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# Concurrent Infections And Proportional Analysis Of Etiological Agents In Pediatric Tropical Fevers: A Tertiary Care Perspective

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## ABSTRACT

**Background:** Pediatric tropical fevers represent a significant burden in many low- and middle-income countries, with multiple pathogens—viral, bacterial, and parasitic—coexisting in endemic regions. Co-infections further complicate clinical presentation and outcomes. Understanding the proportional etiology, clinical profiles, and outcomes among pediatric populations is essential for guiding diagnostic algorithms, targeted therapeutic interventions, and effective public health strategies.

**Methods:** This observational descriptive study was conducted in the pediatric wards of Malda Medical College and Hospital, West Bengal, over one year (December 2022–November 2023). We enrolled 100 children (up to 12 years of age) presenting with fever and at least one of the following: rash/thrombocytopenia, respiratory distress, renal failure, encephalopathy, jaundice, or multi-organ dysfunction syndrome (MODS). Laboratory diagnoses included malaria smears, ELISA for scrub typhus, leptospirosis, chikungunya, dengue (NS1, IgM, IgG), bacterial blood cultures, and other relevant tests. Descriptive and inferential statistics were performed using SPSS version 26.0.

**Results:** Of the 100 enrolled children, the most common confirmed infection was dengue (42%), followed by scrub typhus (31%), enteric fever (3%), malaria (1%), and leptospirosis (1%). Notably, 22% of children presented with concurrent co-infections; dengue plus scrub typhus was the most prevalent combination (14%). The majority of cases (62%) occurred in children aged 5–12 years, and 60% were male. Median fever duration was 8 days. Common clinical features included vomiting (92%) and abdominal pain (82%). Overall mortality was 3% (3/100), predominantly linked to severe co-infections and complications such as hemophagocytic lymphohistiocytosis (HLH) or severe hepatitis with encephalopathy.

**Conclusion:** Dengue and scrub typhus emerged as the major contributors to pediatric tropical fevers in our setting, frequently co-existing and contributing to severe disease. Prompt recognition of co-infections is crucial to avert adverse outcomes. Further large-scale studies are warranted to optimize diagnostic protocols and management pathways in resource-limited settings.

***Keywords:*** *Tropical fevers, Pediatric infections, Dengue, Scrub typhus, Concurrent infections, Etiology*

## 1. INTRODUCTION

Tropical fevers remain a leading cause of pediatric admissions in many developing countries, reflecting complex interactions between environmental factors, socioeconomic conditions, and pathogen epidemiology [1]. In South and Southeast Asia, including India, etiological agents of tropical fever frequently include viral pathogens (e.g., dengue, chikungunya, Japanese encephalitis), bacterial agents (e.g., scrub typhus, leptospirosis, enteric fever), and parasites (e.g., malaria, kala-azar) [2,3]. While dengue remains a major public health threat with recurrent outbreaks, scrub typhus has recently received increasing attention due to its expanding geographic range, variable clinical presentation, and high morbidity if untreated [4]. Furthermore, multi-pathogen concurrent infections can exacerbate clinical severity and pose additional challenges in diagnosis and management.

Children represent a vulnerable population, often with immature immune systems, limited host defense reserves, and higher exposure risk due to environmental and behavioral factors [5]. Early diagnosis is often complicated by overlapping clinical manifestations such as fever, headache, rash, and organ dysfunction, which can be shared among multiple pathogens. For instance, dengue, scrub typhus, and leptospirosis can all present with high fever, hepatitis, thrombocytopenia, and shock [6]. When these infections coexist, therapeutic approaches become more complex, demanding a high index of suspicion and rapid, targeted testing [7]. Additionally, concurrent infections may delay recovery, prolong hospital stays, and potentially heighten mortality risk if not identified promptly.

Despite the abundance of tropical pathogens in resource-limited environments, comprehensive studies focusing on proportional etiologies and co-infections among hospitalized pediatric cases are relatively scarce. Most epidemiological investigations have targeted a single disease, which may underestimate the true burden of mixed pathogens [8]. Understanding the local etiology and distribution of these infections is vital for informing public health interventions such as vector control measures, community-based awareness programs, and the rational use of antibiotics and antivirals.

This study was conceived to assess (a) the predominant etiological factors responsible for tropical fevers in children, (b) the proportion of concurrent infections and their clinical impact, and (c) the mortality profile among pediatric patients admitted with tropical fevers to a tertiary care setting in eastern India. By elucidating the distribution and burden of single vs. co-infections, our work aims to inform clinicians and policymakers about critical diagnostic and management pathways, thereby improving both clinical outcomes and resource allocation. The findings presented here will also serve as a foundation for more extensive investigations into the immune pathogenesis of concurrent infections and the development of integrated diagnostic algorithms.

## 2. MATERIALS AND METHODS

### Study Design

This was an **observational descriptive study** carried out in children admitted with tropical fever in the pediatric wards of Malda Medical College and Hospital, West Bengal.

### Study Setting and Timelines

- **Duration**: December 2022 to November 2023
- **Population**: 100 children (up to 12 years of age) presenting with fever (≥3 days) and one or more of the following clinical signs: (i) rash/thrombocytopenia, (ii) respiratory distress, (iii) renal failure, (iv) encephalopathy, (v) jaundice, or (vi) multi-organ dysfunction syndrome (MODS).

Each patient was followed until discharge or final outcome (death).

### Inclusion and Exclusion Criteria

- **Inclusion**:
  - All children admitted for tropical fever under evaluation.
- **Exclusion**:
  - Parents not willing to provide informed consent.
  - Children younger than 1 month of age.
  - Patients recently hospitalized or having surgery within 2 weeks, or those with known conditions posing increased risk of recurrent fevers (e.g., HIV, congenital heart disease, immunosuppressive therapy).

### Sample Size

A total of **100** consecutive children meeting the inclusion criteria were enrolled during the study period.

### Data Collection

Relevant demographic and clinical details (e.g., age, sex, geographic origin, seasonality, presenting symptoms, comorbidities) were recorded on a predesigned proforma. Laboratory investigations included:

1. **Complete Blood Counts** (hemoglobin, total leukocyte count, platelets).
2. **Serology**:
   - Scrub typhus IgM ELISA (cut-off 0.5 OD), confirmed by indirect immunofluorescence assay (IFA).
   - Leptospira IgM ELISA (with microscopic agglutination test, MAT).
   - Dengue rapid NS1 antigen, IgM/IgG testing, and MAC-ELISA.

- Chikungunya IgM ELISA.

3. **Blood Smears and Rapid Diagnostic Tests** for malaria (both thick and thin smear). Species confirmation by PCR if smears were positive or inconclusive.
4. **Blood Cultures**: Automated (BATEC) or conventional methods, with subsequent pathogen identification and sensitivity testing.
5. **Other Tests**: Liver function tests, renal function tests, chest X-ray, ultrasound abdomen, cerebrospinal fluid (CSF) analysis (where indicated), and relevant biochemical parameters (e.g., LDH, ferritin, PT, INR) as clinically warranted.

**Case Definitions**

- **Dengue**: Positive NS1 antigen and/or MAC-ELISA.
- **Malaria**: Positive smear and/or PCR.
- **Scrub Typhus**: Positive IgM ELISA and IFA.
- **Leptospirosis**: Positive IgM ELISA and confirmatory MAT.
- **Enteric Fever (Typhoid)**: Positive blood culture for Salmonella Typhi/Paratyphi.
- **Chikungunya**: Positive IgM ELISA.
- **Kala Azar**: Demonstration of Leishman–Donovan (LD) bodies in bone marrow aspirate.
- **Japanese Encephalitis**: IgM capture ELISA of serum or CSF.
- **Co-Infection**: Simultaneous laboratory confirmation of ≥2 pathogens.

**Statistical Analysis**

Data were entered and analyzed using **SPSS version 26.0**. Categorical variables are reported as frequencies/percentages, whereas continuous variables are presented as mean ± standard deviation or median (range) as appropriate. Associations were tested using the chi-square test for categorical variables and the Z-test or t-test for continuous variables. A p-value <0.05 was considered statistically significant.

## 3. RESULTS

**Overall Findings**

A total of 100 children (up to 12 years) were included. The most common single infection was dengue (42%), followed by scrub typhus (31%), enteric fever (3%), malaria (1%), and leptospirosis (1%). Con-current (mixed) infections were seen in 22% of children, with dengue-plus-scrub-typhus the predominant combination (14%).

**Table 1. Etiological Distribution of Tropical Fevers (n=100)**

| Etiology | Frequency | Percentage (%) |
|---|---|---|
| Dengue | 42 | 42 |
| Scrub typhus | 31 | 31 |
| Enteric fever | 3 | 3 |
| Malaria | 1 | 1 |
| Leptospirosis | 1 | 1 |
| Other/None | 0 | 0 |
| **Co-infections** | 22 | 22 |
| **Total** | 100 | 100 |

Among co-infections, 14% had dengue plus scrub typhus, 2% had dengue plus enteric fever, 2% had scrub typhus plus enteric fever, 2% had scrub typhus plus malaria, and 1% each had (i) dengue + scrub typhus + malaria, and (ii) scrub typhus + leptospira.

**Demographic and Clinical Profile**

The majority of enrolled children were in the 5–12 year age group (62%), followed by 1–5 years (32%), and <1 year (6%). Males comprised 60% of the study population.

**Table 2. Age and Gender Distribution (n=100)**

| Variable | Frequency | Percentage (%) |
|---|---|---|
| **Age** | | |
| <1 year | 6 | 6 |
| 1–5 years | 32 | 32 |
| >5–12 years | 62 | 62 |
| **Gender** | | |
| Male | 60 | 60 |
| Female | 40 | 40 |

Median duration of fever at presentation was 8 days (range 3–16 days). Common symptoms included vomiting (92%) and abdominal pain (82%). About 58% presented with rash, 54% showed jaundice, and 76% had pallor.

**Co-Infections and Complications**

Dengue plus scrub typhus accounted for the highest proportion of co-infections (14%). Complications seen with dengue included acute hepatitis, pneumonia, hemophagocytic lymphohistiocytosis (HLH), and empyema thoracis. Scrub typhus complications encompassed encephalitis, acute hepatitis, acute cholecystitis, and in one case, tubercular meningitis was also identified.

**Laboratory Findings**

- **Anemia (pallor)** was noted in 76% overall, with mean hemoglobin levels significantly lower in non-survivors (7.43 g/dL) compared to survivors (10.06 g/dL) (p=0.032).
- **Liver function abnormalities** were detected in 54% of patients, more common in those with prolonged fever (>7 days).
- **Platelet counts** varied substantially, but severe thrombocytopenia was observed primarily in dengue and mixed infections.

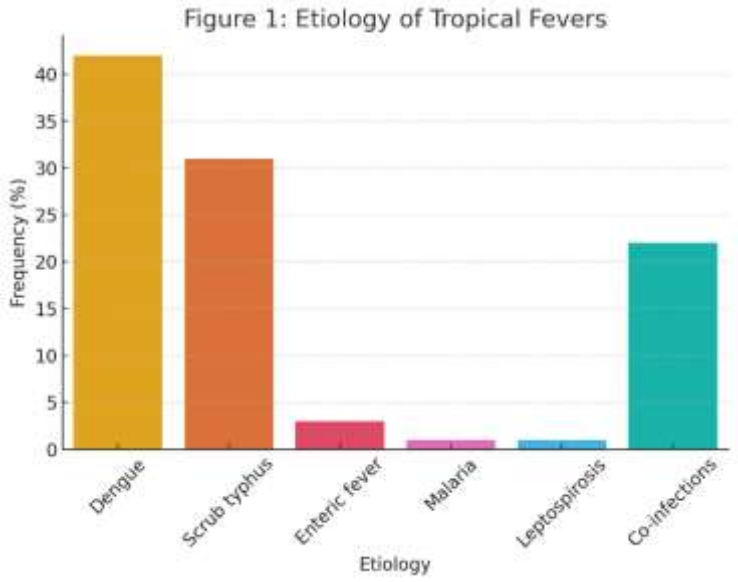
**Outcomes**

Overall mortality was 3% (3/100). Two patients succumbed to severe scrub typhus-related complications (one co-infected with leptospira; another with encephalitis and acute hepatitis), and one child with dengue complicated by HLH died despite intensive care support. The remaining 97% of children recovered and were discharged.

**Table 3. Final Outcomes (n=100)**

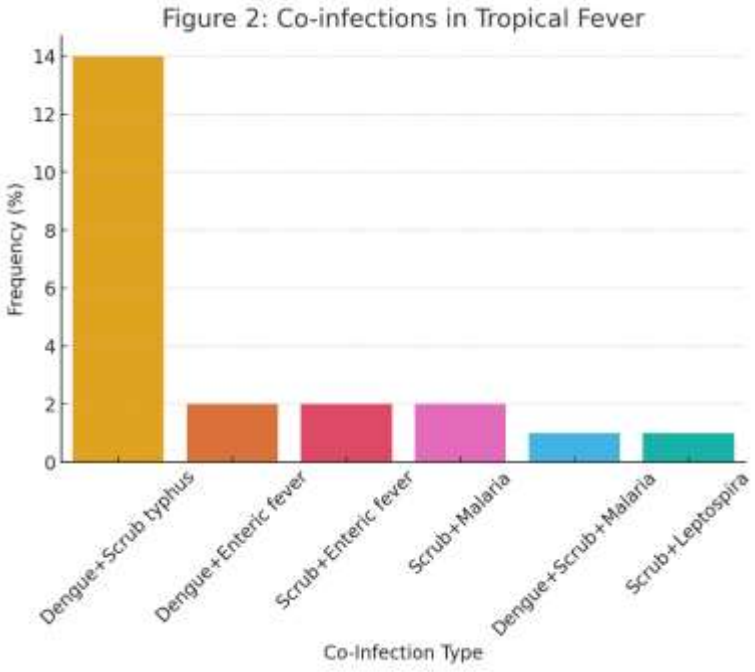
| Outcome | Frequency | Percentage (%) |
|---|---|---|
| Discharged | 97 | 97 |
| Death | 3 | 3 |
| **Total** | 100 | 100 |

**Figure 1. Etiology of Tropical Fevers (Single Infections vs. Co-infections)**




(A bar chart illustrating distribution of etiologies, with 42% dengue, 31% scrub typhus, etc., and 22% co-infections.)

**Figure 2. Co-infections in Tropical Fever**




(A bar chart demonstrating the most frequent co-infections, e.g., dengue + scrub typhus [14%], scrub typhus + malaria [2%], etc.)

## 4. DISCUSSION

In this tertiary care-based observational study, dengue emerged as the predominant cause of pediatric tropical fever, closely followed by scrub typhus. The findings are consistent with other hospital-based reports from the Indian subcontinent, where dengue outbreaks have been recurrent and scrub typhus prevalence has increased, particularly in the foothills and rural areas [1,2]. This shift in epidemiology underscores the need for heightened clinical vigilance and improved laboratory capacity [3].

Importantly, a substantial fraction (22%) of patients harbored co-infections, with dengue plus scrub typhus the most common combination. Co-infections can stem from overlapping ecologies of vectors (e.g., Aedes mosquitoes for dengue and chiggers for scrub typhus) and shared risk factors such as poor sanitation and high rainfall [4]. Concomitant infections may intensify clinical severity through additive or synergistic pathogenic mechanisms, contributing to organ dysfunction and complicating clinical diagnosis [5]. In our cohort, several co-infection cases progressed to severe complications, including hepatitis, encephalopathy, and HLH, reflecting the danger of missing a secondary pathogen.

Anemia and liver dysfunction were notable findings, affecting over half of the patients. In resource-limited settings, factors such as malnutrition, repeated infections, and delayed presentation exacerbate these abnormalities [6]. Interestingly, the mean hemoglobin level was significantly lower in non-survivors, suggesting that severe anemia might be a predictor of poor outcome, warranting early correction and transfusion if necessary. Meanwhile, 54% demonstrated jaundice or abnormal liver function tests, particularly those with a fever duration exceeding seven days. Such hepatic involvement is well-documented in dengue and scrub typhus, potentially reflecting direct viral/bacterial injury or a hyperinflammatory state [7].

Despite these challenges, overall mortality remained relatively low (3%). This may be attributable to increased awareness, earlier diagnosis, and prompt initiation of appropriate antimicrobial therapies, such as doxycycline for scrub typhus and supportive measures for dengue. Nonetheless, the three deaths highlight the lethal potential of complicated or co-infected fevers in pediatric populations, especially when delayed recognition results in multi-organ failure [8]. Strengthening diagnostic protocols with combined rapid tests or point-of-care devices could further reduce mortality.

The current study has certain limitations. Being single-center and having a modest sample size may limit the generalizability of results. Serological tests can yield false positives or negatives, particularly in endemic areas where subclinical infections or cross-reactivity is possible. However, employing confirmatory tests (e.g., IFA for scrub typhus, MAT for leptospirosis) improved specificity. Larger, multi-centric studies evaluating long-term outcomes, immunologic markers, and cost-effectiveness of advanced diagnostics are warranted.

In summary, these findings emphasize that pediatric tropical fevers in endemic regions often involve overlapping clinical pictures, with frequent co-infections. Robust surveillance, early diagnostics, and careful clinical monitoring are pivotal to achieving better outcomes. Strengthening public health infrastructure to address vector control and awareness campaigns can further minimize the morbidity and mortality associated with these infections.

## 5. CONCLUSION

Pediatric tropical fevers in our tertiary care setting were chiefly attributed to dengue and scrub typhus, with a notable 22% of children presenting with co-infections. Co-infections were linked to higher complication rates, including severe hepatitis, encephalopathy, and HLH. Although overall mortality was low (3%), severe anemia and multi-organ dysfunction were key predictors of poor outcome. Prompt, comprehensive diagnostic workups for multiple pathogens are essential. Improving clinical suspicion for mixed infections, along with timely therapeutic interventions, could further reduce complications and mortality among pediatric age groups in resource-limited settings.

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