ORIGINAL ARTICLE

# Clinical and Laboratory Profile of Patients with Tropical Coinfections Admitted at a Tertiary Care Center in North India

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## Abstract

**Background:** Tropical coinfections (CI) are the simultaneous occurrence of two or more vector-borne diseases in a single host. The prevalence of such illnesses is not uncommon among tropical and subtropical regions such as India; however, these CIs have not been systematically studied prospectively. Mixed infections can prove potentially detrimental if underdiagnosed or undertreated. We undertook this study to estimate the prevalence and compare the clinical profile, laboratory characteristics, and various outcomes among the patients with tropical CI who presented with acute undifferentiated febrile illness (AUFI).

**Materials and methods:** A prospective, observational study was conducted on adult patients hospitalized with tropical CIs. As per the clinical suspicion, a panel of tests for dengue fever (D), malaria (M), scrub typhus (S), leptospirosis (L), chikungunya (C), and brucella (B) was carried out. Statistical analysis was done using standard methods.

**Results:** The mean age of the population was 39.4 ± 17.3 years. Among 986 patients presenting with AUFI, 8.1% of the patients had CIs. Of these CIs, 95% had dual infections, and 5% had CIs with three tropical pathogens. We observed 17 diverse tropical CI combinations; four predominant being D + L, D + S, D + C, and S + L with a prevalence of 26.2, 25, 15, and 13.8%, respectively. 16.25% of the patients with tropical CIs died, mostly those suffering from D + S and D + L. Coinfection with D + S had predominant acute kidney injury (AKI), whereas acute transaminitis was highest in the D + L category. Acute respiratory distress syndrome (ARDS) was clinically significant in S + L, and multiorgan dysfunction was highest in the D + S combination. Using logistic regression, AKI, hepatitis, ARDS, shock, gastrointestinal bleeding, and myocarditis were independent risk factors for mortality.

**Conclusion:** Our study identified 17 different combinations of CIs. Four groups, i.e., D + L, D + S, D + C, and S + L—accounted for 80% of CIs. Despite significant organ involvement in certain CI combinations, we conclude that a clinical bedside differentiation of tropical CIs from monomicrobial infections is often difficult. Hence, optimal treatment for a possible CI may well be commenced empirically and early, bearing in mind an 8% probability of a concurrent tropical coinfection.


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## Introduction

Tropical infections are commonly encountered entities in tropical and subtropical regions, including India. The presence of two or more infections simultaneously in one host is generally termed a tropical coinfection (CI). This terminology is synonymous with mixed infection, concurrent infections, or polyinfections. Coinfections tend to have more harmful effects on host health than single infections.

Coinfections (CIs) are emerging as a major causative phenomenon among patients of acute undifferentiated febrile illness (AUFI).[1,2] Numerous studies have shown that scrub typhus, malaria, dengue fever, and leptospirosis CIs have a widespread geographical distribution in our country, right from the Himalayan belt to the coastal regions of South India.[3]

The occurrence of the CIs can be postulated by two diverse mechanisms. These can either happen owing to contracting various infections concurrently in a particular time frame or as a consequence of enhanced pathogenicity of a coincident subclinical infection due to altered immune response.[4] It is often seen that when two organisms coexist, they increase each other's penetration and virulence, resulting in more severe outcomes and mortality.

Tropical diseases usually present with similar and nonspecific symptoms such as fever, headache, body aches, and gastrointestinal issues. This overlapping symptomatology makes accurate diagnosis of CIs extremely challenging, leading to diagnostic confusion and delays in appropriate treatment. The lack of distinctive characteristics in the early stages of AUFI/CIs often creates clinical and therapeutic dilemmas for the physicians, especially if the presentation is atypical. Serological cross-reactivity between different pathogens can further complicate diagnostic test interpretation.

Coinfections need to be strongly suspected and substantiated since underdiagnosis and mistreatment may have adverse consequences. Since the clinical features of AUFI widely overlap, the Indian Society of Critical Care Medicine group endorses a 'syndromic approach' for diagnosis and management to help narrow down the possibilities and simplify the treatment.[5] However, CIs may not always follow this syndromic approach, as the clinical presentation may get distorted. From a treatment perspective, CIs complicate drug regimens, risking interactions and reduced efficacy, necessitating integrated therapeutic approaches.

A better understanding of CI epidemiology helps in assessing the true burden of disease and developing comprehensive preventive strategies, guiding public health interventions, resource allocation, and the development of integrated surveillance systems. It promotes a shift from vertical, disease-specific programs to more horizontal and integrated healthcare systems for better management of complex health scenarios. Our study is an attempt to explore and understand these infections when they occur as CIs and emphasize the need for a multidimensional diagnostic approach and treatment.

## Aims and Objectives

- To estimate the prevalence of various tropical CIs among patients presenting with AUFI.
- To compare the clinico-laboratory profile and outcome of these CIs.

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## Materials and Methods

### Study Design and Setting

A prospective and observational study was carried out in the Departments of General Medicine and Microbiology at our hospital, which caters to the northern states of India. The study commenced after due clearance from the Institutional Ethics Committee, GMCH vide letter no. GMC/IEC/2020/570R/226 dated 12.05.2021, and was conducted over 20 months.

### Sample Size

The study population consisted of all patients hospitalized with AUFI who presented to the medicine emergency department during the study period. The sample size was calculated based on prevalence of tropical infection in patients with undifferentiated fever which was found to be 2.1% in the study by Chitkara et al.[6] Assuming a 95% confidence interval and 5% margin of error, the sample size came out to be 30, but keeping the unpredictable nature of outbreaks, the sample size was kept unlocked for the total duration of the study.

### Inclusion Criteria

Patients older than 18 years who were hospitalized with AUFI (a fever ≤14 days) and without evidence of localized infection and diagnosed to have a tropical CIs were included in the study. AUFI was defined as a fever less than 2 weeks in duration with no organ-specific symptom at the onset. Coinfection was defined as simultaneous infections of the host by multiple (two or more) pathogens.[1]

### Exclusion Criteria

Patients having fever with evidence of localized infections, autoimmune diseases, or malignancy, fever of >14 days' duration, prior antibiotic use, or hospitalization were excluded.

### Methodology

Patients with AUFI were enrolled after written informed consent was obtained. All enrolled cases were examined thoroughly and investigated with complete hemogram, ESR, CRP, urine examination, and liver and renal function tests. Simultaneously, a panel of tests for dengue fever, malaria, scrub typhus, leptospirosis, CHIK, and brucella serology and other viral serology such as hepatitis A and E (CTK Biotech, USA) was carried out judiciously as per the clinical suspicion, keeping in mind the diagnostic possibility and available resources.

Malaria (M) was diagnosed based on rapid diagnostic tests for antigen detection (SD biosensor) and peripheral blood smear for malaria parasite (trophozoite of *Plasmodium falciparum*, *Plasmodium vivax,* or mixed). Dengue fever (D) diagnosis was established by detection of dengue NS1 antigen test (TransAsia Bio-Medicals Ltd., India) or by dengue IgM antibody (National Institute Virology, NIV Pune). Leptospirosis (L), scrub typhus (S), brucellosis (B) and chikungunya (C) were established by IgM ELISA for Leptospira organisms (Nova Tec Immundiagnostica, GmBH), *O. tsutsugamushi* (J. Mitra & Co. Pvt Ltd India), brucella IgM (Calbiotech, CA) and anti-CHIKV antibodies, respectively [National Institute of virology (NIV), Pune]. Widal test/typhi dot IgM/blood cultures were carried out for *Salmonella* Typhi. Specific imaging was performed as and when needed. Patients suffering from more than one infectious etiology at the same time were considered CI. The scheme of enrolling the patients is depicted in Figure 1.

For assessing and documenting the complications, the following study definitions were used. Acute liver injury (ALI) was defined according to EASL guidelines as an elevation of liver enzymes 2–3 times the upper normal limit.[7] Acute kidney injury (AKI) was taken into consideration depending upon KDIGO AKI staging.[8] The diagnosis of acute respiratory distress syndrome (ARDS) was made according to Berlin's criteria.[9]

### Statistical Analysis

Statistical analysis was done using IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. Categorical variables were compared using the chi-square and Fisher's exact test. Continuous variables were analyzed as mean (SD) or median (range) using Student's *t*-test. Logistic regression analyses were performed to find the predictors of mortality/poor outcome. A two-sided $p \leq 0.05$ was considered statistically significant.

## Results

Among 986 patients studied, 8.1% ($n$ = 80) had tropical CIs. Of the 80 patients with CIs, 95% ($n$ = 76) had a dual infection, and 5% ($n$ = 4) had a triple infection. Seventeen different combinations of tropical CIs were obtained with four predominant groups, as shown in Figure 2.

The mean age of our patients was 39.4 ± 17.3 years. 42.5% of patients were aged between 18 and 30 years, 38.8% were between 31 and 50 years, and 18.8% were above 50 years of age. Both genders were equally affected. 62.5% of patients were

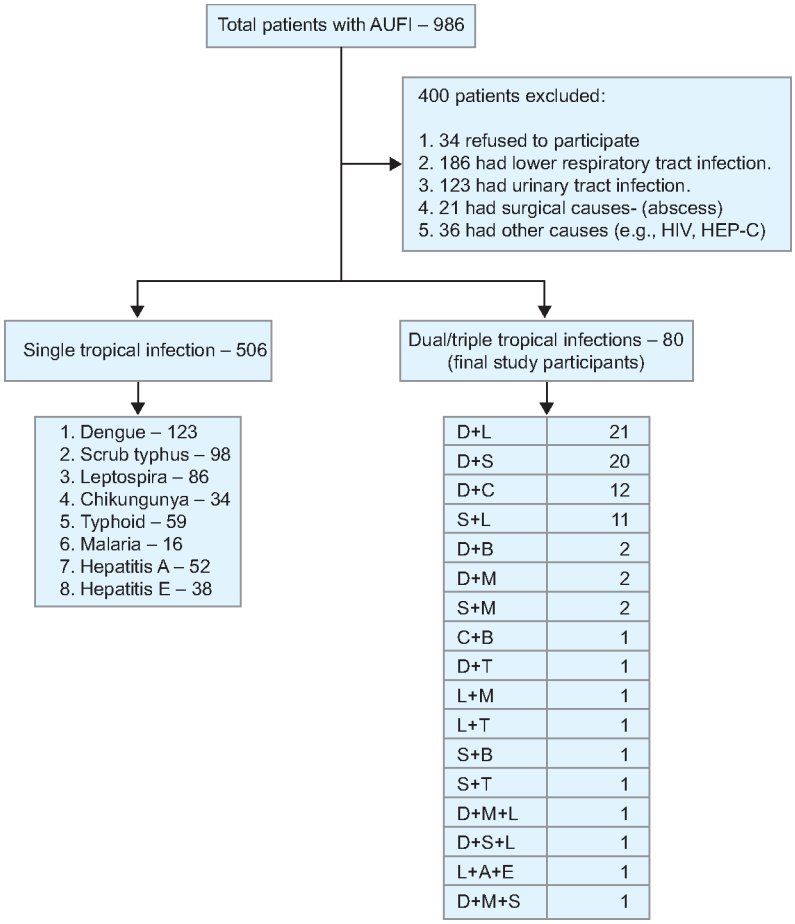


**Fig. 1:** Scheme of enrolling study participants

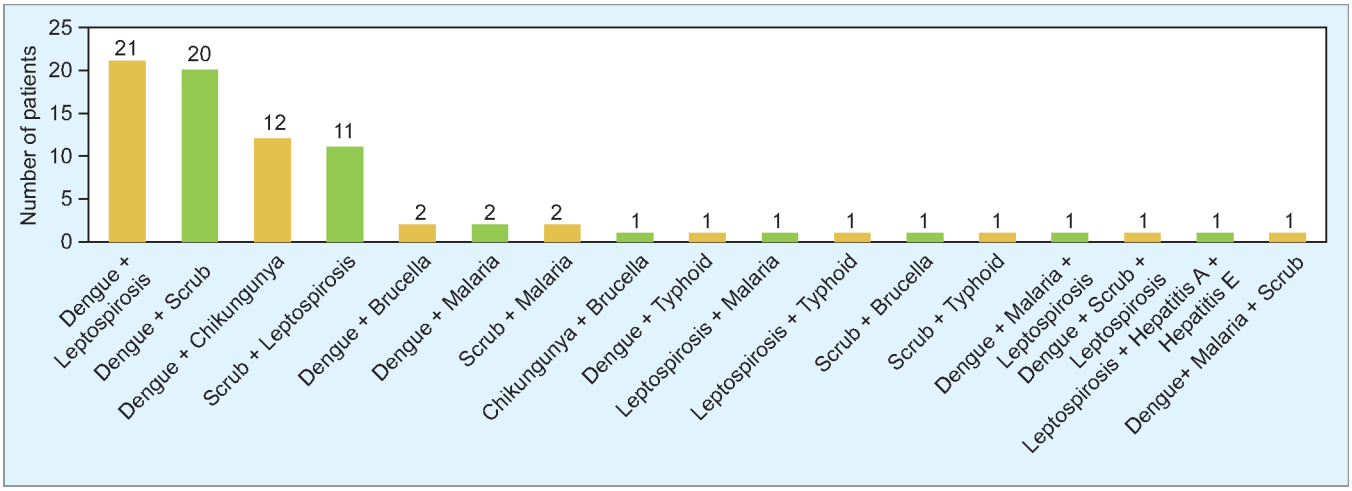


**Fig. 2:** Distribution of tropical coinfections in total study population

**Table 1:** Major laboratory parameters in four major coinfection groups

| *Parameter* | *Total (N = 80)* | *D + L (n = 21)* | *D + S (n = 20)* | *D + C (n = 12)* | *S + L (n = 11)* | *p-value** |
|---|---|---|---|---|---|---|
| Hemoglobin (gm/dL) | 10.86 ± 2.39 | 11.64 ± 2.28 | 10.90 ± 2.09 | 11.13 ± 1.94 | 9.76 ± 2.55 | 0.116 |
| TLC ($\times 10^9$/L) | 9.78 ± 6.43 | 9.23 ± 6.55 | 11.75 ± 5.98 | 6.92 ± 2.62 | 12.78 ± 9.85 | 0.158 |
| Platelet ($\times 10^9$/L) | 76.18 ± 79.36 | 81.90 ± 98.01 | 75.85 ± 59.82 | 81.75 ± 11.08 | 56.72 + 43.84 | 0.672 |
| INR | 1.18 ± 0.27 | 1.13 ± 0.20 | 1.24 ± 0.42 | 1.17 ± 0.26 | 1.13 ± 0.15 | 0.821 |
| Urea (mg/dL) | 69.75 ± 70.14 | 71.95 ± 66.8 | 105.15 ± 102 | 41.25 ± 39.3 | 71 ± 45 | 0.117 |
| Creatinine (mg/dL) | 1.42 ± 1.46 | 1.24 ± 0.66 | 2.30 ± 2.59 | 0.98 ± 0.61 | 1.18 ± 0.49 | 0.261 |
| AST (IU/L) | 769 ± 1659 | 1354.9 ± 2484.7 | 519.5 ± 779.75 | 270.75 ± 516.32 | 471.82 ± 958.46 | 0.253 |
| ALT (IU/L) | 445.16 ± 926.66 | 592.57 ± 918.67 | 381.45 ± 680.10 | 170.33 ± 324.35 | 243.82 ± 413.80 | 0.395 |
| Albumin (gm/dL) | 2.91 ± 0.55 | 3.05 ± 0.62 | 2.91 ± 0.47 | 2.57 ± 0.64 | 2.74 ± 0.44 | 0.093 |
| Alkaline phosphatase (IU/L) | 183.7 ± 132 | 157.62 ± 104.4 | 221.35 ± 143.8 | 171.67 ± 163.6 | 281.45 ± 136.5 | 0.031 |

*Kruskal-Wallis test; D+L: Dengue + Leptospirosis; D + S: Dengue fever + Scrub typhus D + C: Dengue fever + Chikungunya; S + L: Scrub typhus + Leptospirosis; TLC: Total Leucocyte Count; INR: International normalized ratio; AST: Aspartate aminotransferase; ALT: Alanine transaminase; Alkaline phosphatase was the only significant lab parameter consistently elevated in all 4 dual tropical infection groups

from urban backgrounds, and these had predominantly D + C, D + S, and S + L infection. In rural areas, 61.9% had the D + L CIs.

Even in patients with tropical CIs, the most common symptoms were abdominal pain in 36 (45%), followed by shortness of breath in 35 (43.8%), generalized weakness in 28 (35%), and myalgia in 27 (33.8%) patients. Other symptoms were cough and vomiting in 25 (31%) patients each, joint pains in 15 (18.8%), jaundice and diarrhea each in 10%. These symptoms were quite nonspecific and noncontributory. Few symptoms were helpful, for example, abdominal pain, which was predominantly seen in patients with the D + L (57%) CI. Breathlessness was chiefly present in D + S (55%) and D + L (33.3%) CI. However, others, such as mucosal bleeding was observed in all four subgroups: D + S (25%), D + C (33.3%), D + L (14.2%), S + L (27.2%).

Among the physical findings, hepatosplenomegaly was the most consistent sign but had no specific predilection for a particular CI. Nevertheless, pleural effusion seen in 24 (30%) patients did point toward dengue fever, as 54.1% of these had evidence of dengue fever CI (*p*-value 0.002). Eschar was seen exclusively with scrub typhus subgroups. Rash was seen in 90% of patients having dengue fever.

Investigations also helped to narrow down the diagnostic possibilities in AUFI. Aspartate aminotransferase/alanine transaminase (AST/ALT) was found maximally raised in the D + L group. Mild to moderate anemia was part of the spectrum of tropical fevers. Leukocytosis was also noted only in patients having S + L. However, mild to moderate thrombocytopenia was common to all tropical CIs patients. No other parameter showed any significant difference among the CI groups. Table 1 depicts the various laboratory parameters among the four major CI groups in the study population.

Coming to the organ involvement and complications, 86.2% of patients developed at least one complication, namely ALI, AKI, ARDS, pneumonia, myocarditis, or encephalopathy. ALI was seen predominantly in D + S (70%) and D + L (57%) CIs. Similarly, AKI (70%) and ARDS (45%) were predominantly noted in the D + S subgroup. Multiorgan dysfunction was statistically higher in patients with scrub typhus subgroups. On the other hand, polyserositis was noted in the majority having dengue fever as CI. Other complications, such as myocarditis, hemodynamic shock, encephalopathy, and mucosal bleed, were noted only in a small number of patients. Unexpectedly, pneumonia was seen in 85.7% of patients having dengue fever as one of the co-etiologies. The various multiorgan complications in different CI are listed in Table 2. Various syndromic distribution of the four major CIs is shown in Table 3.

Case mortality was seen in 13 (16.25%) patients; the highest among D + L and D + S, resulting in a total of 76.9% deaths. The distribution of mortality among various groups is depicted in Figure 3. We observed that AKI, hepatitis, ARDS, shock, polyserositis, GI bleed, and myocarditis were independent predictors of mortality (Table 4).

## Discussion

Rapid urbanization and immigration without corresponding development of

**Table 2:** Comparison of multiorgan dysfunction in four major coinfection groups

| *Complications* | *D + L (n = 21)* | *D + S (n = 20)* | *D + C (n = 12)* | *S + L (n = 11)* | *p-value** |
|---|---|---|---|---|---|
| Hepatitis + AKI | 11 (52) | 14 (70) | 2 (16.6) | 6 (54.5) | 0.019* |
| Hepatitis + ARDS | 3 (14.2) | 9 (45) | 1 (8.3) | 7 (63.6) | 0.142 |
| Hepatitis + shock | 4 (19) | 3 (15) | 2 (16.6) | 1 (9) | 0.260 |
| Hepatitis + encephalopathy | 4 (19) | 6 (30) | 3 (25) | 1 (9) | 0.679 |
| ARDS + AKI | 3 (14.2) | 9 (45) | 1 (8.3) | 6 (54.5) | 0.010* |
| Encephalopathy + AKI | 4 (19) | 6 (30) | 2 (16.6) | 1 (9) | 0.315 |
| Shock + AKI | 4 (19) | 3 (15) | 2 (16.6) | 1 (9) | 0.190 |
| ARDS + shock | 3 (14.2) | 3 (15) | 1 (8.3) | 1 (9) | 0.037 |
| ARDS + encephalopathy | 3 (14.2) | 6 (30) | 1 (8.3) | 1 (9) | 0.514 |

*Advanced regression analysis; percentage in parenthesis; D + L: Dengue fever + Leptospirosis; D + S: Dengue fever + Scrub typhus; D + C: Dengue fever + Chikungunya; S + L: Scrub typhus + Leptospirosis; AKI: acute kidney injury; ARDS: acute respiratory distress syndrome; Hepatitis in combination with AKI was the most prominent complication seen in the majority followed by ARDS and AKI. These complications were higher in dengue and scrub coinfection

**Table 3:** Syndromic distribution of various tropical coinfections

| *Syndromes* | *N (80)* | *D + L (n = 21)* | *D + S (n = 20)* | *D + C (n = 12)* | *S + L (n = 11)* | *p-value** |
|---|---|---|---|---|---|---|
| Fever with thrombocytopenia | 72 | 16 (76.1) | 18 (90) | 11 (91) | 10 (90.9) | 0.739 |
| Fever with hepatitis | 44 | 12 (57.1) | 14 (70) | 4 (33.3) | 7 (72.7) | 0.327 |
| Fever with renal failure | 36 | 11 (52.3) | 14 (70) | 2 (16.6) | 6 (54.5) | 0.621 |
| Fever with respiratory distress | 22 | 3 (14.2) | 9 (45) | 1 (8.33) | 7 (63.6) | 0.585 |
| Fever with encephalopathy | 14 | 4(19) | 6 (30) | 3 (25) | 1 (9) | 0.186 |

*Advanced regression analysis; percentage in parentheses; D + L: Dengue fever + Leptospirosis; D + S: Dengue fever + Scrub typhus; D + C: Dengue fever + Chikungunya; S + L: Scrub typhus + Leptospirosis; AUFI presented us into five varied syndromes, with majority of the patients presenting with thrombocytopenia. But none of the syndromes was able to predict the presence of mixed tropical infection with a nonsignificant *p*-value

**Table 4:** Logistic regression using complications as independent variables for mortality

| *Complications* | *Mortality* | *p-value #* | *Odds ratio* | *Confidence interval* |
|---|---|---|---|---|
| | *N = 13 (%)* | | | |
| AKI (*n* = 45) | 10 (27.8) | 0.011* | 5.26 | 1.32–20.91 |
| Hepatitis (*n* = 44) | 11 (25) | 0.019* | 5.67 | 1.17–27.54 |
| ARDS (*n* = 22) | 7 (31.8) | 0.037* | 4.04 | 1.18–13.87 |
| Shock (*n* = 13) | 9 (69.2) | 0.001* | 35.44 | 7.51–167.29 |
| Sepsis (*n* = 8) | 1 (12.5) | 1.000 | 0.71 | 0.08–6.35 |
| GI Bleed (*n* = 13) | 5 (38.4) | 0.032* | 2.86 | 0.8–10.3 |
| Encephalopathy (*n* = 14) | 4 (28.5) | 0.227 | 2.53 | 0.65–9.83 |
| Myocarditis (*n* = 2) | 2 (100) | 0.025* | 29.35 | 1.32–651.51 |
| Polyserositis (*n* = 11) | 5 (45.4) | 0.014* | 6.35 | 1.57–25.69 |
| Pneumonia (*n* = 21) | 4 (19) | 0.735 | 1.31 | 0.36–4.8 |
| DIC (*n* = 1) | 1 (100) | 0.162 | 16.2 | 0.62–420.74 |

#Fisher's exact test; percentage in parenthesis; *Indicates a significant predictor of mortality

civic infrastructure have led to increased breeding grounds for arthropod vectors that share common habitats. This leads to ecological co-circulation of vectors and parasites, seasonal epidemics, and co-exposure of pathogens to humans. In recent decades, tropical countries have witnessed an unexpected upsurge of tropical CIs due to these multifactorial reasons.

In hospitalized patients, the clinician is confronted with severe forms of CIs, which can become challenging as the outcomes get compounded due to host–pathogen and pathogen–pathogen interaction. The immune mechanism elicited by one or more pathogens can alter the natural history of an individual disease as well as dysregulate host immunity.

We observed an 8.1% prevalence of CIs in our cases of AUFI. The prevalence of tropical

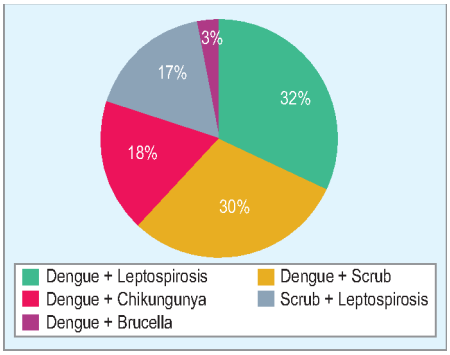


**Fig. 3:** Distribution of mortality among various coinfections

CIs varies tremendously in medical literature. In a Karnataka-based study, 92 (22%) patients had tropical CIs among 420 dengue fever cases, the most common being rickettsia (48.8%) and typhoid fever (22.2%).[10] However, in another study, only 48 (1.9%) patients were found to be suffering from CIs.[11] From western regions of Punjab, of 283 samples tested, 27 sera were positive (9.54%) for dengue and CHIK CIs.[12] A comparative study between mono- and CIs was done by Ahmad et al., which included 233 patients, in which 49 had CIs.[13]

Our study identified 17 different combinations of CIs. Four groups, i.e., D + L, D + S, D + C, and S + L—accounted for 80% CIs. Similar dominant groups were found in a publication by Raina et al.[3] More than 80% of our patients were below 50 years of age, consistent with the demographic profile by Ahmad et al.[13] It is postulated that younger healthy individuals generate aberrant and dysregulated immune responses due to activation of innate immunity and antibody-dependent enhancement.

In the present study, the clinical features across different CI groups were quite nonspecific. Transaminitis was common across all CIs. D+L had the highest AST levels. In 2016, Zubair et al. concluded that severe hepatitis, especially elevated ALT, was a poor prognostic indicator in dengue fever.[14] We noted highest mortality in patients with raised AST levels. Respiratory complications, mainly pneumonia and ARDS, were found to be higher in patients with dengue fever as CI. Secondary bacterial infection in relation to dengue fever has been studied by Thein et al. with similar results.[15] Leptospirosis is another seasonal infection that has outbreaks overlapping with other tropical illnesses.[16] AKI was the only complication which has significant correlation with diagnosis of dual infection, suggesting these patients have more profound kidney injury than monoinfections. Scrub typhus CI with dengue fever and leptospirosis produced the maximum number of complications in our patients. Multiorgan dysfunction was statistically higher in patients with scrub typhus subgroups. Ahmad et al.

also observed a higher incidence of multiorgan dysfunction with D + S CIs.[13]

Mewada et al. conducted a prospective study in Mumbai and suggested a 'syndromic approach' for classifying tropical infections; however, we did not achieve any conclusive differentiation, possibly because the clinical picture becomes transformed in mixed infections.[17] In a recent study conducted on 500 AUFI patients, Kulshrestha et al. stated that CIs are a highly under-recognized entity.[18]

There is no robust data to corroborate the prognosis, survival indices, and mortality rate specifically in patients with tropical CIs. In our study, case fatality was 16.25%, with the D + L and D + S accounting for 76.9% deaths. We have shown that the presence of AKI, hepatitis, ARDS, and shock predicted mortality in the majority of cases.

India, being a vast and diverse country with varying climatic conditions and endemic zones for different pathogens, often requires a region-specific approach to diagnosing and managing tropical CIs. North and North-eastern India have a high prevalence of scrub typhus, dengue, and Japanese encephalitis. Coastal regions have a higher incidence of leptospirosis, especially after floods. In tribal or forested areas, malaria (especially *P. falciparum*) remains a significant concern. In urban centers, dengue and chikungunya are widespread. An algorithmic approach for AUFI often starts with ruling out life-threatening conditions.[19] Based on prevalence in the region and clinical suspicion, specific tests are then ordered in a stepwise manner.[20] If initial tests are negative or the patient does not respond to empirical treatment for common infections, a broader panel of tests for other tropical diseases and CIs is considered. In essence, while formal "region-specific diagnostic protocols" with rigid algorithms for every CI might not be widely published, the Indian medical practice emphasizes a dynamic, syndromic, and context-dependent approach, heavily influenced by the local epidemiology of tropical diseases.

## Limitations

The disease spectrum in our study population was limited to a tertiary hospital setting with a greater number of complicated cases. We could not identify any specific predictors that could guide physicians in formulating the most appropriate diagnostic or management strategy in presence of these CIs. Secondly, in such a clinical setting, the likelihood of cross-reactivity and serological unreliability always remains.[21] Various factors, such as antigenic homology (e.g. viruses with same genus like flaviviruses), original antigenic sin (OAS) mount false positives and mislead diagnosis of CI.[22] Hence, more specific tests such as PCR, paired sera testing, neutralizing tests, and multiplex assays should be incorporated in diagnosis guidelines.

## Conclusion

Coinfections often go unrecognized in community and hospital settings. Through this study, we have ascertained that AUFI is not the domain of a single organism but may host multiple organisms with vectors sharing similar ecological and seasonal disposition. Therefore, we recommend that a thorough exploration of several etiologies must be incorporated into the preliminary diagnostic workup of patients with AUFI. This will ensure that the multiple diagnoses that could contribute to the pathophysiology, manifestations, and complications are not missed. Further research is warranted to better understand how coinfections impact the natural course of individual diseases.

Early recognition, broad-spectrum empirical therapy, and the strategic use of available diagnostic tools are essential, particularly when coinfections are suspected due to atypical clinical features or poor response to treatment. However, the unavailability of reliable point-of-care diagnostics and molecular testing poses a major challenge to evidence-based clinical practice. Until such resources become widely accessible, diagnostic investigations should be guided by local epidemiology and patient presentation. In the interim, an umbrella management covering the spectrum of common tropical fevers, informed by clinical judgment and expert consultation, remains a pragmatic strategy. In addition, there is a paucity of robust, region-specific seroprevalence data on tropical coinfections. Understanding the epidemiology of coinfections is vital for precise disease burden assessment and optimizing public health resource allocation.

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