

COMPARATIVE STUDY OF LABORATORY TESTS IN PATIENTS WITH SCRUB
TYPHUS AT A TERTIARY CARE TEACHING HOSPITAL

Apurva Parate¹,

1. Assistant Professor, Department of Microbiology, Prathima Institute of Medical Sciences, Nagunur, Karimnagar, Telangana State.

Corresponding Author: Dr. Apurva Parate

Abstract

Background: Scrub typhus, an acute febrile infectious disease, affects both male and female patients. This research aimed to compare the laboratory findings of scrub typhus patients based on gender and presentation.

Methods: This retrospective study analyzed diagnosed scrub typhus patients admitted to the intensive care unit of a tertiary care teaching hospital in Karimnagar. Diagnosis involved testing for specific IgM antibodies against *Orientia tsutsugamushi* using a commercial ELISA kit.

Results: The mean serum bilirubin level was higher in male patients (4.01 ± 1.90 mg/dl) compared to female patients (2.39 ± 1.22 mg/dl), with a slight difference that did not reach statistical significance ($p=0.06$). SGOT (IU/l) and SGPT (IU/l): There were no statistically significant differences in the mean levels of serum glutamate oxaloacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT) between male and female patients ($p=0.132$ and $p=0.74$, respectively). Alkaline phosphatase (IU/l): Female patients exhibited a significantly higher mean alkaline phosphatase level (275.81 ± 61.50 IU/l) compared to male patients (162.19 ± 32.36 IU/l), with a statistically significant difference ($p=0.02^*$). Total protein (g/dl), Albumin (g/dl), and Globulin (g/dl): There were no significant differences observed in the mean levels of total protein, albumin, and globulin between male and female patients

Conclusion: Scrub typhus should be considered in the differential diagnosis of acute febrile illness in both male and female patients due to the lack of significant differences in laboratory values.

Keywords: Acute febrile illness, Scrub typhus, *Orientia tsutsugamushi*, ELISA, Laboratory tests

Introduction

Scrub typhus, caused by the bacterium *Orientia tsutsugamushi*, is an acute febrile zoonotic disease transmitted to humans and rodents by certain species of trombiculid mites [1]. The seasonal incidence of scrub typhus varies according to climatic conditions in different regions, with epidemics typically occurring during the rainy season due to increased mite activity [2]. Despite its prevalence, scrub typhus remains significantly underdiagnosed in India due to its nonspecific clinical manifestations, limited awareness among healthcare providers, low suspicion index, and inadequate diagnostic facilities. [3] The disease is more commonly

observed among individuals engaged in farming, labor-intensive occupations, and those exposed to soil [4]. Typical features of scrub typhus include a primary necrotic lesion known as eschar, generalized lymphadenopathy, rash, and nonspecific symptoms such as fever, headache, myalgia, and cough [5]. Severe complications may arise, including prominent encephalitis, interstitial pneumonia, acute respiratory distress syndrome (ARDS), myocarditis, pericarditis, cardiac arrhythmias, acute renal failure, acute hepatic failure, and acute hearing loss [4]. Notably, ARDS is a grave complication associated with scrub typhus [4]. In India, scrub typhus has been documented in various states, including Tamil Nadu, Himachal Pradesh, Jammu, Pondicherry, Andhra Pradesh, Kerala, and Meghalaya, among others [6-11]. Recent studies underscore the significance of scrub typhus as a cause of acute undiagnosed febrile illness in India. Various types of samples are collected for laboratory investigations, but few studies have been conducted in Karimnagar, and no literature comparing male and female laboratory results was found. Therefore, this retrospective study was designed to compare the laboratory findings of scrub typhus patients based on gender.

Material and Methods

This retrospective study was conducted by the Department of Microbiology Prathima Institute of Medical Sciences, Naganoor, Karimnagar. Institutional Ethical approval was obtained for the study. The retrospective data was analyzed from MRD for patients admitted to the intensive care unit of a tertiary care teaching hospital in Karimnagar. Following approval from the institutional ethics committee, medical records of undiagnosed acute febrile illness patients admitted during the rainy season were scrutinized. Only patients diagnosed with scrub typhus were included in the study, while those diagnosed with malaria, leptospirosis, dengue fever, viral infections, enteric fever, or urinary tract infections were excluded. The diagnosis was primarily based on clinical features, further confirmed by testing for specific IgM antibodies against *O. tsutsugamushi* using a commercial ELISA kit.

Laboratory data from all diagnosed patients were analyzed, including hemoglobin, blood counts, serum chemistry (blood sugar, serum creatinine, bilirubin, albumin, SGOT/SGPT, creatinine, and electrolytes), as well as chest radiographs and ECG results. Treatment for all diagnosed scrub typhus patients consisted of doxycycline initially, with azithromycin added if an inadequate response was observed.

Statistical analysis: All the available data was uploaded to an MS Excel spreadsheet and analyzed by SPSS version 15 in Windows format. The continuous variables were expressed as Mean \pm SD and percentage, and the chi-square test and unpaired Student's t-test were employed for data comparison when applicable. The values of p (<0.05) were considered as significant.

Results

Table 1 presents the laboratory results of scrub typhus patients categorized by gender. The table includes various laboratory investigations along with the mean values and standard deviations for male patients ($n=21$), female patients ($n=19$), and the total number of patients ($n=40$). Additionally, the table provides the p -values, indicating the statistical significance of the observed differences between male and female patients.

Table 1: Laboratory results in scrub typhus patients with respect to gender.

Laboratory investigations	Male (n=21)	Female (n=19)	Total patients (n=40)	P value
Mean age	41.25 ± 5.25	38.64 ± 7.65	---	0.156
Haemoglobin (g/dl)	10.99 ± 3.61	9.65 ± 2.18	10.05 ± 3.5	0.02*
Total leucocyte count (/µl)	7550.83 ± 3589.02	7893.36 ± 2915.30	7715.33 ± 3732.91	0.54
Platelets (mm ³)	49551 ± 23347.67	98654 ± 71365.07	85369.27 ± 7232.17	0.032*
Random blood sugar (mg/dl)	103.25 ± 27.62	110.22 ± 30.12	107.35 ± 22.17	0.46
Blood urea (mg/dl)	94.52 ± 40.21	71.22 ± 38.85	81.28 ± 39.55	0.021
Serum creatinine	2.32 ± 1.42	1.37 ± 1.02	1.91 ± 1.2	0.06
Na (mmol/l)	129.19 ± 5.24	131.27 ± 7.35	130.51 ± 6.34	0.05*
K (mmol/l)	3.71 ± 0.90	4.00 ± 1.20	3.90 ± 1.1	0.240

The mean age of male patients was 41.25 years (± 5.25), while for female patients, it was 38.64 years (± 7.65). However, the difference in age between male and female patients was not statistically significant ($p=0.156$). Haemoglobin (g/dl): Male patients had a significantly higher mean hemoglobin level (10.99 ± 3.61 g/dl) compared to female patients (9.65 ± 2.18 g/dl) ($p=0.02^*$). Total leukocyte count (/µl): There was no statistically significant difference in the total leukocyte count between male and female patients ($p=0.54$). Platelets (mm³): Female patients exhibited significantly higher platelet counts ($98,654 \pm 71,365.07$ mm³) compared to male patients ($49,551 \pm 23,347.67$ mm³) ($p=0.032^*$). Random blood sugar (mg/dl): No significant difference in random blood sugar levels was observed between male and female patients ($p=0.46$). Blood urea (mg/dl): Male patients had a significantly higher mean blood urea level (94.52 ± 40.21 mg/dl) compared to female patients (71.22 ± 38.85 mg/dl) ($p=0.021$). Serum creatinine: Although male patients had a higher mean serum creatinine level (2.32 ± 1.42 mg/dl) compared to female patients (1.37 ± 1.02 mg/dl), the difference was not statistically significant ($p=0.06$). Na (mmol/l): There was a marginally significant difference in serum sodium levels between male and female patients ($p=0.05^*$), with male patients having a slightly lower mean level (129.19 ± 5.24 mmol/l) compared to female patients (131.27 ± 7.35 mmol/l). K (mmol/l): No significant difference in serum potassium levels was observed between male and female patients ($p=0.240$).

Table 2 presents the laboratory findings of scrub typhus patients Serum bilirubin (mg/dl): The mean serum bilirubin level was higher in male patients (4.01 ± 1.90 mg/dl) compared to female patients (2.39 ± 1.22 mg/dl), with a slight difference that did not reach statistical significance ($p=0.06$). SGOT (IU/l) and SGPT (IU/l): There were no statistically significant differences in the mean levels of serum glutamate oxaloacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT) between male and female patients ($p=0.132$ and $p=0.74$, respectively).

Table 2: Laboratory results in scrub typhus patients

Parameters	Male (n=21)	Female (n=19)	Total patients (n=40)	P value
Serum bilirubin (mg/dl)	4.01 ± 1.90	2.39 ± 1.22	3.64 ± 1.49	0.06
SGOT (IU/l)	301.34 ± 122.34	219.64 ± 109.76	267 ± 115.36	0.132
SGPT (IU/l)	119.21 ± 53.21	132.32 ± 62.06	124.72 ± 64.18	0.74
Alkaline phosphatase(IU/l)	162.19 ± 32.36	275.81 ± 61.50	264.37 ± 49.48	0.02*
Total protein (g/dl)	4.32 ± 0.75	5.51 ± 0.67	4.85 ± 0.69	0.71
Albumin (g/dl)	2.19 ± 0.52	2.34 ± 0.31	2.22 ± 0.41	0.84
Globulin (g/dl)	3.16 ± 0.42	3.28 ± 0.62	3.21.32 ± 0.52	0.31

Alkaline phosphatase (IU/l): Female patients exhibited a significantly higher mean alkaline phosphatase level (275.81 ± 61.50 IU/l) compared to male patients (162.19 ± 32.36 IU/l), with a statistically significant difference (p=0.02*). Total protein (g/dl), Albumin (g/dl), and Globulin (g/dl): There were no significant differences observed in the mean levels of total protein, albumin, and globulin between male and female patients (p=0.71, p=0.84, and p=0.31, respectively).

Table 3: Laboratory results in scrub typhus patients

Parameters	Male (n=21)	Female (n=19)	Total patients (n=40)	P value
PT (sec)	16.95 ± 2.90	16.58 ± 2.25	16.81 ± 2.48	0.414
aPTT (sec)	47.59 ± 20.21	37.84 ± 10.96	52.32 ± 15.54	0.21
INR ratio	1.51 ± 0.47	1.22 ± 0.30	1.33 ± 0.40	0.32
Ca (mg/dl)	7.03 ± 0.67	7.15 ± 0.76	7.09 ± 0.71	0.78
Mg (mmol/l)	2.75 ± 0.60	2.44 ± 0.49	2.67 ± 0.51	0.26
Phosphate (mg/dl)	4.21 ± 2.10	3.32 ± 1.12	3.81 ± 1.96	0.19
PaO ₂ / FiO ₂ ratio	262.10 ± 48.76	259.40 ± 32.33	260.32 ± 34.66	0.94

Table 3 displays the laboratory results of scrub typhus patients. PT (sec) - Prothrombin Time: The mean prothrombin time was comparable between male (16.95 ± 2.90 sec) and female patients (16.58 ± 2.25 sec), with no statistically significant difference observed (p=0.414). aPTT (sec) - Activated Partial Thromboplastin Time: There was no statistically significant difference in the mean activated partial thromboplastin time between male (47.59 ± 20.21 sec) and female patients (37.84 ± 10.96 sec), with a p-value of 0.21. INR Ratio - International Normalized Ratio: The mean INR ratio was slightly higher in male patients (1.51 ± 0.47) compared to female patients (1.22 ± 0.30), but the difference was not statistically significant (p=0.32). Ca (mg/dl) - Calcium: No significant difference was observed in the mean calcium levels between male (7.03 ± 0.67 mg/dl) and female patients (7.15 ± 0.76 mg/dl), with a p-value of 0.78. Mg (mmol/l) Magnesium: The mean magnesium levels showed no statistically significant difference between male (2.75 ± 0.60 mmol/l) and female patients (2.44 ± 0.49 mmol/l), with a p-value of 0.26. Phosphate (mg/dl): The mean phosphate levels were comparable between male (4.21 ± 2.10 mg/dl) and female patients (3.32 ± 1.12 mg/dl), with no statistically significant difference observed (p=0.19). PaO₂/FiO₂ Ratio - Oxygenation Ratio:

The mean PaO₂/FiO₂ ratio was similar between male (262.10 ± 48.76) and female patients (259.40 ± 32.33), with no statistically significant difference (p=0.94).

Discussion

Early detection plays a crucial role in the management of scrub typhus patients as they typically respond well to antimicrobial therapy. [12] In regions with limited diagnostic capabilities, it is advisable to initiate empirical treatment in individuals presenting with undifferentiated febrile illnesses and evidence of multi-system involvement. Using a combination of elevated liver enzymes, thrombocytopenia, and leukocytosis can yield a specificity and positive predictive value for scrub typhus diagnosis of approximately 80%. [13] Our analysis aimed to examine the laboratory findings of both male and female patients. In our study, out of a total of 40 patients diagnosed with scrub typhus via ELISA testing, there was no significant disparity between male and female patients. Similar findings were reported in a study conducted in Thailand. However, some studies have suggested a male predominance, while others have indicated a higher incidence in females after the age of 30. The discrepancy observed in our study could be attributed to the rural origins of most patients, as both males and females are extensively involved in farming and fieldwork in Rajasthan, India, thereby increasing exposure to scrub typhus.

Among the 40 diagnosed patients in our study, 2(3.33%) fatalities occurred. Comparable mortality rates have been documented in previous studies, ranging from 0% to 30%. Factors contributing to this broad range of mortality may include patient age, geographic region of infection, and missed or delayed diagnoses. Laboratory analyses revealed altered values in both male and female patients, with a more significant incidence of thrombocytopenia in males and lower serum sodium levels in males compared to females. Additionally, elevated serum alkaline phosphatase levels were more prevalent in females. All diagnosed patients exhibited thrombocytopenia, elevated liver enzymes (SGOT, SGPT, alkaline phosphatase), decreased albumin, raised bilirubin, and creatinine levels, indicating multi-organ involvement in scrub typhus cases. [14] The PaO₂/FiO₂ ratio, indicative of acute respiratory distress syndrome (ARDS), ranged between 200 and 300, suggesting respiratory involvement. Elevated SGOT and SGPT levels were observed in all patients, while alkaline phosphatase elevation was noted in 66.67% of patients, particularly more prevalent in females. Previous studies have also highlighted the correlation between elevated hepatic enzyme levels and scrub typhus, reporting increased levels in 74.5% to 96.3% of patients for SGOT, 66.7% to 91.7% for SGPT, and 57.4% to 84.2% for alkaline phosphatase.

There were no statistically significant differences in the mean levels of serum glutamate oxaloacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT) between male and female patients (p=0.132 and p=0.74, respectively). Alkaline phosphatase (IU/l): Female patients exhibited a significantly higher mean alkaline phosphatase level (275.81 ± 61.50 IU/l) compared to male patients (162.19 ± 32.36 IU/l), with a statistically significant difference (p=0.02*).

Conclusion

In conclusion, scrub typhus affects both male and female patients without significant discrepancies in their laboratory parameters. Therefore, when encountering patients with acute febrile illnesses during the rainy season, scrub typhus should be considered in the differential diagnosis for both genders.

References

1. Chakraborty S, Sarma N. Scrub Typhus: An Emerging Threat. *Indian J Dermatol*. 2017 Sep-Oct;62(5):478-485.
2. Xu G, Walker DH, Jupiter D, Melby PC, Arcari CM. A review of the global epidemiology of scrub typhus. *PLoS Negl Trop Dis*. 2017 Nov 3;11(11):e0006062.
3. Mohanty A, Kabi A, Gupta P, Jha MK, Rekha US, Raj AK. Scrub typhus - A case series from the state of Sikkim, India. *Int J Crit Illn Inj Sci*. 2019 Oct-Dec;9(4):194-198.
4. Wang CC, Liu SF, Liu JW, Chung YH, Su MC, Lin MC. Acute respiratory distress syndrome in scrub typhus. *Am J Trop Med Hyg*. 2007; 76:1148-52.
5. 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 N Y Acad Sci*. 2003; 990:359-64.
6. Varghese GM, Trowbridge P, Janardhanan J, Thomas K, Peter JV, Mathews P, Abraham, et al. Clinical profile and improving mortality trend of scrub typhus in South India. *Int J Infect Dis*. 2014. Jun; 23:39-43.
7. Bal M, Mohanta MP, Sahu S, Dwivedi B, Pati S, Ranjit M. Profile of Pediatric Scrub Typhus in Odisha, India. *Indian Pediatr*. 2019. Apr 15;56(4):304-306.
8. Vivekanandan M, Mani A, Priya YS, Singh AP, Jayakumar S, Purty S. Outbreak of scrub typhus in Pondicherry. *J Assoc Physicians India*. 2010; 58:24- 8.
9. 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; 8:208-10.
10. Narvencar KPS, Rodrigues S, Nevrekar RP, Dias L, Dias A, Vaz M, et al. Scrub typhus in patients reporting with acute febrile illness at a tertiary health care institution in Goa. *Indian J Med Res*. 2012. Dec;136(6):1020-24.
11. Devasagayam E, Dayanand D, Kundu D, Kamath MS, Kirubakaran R, Varghese GM. The burden of scrub typhus in India: A systematic review. *PLoS Negl Trop Dis*. 2021 Jul 27;15(7): e0009619.
12. Kala D, Gupta S, Nagraik R, Verma V, Thakur A, Kaushal A. Diagnosis of scrub typhus: recent advancements and challenges. *3 Biotech*. 2020 Sep;10(9):396.
13. Chogle AR. Diagnosis and treatment of scrub typhus: The Indian scenario. *J Assoc Physicians India*. 2010; 58:11-12.
14. Kumar BA, Kumar AS, Sharvanan E. Rhabdomyolysis in scrub typhus: an unusual presentation. *Int J Prev Med*. 2013 Dec;4(12):1472-75.
15. Chanta C, Triratanapa K, Ratanasirichup P, Mahaprom W. Hepatic dysfunction in pediatric scrub typhus: role of liver function test in diagnosis and marker of disease severity. *J Med Assoc Thai*. 2007; 90:2366-69.
16. Hu ML, Liu JW, Wu KL, Lu SN, Chios SS, Kuo CH, et al. Short report: abnormal liver function in scrub typhus. *Am J Trop Med Hyg*. 2005;73: 667-68.
17. Yang CH, Hsu GJ, Peng MY, Young TG. Hepatic dysfunction in scrub typhus. *J Formos Med Assoc*. 1995; 94:101-05.