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# Clinico-Demographic Profile and Economic Impact of Diagnostic Stewardship in Acute Febrile Illness: A Cross-Sectional Analysis

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## ABSTRACT

**Background:** Acute febrile illness (AFI) is a major diagnostic challenge in tropical, resource-limited settings due to overlapping clinical features and multiple etiologies. Empirical treatment without confirmation contributes to antimicrobial resistance, longer hospital stays, and higher costs. Diagnostic stewardship is therefore essential for effective management.

**Methods:** A prospective cross-sectional study was conducted in the Department of Microbiology, IIMSR, Lucknow, from April 2023 to March 2025. A total of 384 blood samples from suspected AFI patients were tested for dengue (NS1, IgM, IgG), malaria (MalCard, peripheral smear), typhoid (Widal, rapid test), and scrub typhus (rapid card test). Patient demographics, clinical features, and laboratory findings were analyzed.

**Results:** AFI was more common in females (54%) and peaked in the 11–20-year age group. Among suspected cases, malaria (38.6%), dengue (27.1%), typhoid (21.9%), and scrub typhus (2%) were most frequent, with confirmed positivity rates of 28.6%, 24.3%, 16.1%, and 1%, respectively. Co-infections occurred in 12.3% of patients. Accurate diagnosis reduced empirical antibiotic use from 53% to 5% and shortened hospital stays, generating substantial cost savings.

**Conclusion:** AFI demonstrates diverse etiologies and frequent co-infections. Accurate diagnostics are pivotal in guiding therapy, minimizing antibiotic misuse, improving outcomes, and reducing healthcare costs.

**Key-words:** Acute febrile illness (AFI), Antimicrobial Stewardship, Economic Impact, Diagnostics, Misdiagnosis, Clinico-Demographic Profile

## INTRODUCTION

Acute febrile illness (AFI) remains one of the most common reasons for outpatient visits and hospital admissions in tropical and developing countries, including India. It represents a clinical syndrome characterized by a sudden onset of fever, often accompanied by non-specific symptoms such as myalgia, chills, headache, and gastrointestinal disturbances.

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The etiologies of AFI are diverse and range from viral, bacterial, to parasitic infections—commonly including dengue, malaria, typhoid fever, and scrub typhus [1,2]. These infections often share overlapping clinical features, complicating prompt and accurate diagnosis in resource-limited settings.

Misdiagnosis or delayed diagnosis of AFI can result in poor clinical outcomes, including increased morbidity and mortality, particularly when empirical antibiotic therapy is used without microbiological confirmation [3]. This practice contributes to the global threat of antimicrobial resistance (AMR), increases patient burden, and prolongs hospital stays [4]. Therefore, the accurate identification of the causative agent is essential not only for guiding appropriate treatment but also for improving antibiotic stewardship and reducing healthcare costs.

 

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Recent studies have demonstrated the utility of rapid, high-sensitivity diagnostic tests for differentiating AFI etiologies, thereby reducing reliance on empirical treatment and promoting targeted therapy [5,6]. Moreover, the economic implications of accurate diagnosis are significant, especially in low-resource settings where healthcare expenditures are primarily out-of-pocket. Effective diagnostic strategies can substantially reduce unnecessary hospitalizations, limit diagnostic delays, and improve the overall cost-effectiveness of care.

This study aims to evaluate the clinical-demographic patterns of patients presenting with AFI and to assess the impact of accurate diagnosis on antibiotic use and healthcare expenditure in a tertiary care hospital in northern India. Understanding regional disease prevalence and associated clinical profiles can help formulate tailored diagnostic algorithms and treatment guidelines that enhance patient outcomes while addressing broader issues of antimicrobial misuse.

## MATERIALS AND METHODS

**Study Design and Setting-** A prospective cross-sectional study was conducted at a tertiary care teaching hospital in North India over two years, from April 2023 to March 2025. The study was undertaken in the Department of Microbiology in coordination with clinical departments managing patients presenting with acute febrile illness (AFI).

### Study Population

**Inclusion Criteria-** All patients presenting with acute febrile illness during the study period were screened and consecutively enrolled. Acute febrile illness was defined as an axillary temperature of ≥38.0°C with a duration of fever of ≤14 days at the time of presentation, in the absence of an identifiable localising focus of infection on initial clinical evaluation. Patients presenting at any stage of illness, including early febrile illness (≤5 days), were eligible for inclusion.

**Exclusion Criteria-** Patients were excluded if informed consent was not obtained, or if collected specimens were inadequate, mislabeled, lipemic, or hemolytic.

**Data Collection-** Demographic and clinical data were collected for all enrolled participants. Information for hospitalized patients was obtained from medical records, while outpatient data were collected using a predesigned, structured pro forma through direct patient interviews. Variables recorded included age, sex, clinical presentation, laboratory parameters, antimicrobial use, duration of hospital stay, and final laboratory-confirmed diagnosis.

**Sample Collection and Laboratory Investigations-** Venous blood samples were collected under aseptic conditions for hematological and serological evaluation. EDTA-anticoagulated blood was used for complete blood counts, rapid diagnostic testing, and peripheral blood smear examination, while serum samples were separated for serological assays.

Laboratory diagnosis was performed on 384 samples using standard diagnostic protocols. Dengue infection was detected by NS1 antigen and IgM/IgG capture ELISA (J. Mitra & Co. Pvt. Ltd). Malaria screening was carried out using a rapid antigen test (ADVANTAGE MALCARD), with confirmation by Leishman-stained peripheral blood smear microscopy. Typhoid fever was assessed using the slide agglutination Widal test, with significant titers defined as O ≥ 1:80, H ≥ 1:160, or a fourfold rise in paired sera. Rapid diagnostic kits (Tydal, Tulip Diagnostics; OnSite Rapid Test, CTK Biotech) were used as supportive tools. Scrub typhus was identified using an immunochromatographic rapid card test (J. Mitra & Co. Pvt. Ltd).

Hematological and biochemical abnormalities were defined according to institutional laboratory reference ranges. Thrombocytopenia was defined as a platelet count <150,000/µL; leukopenia as a total leukocyte count <4,000/µL; anemia as hemoglobin <12 g/dL in adults with age-adjusted values for children; and elevated liver enzymes as serum SGOT or SGPT levels exceeding 40 IU/L. Renal and other biochemical parameters were interpreted based on age- and sex-specific reference values.

**Definition of Empirical Antibiotic Use-** Empirical antibiotic therapy was defined as the initiation of systemic antibacterial treatment before laboratory confirmation of the etiological diagnosis, based solely on clinical assessment.

 

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**Statistical Analysis-** Data were entered into Microsoft Excel and analyzed using SPSS version 20. Categorical variables were expressed as proportions with 95% confidence intervals. Associations between categorical variables were assessed using the Chi-square test or Fisher's exact test, as appropriate. A p-value <0.05 was considered statistically significant. Conditions with low prevalence were analysed descriptively due to limited statistical power. No multivariable analysis was performed. Prevalence estimates were calculated using the binomial exact method.

**Economic Analysis-** A descriptive cost-offset analysis was conducted to assess the potential economic impact of diagnostic stewardship from the hospital perspective. The analysis included direct inpatient costs related to the length of hospital stay. The estimated cost per inpatient day (US$430) was obtained from institutional administrative billing records for the financial year 2023–2024 and included bed charges, nursing care, and routine inpatient services. Costs related to laboratory investigations, imaging, medications, and indirect expenses were excluded. All costs were reported in US dollars using the average exchange rate applicable during the study period.

**Sample Size Considerations-** The sample size was determined pragmatically based on the number of eligible AFI cases presenting during the study period. With a total of 384 participants, the study estimated the prevalence of common AFI etiologies with precision of approximately ±4–5% at the 95% confidence level. The study was not designed to detect small differences between etiological subgroups or patterns of antibiotic use; therefore, comparative findings were interpreted descriptively.

**Ethical Approval-** This study was approved by the Institutional Ethics Committee of Integral Institute of Medical Sciences and Research, Integral University, Lucknow. (IEC/IIMSR/2023/50 dated 16th May 2023).

## RESULTS

A total of 384 patients presenting with acute febrile illness were evaluated during the study period. The etiological distribution of AFI is shown in Figure 1. Malaria was the most frequently identified cause, accounting for 28.6% of cases, followed by dengue fever (24.4%), typhoid fever (16.1%), and scrub typhus (1.0%). Overall, etiology was confirmed in 270 patients (70.3%).

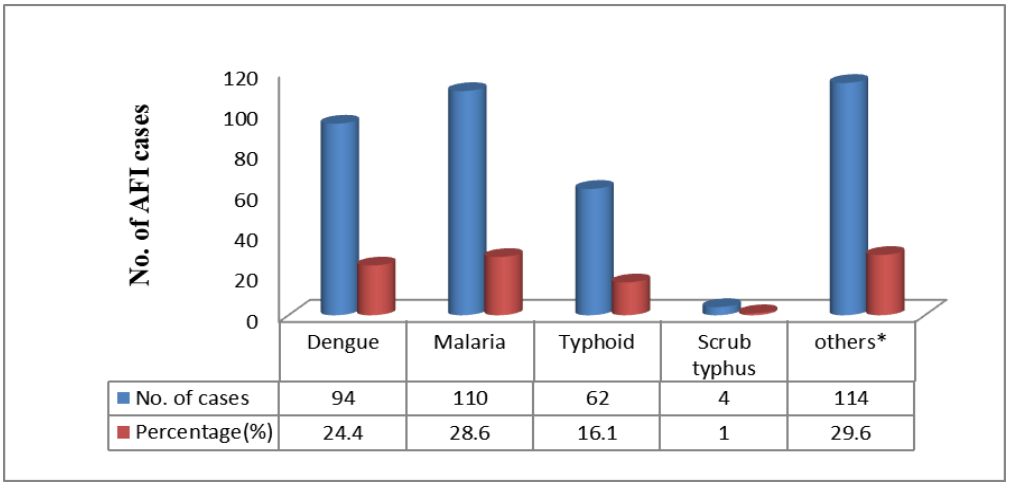


**Fig. 1:** Etiological distribution of acute febrile illness cases

*Note: Others* include viral infections, bacterial infections and undetectable causes*

Of the 384 patients included, 210 (54.7%) were female and 174 (45.3%) were male, showing a slight female predominance. The most affected age group was 11–20 years (35%), followed by 21–30 years (23%) and 31–40 years (11%). Children aged 0–10 years accounted for 7% of cases, while patients aged 41–50 years, 51–60 years, and 60+ years accounted for 10%, 8%, and 4%, respectively. Fever was present in all patients (100%). Other frequently reported symptoms included body ache (97.6%), headache (73%), and vomiting (40%). Respiratory and gastrointestinal symptoms, such as breathlessness (32.8%), restlessness (27.6%), and abdominal pain (22%), were less common. The distribution of clinical features is summarised in Table 1.

 

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**Table 1:** Clinico-demographic characteristics of patients with acute febrile illness (n=384)

| Variable | Category | No. of Patients (N=384) | Percentage (%) |
|---|---|---|---|
| Gender | Male | 174 | 45 |
| | Female | 210 | 54 |
| Age Group (years) | 0–10 | 27 | 7 |
| | 11–20 | 135 | 35 |
| | 21–30 | 90 | 23 |
| | 31–40 | 45 | 11 |
| | 41–50 | 39 | 10 |
| | 51–60 | 31 | 8 |
| | >60 | 17 | 4 |
| Clinical Symptoms | Fever | 384 | 100 |
| | Bodyache | 375 | 97.6 |
| | Headache | 281 | 73 |
| | Restlessness | 106 | 27.6 |
| | Breathlessness | 126 | 32.8 |
| | Vomiting | 154 | 40 |
| | Abdominal pain | 86 | 22 |

Comparative analysis of laboratory parameters across dengue, malaria, typhoid, and scrub typhus revealed several significant findings (Table 2). Thrombocytopenia was commonly observed across all etiologies and was most frequent in malaria (85.5%), followed by dengue (80.4%) and typhoid (58.1%), with the difference being statistically significant (p = 0.0002).

Anemia was significantly more prevalent in malaria (78.2%) and typhoid (67.7%) compared to dengue (56.4%) (p = 0.0046). Elevated serum urea levels were observed more frequently in malaria (55.5%) and dengue (35.1%) cases (p = 0.0001), whereas no elevation was noted among scrub typhus cases. Elevated alkaline phosphatase levels were significantly associated with malaria (50%) and typhoid (25.8%) (p = 0.0081). No statistically significant differences were observed for leukopenia, elevated SGOT, or elevated SGPT across the etiological groups.

**Table 2:** Distribution of laboratory abnormalities across confirmed AFI etiologies

| Lab Parameter | Dengue (n = 94) | Malaria (n = 110) | Typhoid (n = 62) | Scrub Typhus (n = 4) | p-value |
|---|---|---|---|---|---|
| Thrombocytopenia | 76 (80.4%) | 94 (85.5%) | 36 (58.1%) | 4 (100%) | 0.0002 |
| Leucopenia | 26 (27.7%) | 24 (21.8%) | 15 (24.2%) | 0 (0%) | 0.52 |
| Anemia | 53 (56.4%) | 86 (78.2%) | 42 (67.7%) | 4 (100%) | 0.004 |
| Elevated SGOT | 55 (58.5%) | 70 (63.6%) | 38 (61.3%) | 2 (50%) | 0.86 |
| Elevated SGPT | 59 (62.8%) | 59 (53.6%) | 38 (61.3%) | 0 (0%) | 0.06 |
| Elevated ALP | 31 (33.0%) | 55 (50.0%) | 16 (25.8%) | 2 (50%) | 0.01 |
| Elevated Serum Urea | 33 (35.1%) | 61 (55.5%) | 15 (24.2%) | 0 (0%) | 0.0001 |
| Elevated Serum Creatinine | 41 (43.6%) | 53 (48.2%) | 27 (43.5%) | 0 (0%) | 0.28 |

***Note:*** *p-values<0.05 are considered statistically significant and indicate a meaningful difference in that parameter across* the different disease groups.

 

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Co-infections were identified in 48 patients (12.3%), as detailed in Table 3. The most frequently observed co-infection was dengue with typhoid, documented in 16 cases (4.2%). Other combinations were less common.

**Table 3:** Prevalence of co-infections among AFI patients with 95% confidence intervals

| Co–infections | No. of Patients | Percentage (%) | % (95% CI) |
|---|---|---|---|
| Dengue /Typhoid | 16 | 4.2 | 2.4–6.7 |
| Dengue /Malaria | 12 | 3.1 | 1.6–5.4 |
| Malaria /Typhoid | 10 | 2.6 | 1.3–4.8 |
| Dengue/ Malaria /Typhoid | 8 | 2 | 0.9–4.1 |
| Malaria/ Scrub Typhus | 2 | 0.5 | 0.1–1.8 |
| Total | 48 | 12.3 | - |

As shown in Table 4, Empirical antibiotic therapy was initiated in 53% of patients at presentation, before diagnostic results were available. After laboratory confirmation, only 5% of patients continued antibiotics without microbiological indication, demonstrating a marked reduction in inappropriate antibiotic use. Among the 270 patients (70.3%) with laboratory-confirmed diagnoses, an earlier transition from empirical to targeted therapy was associated with a shorter duration of hospital stay. Based on an assumed reduction of 5–7 inpatient days and an estimated cost of US$430 per inpatient day, the potential diagnostic-associated cost offset was estimated to range from US$316,050 to US$442,470. These findings reflect observed associations between diagnostic confirmation, improved antibiotic prescribing practices, and more efficient use of hospital resources.

**Table 4:** Diagnostic-associated antibiotic utilisation patterns and estimated cost offsets

| Parameter | Value | Unit / Remarks |
|---|---|---|
| Total number of patients evaluated | 384 | Patients with AFI |
| Laboratory-confirmed diagnoses | 270 (70.3%) | Microbiologically confirmed cases |
| Assumed reduction in hospital stay | 5–7 days | Based on observed differences, not a comparator |
| Empirical antibiotics commonly used | Ceftriaxone, Amoxicillin–clavulanate | Initiated before diagnostic confirmation |
| Empirical antibiotic use at presentation | 53% | Antibiotics started without microbiological confirmation |
| Continued antibiotic use after diagnostics | 5% | Antibiotics without microbiological indication |
| Estimated reduction in empirical antibiotic use | 48% | Descriptive difference, not causal |
| Estimated cost per inpatient day | US$430 | Institutional billing estimate (2023–2024) |
| Estimated diagnostic-associated cost offset | US$316,050–442,470 | Exploratory estimate based on assumptions |
| Key interpretation | Association with improved prescribing practices | Causal inference not established |

 

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Cost estimates are based on assumed reductions in length of stay and institutional per-day inpatient costs. These figures represent hypothetical cost offsets and not observed or causally attributable savings.

**DISCUSSION**

Acute febrile illness (AFI) continues to represent a major diagnostic and therapeutic challenge in tropical, resource-limited settings because of its nonspecific clinical presentation and the overlapping epidemiology of multiple infectious diseases [7]. In this study, we evaluated 384 patients presenting with AFI. We demonstrated that malaria, dengue, typhoid, and scrub typhus remain the predominant etiologies, with laboratory confirmation achieved in over two-thirds of cases. These findings underscore the importance of systematic diagnostic evaluation in guiding appropriate clinical management.

Malaria was identified as the most common cause of AFI (28.6%), followed by dengue (24.4%), typhoid (16.1%), and scrub typhus (1.0%). This distribution is comparable to reports from several regions of North and Central India, where vector-borne and enteric infections predominate [8,9]. However, marked regional variation in AFI etiology has been documented across India. Studies from southern and coastal regions have reported a higher burden of scrub typhus and leptospirosis, reflecting differences in climate, vector ecology, and occupational exposure [10,11]. These variations highlight the need for region-specific AFI surveillance data to inform diagnostic algorithms and empirical treatment strategies.

A slight female predominance was observed in the present study, with females constituting 54.7% of cases. Similar gender distributions have been reported in some AFI cohorts [7,12], although other studies have demonstrated male predominance, often attributed to occupational exposure and healthcare-seeking behaviour [13]. The highest burden of AFI was observed among adolescents and young adults (11–20 years), followed by those aged 21–30 years. Increased outdoor activity and greater exposure to vectors and contaminated environments may account for this pattern, as suggested in earlier studies [13].

Clinically, fever was universal, while body ache, headache, and vomiting were common accompanying symptoms. This symptom profile is consistent with previous AFI studies and reflects the substantial clinical overlap among malaria, dengue, and typhoid fever [14,15]. Gastrointestinal symptoms such as vomiting and abdominal pain were frequently observed, particularly in dengue and typhoid cases, as reported earlier by Sarkar *et al.* [16]. Less frequent symptoms such as breathlessness and restlessness may indicate severe systemic involvement and have been described in complicated malaria and scrub typhus [17,18].

Laboratory parameters provided important discriminatory value across etiologies. Thrombocytopenia was a prominent finding, particularly in malaria and dengue, with statistically significant differences between disease groups. Similar observations have been reported by Yogeesha *et al*., Karoli *et al*., and Dasari *et al*., who identified thrombocytopenia as a key laboratory marker in AFI, especially in dengue and malaria [19–21]. Anemia was significantly more prevalent in malaria and typhoid, likely reflecting hemolysis, bone marrow suppression, and chronic inflammation, as described by Kochar *et al*. [22]. Renal dysfunction, evidenced by elevated urea levels, was most frequent in malaria, followed by dengue, consistent with previous reports identifying malaria as a leading cause of febrile renal impairment [23]. Although transaminase elevations were commonly observed, differences in SGOT and SGPT across etiologies were not statistically significant; however, alkaline phosphatase elevation was significantly associated with malaria and typhoid, suggesting hepatobiliary involvement in these infections.

Co-infections were identified in 12.3% of patients, with dengue–typhoid being the most common combination. This finding aligns with earlier studies reporting similar co-infection patterns in endemic settings [24]. The presence of co-infections further complicates clinical diagnosis and management, particularly during peak transmission seasons, and reinforces the importance of comprehensive diagnostic testing in AFI.

An important observation in this study was the association between laboratory confirmation and changes in antibiotic prescribing practices. Empirical antibiotic therapy was initiated in over half of patients at presentation; however, following diagnostic confirmation, only a small proportion continued antibiotics without microbiological indication. This reduction occurred in the absence of a formal

 

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antimicrobial stewardship intervention, suggesting that access to timely diagnostic information alone can influence clinician prescribing behaviour. These findings are consistent with global recommendations advocating diagnostic-informed antimicrobial use as a key strategy to curb unnecessary antibiotic exposure and antimicrobial resistance [3].

Additionally, diagnostic confirmation was associated with a shorter observed duration of hospital stay among patients who transitioned from empirical to targeted therapy. The estimated diagnostic-associated cost offsets, based on assumed reductions in hospital stay, are exploratory and should be interpreted cautiously. Nevertheless, similar associations between diagnostic-guided care, reduced length of stay, and improved resource utilisation have been reported in other healthcare settings [4,5]. Given the cross-sectional design and absence of a control group, causal inference cannot be established, and these findings should be viewed as hypothesis-generating.

Overall, this study highlights the continued burden of AFI due to malaria, dengue, and typhoid in endemic regions and demonstrates the clinical and potential economic value of laboratory-based diagnostic confirmation. Strengthening access to reliable diagnostics and integrating region-specific AFI algorithms into routine care may facilitate timely targeted therapy, reduce unnecessary antimicrobial use, and support antimicrobial stewardship efforts in resource-limited settings.

## LIMITATIONS

The cross-sectional design, the absence of a comparator group, and the lack of a formal antimicrobial stewardship intervention limit causal interpretation of the observed reductions in antibiotic use and hospital stay. Economic estimates were exploratory and based on assumptions rather than observed cost differentials. The study was not powered to detect subgroup differences, and findings regarding rare infections should be interpreted cautiously.

## CONCLUSIONS

This study highlights the complex clinico-demographic spectrum of acute febrile illness in a tropical setting, with malaria, dengue, and typhoid fever as the predominant etiologies. The findings demonstrate that diagnostic stewardship—through timely and accurate laboratory confirmation—plays a pivotal role in improving etiological identification, reducing inappropriate empirical antibiotic use, shortening hospital stay, and potentially lowering healthcare costs. These results underscore the clinical and economic value of strengthening diagnostic infrastructure and integrating region-specific diagnostic algorithms to support targeted therapy, enhance antimicrobial stewardship, and optimise resource utilisation in endemic settings.

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