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Multilevel determinants of scrub typhus incidence and hospitalization in Mizoram, North East India

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Abstract

Background

The state of Mizoram in North-East India is reporting the highest burden of scrub typhus in recent years. Despite it being a major public health problem, evidence on village-level determinants of incidence and severity of scrub typhus remains limited. By combining individual-level surveillance data with village-level infrastructure and socioeconomic data to examine the individual- and village-level determinants of scrub typhus incidence and hospitalization in Mizoram, we aim to identify high-risk communities and inform locally tailored prevention strategies.

Methods

De-identified passive surveillance data of scrub typhus cases from Integrated Disease Surveillance Programme (IDSP), Mizoram from 2023 to 2025 was used for the analysis. Individual-level determinants of hospitalization were assessed using mixed-effects logistic regression with district- and facility-level random intercepts. Aggregated village-level cases were linked to Mission Antyodaya village-level data and assessed using mixed-effects negative binomial regression with a population offset and district random intercept to identify village-level determinants of scrub typhus incidence and hospitalization. Model diagnostics included multicollinearity, calibration, and DHARMa residual checks.

Results

Scrub typhus cases showed a rising annual burden and heterogeneous, expanding geographic distribution across Mizoram. The disease showed a distinct seasonal pattern throughout the study period, peaking during the monsoon and/ or post-monsoon. Out of 49,452 scrub typhus cases, 2,411 (4.9%) required hospitalization. Prolonged fever (≥7 days) (1.27, $p=0.02$) and admission to private (36.27, $p<0.001$) and tertiary hospitals (22.22, $p<0.001$) were risk factors for longer hospital stays. The model showed excellent discrimination (AUC = 0.92) and good calibration. Village-level analysis (1,803 village-years) showed higher disease incidence in villages with community forest (1.30, $p=0.029$) and road connectivity (1.97, $p<0.001$), and lower disease incidence in villages with longer distance to Primary Health Ccntre (PHC) (0.58, $p<0.001$), and lesser access to public

transport (0.88, p=0.034); while hospitalization rate was lesser in villages farther from PHC (0.81, p<0.001). In addition, a significant upward temporal trend was observed in both cases (~27% annually; ICC = 28.02%) and hospitalizations (~35% annually; ICC = 13.95%).

Conclusion

The rise in scrub typhus incidence and hospitalizations in Mizoram is shaped by individual demographic and clinical characteristics, along with village infrastructure and healthcare accessibility. Community-level prevention such as targeted awareness among farmers and agriculture-related workers, rodent control, and measures to control chigger exposure, alongside strengthened surveillance and early diagnosis, is essential to control scrub typhus in this region.

Introduction:

Scrub typhus is an important but historically neglected acute undifferentiated febrile illness. It is one of the most underdiagnosed and underreported febrile illnesses [1], with roughly one billion people at risk of infection and ~one million cases annually [2]. The disease has geographically expanded from its traditional "Tsutsugamushi Triangle" to other continents, with reports from Asia, the Middle East, South America, and Africa [3–6]. In India, scrub typhus is recognized as an important cause of acute febrile illness, with a pooled seroprevalence of 26.41% (95% CI, 22.03–31.03%) distributed heterogeneously across the country [7]. Although the disease is prevalent nationwide, its exact distribution is unknown, as the surveillance remains largely hospital-based and often goes underdiagnosed or underreported. A recent spatiotemporal analysis spanning two decades identified 47,650 cumulative cases of scrub typhus in India, with the northeast (NE) Indian state of Mizoram accounting for nearly half the burden in a decade (2012-2022) [8].

Mizoram, with 88.48% forest cover, is situated in one of the biodiversity hotspots, and farmers constitute ~60% of the population [9–11]. Since the first report of scrub typhus cases in 2012, cases have increased substantially in Mizoram, with an average annual incidence of 304 cases per 100,000 persons from 2018 to 2022, indicating endemic transmission rather than sporadic outbreaks [12]. The persistent occurrence of scrub typhus in Mizoram necessitates the need to understand the factors that facilitate transmission within communities at the village level.

The unique ecological characteristics of Mizoram, such as mountainous landscape, extensive forest cover, humid climate, and widespread agricultural practices, provide favourable conditions for natural transmission cycle of *Orientia tsutsugamushi*, the causative organism of scrub typhus [12, 13]. However, environmental suitability alone is unlikely to explain the differences in disease occurrence between communities. Household conditions, occupational practices, socioeconomic circumstances, and health-seeking behavior may also shape both the risk of infection and the likelihood of timely diagnosis. A large proportion of the rural population is engaged in agricultural practices, particularly shifting cultivation, and other outdoor activities that may increase exposure to infected chiggers. Understanding how these environmental, social, occupational, and healthcare-related factors interact is therefore important for identifying communities at greater risk and strengthening the prevention, early detection, and management of scrub typhus in Mizoram.

Even though recent reports have described the epidemiology, clinical characteristics, and surveillance trends of scrub typhus in Mizoram, there is little information available on the community-level determinants of the disease and severity. Since socioeconomic conditions, infrastructure, accessibility, and healthcare-seeking patterns vary across villages, locally generated evidence is essential for identifying high-risk areas and informing context-specific prevention strategies. Given the background, the study aims to investigate the individual and village-level determinants of scrub typhus incidence and hospitalization rates in Mizoram.

Methods

Study design and data source:

The study follows an ecological study design using de-identified passive surveillance line-listing data (2022-2025) from the Integrated Disease Surveillance Program, Health and Family Welfare Department, Mizoram. Scrub typhus data were obtained from public and private healthcare facilities, including primary and community health centers, subdistrict and district hospitals, Zoram Medical College, and Civil Hospital. The Weil-Felix test, Rapid diagnostic Test (RDT), and IgM Enzyme-Linked Immunosorbent Assay (ELISA) were used to diagnose the scrub typhus cases in this dataset. The line listing data was aggregated into 853 villages as per the 2011 census [14]. Village-level sociodemographic, infrastructure, and healthcare accessibility variables were sourced from the Antyodaya Mission village-level dataset, a Government of India initiative that compiles administrative data for grama panchayats across all villages in Mizoram [15].

Spatiotemporal analysis:

The line-listing data were consolidated into 853 villages across Mizoram's 11 districts, obtained from Census 2011, and unique spatial identifiers were assigned to prepare a spatial database using ArcGIS 10.4 software (https://desktop.arcgis.com). The year-wise distribution of scrub typhus cases from 2023 to 2025 was mapped using choropleth maps, with color intensity proportional to case numbers.

Individual level analysis:

Categorical variables such as year, season, sex, age group, presenting symptoms, diagnostic test performed, and type of healthcare facility were compared based on hospitalization status—

inpatient department (IPD) and outpatient department (OPD). These variables were summarized using frequencies and percentages for the overall study population and separately for IPD and OPD cases. The differences in the distribution were assessed using the Pearson chi-square test. A two-sided P value <0.05 was considered statistically significant. Factors associated with IPD among scrub typhus cases were assessed using mixed-effects logistic regression, with the outcome variable being hospitalization status (IPD = 1, OPD = 0). Candidate variables that were significant for the Pearson chi-square test were included for the analysis. A random intercept at the district- and health facility- level was incorporated into the model to account for potential correlation among individuals from the same district and health facility.

The formula of the model is:

$$\mathbf{logit[P(IPD)] = \beta_0 + \sum_{k=1}^{k} \beta_k X_{ki} + u_{d(i)} + v_{f(i)}}$$

where $u_{d(i)}$ represents the district-specific random intercept and $v_{f(i)}$ represents the health facility- specific random intercept. Statistical significance was assessed using two-sided tests, with P <0.05 considered statistically significant.

Model diagnostics were performed by evaluating model discrimination using the area under the curve (AUC) of the receiver operating characteristic curve (ROC), assessment of multicollinearity among predictors using variance inflation factors (VIF). Model calibration was assessed using the Hosmer-Lemeshow test along with a visual 10-decile calibration plot to account for sample size sensitivity. Calibration quality was determined by calculating calibration intercept and slope through a logistic validation framework. Further, sensitivity analyses were performed to assess the robustness of the model estimates to alternative analytical specifications.

Village level analysis:

Variables included in the village-level analysis are provided in Supplementary Table 1. The village-level dataset of 853 villages was merged with the Anthyodaya dataset using village IDs (852 villages), resulting in a final dataset of 601 villages containing both datasets; the remaining 251 villages were excluded because the village IDs and names didn't match. The

merged data was restructured into a longitudinal format for 2023–2025 for analysis, with separate outcomes for IPD and total scrub typhus cases.

Two-step multicollinearity testing was performed to select the variables for the model. First, Spearman's rank correlation was used to check collinearity among all independent variables using the psych package. Variables with collinearity > 0.7 were removed, except for one theoretically relevant variable, to maintain data completeness. Then, the selected variables were tested for VIF using a dummy Poisson regression, and variables with VIF < 2 were retained for analysis. Data visualization was performed using ggplot2.

The distribution of scrub typhus cases and IPD cases were tested for overdispersion. Poisson regression showed no overdispersion in either model (scrub typhus cases: dispersion ratio = 0.260, P = 0.832; IPD cases: dispersion ratio = 0.978, P = 0.664). To determine the most appropriate distribution for the count outcomes, a null mixed-effects model with Poisson, negative binomial and zero-inflated negative binomial distributions, containing village and district-level random intercept, was fitted. Model fit was compared using Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), and log-likelihood using performance package to assess model fit. Based on the lower AIC, BIC, and log-likelihood values among all three models, multivariable mixed-effects negative binomial model was fitted to total scrub typhus cases and scrub typhus inpatient cases, with village and district included as random intercepts to account for clustering of 601 villages within the 11 districts, using the glmmTMB framework. The model included population as an offset to estimate incidence rates while accounting for differences in village population size, while village and district were specified as random intercepts to account for repeated observations of the 601 villages across 2023–2025 and clustering within the 11 districts.

$$\boldsymbol{Log}\left[\boldsymbol{E}\left(\boldsymbol{Y}_{\{ijt\}}\right)\right] = \boldsymbol{\beta_0} + \sum_{\boldsymbol{k=1}}^{\boldsymbol{K}} \boldsymbol{\beta_K X}_{\{kijt\}} + \boldsymbol{uj} + \boldsymbol{vij} + \boldsymbol{log}\left(\boldsymbol{Population}_{\boldsymbol{ij}}\right)$$

where Y is scrub typhus cases or IPD cases in village I, district j, and time t. X_{kijt} represents independent variables, β_k is the fixed-effect coefficient, uj is the district-level random intercept, vij is the village-level random intercept nested within the district, and log(Populationij) is the population offset.

Independent variables were standardized as z-scores before model fitting. Model estimates were extracted and summarized using broom.mixed package. The adjusted associations were expressed as incidence rate ratios (IRRs) with 95% confidence intervals (CIs). The magnitude of between-district clustering was assessed using the intraclass correlation coefficient (ICC). Model adequacy was assessed using DHARMa simulated residual diagnostics based on 1,000 simulations using DHARMa package. The diagnostics included tests of residual uniformity, dispersion, and zero inflation. DHARMa residual plots were used to identify potential departures from model assumptions. Spearman's rank correlation coefficient was used to compare observed and model-predicted village-level scrub typhus cases and IPD cases. A two-sided *P* value <0.05 was considered statistically significant for all the analyses.

3. Results

Spatiotemporal distribution of scrub typhus cases in Mizoram:

Scrub typhus cases were distributed heterogeneously across Mizoram, with urban areas reporting higher numbers (Figure 1). The number of cases increased in the eastern districts compared to the other parts of the state and expanded geographically over the years; Saitual and Serchhip continued to have cases in most of their villages, while scrub typhus expanded across the villages in Champhai, with an overall increase in cases from 1908 in 2023 to 5260 in 2025.

Figure 1.

The cases were reported year-round but showed a clear seasonal pattern in all three years (Figure 2). The cases increased from June and peaked during July–October, which coincides with the monsoon and post-monsoon seasons, and declined towards the end of the year. The number of cases increased consistently over the years, indicating a growing burden of scrub typhus during the study period.

Figure 2.

Socio-demographic and clinical characteristics of scrub typhus cases and their association with hospitalization

Overall, 49,462 scrub typhus cases were reported in the study period (2023-25), of which 2,411 (4.87%) were hospitalized (Table 1). Along with the increase in cases, the proportion of hospitalizations increased from 525 cases (21.8%) in 2023 to 19,357 cases (42.6%) in 2025. The highest numbers of scrub typhus cases and hospitalizations (37.8%) occurred during the summer (May to August) (18,133; 40.7%). Males accounted for a higher proportion of hospitalized cases than females (1,305; 54.1% vs. 1,106; 45.9%], and older adults aged ≥45 years comprised the largest age group among inpatients (1,086; 45.0%), followed by younger adults aged 15–44 years (869; 36.0%). Cases with acute fever (<7 days) accounted for the highest number of hospitalizations (1086; 45%). Rapid diagnostic tests were the most commonly used diagnostic method (14,618; 49.96%); they were used highly among both IPD (1212; 50.6%) and OPD cases (23,406; 49.7%). Higher hospitalized cases were reported from Medical college and surveillance-linked facilities (873; 36.2%) and private hospitals (862; 35.8%). All variables were significantly associated with hospitalization.

Table 1.

Multivariable Mixed-Effects Logistic Regression

After adjustment for demographic, clinical, temporal, and health system variables, several factors were associated with inpatient disease (Table 2). Cases from 5–14 (aOR = 0.67, P = 0.011) and 15–44-year-old age groups (aOR = 0.63, P = 0.001) had significantly lower odds of hospitalization compared to children aged <2 years, whereas no significant differences were found in children of the 2–4 year-old age group and adults aged ≥45 years. Gender had no significant differences in hospitalization. Cases in winter (OR = 1.34, P < 0.001) and summer (OR = 1.24, P = 0.004) showed higher odds of inpatient cases than in spring, whereas autumn showed no significant association. A strong association with hospitalization was observed by hospital type; compared with PHCs, patients diagnosed in private (aOR = 33.47, P < 0.001) and tertiary referral hospitals (aOR = 21.51, P < 0.001) had higher odds of hospitalization, whereas CHCs and SD/DHs showed no difference. Patients with prolonged fever (≥7 days) had higher odds of hospitalization than those with other scrub typhus-specific clinical presentations (aOR = 1.26, P = 0.025), whereas acute fever lasting <7 days was not significantly associated. Compared with Weil–Felix testing, hospitalization was higher among patients diagnosed with IgM ELISA (aOR = 2.11, P < 0.001), whereas rapid diagnostic testing showed no significant association. Higher odds of inpatient cases were reported in 2024 (aOR 1.72, P < 0.001) and 2025 (aOR 1.47, P < 0.001) compared with 2023. The district-level and facility-

level random intercept variances were 3.08 and 0.10, respectively, indicating variation in hospitalization cases across districts and health facilities.

Table 2.

Model discrimination was evaluated using the receiver operating characteristic (ROC) curve, and the area under the curve (AUC) was 0.92, indicating excellent discrimination between inpatient and non-inpatient cases (Supplementary Figure 1). The mean VIF was 1.07, well below the threshold of 2.0 (Supplementary figure 2). Due to the low prevalence of IPD cases among the study population (IPD = 4.88%), model performance was further assessed (Supplementary table 1) at a predicted probability of 0.051 (using the Youden index). The model achieved a sensitivity and specificity of 78.55% and 89.93%, respectively. The positive predictive value was 28.57%, while the negative predictive value was 98.79%. The model showed a balanced accuracy of 84.25%. Cohen's kappa was 0.37, indicating fair agreement between predicted and observed IPD status. The Hosmer-Lemeshow goodness-of-fit test was statistically significant (P=0.03), possibly due to the large sample size. However, the calibration plot (Supplementary figure 3) showed strong agreement with risk deciles. This was confirmed by logistic calibration metrics—a calibration intercept of 0.015 (ideal: 0) and a calibration slope of 1.031 (ideal: 1), suggesting good agreement between predicted risks and observed proportions with no systematic over- or under-estimation.

Village-Level Determinants of Scrub Typhus cases and hospitalization

Supplementary Table 1 showed variation in socioeconomic, environmental, infrastructure, and healthcare-access characteristics among 601 villages. 97.3% of the villages had open drainage (n=585), 75.7% had all-weather road connectivity (n=455), and 66.9% were located more than 10 km from the nearest PHC (n=402).

Village-level analysis included 1,803 village-year observations from 601 villages across 2023-2025. Spearman correlation analysis showed no strong pairwise correlations ($\rho < |0.6|$) among the predictors included in the analysis (Supplementary Figure 4). Multicollinearity was also low, with all variance inflation factor (VIF) values below the predefined threshold of 2.0 (Supplementary Figure 5), except for one variable (Anganwadi centers with requisite infrastructure – VIF >2.0). Finally, ten variables were selected for the analysis.

Null model with lower AIC, BIC, and log-likelihood as selected for analysis. For scrub typhus cases, the negative binomial model had the lowest AIC (10,187.86), lowest BIC (10,209.85), and a higher log-likelihood (−5,089.93) than the Poisson model (AIC = 15,381.12; BIC = 15,397.61; log-likelihood = −7,687.56) and the zero-inflated negative binomial model (AIC = 10,189.86; BIC = 10,217.35; log-likelihood = −5,089.93). Similarly, for IPD cases, the negative binomial model provided the best fit (AIC = 3,204.17; BIC = 3,226.16; log-likelihood = −1,598.09) compared with the Poisson model (AIC = 3,308.22; BIC = 3,324.71; log-likelihood = −1,651.11) and zero-inflated negative binomial model (AIC = 3,206.17; BIC = 3,233.66; log-likelihood = −1,598.09). Although 24.3% of village-year observations for scrub typhus cases were zero, the zero-inflated negative binomial model did not improve model fit over the standard negative binomial model.

A mixed-effects negative binomial regression model with district-level random intercepts was selected to account for geographic clustering in the data (Table 3). The model showed a higher incidence of scrub typhus cases in villages that had community forest (IRR = 1.30, P = 0.029) and all-weather road (IRR = 1.97, P < 0.001). On the other hand, villages with higher population (IRR = 0.77, P <0.001), lesser access to public transport (IRR = 0.88, P = 0.034), and longer distance to PHC (IRR = 0.58, P <0.001) showed lower scrub typhus cases in villages. For IPD cases of scrub typhus, only greater PHC distance (IRR = 0.81, P <0.001) remained a significant predictor. A significant positive temporal trend was observed over the study period, with ~27% increase in scrub typhus incidence (IRR = 1.25, p < 0.001) and 35% increase in IPD cases (IRR = 1.35, p < 0.001) per year. The model showed a district-level random-effects variance of 0.324 and village-level random-effects variance of 0.855, indicating geographic heterogeneity among districts. The adjusted ICCs were 28% and 13.95% for the scrub typhus cases model and the scrub typhus IPD model, respectively, indicating between-district differences after adjustment for village-level characteristics.

Table 3.

The multivariable negative binomial mixed-effects model demonstrated a strong positive correlation between observed and predicted scrub typhus case counts (Spearman's ρ = 0.90, P < 0.001) and IPD Case counts (Spearman's ρ = 0.63, P < 0.001), indicating good correspondence between model estimates and observed village-level counts (Supplementary figure 6). District-specific random effects demonstrated geographic heterogeneity after adjustment for measured village-level predictors and a population offset (Supplementary figure

7). DHARMa diagnostics for the model (Supplementary figure 8) showed no overdispersion ($P = 0.416$) or zero inflation ($P = 0.186$), although the KS test indicated deviation from the expected residual distribution ($P < 0.001$). The mixed-effects negative binomial regression model for IPD cases showed slight residual non-uniformity (P = 0.0445), but no evidence of overdispersion (P = 0.528) or zero inflation (P = 0.642), indicating a good model fit.

Discussion:

Scrub typhus in Mizoram has evolved from an emerging infection to an endemic public health concern with year-round transmission and predictable seasonal peaks during the monsoon and post-monsoon months of May to September. While earlier surveillance-based studies had already established the widespread endemicity of the disease across the state [12, 16], this study identifies factors affecting disease transmission at individual and community levels. The 49462 scrub typhus cases reported from 2023-25 is 2.5 times higher than the number of cases over the previous 5 years (2018-2022; 19651 cases) [12]. The overall rise in scrub typhus cases in Mizoram could be attributed to the government-led expansion of efficient testing and reporting of scrub typhus cases among febrile cases attending all health facilities across the state. In addition, sustained increase in cases reflects increased disease transmission, warranting urgent attention.

In Mizoram's Champhai district, bordering Myanmar was observed over the last 3 years (2023-2025), a steep 2.7-fold increase in the last 3 years (2023-2025) was observed. Champhai is predominantly rural and has a strong dependence on agriculture, with approximately 76.6% of the population is engaged in agricultural activities, indicating substantial occupational exposure to scrub typhus. In addition, Mizoram shares a porous boundary with Myanmar, characterized by historical social, cultural, and economic linkages, with movement of people and goods between communities on both sides [17]. Recent regulation of movement across the Mizoram–Myanmar border further confirms the substantial population mobility associated with this border region [18]. Although direct cross-border transmission of scrub typhus was not assessed in the present study, such mobility, together with shared agricultural and forest ecosystems, may facilitate epidemiological connectivity between transmission foci. Therefore, sentinel surveillance in the border areas should be integrated with routine passive surveillance in Mizoram for scrub typhus and other endemic febrile illnesses, and should be reported to health authorities and communities on both sides of the border [19, 20].

In Mizoram, scrub typhus transmission follows a seasonal pattern, with higher cases reported during the monsoon and post-monsoon months; this pattern is consistent with previous studies from Mizoram [12, 21] and other parts of India [22–24]. In addition to cases, distinct seasonal variation was observed in hospitalization, with higher odds in summer (May–August) and winter (November–January). Summer coincides with the onset of the monsoon and peak agricultural activity in Mizoram [13]. In contrast, high odds of hospitalization in winters could be attributed to post-harvest rice-field rat hunting, Rats harboring *O. tsutsugamushi*-infected chiggers, could facilitate a rat–chigger–human transmission pathway [16]. These are plausible explanations rather than a demonstrated cause of the higher odds of hospitalization, as the study did not directly measure agricultural activities, individual exposure to rat hunting, or the timing of infection. The study also found lower odds of hospitalization among children aged 5-14 years and adults, compared to children <2 years, possibly due to immunity developed from past infections in this endemic setting [25]. Increased hospitalization was observed among cases presenting with fever ≥7 days. Prolonged infection due to delayed diagnosis increases the risk of complications and subsequent hospitalization among scrub typhus cases [26–28]. Studies showed cases with fever lasting >7 days were independently associated with severe scrub typhus, including respiratory complications, shock, and acute kidney injury, and had poorer survival chances [29, 30]. Rise in infectious disease hospitalization will increase the economic burden of scrub typhus in Mizoram, particularly through higher healthcare expenditure and productivity losses among affected working-age populations. The average annual economic burden for scrub typhus in Mizoram was estimated to be US$243,334.60, which accounts for 0.08% of the Gross State Domestic Product (GSDP), and showed an increasing trend during the study period [31]. This highlights the importance of strengthening early diagnosis and treatment at peripheral health facilities and community, particularly among high-risk populations, to reduce progression to severe disease, hospitalization, and the associated disease and financial burden. PHCs are the first referral for diagnosis of scrub typhus cases in Mizoram, but the odds of hospitalization was higher in tertiary and private hospitals and spiked to around 20- and 30-fold in medical college hospitals and private hospitals, respectively. The referral pathways and the availability of hospital beds and staffing, indicate the differences in healthcare service capacity that shape where patients ultimately receive care [32, 33].

Village-level analysis highlighted the influence of the village structure in which people live and their access to health facilities on scrub typhus prevalence, rather than by population size alone. The presence of community forests in villages increases the incidence of scrub typhus

by 30%. Jhum cultivation is the major occupation in Mizoram, particularly in rural areas, thereby increasing the risk of exposure to infected chigger mites through frequent contact with soil, vegetation and agricultural environments. Recent evidence from Mizoram shows a direct occupational risk through the ecological link—rice-field rats [16]. *Rattus tanezumi* and *Rattus nitidus*, traditionally hunted and consumed by Mizo communities, were found to harbor trombiculid mites infected with *Orientia tsutsugamushi*; Kato- and Karp-related genotypes of *O. tsutsugamushi* were the dominant strains in the infected mites [16]. Studies show that Karp-like strains are associated with severe complications and greater resource utilization, which may explain the higher rates of hospitalization in acute infection [34, 35]. In addition, a statewide serosurvey of rodents in Mizoram revealed >60% seropositivity to rickettsial antigens and a high chigger index, indicating active rodent–chigger interactions within and around human settlements [36]. Thus, scrub typhus transmission in Mizoram occurs in multiple interconnected pathways—agricultural activities, forest and vegetation contact, rat hunting practices, and peri-domestic rodent–chigger prevalence. It is important to integrate prevention strategies focusing on agricultural workers and rural households, including awareness of chigger exposure, personal protective measures during agricultural activities, environmental and rodent control around households and farms, and strengthened surveillance in villages with high agricultural and rodent exposure. Notably, accessibility remains a major issue for reporting scrub typhus cases—villages with greater PHC distance, poor road connectivity, and lesser access to public transport had a lower incidence of scrub typhus. These negative associations should not be interpreted as a protective effect but instead captured as differences in healthcare access, i.e., people from less-connected villages are less likely to reach health facilities and get diagnosed for fevers.

This study has several strengths. By utilizing statewide IDSP surveillance data, instead of a single facility or a district, the study provides accurate information on the overall distribution and trends of scrub typhus in Mizoram at the population level. Linking IDSP case data with village-level Mission Antyodaya infrastructure data has allowed to examine scrub typhus simultaneously as an individual clinical event and also as a village-level phenomenon shaped by geography and access—an approach rarely attempted for scrub typhus in India. The mixed-effects negative binomial model accounts for clustering and overdispersion in village-level case counts, and the findings are directly actionable for a state health system already investing in scrub typhus surveillance.

The study also has important limitations. The IDSP data is generated through passive, routine surveillance from the health centers and hospitals; the case reporting depends on patients seeking care and being tested, and therefore the true burden could be over- or under-estimated. Associations observed at the village level—the presence of community forest or connectivity—describe area-level exposure and cannot be assumed to uniformly apply for all individuals within that village. 250 villages were not included for the analysis as the name and village ID didn't match the 2011 census villages. Person-level behavioral and occupational data, such as actual participation in rat hunting, personal protective equipment use, or hours of farm work, were not available in either dataset and could not be modelled directly. The village-level model could not fully capture confounders, particularly the climatic variables, which could influence scrub typhus risk.

Mizoram has made tremendous progress in detecting and managing scrub typhus. Despite increased surveillance efforts in Mizoram, transmission of scrub typhus has increased over the years, as reflected in numbers and severity. For effective disease reduction in the state, community-level prevention strategies such as targeted health education in the high-risk areas (particularly among farmers and individuals involved in rice-field activities and rat hunting), promotion of personal protective measures in agricultural and related activities, improved household and community-level rodent control, and reduction of exposure to chigger-infested environments. Ultimately, sustained reductions in scrub typhus in Mizoram will require combining effective surveillance, early diagnosis, and treatment with interventions that reduce exposure before infection occurs.

Declaration

Ethics approval and consent to participate

The IRB that waived informed consent for the secondary data analysis was the Institutional Human Ethics Committee (IHEC), Central University of Kerala (CUK/IHEC/2024/D/07). We confirm that all methods performed in this study were in accordance with the protocol reviewed and approved by the IHEC.

Consent for publication

Not applicable.

Availability of data and materials

The data that support the findings of this study are available from the Integrated Disease Surveillance Program of Mizoram's Health and Family Welfare Department and are not publicly available. The request for de-identified datasets should be made to Dr. Lalfakzuala Pautu, State Vector Borne Disease Control Programme, Health & Family Welfare Department, Mizoram, Email ID: fakaento@gmail.com. Data for village-level predictors were obtained Mission Antyodaya survey 2020 from the India Data Portal (IDP) (https://indiadataportal.com/).

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

PTP and PBN conceptualized, designed, and wrote the first draft of the manuscript. PTP and AC contributed to the literature search. PBN, LP, ZS, and VD contributed to the review and editing of the manuscript. PTP and AC analyzed the data, and KB made the figures. All authors have read and agreed to the final version of the manuscript.

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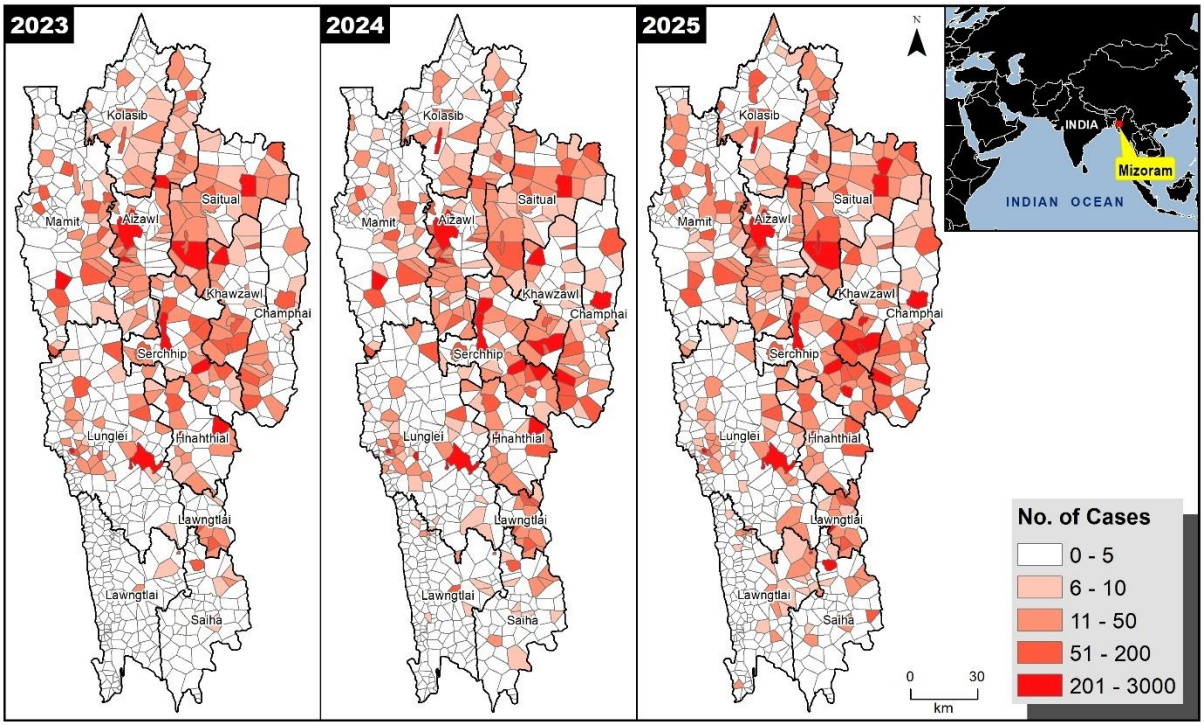
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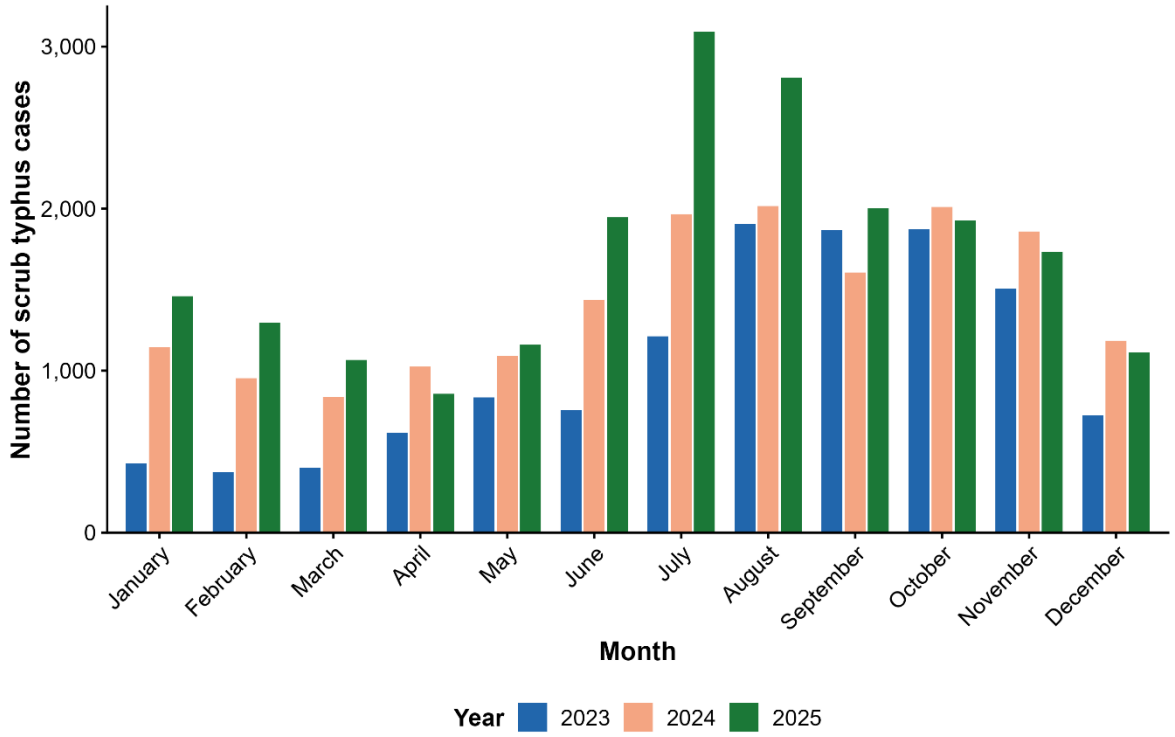
Figures and tables

Figure 1: Spatial distribution of scrub typhus cases across villages in Mizoram, India, 2023–2025 (N= 50,086).



Footnote: *Maps show the village-level distribution of scrub typhus cases for the years 2023, 2024, and 2025. The intensity of the color index represents the increasing number of cases in each village. The inset map (top right) shows the location of Mizoram within India.*

Figure 2: Monthly distribution of scrub typhus cases in Mizoram from 2023 to 2025 (N= 50,086)



576

577 ***Footnote:*** *The bar graph compares monthly case counts for 2023 (blue), 2024 (orange), and*
578 *2025 (green). The x-axis represents the months of the year, and the y-axis shows the number*
579 *of reported scrub typhus cases.*

580

581 **Table 1. Baseline characteristics of scrub typhus cases and their association with**
582 **hospitalization in Mizoram (N= 49462)**

Variable	Outpatient department n (%)	Inpatient department n (%)	Total n (%)	P value
Year				<0.001
2023	11,972 (25.4%)	525 (21.8%)	12,497 (25.3%)	
2024	15,722 (33.4%)	859 (35.6%)	16,581 (33.5%)	
2025	19,357 (41.1%)	1,027 (42.6%)	20,384 (41.2%)	
Season				<0.001
Autumn (September to October)	10,734 (22.8%)	431 (17.9%)	11,165 (22.6%)	
Spring (February to April)	7,037 (15.0%)	310 (12.9%)	7,347 (14.9%)	
Summer (May to August)	19,133 (40.7%)	912 (37.8%)	20,045 (40.5%)	

Winter (November to January)	10,147 (21.6%)	758 (31.4%)	10,905 (22.0%)	
Sex[#]				<0.001
Male	22,992 (48.9%)	1,305 (54.1%)	24,297 (49.1%)	
Female	24,051 (51.1%)	1,106 (45.9%)	25,157 (50.9%)	
Age group				<0.001
<2 years	1,479 (3.1%)	98 (4.1%)	1,577 (3.2%)	
2–4 years	1,965 (4.2%)	131 (5.4%)	2,096 (4.2%)	
5–14 years	5,417 (11.5%)	227 (9.4%)	5,644 (11.4%)	
15–44 years	19,272 (41.0%)	869 (36.0%)	20,141 (40.7%)	
≥45 years	18,918 (40.2%)	1,086 (45.0%)	20,004 (40.4%)	
Symptom[$]				<0.001
Only fever <7 days	20,538 (43.7%)	1,086 (45.0%)	21,624 (43.7%)	
Only fever ≥7 days	9,505 (20.2%)	621 (25.8%)	10,126 (20.5%)	
High fever, headache with rashes, and altered sensorium	17,007 (36.1%)	704 (29.2%)	17,711 (35.8%)	
Test performed[^]				<0.001
Rapid Diagnostic Test	23,406 (49.7%)	1,212 (50.63%)	24,618 (49.96%)	
Weil–Felix Test	21,867 (46.5%)	509 (21.1%)	22,376 (45.2%)	
IgM ELISA	1,602 (3.42%)	673 (28.11%)	2,275 (4.62%)	
Hospital type				<0.001
Primary health centers	23,332 (49.6%)	278 (11.5%)	23,610 (47.7%)	
Community health centers	4,657 (9.9%)	237 (9.8%)	4,894 (9.9%)	
Sub-district and district hospitals	12,267 (26.1%)	161 (6.7%)	12,428 (25.1%)	
Medical college and surveillance-linked facilities	2,938 (6.2%)	873 (36.2%)	3,811 (7.7%)	
Private hospital	3,857 (8.2%)	862 (35.8%)	4,719 (9.5%)	
Total	**47,051**	**2,411**	**49,462***	

Footnote: *Data are presented as n (%). Variables are compared using Pearson's χ^2 test. P<0.05 is considered statistically significant.* ***Missing variables****: *Hospitalization = 624 cases; [#]Age = 8 cases were transgender and were removed due to negligible count; [$] Symptom = 01 case; [^]Test Performed = 193 cases.*

588 **Table 2. Mixed-logistic effects regression model of factors associated with hospitalization**
589 **among scrub typhus cases in Mizoram (N= 49462)**

Variable	adjusted odds ratio (95% confidence interval)	P value
Year		
2023	Reference	
2024	1.72 (1.49–1.99)	<0.001**
2025	1.47 (1.28–1.69)	<0.001**
Season		
Autumn (September to October)	Reference	
Spring (February to April)	1.09 (0.90–1.32)	0.366
Summer (May to August)	1.24 (1.07–1.43)	0.004*
Winter (November to January)	1.35 (1.16–1.57)	<0.001**
Age group		
<2 years	Reference	
2–4 years	1.01 (0.71–1.43)	0.970
5–14 years	0.67 (0.49–0.92)	0.013*
15–44 years	0.63 (0.48–0.84)	0.001*
≥45 years	0.90 (0.68–1.20)	0.472
Sex		
Female	Reference	
Male	1.10 (0.99–1.22)	0.069
Symptoms		
Other symptoms	Reference	
Fever <7 days	1.02 (0.84–1.25)	0.826
Fever ≥7 days	1.27 (1.03–1.55)	0.024*
Diagnostic test		
Weil–Felix	Reference	
Rapid Diagnostic Test	1.02 (0.87–1.21)	0.780
IgM ELISA	2.11 (1.70–2.63)	<0.001**
Hospital type		
Primary health center	Reference	
Community health center	3.21 (0.88–11.72)	0.077
Sub-district hospital and district hospital	1.32 (0.38–4.57)	0.658

Private hospital	36.27 (14.46–91.00)	<0.001**
Medical college and surveillance units[$]	22.22 (3.90–126.60)	<0.001**

Note: *AORs were estimated using a generalized linear mixed-effects logistic regression model with inpatient department (IPD) cases as the outcome and outpatient department (OPD) as the reference category. The model was adjusted for age group, gender, season, year, hospital type, symptom, and test performed. 11 Districts and 118 health facilities were included as random intercepts to account for clustering of observations within districts and healthcare facilities.*
Statistical significance: **P <0.05; **P <0.001*

Table 3. Village-level mixed-effects negative binomial regression of factors associated with scrub typhus cases and hospitalization in Mizoram from 2023–2025 (n=1803 observations)

Variable	Scrub typhus cases IRR (95% CI)	P value	Scrub typhus IPD cases IRR (95% CI)	P value
Population in the village	0.77 (0.69–0.87)	<0.001	1.04 (0.91–1.18)	0.584
Average household size	1.01 (0.90–1.12)	0.905	1.07 (0.93–1.23)	0.374
Households practicing organic farming	1.05 (0.95–1.16)	0.315	1.00 (0.90–1.12)	0.991
Presence of community forest	1.30 (1.03–1.64)	0.029	0.92 (0.69–1.23)	0.573
Presence of open drainage	0.76 (0.42–1.36)	0.352	0.89 (0.43–1.86)	0.764
Presence of solid waste disposal	1.07 (0.85–1.37)	0.556	1.11 (0.83–1.48)	0.497
Presence of all-weather road	1.97 (1.44–2.69)	<0.001	0.88 (0.58–1.32)	0.533
Availability of public transport	0.88 (0.78–0.99)	0.034	0.98 (0.84–1.14)	0.780
Presence of sub-centre	1.15 (0.91–1.45)	0.239	0.96 (0.71–1.30)	0.775
Distance to nearest primary health centre	0.58 (0.52–0.65)	<0.001	0.81 (0.72–0.91)	<0.001
Year	1.27 (1.21–1.33)	<0.001	1.35 (1.23–1.49)	<0.001

Footnote: *Models were fitted using mixed-effects negative binomial regression with a log link, population as an offset, and random intercepts for district and village to account for clustering and repeated observations of villages over the three study years. The analysis included 1,803 village-year observations from 601 villages across 2023–2025; year was centered at 2023. Continuous predictors were standardized; binary predictors were coded as 0/1. For the scrub typhus cases model, the district-level random-effect variance was 0.377 (SD = 0.614) and the village-level random-effect variance was 1.139 (SD = 1.067). For the scrub typhus IPD cases model, the district-level random-effect variance was 0.324 (SD = 0.569) and the village-level random-effect variance was 0.855 (SD = 0.925). The negative binomial dispersion parameters were 2.94 and 2.20 for scrub typhus cases and IPD cases, respectively. Statistical significance was defined as $P < 0.05$. IRR = incidence rate ratio; CI = confidence interval; IPD = inpatient department.*

Supplementary Files

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