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A study of peripheral smear findings along with haematological and biochemical parameters in assessing morbidity among seropositive scrub typhus cases at a tertiary care centre: A cross-sectional study.

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Abstract

Background:

Scrub typhus, caused by *Orientia tsutsugamushi*, is a re-emerging rickettsial infection characterized by systemic vasculitis and multi-organ involvement. Haematological and biochemical abnormalities are frequently observed and may help in assessing disease morbidity. This study aimed to evaluate peripheral smear findings along with haematological and biochemical parameters in seropositive scrub typhus cases and correlate them with clinical severity.

Methods:

A cross-sectional study was conducted in the Department of Pathology, Sri Venkateswara Ramnarayan Ruia Government General Hospital, Tirupati, over nine months. A total of 45 serologically confirmed scrub typhus cases were included. Complete blood counts were performed using a five-part haematology analyser, ERBA Elite 580. Peripheral blood smears were stained with Leishman stain and examined for morphological changes. Liver and renal function tests were analysed using ERBA XL-640. Associations between laboratory abnormalities and morbidity were assessed using the odds ratio and Fisher's exact test.

Results:

Most cases occurred between October and December. Males constituted 60% and females 40% of cases. Common haematological abnormalities included thrombocytopenia (66.7%), leucocytosis (35.6%), and neutrophilia with toxic granulation or cytoplasmic vacuolation (31.1%). Biochemical abnormalities included elevated AST (57.8%), ALT (53.3%), hyperbilirubinaemia (40.0%), and raised serum creatinine (20.0%). Severe thrombocytopenia was strongly associated with morbidity (OR 9.75, 95% CI 2.01–47.2; p = 0.001). Significant associations were also observed for elevated transaminases (OR 4.20, 95% CI 1.58–11.1; p = 0.003), hyperbilirubinaemia (OR 3.68, 95% CI 1.22–9.80; p = 0.022), raised serum creatinine (OR 6.10, 95% CI 1.85–20.4; p < 0.001), and neutrophilia with toxic changes (OR 2.95, 95% CI 1.05–8.40; p = 0.020).

Conclusion:

Integrated evaluation of peripheral smear, haematological, and biochemical parameters provides a rapid and cost-effective approach for predicting morbidity in scrub typhus.

Recommendations:

Routine peripheral smear, platelet count, liver, and renal parameters should guide early morbidity assessment in scrub typhus.

Keywords: *Scrub typhus, peripheral smear, thrombocytopenia, hepatic dysfunction, renal impairment, morbidity predictors.*
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Introduction

Scrub typhus is an acute febrile zoonotic illness caused by *Orientia tsutsugamushi*, an obligate intracellular Gram-negative bacterium transmitted to humans through the bite of infected larval trombiculid mites, commonly known as chiggers. The disease is widely distributed within the tsutsugamushi triangle, which extends across South and Southeast Asia, the Western Pacific region, and northern Australia [1]. In India, scrub typhus has re-emerged as an important cause of acute undifferentiated febrile illness, particularly in rural and semi-urban populations. Its occurrence is commonly reported during and after the monsoon season, when environmental conditions favour mite activity and human exposure [2,3].

The clinical spectrum of scrub typhus is broad, ranging from a self-limiting febrile illness to severe disease with multi-organ involvement. Patients usually present with fever, headache, myalgia, malaise, and, in some cases, a characteristic eschar at the site of a mite bite. However, the eschar may be absent or overlooked, especially in dark-skinned individuals or when located in covered body areas, which may delay clinical suspicion and diagnosis. Untreated or late-diagnosed scrub typhus may progress to serious complications such as acute respiratory distress syndrome, myocarditis, meningoencephalitis, acute kidney injury, hepatic dysfunction, shock, and disseminated intravascular coagulation [4,5]. Mortality in untreated cases has been reported to vary considerably, emphasizing the need for early recognition, timely treatment, and assessment of disease severity [6].

Laboratory evaluation plays a crucial role in diagnosis, severity assessment, and monitoring of scrub typhus. Haematological abnormalities such as thrombocytopenia, leukocytosis or leukopenia, neutrophilia, and reactive lymphocytosis have been reported in scrub typhus, particularly in patients with severe disease [6]. Peripheral blood smear examination may reveal important morphological changes, including neutrophils with toxic granulations and cytoplasmic vacuolations, reactive lymphocytes, and platelet reduction. Although peripheral smear examination is simple, rapid, and inexpensive, it is often underutilized in routine evaluation. When interpreted along with complete blood count parameters, it may provide early clues regarding systemic inflammation, sepsis-like response, platelet consumption, or impending complications.

Biochemical abnormalities are also frequently observed in scrub typhus and may reflect multi-organ involvement. Elevated serum transaminases, hyperbilirubinemia, hypoalbuminemia, raised serum creatinine, and other indicators of hepatic and renal dysfunction have been associated with increased disease severity and morbidity [7, 8]. These changes are clinically relevant because they may precede overt organ failure and assist in identifying patients who require closer monitoring, intensive care support, or early therapeutic intervention.

In resource-limited settings, the combined assessment of peripheral smear findings, haematological indices, and biochemical parameters can serve as a practical and cost-effective approach for evaluating morbidity in scrub typhus. Such an integrated laboratory profile may help clinicians recognize severe disease at an early stage, guide appropriate management, reduce complications, and improve patient outcomes. Considering the increasing burden of scrub typhus in India and its potential to cause significant morbidity, there is a need to identify simple and reliable laboratory markers that correlate with clinical severity.

The present study was undertaken to evaluate peripheral smear findings, including thrombocytopenia, neutrophils with toxic granulations and cytoplasmic vacuolations, and reactive lymphocytes, along with haematological and biochemical parameters in seropositive scrub typhus cases. The study further aimed to correlate these laboratory findings with clinical morbidity among patients admitted to a tertiary care centre.

Materials and Methods

Study Design and Setting

This hospital-based cross-sectional observational study was conducted in the Department of Pathology and the Clinical Pathology Central Laboratory at Sri Venkateswara Ramnarayan Ruia Government General Hospital (SVRRGGH), Tirupati, Andhra Pradesh. SVRRGGH is a government teaching and tertiary referral hospital affiliated with S. V. Medical College. It provides round-the-clock emergency care and comprehensive outpatient, inpatient, intensive care, medical, surgical, paediatric, obstetric, and diagnostic laboratory services to patients from Tirupati and the surrounding districts of the Rayalaseema region. The study was conducted over 12 months, from January 2025 to December 2025.

Study Size

A census-based consecutive sampling approach was used. Because scrub typhus is seasonal and the number of seropositive admissions during the fixed study period could not be predicted reliably, a separate prevalence-based sample-size calculation was not undertaken. All 45 patients who met the eligibility criteria and had complete clinical and laboratory data during the prespecified nine-month period

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were included. Therefore, the final study size represented the entire accessible population of confirmed cases available at the study centre during the study period.

Study Population

The study population comprised patients of all age groups who presented to Sri Venkateswara Ramnarayan Ruia Government General Hospital, Tirupati, with acute febrile illness during the study period. Patients who were serologically confirmed to be positive for scrub typhus by detection of *Orientia tsutsugamushi* IgM antibodies using ELISA were considered eligible for inclusion.

A total of 45 seropositive scrub typhus cases fulfilling the inclusion criteria were enrolled in the study. Patients with evidence of concurrent infections such as dengue, leptospirosis, malaria, or typhoid fever, and pregnant women, were excluded.

Inclusion Criteria

Patients of all age groups presenting with acute febrile illness and serologically confirmed to be positive for scrub typhus by detection of *Orientia tsutsugamushi* IgM antibodies using ELISA were included in the study. Only patients admitted to the tertiary care centre during the study period, and those with available clinical and laboratory data, were considered for analysis.

Exclusion Criteria

Patients with evidence of concurrent infections such as dengue fever, leptospirosis, malaria, or typhoid fever, confirmed by appropriate laboratory or serological tests, were excluded from the study. Pregnant women, patients with acute febrile illness but negative scrub typhus serology, and cases with incomplete clinical or laboratory records were also excluded.

Data Collection

Relevant clinical details, including presenting symptoms, signs of organ involvement, complications, and requirement for intensive care unit admission, were recorded from patient case sheets and laboratory records.

Venous blood samples were collected aseptically from each patient in two vacutainers. One sample was collected in an ethylenediaminetetraacetic acid vacutainer for haematological analysis, and another was collected in a plain tube for serum separation and biochemical investigations. All samples were processed in the central laboratory under standard biosafety precautions.

Laboratory Investigations

Haematological Investigations

Complete blood count analysis was performed using an automated five-part haematology analyser, ERBA Elite 580. The parameters recorded included haemoglobin concentration, total leukocyte count, differential leukocyte count, and platelet count.

Peripheral blood smears were prepared from EDTA-anticoagulated blood samples and stained with Leishman stain. Each smear was examined by a qualified pathologist. The smear findings assessed included red cell morphology, leukocyte abnormalities, neutrophils showing toxic granulations and cytoplasmic vacuolations, reactive lymphocytes, platelet clumping, and platelet reduction.

Biochemical Investigations

Liver function tests and renal function tests were performed using a fully automated biochemical analyser, ERBA XL-640. The biochemical parameters assessed included total bilirubin, total protein, serum albumin, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, blood urea, and serum creatinine. Abnormal values were interpreted according to standard laboratory reference ranges.

Morbidity Assessment

Clinical morbidity was assessed based on the presence of organ dysfunction and/or requirement for intensive care unit admission. Laboratory parameters were correlated with clinical findings such as bleeding manifestations, jaundice, oliguria, rash, and respiratory distress to evaluate disease severity.

The following laboratory variables were analysed for their association with morbidity: thrombocytopenia, defined as platelet count less than 1.5 lakh/mm^3; severe thrombocytopenia, defined as platelet count less than 50,000/mm^3; elevated transaminases, defined as AST or ALT greater than 40 IU/L; raised serum creatinine, defined as serum creatinine greater than 1.2 mg/dL; and hyperbilirubinemia, defined as total bilirubin greater than 1.2 mg/dL.

Ethical Considerations

The study was conducted after obtaining approval from the Institutional Scientific and Ethics Committee of S. V. Medical College, Tirupati, Andhra Pradesh, India. All procedures followed in the study were in accordance with institutional ethical standards and the principles of biomedical research involving human participants.

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Informed Consent

Written informed consent was obtained from all adult participants before enrolment. For participants younger than 18 years, written consent was obtained from a parent or legally authorised guardian, with age-appropriate assent wherever applicable. Participants were informed about the study purpose, procedures, confidentiality safeguards, voluntary participation, and their right to withdraw without any effect on clinical care.

Bias

Consecutive enrolment of all eligible seropositive cases during the study period was used to reduce selection bias. Predefined inclusion and exclusion criteria were applied uniformly. Haematological and biochemical analyses were performed using standardised automated analysers with routine internal quality-control procedures. Peripheral smears were examined by qualified pathologists using predefined morphological criteria, and clinical information was extracted with a structured data collection format. Cases with concurrent infections or incomplete records were excluded to reduce confounding and information bias. Data entries were cross-checked before analysis, and identical morbidity definitions and laboratory cut-offs were applied to all participants.

Statistical Analysis

Data were compiled using Microsoft Excel and analysed using JASP version 0.18.3. Descriptive statistics were used to summarise the data. Continuous variables were expressed as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages. The association between laboratory parameters and morbidity outcomes was assessed using the odds ratio and Fisher's exact test, wherever appropriate. A p-value of less than 0.05 was considered statistically significant.

Results

Participant Flow

During the study period, 45 potentially eligible seropositive scrub typhus cases were identified and assessed for eligibility. All 45 fulfilled the prespecified eligibility criteria, had complete clinical and laboratory data, and provided informed consent. No confirmed case was excluded after eligibility assessment. Consequently, 45 participants were enrolled, and all 45 were included in the final analysis (Figure 5).

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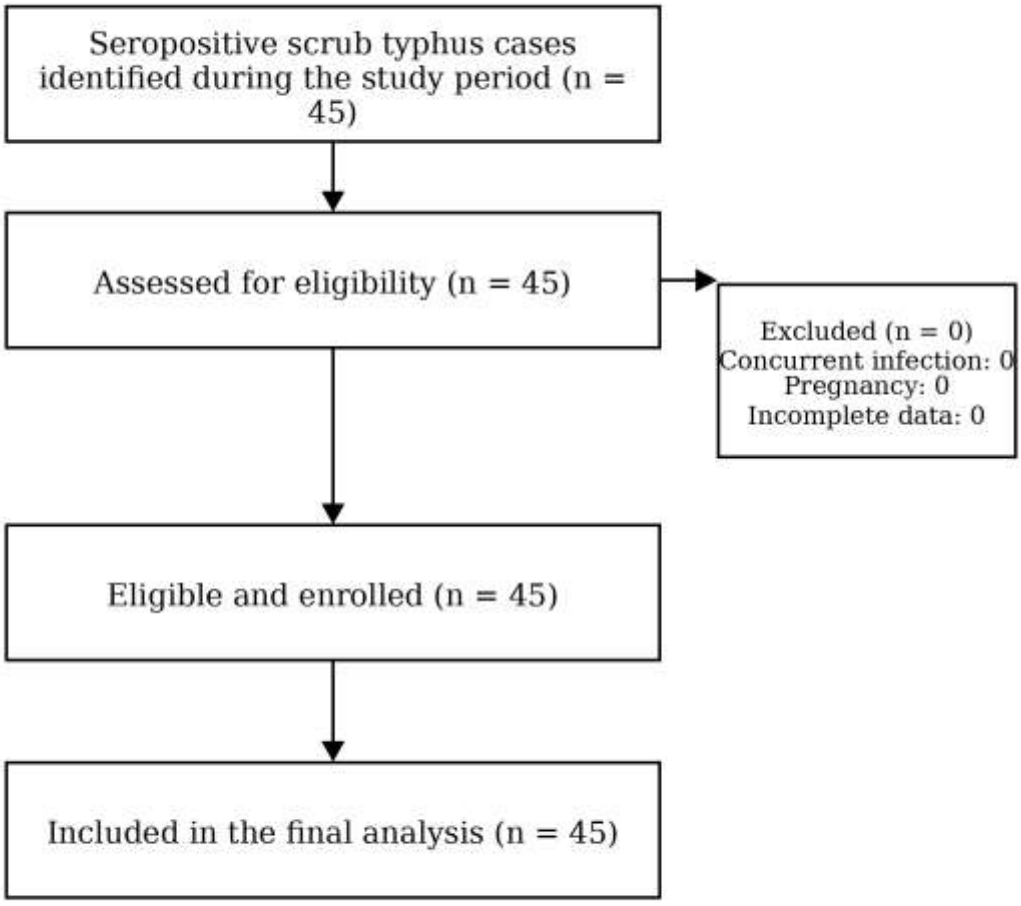

Figure 5. Participant flow through the study.

Demographic and Seasonal Distribution

A total of 45 serologically confirmed scrub typhus cases were included in the study. The demographic and seasonal profile is shown in Table 1. The highest number of cases was observed in the 31–45 years age group [15 cases, 33.3%], followed by the 16–30 years age group [12 cases, 26.7%]. Male patients constituted 27 cases [60.0%], while females accounted for 18 cases [40.0%], giving a male-to-female ratio of 1.5:1.

Seasonal distribution, as presented in Table 1, showed maximum case occurrence during October–December [22 cases, 48.9%], followed by January–March [9 cases, 20.0%]. This indicates a clear post-monsoon clustering of scrub typhus cases.

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Table 1: Demographic and seasonal distribution of seropositive scrub typhus cases [n = 45]

Variable	Category	Frequency [n]	Percentage [%]
Age group [years]	1–15	4	8.9
	16–30	12	26.7
	31–45	15	33.3
	46–60	9	20.0
	>60	5	11.1
Sex	Male	27	60.0
	Female	18	40.0
Season of occurrence	October–December	22	48.9
	January–March	9	20.0
	April–June	6	13.3
	July–September	8	17.8

Haematological Profile

The haematological abnormalities observed among scrub typhus patients are summarized in Table 2. Thrombocytopenia was the most frequent abnormality, noted in 30 cases [66.7%]. Leucocytosis was observed in 16 cases [35.6%], whereas leucopenia was seen in 6 cases [13.3%]. Anaemia, defined as haemoglobin <10 g/dL, was present in 10 cases [22.2%].

Severe thrombocytopenia, defined as platelet count <50,000/mm³, was observed in 8 cases [17.8%], indicating a clinically important subgroup with increased risk of morbidity.

Table 2: Haematological abnormalities among seropositive scrub typhus cases

Haematological parameter	Abnormal cases [n]	Percentage [%]
Haemoglobin <10 g/dL	10	22.2
Total leukocyte count <4,000/mm³	6	13.3
Total leukocyte count >11,000/mm³	16	35.6
Platelet count <1.5 lakh/mm³	30	66.7
Severe thrombocytopenia <50,000/mm³	8	17.8

Biochemical Parameters

Biochemical derangements are presented in Table 3. Liver function abnormalities were common among the study population. Raised SGOT/AST >40 IU/L was observed in 26 cases [57.8%], while raised SGPT/ALT >40 IU/L was seen in 24 cases [53.3%]. Hyperbilirubinaemia was present in 18 cases [40.0%].

Hypoalbuminaemia was noted in 15 cases [33.3%], and low total protein was observed in 10 cases [22.2%]. Renal involvement, indicated by serum creatinine

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>1.2 mg/dL, was found in 9 cases [20.0%]. Raised alkaline phosphatase was seen in 10 cases [22.2%].

Table 3: Biochemical abnormalities among seropositive scrub typhus cases

Biochemical parameter	Abnormal cases [n]	Percentage [%]
Total bilirubin >1.2 mg/dL	18	40.0
Total protein <6 g/dL	10	22.2
Serum albumin <3.5 g/dL	15	33.3
SGOT/AST >40 IU/L	26	57.8
SGPT/ALT >40 IU/L	24	53.3
Alkaline phosphatase >120 IU/L	10	22.2
Serum creatinine >1.2 mg/dL	9	20.0

Peripheral Smear Findings

Peripheral smear findings are shown in Table 4. Thrombocytopenia was the most common smear finding, observed in 30 cases [66.7%]. Leucocytosis was seen in 16 cases [35.6%]. Neutrophilia with toxic granulation and/or cytoplasmic vacuolation was observed in 14 cases [31.1%], while reactive lymphocytes were identified in 13 cases [28.9%].

Mild anaemia with hypochromic red cell morphology was present in 10 cases [22.2%]. Platelet clumping, suggestive of pseudothrombocytopenia, was observed in 5 cases [11.1%].

Table 4: Peripheral smear findings in seropositive scrub typhus cases

Peripheral smear finding	Cases [n]	Percentage [%]
Mild anaemia / hypochromia	10	22.2
Leucocytosis	16	35.6
Neutrophilia with toxic granulation/vacuolation	14	31.1
Reactive lymphocytes	13	28.9
Thrombocytopenia	30	66.7
Platelet clumping / pseudothrombocytopenia	5	11.1

Figure 1 shows neutrophilia, indicated by an increased number of neutrophils in the peripheral smear. Neutrophilia reflects acute inflammatory or infective response and may be seen in patients with scrub typhus presenting with systemic illness. Figure 2 shows neutrophils with toxic granulations and cytoplasmic vacuolation. These are reactive morphological changes usually associated with severe infection, sepsis-like response, or intense inflammatory stimulation. Their presence may suggest increased disease activity and possible morbidity. Figure 3 shows reactive lymphocytes, which indicate immune activation during acute infection. Reactive lymphocytes are commonly seen in infectious conditions and may support the diagnosis when correlated with clinical and serological findings. Figure 4 shows severe thrombocytopenia, demonstrated by a marked reduction in platelet number on the smear. This is an important finding in scrub typhus because severe thrombocytopenia may be associated with bleeding risk, organ dysfunction, and increased morbidity.

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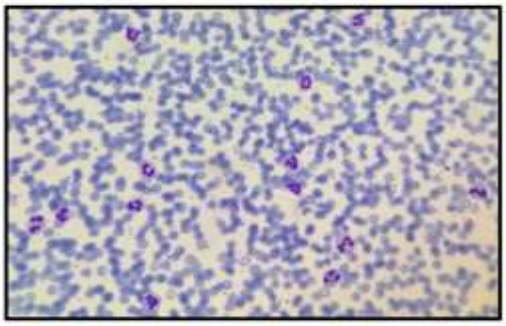
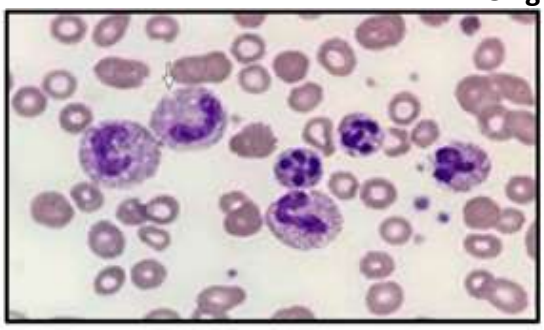


Figure- 1



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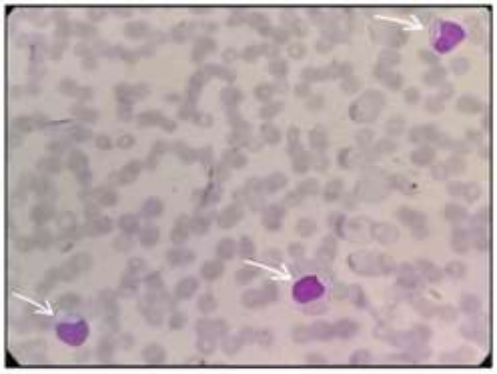

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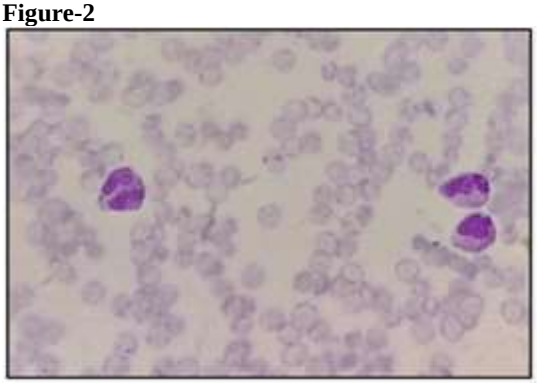

Figure- 4

Figure 1–4: Peripheral blood smear findings in seropositive scrub typhus cases.

Figure 1: Peripheral blood smear showing neutrophilia, Leishman stain, 40X; Figure 2: Peripheral blood smear showing neutrophils with toxic granulations and cytoplasmic vacuolation. Leishman stain, 100X; Figure 3: Peripheral blood smear showing reactive lymphocytes, Leishman stain, 100X; Figure 4: Peripheral blood smear showing severe thrombocytopenia, Leishman stain, 100X.

Correlation of Laboratory Parameters with Morbidity

The association between laboratory abnormalities and morbidity is shown in Table 5. Morbidity was defined by severe scrub typhus requiring intensive care unit admission and/or evidence of organ dysfunction. Severe thrombocytopenia showed the strongest association with morbidity. Among patients with platelet count <50,000/mm³, 5 out of 8 cases [62.5%] had morbidity, with an odds ratio of 9.75 [95% CI: 2.01–47.2; p = 0.001].

Raised serum creatinine was also significantly associated with morbidity, with 4 out of 9 cases [44.4%] showing morbidity [OR: 6.10; 95% CI: 1.85–20.4; p <0.001]. Elevated transaminases were present in 26 cases, of which 11 cases [42.3%] had morbidity [OR: 4.20; 95% CI: 1.58–11.1; p = 0.003].

Hyperbilirubinaemia, leucocytosis, and neutrophilia with toxic changes also showed statistically significant associations with morbidity, as detailed in Table 5.

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Table 5: Correlation between laboratory abnormalities and morbidity in seropositive scrub typhus cases

Laboratory abnormality	Abnormal cases [n]	Morbidity present n [%]	Morbidity absent n [%]	Odds ratio [95% CI]	p-value
Severe thrombocytopenia <50,000/mm³	8	5 [62.5]	3 [37.5]	9.75 [2.01–47.2]	0.001
Transaminases AST/ALT >40 IU/L	26	11 [42.3]	15 [57.7]	4.20 [1.58–11.1]	0.003
Serum creatinine >1.2 mg/dL	9	4 [44.4]	5 [55.6]	6.10 [1.85–20.4]	<0.001
Total bilirubin >1.2 mg/dL	18	8 [44.4]	10 [55.6]	3.68 [1.22–9.80]	0.022
Leucocytosis >11 × 10³/mm³	16	7 [43.8]	9 [56.2]	3.25 [1.01–8.90]	0.040
Neutrophilia with toxic changes	14	6 [42.9]	8 [57.1]	2.95 [1.05–8.40]	0.020

Discussion

The present study evaluated the role of peripheral smear findings, haematological parameters, and biochemical abnormalities in assessing morbidity and disease severity among seropositive scrub typhus patients admitted to a tertiary care centre. A total of 45 serologically confirmed cases were included. The majority of patients belonged to the adult age group of 31–45 years, with male predominance and a male-to-female ratio of 1.5:1. This demographic pattern is comparable with previous Indian studies, where adult males in the economically active age group were more commonly affected, probably due to greater occupational and outdoor exposure to mite-infested vegetation, agricultural fields, and rural environments [9, 10]. Seasonal clustering was observed during October to December, which supports the known post-monsoon rise in scrub typhus incidence due to favourable climatic conditions for vector proliferation [11].

Haematological abnormalities were frequent in the present study and formed an important basis for assessing disease severity. Thrombocytopenia was the most common abnormality, observed in 66.7% of cases. This finding is consistent with earlier studies by Kumar et al. [10] and Itani et al. [12], who reported thrombocytopenia in 69% and 71% of cases, respectively. Kala et al. [13] also observed a comparable frequency of thrombocytopenia, indicating that platelet reduction is one of the most consistent haematological abnormalities in scrub typhus.

Severe thrombocytopenia, defined as a platelet count below 50,000/mm³, showed a significant association with morbidity in the present study. Patients with marked platelet reduction were more likely to develop bleeding manifestations, require intensive care, and have prolonged hospitalization. This suggests that severe thrombocytopenia may serve as a useful prognostic marker for identifying high-risk scrub typhus patients. The mechanism of thrombocytopenia in scrub typhus is multifactorial and may include endothelial injury, systemic vasculitis, increased platelet consumption, immune-mediated platelet destruction, and capillary leakage [14].

Leucocytosis was observed in 35.6% of cases, while leucopenia was noted in 13.3%. The frequency of leucocytosis in the present study was higher than that reported by Kumar et al. [10] and Kala et al. [13], who documented lower rates of leucocytosis. This variation may be due to differences in disease severity, timing of hospital presentation, associated secondary infections, or referral bias in tertiary care settings. Leucocytosis in scrub typhus reflects systemic inflammatory response and may indicate more severe disease when associated with organ dysfunction.

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Peripheral smear examination provided additional morphological evidence of systemic inflammation. Neutrophilia with toxic granulation and cytoplasmic vacuolation was observed in 31.1% of cases. This finding was slightly higher than the observations reported in previous studies, where toxic neutrophilic changes were documented in approximately 18–25% of cases [13]. Toxic granulation and vacuolation are indicators of acute inflammatory stress and marrow activation during infection. Their presence in scrub typhus may help distinguish bacterial or rickettsial febrile illness from uncomplicated viral infections.

Reactive lymphocytes were identified in 28.9% of peripheral smears. This proportion was also higher than that reported in some earlier studies, where reactive lymphocytes were observed in nearly 18–23% of cases [13]. Reactive lymphocytosis indicates immune activation during the acute phase of infection. When assessed together with thrombocytopenia and toxic neutrophilic changes, reactive lymphocytes may provide supportive evidence of systemic involvement.

Mild anaemia with hypochromic red cell morphology was observed in a subset of patients. Platelet clumping was also noted in some smears, highlighting the importance of peripheral smear review to exclude pseudothrombocytopenia. Thus, peripheral smear examination remains a simple, rapid, and cost-effective investigation that provides clinically useful information beyond automated cell counts.

Biochemical analysis showed hepatic and renal involvement in a considerable proportion of patients. Elevated AST and ALT levels were observed in 57.8% and 53.3% of cases, respectively. These findings are comparable with earlier studies by Jantikar et al. [15] and Kumar et al. [10], where transaminase elevation was frequently reported in scrub typhus. Hepatic dysfunction in scrub typhus may result from endothelial injury, focal hepatic necrosis, systemic vasculitis, direct rickettsial invasion, and immune-mediated inflammatory damage [13].

Hyperbilirubinaemia was observed in 40.0% of cases, while hypoalbuminaemia was present in 33.3%. These abnormalities reflect hepatic involvement, systemic inflammation, increased vascular permeability, and capillary leakage. The frequency of hyperbilirubinaemia in the present study was slightly higher than that reported in some previous studies [10]. This may be related to delayed hospital presentation, greater disease severity, or regional variation in the infecting strain of *Orientia tsutsugamushi*.

Renal dysfunction, indicated by raised serum creatinine, was observed in 20.0% of patients. This finding is comparable with earlier reports by Kala et al. [13]. Renal involvement in scrub typhus may occur due to hypovolaemia, pre-renal azotaemia, direct renal vasculitis, acute tubular injury, or multiorgan dysfunction. In the present study, raised serum creatinine showed a significant association with morbidity, suggesting that renal function assessment should be an essential part of routine evaluation in scrub typhus patients.

In the present study, severe thrombocytopenia, elevated transaminases, raised serum creatinine, hyperbilirubinaemia, leucocytosis, and neutrophilia with toxic changes showed statistically significant associations with morbidity. These findings are in agreement with the observations of Varghese et al. [9] and Vivekanandan et al. [11], who identified hepatic dysfunction, renal impairment, and haematological abnormalities as important predictors of severe scrub typhus.

Severe thrombocytopenia had the strongest association with morbidity and showed the highest odds ratio among the evaluated parameters. Patients with platelet counts below 50,000/mm^3 were more likely to have bleeding manifestations, intensive care requirements, and prolonged hospital stays. This emphasizes the importance of serial platelet monitoring in scrub typhus patients, particularly during the acute phase of illness.

Elevated transaminases were also significantly associated with morbidity. Raised AST and ALT levels may indicate hepatic involvement as well as systemic endothelial injury. Hyperbilirubinaemia further reflected more severe hepatic dysfunction and was associated with adverse clinical outcomes. Similarly, raised serum creatinine was an important marker of renal involvement and possible progression toward multiorgan dysfunction.

Peripheral smear findings, especially neutrophilia with toxic granulation and cytoplasmic vacuolation, also showed a significant association with morbidity. These changes reflect an intense systemic inflammatory response and may help identify patients at increased risk of clinical deterioration. Therefore, the combined interpretation of complete blood count, peripheral smear findings, liver function tests, and renal function tests can support early risk stratification in seropositive scrub typhus cases.

The laboratory abnormalities observed in this study are consistent with the known pathophysiology of scrub typhus. *Orientia tsutsugamushi* primarily infects endothelial cells, leading to disseminated vasculitis, microangiitis, increased vascular permeability, and multiorgan involvement [16, 17]. Endothelial damage contributes to platelet consumption, thrombocytopenia, capillary leakage, hepatic dysfunction, renal impairment, and systemic inflammation.

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Raised transaminases and serum creatinine may be considered biochemical consequences of endothelial injury in organs with rich microvascular networks, particularly the liver and kidneys. Peripheral smear findings such as toxic granulation, cytoplasmic vacuolation, and reactive lymphocytes reflect cytokine-mediated marrow activation and immune response during acute infection. These findings support the role of routine laboratory investigations as practical markers of disease severity.

The haematological and biochemical profile observed in the present study is broadly consistent with findings from other endemic regions of India and Asia. Indian studies have repeatedly reported thrombocytopenia as one of the most frequent abnormalities in scrub typhus, with rates generally ranging from approximately 64% to 71% [11]. The present study showed a similar frequency of thrombocytopenia at 66.7%, supporting its reliability as a common laboratory feature of scrub typhus.

The frequency of leucocytosis and toxic neutrophilic changes in the present study was relatively higher than that reported in some previous studies. This may reflect a more severe inflammatory response among patients admitted to a tertiary care centre. Reactive lymphocytes were also noted more frequently in the present study compared with earlier reports. These variations suggest that peripheral smear morphology may differ according to disease stage, severity, immune response, and timing of sample collection.

Studies from Nepal, Korea, Thailand, and southern China have also reported similar laboratory patterns, including thrombocytopenia, raised transaminases, renal dysfunction, and systemic inflammatory changes. Gautam et al. [18] reported transaminase elevation in nearly 55–60% of cases, which closely matches the present findings. Kim et al. [19] documented thrombocytopenia in more than two-thirds of hospitalized scrub typhus patients. Despite regional variation, the recurring pattern of platelet reduction, hepatic enzyme elevation, renal impairment, and inflammatory smear changes across different endemic regions supports the diagnostic and prognostic value of these parameters.

Generalizability

Because the study included consecutive seropositive patients across all age groups and used routine haematological, peripheral smear, liver, and renal investigations, the findings are most applicable to hospitalised scrub typhus patients managed in comparable government tertiary-care centres in endemic regions of South India. The observed associations can support early risk stratification where similar laboratory methods and morbidity definitions are used. However, extrapolation to community-managed patients, primary-care settings, non-endemic regions, pregnant women, and patients with concurrent infections should be cautious because these populations were not represented in the study.

Conclusion

The present study demonstrates that selected haematological, biochemical, and peripheral smear findings are useful indicators of morbidity in seropositive scrub typhus cases. Severe thrombocytopenia, neutrophilia with toxic changes, elevated transaminases, hyperbilirubinaemia, and raised serum creatinine showed an important association with increased disease severity.

Peripheral smear examination, when interpreted together with complete blood count and biochemical parameters, provides a simple, rapid, and cost-effective approach for early identification of patients at risk of morbidity. The presence of marked platelet reduction and toxic neutrophilic changes should alert clinicians to possible severe disease. Routine assessment of these parameters may help in timely risk stratification, early supportive management, and improved clinical outcomes in tertiary care settings.

Limitations

The study had several limitations. The sample comprised 45 serologically confirmed cases, which reduced statistical precision and resulted in wide confidence intervals for some associations. The cross-sectional design permitted assessment of relationships but did not establish temporal or causal effects. Long-term outcomes and serial trends in haematological and biochemical parameters were not evaluated. Morbidity was defined using organ dysfunction and/or intensive care admission, which can be influenced by referral patterns and local clinical practice. Larger prospective multicentre studies with repeated measurements and standardised severity outcomes are required to validate these findings.

Recommendations

Routine complete blood count, platelet count, peripheral smear examination, liver function tests, and renal function tests should be performed in all seropositive scrub typhus patients at admission. Patients with severe thrombocytopenia, toxic neutrophilic changes, elevated transaminases, hyperbilirubinaemia, or raised serum creatinine should be closely monitored for morbidity and organ dysfunction. Peripheral smear examination should be used as a rapid, inexpensive supportive tool for early risk

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assessment, especially in resource-limited settings. Serial monitoring of platelet count, liver enzymes, bilirubin, and creatinine is recommended during hospitalization. Larger multicentric studies are needed to validate these parameters as predictors of disease severity.

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Abbreviations
ALP- Alkaline Phosphatase
ALT- Alanine Aminotransferase
AST- Aspartate Aminotransferase
CBC- Complete Blood Count
CI-Confidence Interval
DIC-Disseminated Intravascular Coagulation
EDTA-Ethylenediaminetetraacetic Acid
ELISA-Enzyme-Linked Immunosorbent Assay
Hb- Haemoglobin
ICU- Intensive Care Unit
IgM- Immunoglobulin M
LFT- Liver Function Test
OR- Odds Ratio
RFT- Renal Function Test
SGOT-Serum Glutamic-Oxaloacetic Transaminase
SGPT- Serum Glutamic-Pyruvic Transaminase
SVRRGGH- Sri Venkateswara Ramnarayan Ruia Government General Hospital
TLC- Total Leukocyte Count

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The author declares no conflict of interest.

Data Availability
Data available on request

Author's contribution:
Dr. R. Rajakumari contributed to the conception of the study, data collection, sample processing, peripheral smear evaluation, compilation of clinical and laboratory findings, statistical analysis, interpretation of results, and drafting of the manuscript. **Dr. S. Rajasekhar Reddy** contributed to study design, supervision of laboratory investigations, interpretation of haematological and biochemical parameters, critical review of the manuscript, and overall academic guidance. **Dr. C. Sarada Devi** contributed to peripheral smear assessment, review of clinical correlations, interpretation of morbidity-related findings, manuscript revision, and final approval of the article. All authors read and approved the final manuscript and agree to be accountable for the accuracy and integrity of the work.

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