Le Infezioni in Medicina, n. 1, 106-113, 2025
doi: 10.53854/liim-3301-10

Scrub Typhus in Kerala: Demographic, Clinical, and Laboratory Predictors of ICU Admission in a Tertiary Care Setting

Shazia Zahara Saheed[1], Debajyoti Goswami[1], Vettakkara Kandy Muhammed Niyas[2], Rajalakshmi Ananthanaryanan[2]

[1]Department of Internal Medicine, KIMSHEALTH, Thiruvananthapuram, Kerala, India;
[2]Department of Infectious Diseases, KIMSHEALTH, Thiruvananthapuram, Kerala, India.

Article received 5 December 2024 and accepted 5 February 2025

SUMMARY

Background: Scrub typhus, a mite-borne infection caused by *Orientia tsutsugamushi*, is endemic in South and Southeast Asia, including India. Although increasing awareness and improved healthcare access have reduced mortality, the disease remains a significant public health concern. Kerala, a southern Indian state, has reported scrub typhus cases for decades; however, comprehensive data on its clinical profile and severity indicators are limited. This study aimed to describe the clinical characteristics of scrub typhus and identify predictors of intensive care unit (ICU) admission.

Methods: A retrospective study was conducted on scrub typhus cases diagnosed at KIMSHEALTH, Thiruvananthapuram, India, from 2015 to 2021 using electronic medical records (EMR). Scrub typhus was defined as an acute febrile disease with positive IgM ELISA. Patients with other diagnoses explaining the febrile illness or those with incomplete data were excluded. Demographic characteristics, clinical features, laboratory findings, and patient outcomes were analyzed. ICU admission was the primary outcome. Binary logistic regression was used to identify independent predictors of ICU admission.

Results: A total of 241 patients were included in the study, of whom 74 (30.7%) required ICU admission. Most cases occurred between September and January, with a peak in December. The median age was 45 years (IQR: 24.5–60.5), and 122 (50.6%) were female. Fever lasting >7 days was present in 46.1% of patients. Common symptoms included headache (38.2%), myalgia (37.3%), vomiting (31.5%), and breathlessness (19.5%). Hepatomegaly and splenomegaly were observed in 33.2% and 28.6% of cases, respectively, while eschar was noted in 20.3%. Most patients received doxycycline (82.6%), with some receiving azithromycin (7.1%) or both (10.4%).

In multivariable analysis using binary logistic regression, altered sensorium (adjusted odds ratio [aOR]: 6.63, 95% CI: 1.83–24.12, p=0.004) and breathlessness (aOR: 5.02, 95% CI: 2.31–10.90, p<0.001) were independent predictors of ICU admission.

Conclusions: Scrub typhus in Kerala exhibits seasonal variation, peaking from September to January. Breathlessness and altered sensorium present at admission were the strongest predictors of ICU admission The lower mortality in our study (2.1%) compared to national estimates may be attributed to improved healthcare access, early diagnosis, and prompt treatment. Further multicenter prospective studies are needed to validate these findings and improve risk stratification for severe disease.

Keywords: Scrub typhus, *Orientia tsutsugamushi*, ICU Admission Predictors, Kerala.

INTRODUCTION

Scrub typhus is a mite borne infection caused by *Orientia tsutsugamushi* and is endemic to many regions in South and Southeast Asia, including India [1]. The disease is transmitted by the bite of lar-

Corresponding author
Vettakkara Kandy Muhammed Niyas
E-mail: niyas987@gmail.com

val trombiculid mites of the genus *Leptotrombidium*. Clinical manifestations range from nonspecific febrile illness to severe complications that require intensive care admissions. Though with increasing awareness the mortality in scrub typhus has been brought down significantly, it remains a serious public health issue with life threatening complications [2].

Kerala, a southern Indian state, has been reporting cases of scrub typhus for the past three decades [3]. However, most studies on clinical manifestations of the disease are limited to case reports. Given Kerala's reputation for robust healthcare facilities compared to other Indian states, it is important to examine scrub typhus in this context, as differences in outcomes may exist [4]. Understanding the demographic and clinical profile of the disease is essential for improving patient care in endemic areas. Although recent studies have demonstrated low mortality rates, a significant number of patients develop severe complications that require intensive care unit (ICU) admission [1, 5, 6]. Identifying predictors of ICU care may facilitate better triage and closer monitoring of scrub typhus patients. We conducted a retrospective study of scrub typhus cases presenting to our hospital, KIMSHEALTH, Thiruvananthapuram, iNDIA, focusing on the demographic and clinical profile and predictors of ICU admission. KIMSHEALTH, a tertiary care facility in Thiruvananthapuram, southern Kerala, primarily serves patients from the Thiruvananthapuram and Kollam districts of Kerala, as well as the neighboring Kanyakumari district in Tamil Nadu.

METHODS

A retrospective analysis of scrub typhus cases from 2015 to 2021 was conducted using electronic medical records (EMR). Scrub typhus was defined as an acute febrile disease with positive IgM ELISA (InBios International, Inc., Seattle, WA, USA) against scrub typhus. The optical density (OD) cut-off used was 0.55. Patients of all age groups were included. Patients with an additional diagnosis that could account for the febrile illness or those with incomplete data were excluded. As this study utilized all available cases during the study period, a formal sample size calculation was not performed. Instead, our analysis is based on the complete dataset of patients diagnosed with scrub typhus over these years.

Demographic characteristics (age, sex and area of residence), symptoms, physical examination findings, laboratory findings, and patient outcomes (ICU admission and in-hospital mortality) were obtained from the EMR. Both physical examination findings and ultrasonographic findings were used to assess hepatomegaly and splenomegaly. Continuous variables were summarized as medians with interquartile ranges (IQRs), while categorical variables were presented as frequencies and percentages.

Comparisons were made between patients requiring ICU admission and those who did not. ICU admission was recorded as a binary outcome (yes/no) based solely on whether the patient was transferred to the intensive care unit. It is important to note that the specific criteria used to decide ICU admission were not evaluated in this study. Continuous variables were summarized as medians with interquartile ranges (IQRs), and categorical variables were presented as frequencies and percentages. Comparisons between patients requiring ICU admission and those who did not were performed using the Mann-Whitney U test for non-normally distributed continuous variables and the χ^2 test for categorical variables. Variables that were significantly different between the two groups ($p<0.05$) in univariate analysis were subsequently entered into a binary logistic regression model to identify independent predictors of ICU admission. To assess potential multicollinearity among the independent variables, Variance Inflation Factor (VIF) values were calculated for all predictor variables included in the multivariable binary logistic regression model. A VIF threshold of 5 was used to identify potential collinearity concerns, with values below this threshold considered acceptable.

RESULTS

A total of 241 patients met the inclusion criteria for this study. Most cases occurred between September and January (Figure 1), with the maximum number of cases reported in December. A smaller peak was observed from June to August. Patients were from both rural and urban areas of the Thiruvananthapuram and Kollam districts in Kerala and the adjacent Kanyakumari district in Tamil Nadu (Figure 2). The median age of the patients was 45 years (interquartile range: 24.5–60.5), with

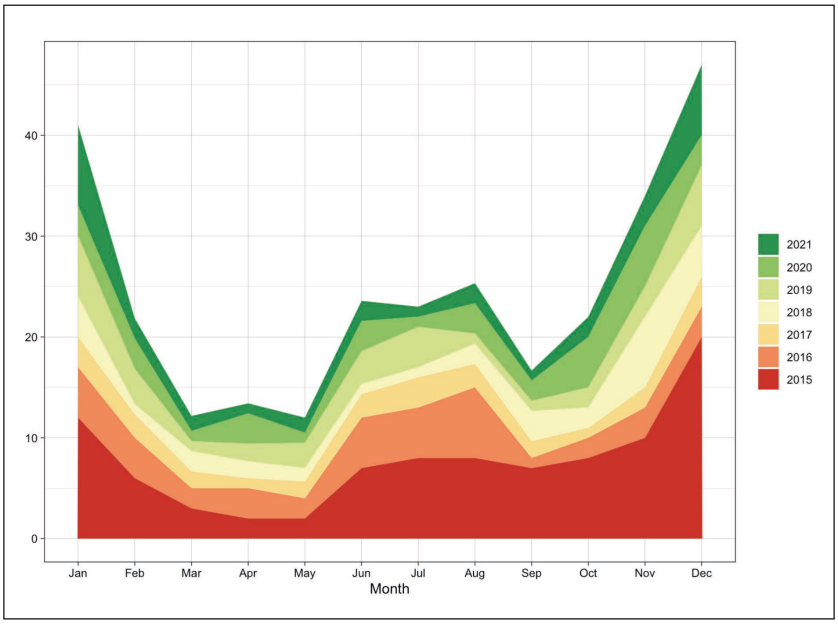

Figure 1
Monthly distribution of scrub typhus cases (2015 to 2021).

Figure 2
Geographic distribution of scrub typhus cases. The hospital, located in Thiruvananthapuram, receives cases primarily from Thiruvananthapuram and Kollam districts in Kerala and the Kanyakumari district in Tamil Nadu.

122 males and remainder females. 47 patients (19.5%) belonged to the pediatric age group (<18 years). Figure 3 depicts the age distribution of males and females. Common comorbidities included type 2 diabetes mellitus (19.5%), coronary artery disease (5.8%), chronic respiratory diseases (5.4%), and chronic liver disease (2.1%).

Fever lasting more than one week was noted in 46.1% of patients. Other frequent symptoms included headache (38.2%), myalgia (37.3%), vomiting (31.5%), cough (27.4%), breathlessness (19.5%), abdominal pain (15.8%), arthralgia (8.7%), and altered sensorium (6.2%). Hepatomegaly and splenomegaly were observed in 33.2% and 28.6% of patients, respectively, and an eschar was identified in 20.3% of cases. Most common site of eschar included the inguinal area and lower abdominal area. Antibiotics used for management were looked

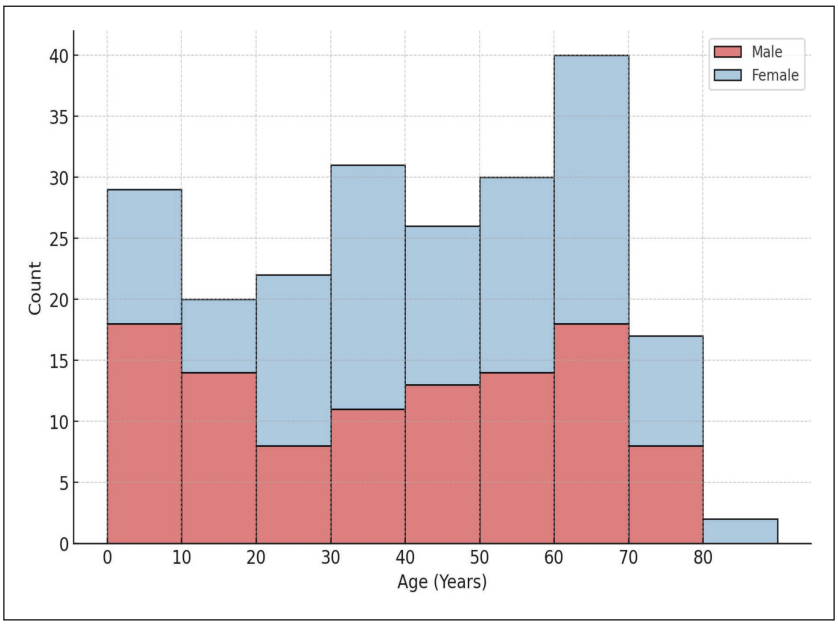

Figure 3
Age and Sex Distribution of Scrub Typhus Cases.

at; 199 patients received doxycycline, 17 received azithromycin, and 25 were treated with both. The overall in-hospital mortality rate was 2.1%.

A total of 74 (30.7%) patients required ICU admission. Clinical and laboratory parameters at admission were compared between those requiring ICU admission and those who did not. In univariate analysis, age, sex, breathlessness, altered sensorium, hemoglobin, and platelet count differed significantly between the groups (p value<0.05) (Table 1). These variables were then assessed through binary logistic regression to iden-

Table 1 - Comparison of clinical parameters between patients who did not require ICU admission and those who required ICU admission. Continuous variables are expressed in median (interquartile range). Categorical variables are expressed as number(percentage).

Variable (at admission)	*Total patients (n=241)*	*No ICU admission (n=167)*	*ICU admission (n=74)*	*p-value*
Male Sex	122 (50.62%)	77 (46.11%)	45 (60.81%)	0.04
Age (years)	45.0 (24.5-60.5)	42 (24-58)	51.5 (25.75-65.25)	0.04
Received doxycycline or azithromycin prior to presentation	19 (7.88%)	12 (7.19%)	7 (9.46%)	0.73
Diabetes mellitus	47 (19.50%)	28 (16.77%)	19 (25.68%)	0.15
Chronic kidney disease	2 (0.83%)	0 (0.00%)	2 (2.70%)	0.17
Coronary artery disease	14 (5.81%)	10 (5.99%)	4 (5.41%)	1.00
Chronic liver disease	5 (2.07%)	4 (2.40%)	1 (1.35%)	0.97
Chronic respiratory disease	13 (5.39%)	9 (5.39%)	4 (5.41%)	1.00
Active malignancy	2 (0.83%)	2 (1.20%)	0 (0.00%)	0.86
Connective tissue diseases	3 (1.24%)	1 (0.60%)	2 (2.70%)	0.46
HIV infection	1 (0.41%)	1 (0.60%)	0 (0.00%)	1.00
Immunosuppressive drugs	2 (0.83%)	0 (0.00%)	2 (2.70%)	0.17

Continue >>>

>>> *Continue*

Variable (at admission)	*Total patients (n=241)*	*No ICU admission (n=167)*	*ICU admission (n=74)*	*p-value*
Myalgia	90 (37.34%)	58 (34.73%)	32 (43.24%)	0.26
Arthralgia	21.0 (8.71%)	12.0 (7.19%)	9.0 (12.16%)	0.31
Headache	92 (38.17%)	64 (38.32%)	28 (37.84%)	1.00
Altered sensorium	15 (6.22%)	4 (2.40%)	11 (14.86%)	<0.01
Seizure	5 (2.07%)	1 (0.60%)	4 (5.41%)	0.05
Abdominal pain	38.0 (15.77%)	23.0 (13.77%)	15.0 (20.27%)	0.30
Cough	66 (27.39%)	52 (31.14%)	14 (18.92%)	0.07
Breathlessness	47 (19.50%)	19 (11.38%)	28 (37.84%)	<0.01
Total leucocyte count (cells/µL)	9700 (7600-12700)	9300 (7500-12500)	10400 (8175-13325)	0.13
Hemoglobin (g/dL)	12.15 (10.82-13.50)	12.7 (11.40-13.80)	11.20 (10.20-12.25)	<0.01
Platelet count (x 10^3 cells/µL)	156.00 (116.25-224.75)	166.00 (127.00-239.00)	135.00 (83.00-192.00)	<0.01
Bilirubin mg/dL	0.6 (0.2-1.2)	0.50 (0.40-1.10)	0.80 (0.40-1.20)	0.065
Alanine aminotransferase(U/L)	88 (50-152)	96.00 (48.00-156.50)	80 (52.50-133.75)	0.32
Aspartate aminotransferase (U/L)	79.5 (45-145)	80.50 (45.25-145)	76.00 (45.00-135.00)	0.86
Alkaline phosphatase (U/L)	122 (84-192)	123.00 (76.50-186.00)	121.00 (92.00-241.00)	0.17
Creatinine (mg/dL)	0.8 (0. 60-1.10)	0.80 (0.60-1.00)	0.80 (0.55-1)	0.73

tify independent predictors of ICU admission (Table 2).

Altered sensorium (adjusted odds ratio [aOR]: 6.63, 95% CI: 1.83–24.12, p<0.01) and breathlessness (aOR: 5.0, 95% CI: 2.31–10.90, p<0.01) were associated with higher odds of ICU admission. Although higher hemoglobin levels (aOR: 0.68, 95% CI: 0.56–0.84, p< 0.01) and higher platelet counts (aOR: 0.996, 95% CI: 0.993–0.999, p=0.01) were statistically associated with a lower risk of ICU admission, the absolute differences in their median values between groups were small, making their clinical significance uncertain. Collinearity diagnostics showed no significant multicollinearity among the predictor variables, with all Variance Inflation Factor (VIF) values below 1.3 (range: 1.10–1.26), indicating that multicollinearity is unlikely to affect the model. The model demonstrated a reasonable fit, with a McFadden's pseudo R^2 of 0.328.

DISCUSSION

Our study describes the epidemiological and clinical profile of patients with scrub typhus, along with the predictors of ICU admission in a tertiary

Table 2 - Multivariable Binary Logistic Regression: Adjusted Odds Ratios (aORs) for Predictors of ICU Admission in Scrub Typhus Patients.

Variable	*Adjusted Odds Ratio (aOR)*	*95% CI*	*p-value*
Age	0.995	0.980 - 1.011	0.572
Sex (Male as reference)	0.925	0.465 - 1.841	0.825
Breathlessness	5.019	2.310 - 10.903	< 0.001
Altered Sensorium	6.636	1.826 - 24.122	0.004
Hemoglobin	0.684	0.559 - 0.836	< 0.001
Platelet Count	0.996	0.993 - 0.999	0.014

care center in Kerala, southern India. The disease affected males and females equally, with a median age of 45 years. Majority of cases were reported during the relatively cool months from September to January, with maximum cases occurring in December. A similar pattern of the disease has been observed in previous studies in this region [3, 5]. The seasonality of scrub typhus has been well documented, with multiple studies showing that scrub typhus cases peak during the cooler months of the year. A study from Vellore, Tamil Nadu has shown that mean temperature had a negative correlation with the scrub typhus cases [7]. However, humidity showed a positive correlation with the number of scrub typhus cases. Low temperature, high humidity and rainfall are considered favorable for the mites' egg-laying and survival [7]. Thus, the cooler, post monsoon months records the maximum number of scrub typhus cases.

Around half of the patients had a febrile period lasting more than 7 days. Previous studies also have noted a fever lasting more than 1 week in majority of the patients. In a study from Vellore, the median duration of fever was 8.8 days [8]. Previous studies from Kerala has observed a fever duration of 6.4- 13.5 days in scrub typhus cases [5, 9, 10]. It should be noted that the duration of fever can be affected by treatment initiation, as scrub typhus responds readily to antibiotics. In our study 7.88% of patients had received a drug active against scrub typhus, by the time they had presented to our hospital. Other common symptoms of scrub typhus in our study included headache, myalgia, cough, breathlessness, abdominal pain, vomiting, arthralgia, and altered sensorium, similar to previous published studies. Headache has been identified as the most common symptom after fever in previous studies as well [1, 9-11].

Hepatomegaly and splenomegaly were observed in 33.2% and 28.6% of the cases. The reported prevalence of hepatomegaly and splenomegaly has shown considerable variation across studies. One prospective study from north India noted hepatomegaly in 61% of patients and splenomegaly in 45% [12]. Another study from Goa reported hepatomegaly in 60% and splenomegaly in 26.7% of the patients [13]. This variation may be attributed to the inherent subjectivity in clinical assessment of organ enlargement and differences in diagnostic tools, such as ultrasonography, used to confirm hepatomegaly and splenomegaly across studies.

Eschar is an important physical examination finding in a patient with scrub typhus, that can strongly suggest the diagnosis. In our study an eschar was noted in 20.3% of the scrub typhus cases. The prevalence of eschar in previous studies has varied significantly. In a systematic review of scrub typhus cases in India, the median prevalence of eschar was 22.1%, but ranged from 1 to 100 [1]. In another systematic review that specifically looked at the frequency and distribution of eschar in scrub typhus, the pooled eschar positivity varied from ≤12% in Haryana, Rajasthan, Madhya Pradesh, Punjab, and Meghalaya to ≥46% in Tamil Nadu and Tripura [14]. We acknowledge that the retrospective design of our study may have contributed to an underestimation of eschar prevalence, as this clinical sign requires thorough physical examination for detection.

We also assessed the factors that predicted ICU admission in scrub typhus patients. Among symptoms, breathlessness and altered sensorium were associated with an increased odds of ICU admission. Among laboratory parameters, a higher hemoglobin and platelet values were associated with a lower odds of ICU admission. However, although the differences in hemoglobin and platelet counts between groups were statistically significant, the magnitude of these differences was small and unlikely to provide meaningful predictive value for ICU admission. A study from Vellore had shown that ARDS and increasing SOFA scores were the independent predictors of ICU admission, two variables that were not assessed in our study [8]. Another study from north India in pediatric population, lymphadenopathy, respiratory distress, shock, elevated lactate, and meningoencephalitis predicted the requirement of PICU admission [15]. Other studies have assessed the factors that predicted severity of the disease. A study from north India identified leukocytosis, hyperbilirubinemia, transaminitis, hypoalbuminemia, and uremia were significantly associated with organ failure [16]. A Chinese study examining predictors of severe scrub typhus found that, in pediatric patients, peripheral edema and reduced hemoglobin levels were the strongest indicators of severe illness. In elderly patients, dyspnea and elevated total bilirubin were identified as potential determinants of severe disease [17]. Across these studies, breathlessness and altered sensorium consistently emerge as common indicators of disease severity and ICU admission.

The overall mortality in our study was 2.1%. In a systematic review of published studies on scrub typhus from India, the overall mortality was 6.3% (1). The study also noticed a regional difference in mortality: 8.5% in northern India vs 4.7% in southern India [1]. In another systematic review that assessed global mortality rates in scrub typhus, median mortality was 5.00% (range: 0.00-56.00%) among hospital inpatients [18]. With increased awareness of the disease and the prompt initiation of empiric treatment, there is a decreasing trend in mortality from scrub typhus [2]. Previous studies from Kerala have also documented low mortality rates, though their conclusions were limited by small sample sizes [5, 9, 10]. Increased access to healthcare facilities in the region, proactive healthcare-seeking behavior in Kerala, heightened awareness among treating physicians, and the availability of better critical care services may have contributed to improved outcomes [4]. A younger patient population and a lower prevalence of comorbidities in our study may have also played a role in the lower mortality observed. Early diagnosis and prompt initiation of appropriate antibiotic therapy are key factors in reducing mortality. However, we did not specifically evaluate the impact of these factors, and further research is needed to assess their contribution to improved outcomes.

Our study describes the clinical features of scrub typhus in patients from Kerala, a region where major studies on the disease are scarce. However, the retrospective design of our study presents limitations, potentially leading to underestimation of clinical signs such as eschar, hepatomegaly and splenomegaly. Additionally, this is a single-center study conducted at a tertiary care hospital in Kerala, which may limit the generalizability of our findings to other settings, particularly primary care or community-level healthcare facilities. It should also be noted that ICU admission often follows subjective assessment, which may not always correlate with disease severity. Larger, prospective multi-centric studies from this region are needed to validate our findings.

CONCLUSIONS

In summary, our study provides valuable insights into the clinical characteristics and predictors of ICU admission for scrub typhus patients in Kerala, highlighting the need for further investigation in this region where data is limited. Although our findings underscore breathlessness and altered sensorium present at admission as key indicators of severity, larger, prospective studies are required to confirm these observations and address the limitations inherent in retrospective analysis.

Conflicts of interest
None

Funding
None

Acknowledgements
We extend our gratitude to StatSolutions India for their invaluable support in statistical analysis and data visualization. We also appreciate the efforts of the Audiovisual Team at KIMSHEALTH, Thiruvananthapuram, for their assistance in enhancing the figures. We thank Dr. Viji Mohan from the Department of Microbiology, KIMSHEALTH, for her expertise in interpreting the ELISA reports.

Author declaration
All authors have seen and approved the manuscript, contributed significantly to the work, and the manuscript has not been previously published nor is under consideration for publication elsewhere.

REFERENCES

[1] Devasagayam E, Dayanand D, Kundu D, Varghese GM. The burden of scrub typhus in India: A systematic review. *PLoS Negl Trop Dis.* 2021; 15(7): e0009619.
[2] Varghese GM, Trowbridge P, Janardhanan J, et al. Clinical profile and improving mortality trend of scrub typhus in South India. *Int J Infect Dis.* 2014; 23: 39-43.
[3] Ali A, Haridasan RK, Kumar SK, Suni KA, Farook UM. A study on scrub typhus in a tertiary care hospital. *Kerala Med J.* 2009; 2(1): 7-9.
[4] Adithyan GS, Ranjan A, Muraleedharan VR, Sundararaman T. Kerala's progress towards universal health coverage: the road travelled and beyond. *Int J Equity Health.* 2024; 23(1): 152.
[5] Krishnan R, Pillai RK, E KE, A S, Bindusha S. Pediatric scrub typhus in Southern Kerala: An emerging public health problem. *Clin Epidemiol Glob Health.* 2016; 4(2): 89-94.
[6] Ravikumar DB, Sivasubramanian BP, Shanmugam SN, et al. Multifaceted realities of scrub typhus: a case series from southern India. *Infez Med.* 2023; 31(3): 384-393.
[7] D'Cruz S, Sreedevi K, Lynette C, Gunasekaran K,

Prakash JAJ. Climate influences scrub typhus occurrence in Vellore, Tamil Nadu, India: Analysis of a 15-year dataset. *Sci Rep.* 2024; 14(1): 1532.
[8] John KJ, George TK, Joy M, et al. Costs & outcomes of hospitalized scrub typhus infection in a tertiary hospital in South India. *Indian J Med Res.* 2023; 157(6): 559-567.
[9] Jose RA, Jose H, Jacob AA, Thomas P, Mathew R, Thomas M. Seroprevalence and clinical profile of scrub typhus in patients presenting with undifferentiated acute febrile illness in a tertiary care centre. *Asian J Med Sci.* 2021; 12(4): 54-60.
[10] Balasubramanian P, Moorkoth AP, Valuvil U, Kumar J, Thottathil J, George K. Clinical profile, epidemiology and prognostic factors of scrub typhus in a tertiary care centre. *J Acad Clin Microbiol.* 2015; 17(1): 29.
[11] Meenakumari PB, Reddy SD, Anoop AR, Bhaskar A. A study of clinical presentation, laboratory findings and outcome among patients of scrub typhus in General Hospital Thiruvananthapuram. *Kerala Med J.* 2016; 9(2): 55-59.
[12] Sharma N, Biswal M, Kumar A, Zaman K, Jain S, Bhalla A. Scrub typhus in a tertiary care hospital in North India. *Am J Trop Med Hyg.* 2016; 95(2): 447.
[13] Narvencar KP, Rodrigues S, Nevrekar RP, et al. Scrub typhus in patients reporting with acute febrile illness at a tertiary health care institution in Goa. *Indian J Med Res.* 2012; 136(6): 1020.
[14] Gupta N, Kumar TP, Boodman C, et al. Frequency and distribution of eschar in patients with scrub typhus in India: Systematic review of literature and meta-analysis. *Infez Med.* 2024; 32(3): 312-322.
[15] Nallasamy K, Gupta S, Bansal A, et al. Clinical profile and predictors of intensive care unit admission in pediatric scrub typhus: A retrospective observational study from North India. *Indian J Crit Care Med.* 2020; 24(6): 445-450.
[16] Sharma R, Mahajan SK, Singh B, et al. Predictors of severity in scrub typhus. *J Assoc Physicians India.* 2019; 67(4): 35-38.
[17] Guan XG, Wei YH, Jiang BG, et al. Clinical characteristics and risk factors for severe scrub typhus in pediatric and elderly patients. *PLoS Negl Trop Dis.* 2022; 16(4): e0010357.
[18] Wang Q, Ma T, Ding F, et al. Global and regional seroprevalence, incidence, mortality of, and risk factors for scrub typhus: A systematic review and meta-analysis. *Int J Infect Dis.* 2024; 146: 107151.