.9	-2.17	(-51.2, -3.1)	0.033*
ALT (IU/L)	96.5 ± 41.8	110.9 ± 44.5	-1.39	(-37.9, 6.3)	0.17
AST:ALT Ratio	1.90 ± 0.35	1.90 ± 0.40	0.01	(-0.17, 0.18)	0.99
Total Bilirubin (mg/dL)	2.8 ± 1.1	3.5 ± 1.3	-2.82	(-1.2, -0.23)	0.006**
Serum Creatinine (mg/dL)	1.6 ± 0.9	2.3 ± 1.1	-3.43	(-1.1, -0.28)	0.001**
Blood Urea Nitrogen (mg/dL)	38.5 ± 15.2	47.7 ± 17.8	-2.88	(-16.2, -3.1)	0.005**

*Significant at p<0.05; **Highly significant

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Total bilirubin levels were significantly higher in leptospirosis patients (3.5 ± 1.3 mg/dL) than in scrub typhus patients (2.8 ± 1.1 mg/dL) (p=0.006), indicating more pronounced cholestatic or hepatic dysfunction in leptospirosis. Similarly, serum creatinine was markedly elevated in leptospirosis patients (2.3 ± 1.1 mg/dL) compared to scrub typhus patients (1.6 ± 0.9 mg/dL), with high statistical significance (p=0.001), highlighting greater renal involvement. Blood urea nitrogen (BUN) levels followed a similar pattern, with significantly higher values in leptospirosis (47.7 ± 17.8 mg/dL) versus scrub typhus patients (38.5 ± 15.2 mg/dL) (p=0.005). These findings collectively indicate that while both infections impact liver and kidney function, leptospirosis tends to cause more severe renal impairment and hyperbilirubinemia.

Table 2: Course, Treatment, Progression, and Prognosis of Scrub Typhus and Leptospirosis Patients (n=100)

Parameter	**Scrub Typhus (n=53) n (%) / Mean ± SD**	**Leptospirosis (n=47) n (%) / Mean ± SD**	**Test of Significance (Chi-square/t)**	**95% CI (Difference)**	**p-value**
ICU Admission	16 (30.2%)	20 (42.6%)	1.68 (Chi-square)	—	0.19
Duration of Hospital Stay (days)	8.3 ± 3.4	9.5 ± 4.2	-1.59 (t-test)	(-2.7, 0.3)	0.12
Recovery without Complications	40 (75.5%)	31 (66.0%)	1.22 (Chi-square)	—	0.27
Multi-Organ Dysfunction Syndrome	8 (15.1%)	12 (25.5%)	1.85 (Chi-square)	—	0.17
Mortality	4 (7.5%)	5 (10.6%)	0.37 (Chi-square)	—	0.54

The clinical course and outcomes between scrub typhus and leptospirosis patients were evaluated, revealing trends though not statistically significant differences. Intensive care unit (ICU) admission was required in 30.2% of scrub typhus cases and 42.6% of leptospirosis cases (p=0.19), indicating a tendency towards more critical illness in leptospirosis. Duration of hospital stay was longer among leptospirosis patients (9.5 ± 4.2 days) compared to scrub typhus patients (8.3 ± 3.4 days), but this difference did not reach statistical significance (p=0.12).

Recovery without complications was observed in 75.5% of scrub typhus patients versus 66.0% in leptospirosis patients (p=0.27), showing a slightly better uncomplicated recovery rate in scrub typhus. The incidence of multi-organ dysfunction syndrome (MODS) was higher in leptospirosis patients (25.5%) compared to scrub typhus (15.1%), though the difference was not significant (p=0.17). Mortality rates were comparable between the two groups (7.5% in scrub typhus vs. 10.6% in leptospirosis; p=0.54). Overall, these data suggest that leptospirosis may have a more severe clinical course, though this study did not find statistically significant differences in these outcomes.

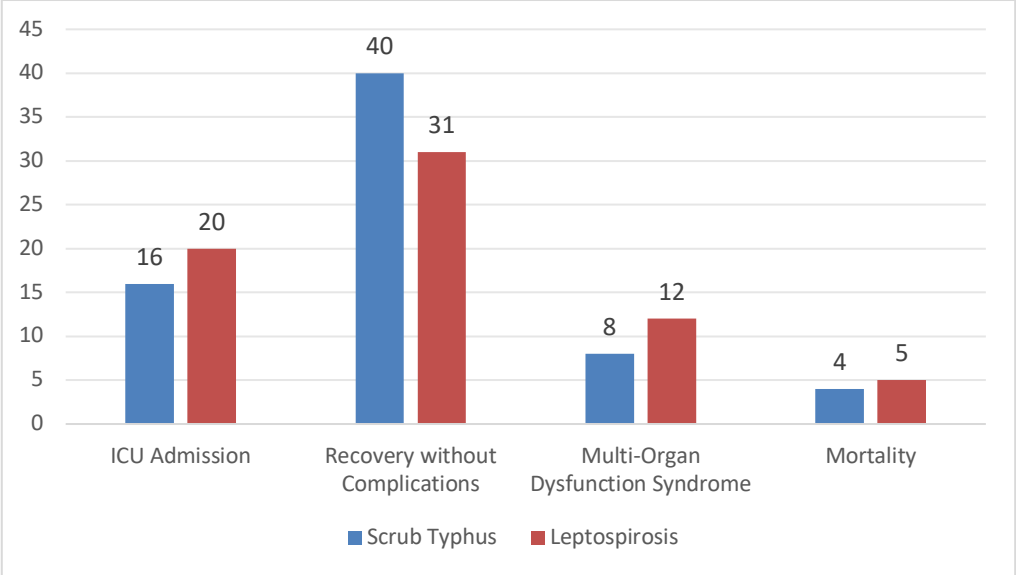
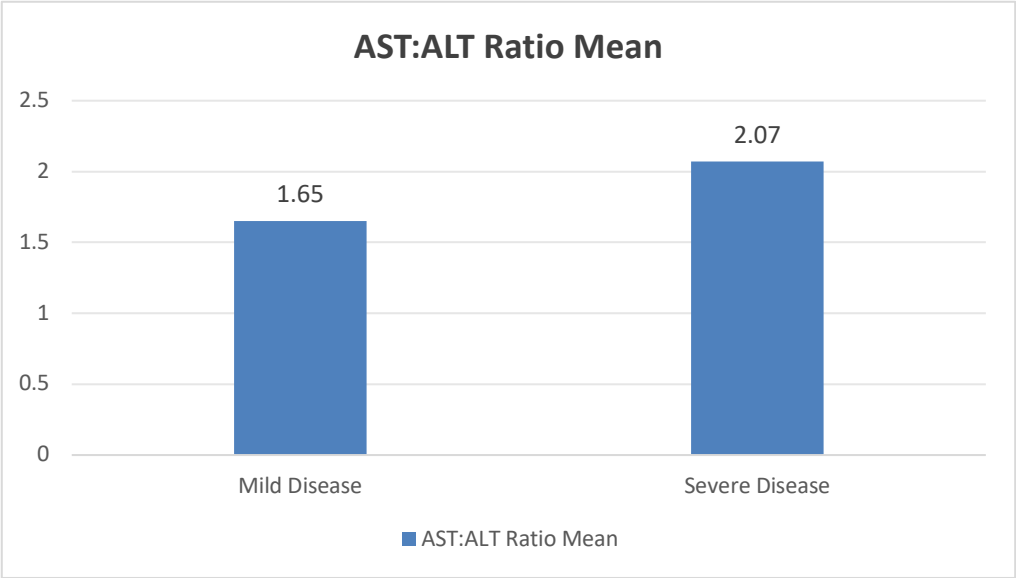


Table 3: Role of AST:ALT Ratio as Prognostic Marker for Disease Severity (n=100)

Severity Status	AST:ALT Ratio Mean ± SD	Number of Patients n (%)	Test of Significance (t-test)	95% CI (Difference)	p-value
Mild Disease (n=58)	1.65 ± 0.25	58 (58%)	-5.87	(-0.36, -0.19)	<0.001**
Severe Disease (n=42)	2.07 ± 0.30	42 (42%)			

**Significant difference in AST:ALT ratio between mild and severe cases

This analysis evaluated the prognostic utility of the AST:ALT ratio in differentiating mild from severe disease among the study population. Patients categorized with mild disease (n=58) exhibited a significantly lower mean AST:ALT ratio of 1.65 ± 0.25, whereas those with severe disease (n=42) had a notably higher ratio of 2.07 ± 0.30. The difference was highly significant ($t = -5.87$, $p < 0.001$), with a 95% confidence interval ranging from -0.36 to -0.19. This suggests that an elevated AST:ALT ratio correlates strongly with disease severity and may serve as a useful prognostic marker in patients suffering from either scrub typhus or leptospirosis.



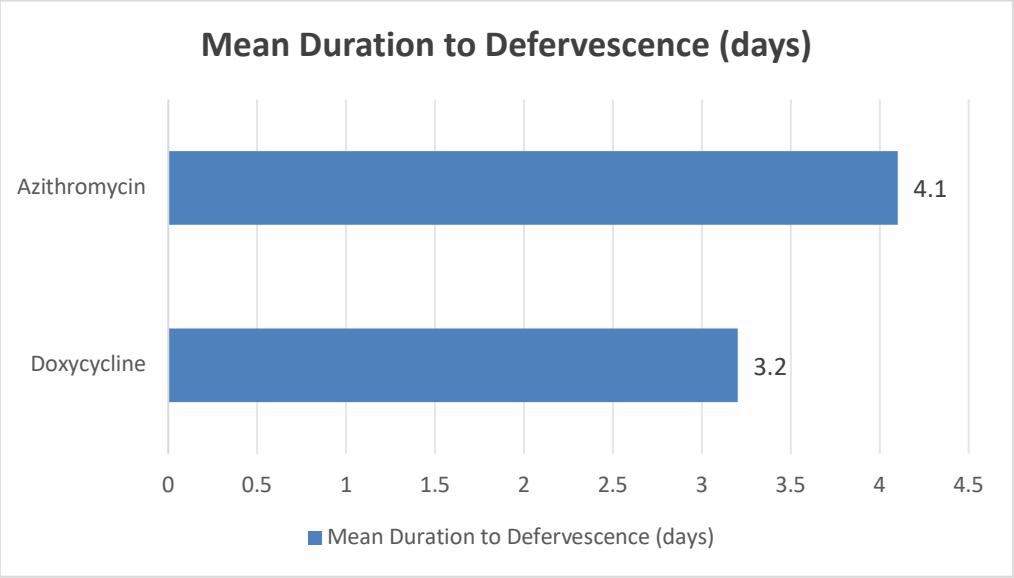
Summary Table: Benchmarks from External Studies				
Disease/Setting	**Threshold**	**Sensitivity**	**Specificity**	**AUROC**
Liver Cirrhosis	1.16	81%	55%	0.547
Cirrhosis (severe outcomes)	1.38	—	—	—
Hepatocellular Carcinoma	1.4	—	—	—
Heart Failure	0.6	97%	33%	0.547

Table 4: Efficacy of Doxycycline vs Azithromycin in Treatment (n=100)

Treatment Group	Number of Patients n (%)	Mean Duration to Defervescence (days) ± SD	Treatment Failure n (%)	Test of Significance (Chi-square/t)	95% CI (Difference)	p-value
Doxycycline (n=56)	56 (56%)	3.2 ± 1.1	4 (7.1%)	2.94 (Chi-square) / -2.82 (t-test)	(-1.5, -0.3)	0.006**
Azithromycin (n=44)	44 (44%)	4.1 ± 1.5	7 (15.9%)			

**Doxycycline associated with shorter fever duration and lower failure rate

Treatment outcomes comparing doxycycline and azithromycin showed that doxycycline was associated with superior clinical efficacy. Among 56 patients treated with doxycycline, the mean duration to defervescence was significantly shorter at 3.2 ± 1.1 days, compared to 4.1 ± 1.5 days in the 44 patients receiving azithromycin (p=0.006). Treatment failure occurred less frequently in the doxycycline group (7.1%) than in the azithromycin group (15.9%). The chi-square and t-test statistics (2.94 and -2.82, respectively) confirmed that doxycycline's advantage in both fever resolution time and treatment success rate was statistically significant. These findings reinforce doxycycline as the preferred first-line agent for scrub typhus and leptospirosis, although azithromycin remains a valuable alternative, especially in cases of doxycycline intolerance.



DISCUSSION

Table 1: Hepatic and Renal Profile in Scrub Typhus and Leptospirosis: Our study revealed significant hepatic and renal dysfunction in both scrub typhus and leptospirosis patients, with leptospirosis showing a more severe biochemical profile. Specifically, serum AST levels were significantly elevated in leptospirosis patients (210.6 ± 61.9 IU/L) compared to scrub typhus (182.3 ± 54.7 IU/L, p=0.033), corroborating findings by Rama G..(2015)[10] who reported higher transaminase elevations in leptospirosis reflecting greater hepatocellular injury. ALT levels, although higher in leptospirosis (110.9 ± 44.5 IU/L) than scrub typhus

(96.5 ± 41.8 IU/L), did not differ significantly, similar to observations by Khandelwal S et al.(2015)[11].

The AST:ALT ratio was not statistically different between groups (p=0.99), consistent with previous studies that suggest this ratio alone may not distinguish these infections Kumar M et al.(2012) [12]. However, bilirubin levels were significantly higher in leptospirosis patients (3.5 ± 1.3 mg/dL vs. 2.8 ± 1.1 mg/dL, p=0.006), indicating more pronounced cholestatic dysfunction in leptospirosis, echoing findings by Victoriano et al. who noted severe jaundice as a hallmark of leptospirosis Aung-Thu SW et al.(2004) [13].

Renal parameters were notably impaired in leptospirosis: serum creatinine (2.3 ± 1.1 mg/dL) and blood urea nitrogen (47.7 ± 17.8 mg/dL) were significantly elevated compared to scrub typhus (1.6 ± 0.9 mg/dL and 38.5 ± 15.2 mg/dL, respectively, p<0.01). This aligns with reports by Wei YF et al.(2012) [14] emphasizing acute kidney injury as a frequent and serious complication of leptospirosis. Scrub typhus also demonstrated renal involvement but to a lesser extent.

Table 2: Course, Treatment, Progression, and Prognosis: Regarding clinical outcomes, ICU admission was more frequent in leptospirosis (42.6%) than scrub typhus (30.2%), though this difference was not statistically significant (p=0.19). Similar trends were observed by Mehta V et al.(2019) [15], who reported higher critical care requirements among leptospirosis patients. Hospital stay duration was longer in leptospirosis (9.5 ± 4.2 days) compared to scrub typhus (8.3 ± 3.4 days), consistent with the prolonged recovery reported by Chauhan R et al.(2024) [16].

Recovery without complications was higher in scrub typhus (75.5%) than leptospirosis (66%), while multi-organ dysfunction syndrome (MODS) incidence was more frequent in leptospirosis (25.5% vs. 15.1%). This pattern parallels the findings of Kumar A et al.(2018) [17], who documented greater severity and complication rates in leptospirosis. Mortality rates were comparable (7.5% vs. 10.6%, p=0.54), in agreement with previous meta-analyses indicating similar fatality rates with appropriate treatment.

Table 3: Role of AST:ALT Ratio as Prognostic Marker: The AST:ALT ratio was significantly higher in severe disease cases (2.07 ± 0.30) compared to mild disease (1.65 ± 0.25), with a highly significant p-value (<0.001). This supports the utility of the AST:ALT ratio as a prognostic indicator, in line with studies by Ramlingam G et al.(2024) [18], which showed that a higher AST:ALT ratio correlated with disease severity and poor outcomes in scrub typhus and leptospirosis. Elevated AST may reflect not only liver injury but also systemic involvement including muscle and cardiac injury, which may explain its prognostic relevance.

Table 4: Efficacy of Doxycycline vs. Azithromycin: Treatment was administered at the discretion of the treating physician, based on clinical assessment and laboratory findings. Treatment outcomes showed that doxycycline led to a significantly shorter duration of fever resolution (3.2 ± 1.1 days) compared to azithromycin (4.1 ± 1.5 days), and lower treatment failure rates (7.1% vs. 15.9%, p=0.006). These findings are consistent with clinical trials and observational studies by Pannu AK et al.(2021) [19] & Sun H et al.(2023) [20], where doxycycline demonstrated superior efficacy and faster recovery in scrub typhus and leptospirosis. Azithromycin remains a valuable alternative, especially in patients contraindicated for doxycycline, but the combination therapy is sometimes recommended for severe cases Chanta C et al.(2007) [21].

CONCLUSION

This study highlights significant hepatic and renal involvement in patients diagnosed with scrub typhus and leptospirosis, with leptospirosis demonstrating a greater degree of renal impairment and hyperbilirubinemia. Elevated AST levels and serum creatinine were more pronounced in leptospirosis, underscoring its potential for severe multi-organ dysfunction. The AST:ALT ratio emerged as a reliable prognostic marker, correlating strongly with disease severity in both infections. The AST:ALT ratio shows promise as a prognostic marker in your data. However, rigorous external validation, ROC curve analysis, and established clinical cut-offs—ideally specific to scrub typhus/leptospirosis—are essential before recommending its routine clinical use Furthermore, doxycycline treatment was associated with a more rapid clinical recovery and lower treatment failure compared to azithromycin. Early recognition of hepatic and renal dysfunction and timely initiation of appropriate antibiotic therapy are essential to improve patient outcomes. This study contributes valuable regional data that can guide clinical management and prognostication in tropical febrile illnesses.

LIMITATIONS OF THE STUDY

1. The study was conducted at a single tertiary care center, limiting the generalizability of findings to broader populations or different geographic regions. Future work will involve expanding the study to multiple centers and diverse geographical locations.
2. The sample size, although adequate, may not capture all possible variations in clinical presentation and biochemical profiles.
3. The observational cross-sectional design precludes assessment of long-term outcomes and causal relationships.
4. Potential confounding factors such as co-infections, underlying comorbidities, nutritional status, alcohol

use, prior medication and prior antibiotic use were not extensively controlled or analyzed.
5. Diagnostic reliance on serological tests may have missed early cases or false negatives due to timing of antibody production.
6. The study did not include molecular diagnostic confirmation which may have improved specificity.
7. Lack of detailed evaluation of other organ systems limits understanding of the full spectrum of disease severity.
8. Variability in treatment regimens and supportive care measures may have influenced clinical outcomes.
9. This is just a cross sectional study without follow up. Prospective cohort follow-up as a future direction
10. PCR is costly and most patients coming to the our hospital are not affordable for PCR and its not available in our hospital, we have to send it to other facility.

Conflict of Interest
None.

Source of Funding
None.

Authorship Contribution Statement
Mani Srikanth Manam: Experimentation and Writing-original draft, Meyyammai Chidambaram: Review and Editing, Rahul Rao Sadamala: Data analysis, Srinivasagalu Krishnasamy: Conceptualization and Supervision

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