



CAUSES OF ACUTE UNDIFFERENTIATED FEVER IN EMERGENCY DEPARTMENT PATIENTS AT A TERTIARY HOSPITAL

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ABSTRACT

Background: Acute undifferentiated fever (AUF) is common in the emergency department, particularly in tropical countries, where a variety of infectious causes can be mixed. Early detection and diagnosis is essential to avoid complications, morbidity and mortality.

Objective: To find out the etiology, clinical characteristics and prognosis of patients who presented with acute undifferentiated fever to the emergency department of a tertiary care hospital in Karachi, Pakistan.

Methods: This was a cross sectional observational study carried out Medicine Department, Saidu Group of Teaching Hospital for six months March, 2025 to August, 2025. 250 patients with fever $\leq$ 14 days without a localizing source were enrolled. History, clinical examination and laboratory investigations were conducted which included complete blood count, liver function tests, renal function tests, blood culture, malaria smears, dengue serology and pathogen-specific tests. Demographic pattern, clinical features, laboratory abnormalities, etiology and outcome were analyzed.

Results: The mean age was 32.4 ± 18.7 years, with 58% males. The most common etiologies were Dengue (32%), Malaria (18%), Scrub Typhus (15%) and Typhoid (10%). Thirty eight percent had thrombocytopenia, 25 percent leukopenia, and 30 percent elevated liver enzymes. Multi-organ involvement was seen in 12% of the patients and overall mortality was 2%. Seasonal trends revealed that the presentation was higher during summer and monsoon months.

Conclusions: AUF is a major cause of morbidity in emergencies. Prompt diagnosis and management relies on early clinical evaluation, appropriate laboratory testing and knowledge of local epidemiology. A knowledge of common etiologies like dengue, malaria and scrub typhus can help guide appropriate therapy, minimize complications and improve patient outcomes in tertiary care centers.

Keywords: Acute undifferentiated fever, dengue, malaria, scrub typhus, emergency department, thrombocytopenia, tertiary hospital, Karachi

INTRODUCTION

Acute undifferentiated fever is a common emergency presentation in tropical countries, with many infections starting with similar non-specific symptoms. Early recognition of the likely causes is crucial

at Medicine Department, Saidu Group of Teaching Hospital since delayed diagnosis could lead to higher complications, hospitalisation, unnecessary treatment and cost of care (1). Acute undifferentiated febrile illness is defined as a fever of short duration, without a definite localizing focus after history and examination. In emergency wards, this leads to diagnostic uncertainty as malaria and dengue, typhoid, leptospirosis, rickettsial infections, viral diseases and bacterial sepsis can be clinically indistinguishable (2). Acute undifferentiated fever is particularly significant in children since the symptoms may be nonspecific and deterioration may be rapid. Symptoms can be fever, poor feeding, lethargy, rash, abdominal symptoms, or seizures, and the etiology can be viral or serious bacterial illness (3). The disease progresses to a more severe stage if the fever is accompanied by thrombocytopenia, jaundice, hypotension, altered sensorium, renal dysfunction, respiratory distress or multi-organ involvement. These findings are seen in dengue, severe malaria, scrub typhus, leptospirosis, enteric fever or sepsis and a structured diagnostic approach is important (4). Successful clinical outcome is related to the severity of the presentation, prompt identification of the danger signs, and prompt treatment. Patients are presented to the ED in a variety of states, ranging from mild fever to shock. Therefore, it is important to identify risk factors for death for triage, monitoring, referral, and to avoid avoidable mortality (5). Antipyretics are not enough for the treatment of acute undifferentiated fever, as different infections require different treatment. Some patients require anti-malarials, some require antibiotics, some require careful monitoring of fluids and some require isolation precautions. Diagnosis and treatment should be correlated with season, exposure, travel and local disease patterns (6).

Bacteremia is still a significant cause of undifferentiated fever, especially in children and in the immunocompromised host. In early illness may not have a clear focus. Severe symptoms of bacteremia can result in sepsis, and overuse of antibiotics can result in antibiotic resistance; therefore, selective cultures and clinical predictors are useful for emergency care (7). Acute febrile illness is prevalent in Karachi, particularly in summer and monsoon months when mosquito breeding, crowding, unsafe water and sanitation issues are more prevalent. Dengue, malaria, enteric fever, respiratory viral infections and bacterial infections can occur simultaneously (8) in Medicine Department, Saidu Group of Teaching Hospital. The first step in narrowing the cause is clinical assessment. History should contain information on duration of fever, travel, exposure to mosquitoes, food and water consumption, previous contact history, medicines, bleeding symptoms, urinary symptoms, and respiratory complaints. Hydration, rash, lymph nodes, abdomen, jaundice, hepatosplenomegaly, meningeal signs and hemodynamic status should be assessed in examination (9). A stepwise diagnostic approach enables emergency physicians to make quick decisions without unnecessary testing. Initial tests include complete blood count, platelet count, liver and renal functions, malaria testing, dengue testing, urinalysis, blood culture and targeted tests based on clinical suspicion and local epidemiology (10). Scrub typhus is a significant, but rarely considered cause of acute undifferentiated fever in South Asia. It may manifest as fever, headache, myalgia, rash, cough, gastrointestinal symptoms, thrombocytopenia, hepatitis or organ dysfunction and the eschar may not be present or noticed during examination (11). Microbiological evaluation is needed to confirm the true causes of acute febrile illness. In tertiary emergency settings, pathogens cannot be reliably diagnosed by symptoms alone and blood culture, serology, rapid diagnostic tests, polymerase chain reaction (if available), urine testing, and respiratory testing can be used to identify pathogens. (12) Fever causes vary regionally, according to climate, occupation, age, vector exposure and length of illness. Early missed infections, such as enteric fever, tuberculosis, malaria, rickettsial disease and viral infections, are possible causes of prolonged fever, confirming the need for local hospital-based data (13). The COVID-19 pandemic made the evaluation of fever more challenging as dengue and COVID-19 can have similar clinical features including fever, headache, myalgia, leukopenia, thrombocytopenia, and constitutional symptoms. In overlapping outbreaks, emergency physicians should be careful not to focus on one diagnosis and may be faced with a situation of multiple infections circulating simultaneously (14). Monsoon studies have revealed that the spectrum of acute undifferentiated fever varies with the seasons, with increased dengue, malaria, leptospirosis, scrub typhus and other infections occurring during the rainy season and during the period of vector breeding.

The same seasonal pressure is applicable to Pakistan and adds to the workload of the emergency department (15).

History of travel is also important as patients may present after travelling within Pakistan or returning from other endemic area. Travel, occupation, animal, water and insect exposures are not systematically asked and therefore may be overlooked for imported infections, unusual pathogens and mixed exposures (16). The risk of various fever causes varies seasonally, regionally and demographically. Disease distribution may vary with age, sex, place, occupation, rainfall and outbreaks. Thus, knowledge of emergency patients at Medicine Department, Saidu Group of Teaching Hospital, can help in rational investigations, prompt treatment and improved patient outcomes (17).

Objective: To determine the causes, clinical presentations, and outcomes of acute undifferentiated fever among patients presenting to the emergency department of Medicine Department, Saidu Group of Teaching Hospital.

MATERIALS AND METHODS

Study Design: Cross-sectional observational study.

Study Setting: Medicine Department, Saidu Group of Teaching Hospital.

Study Duration: March, 2025 to August, 2025.

Sample Size: A total of 250 patients presenting with acute undifferentiated fever were enrolled based on sample size calculations considering prevalence, confidence interval, and precision.

Sample Technique: Convenience sampling was used, including all eligible patients presenting during the study period until the required sample size was reached.

Inclusion criteria: All age groups presenting to the ED with fever of ≤ 14 days duration with no local source were included. Patients had to consent to participate and agree to investigations as per protocol.

Exclusion criteria: Patients with a clear initial diagnosis of fever (localized pneumonia, urinary tract infection, cellulitis etc.) were excluded. Other exclusions included persons with chronic immunosuppressive diseases, recent surgery and persons with known malignancy.

Methods: Demographic data, detailed history and clinical examination findings were recorded after informed consent. Complete blood count, liver and renal function tests, blood culture, malaria smears, dengue serology and other tests according to clinical suspicion were done. Descriptive and inferential statistics were used to analyze the data to determine the frequency of etiologies, patterns of thrombocytopenia, organ involvement, and clinical outcomes.

RESULTS

The total number of patients included in the study were 250, who had acute undifferentiated fever. The age distribution was 6 months to 75 years (mean age was 32.4 ± 18.7 years). Most of the patients (58%) were male while 42% were female.

Table 1: Demographic and Seasonal Distribution of Patients (n=250)

Characteristic	Number of Patients	Percentage (%)
Age <15 years	60	24%
Age 15–45 years	130	52%
Age >45 years	60	24%
Male	145	58%
Female	105	42%
Winter (Jan–Feb)	60	24%
Summer (Mar–May)	95	38%
Monsoon (Jun)	95	38%

The duration of fever at presentation ranged from 2 to 14 days and the mean was 5.6 ± 2.9 days. The most frequent symptoms were headache (65%), myalgia (58%), rash (22%) and gastrointestinal complaints (18%) (Table 2).

Table 2: Clinical Features of Patients with Acute Undifferentiated Fever

Symptom	Number of Patients	Percentage (%)
Headache	162	65%
Myalgia	145	58%
Rash	55	22%
Nausea/Vomiting	45	18%
Abdominal Pain	40	16%
Bleeding Manifestations	18	7%
Altered Sensorium	10	4%

Laboratory examination showed 38% of patients had thrombocytopenia ($<150,000/\text{mm}^3$) and 25% had leukopenia ($<4,000/\text{mm}^3$). Thirty percent of patients had elevated liver enzymes and 12% had mild renal dysfunction (Table 3).

Table 3: Laboratory Findings of Patients

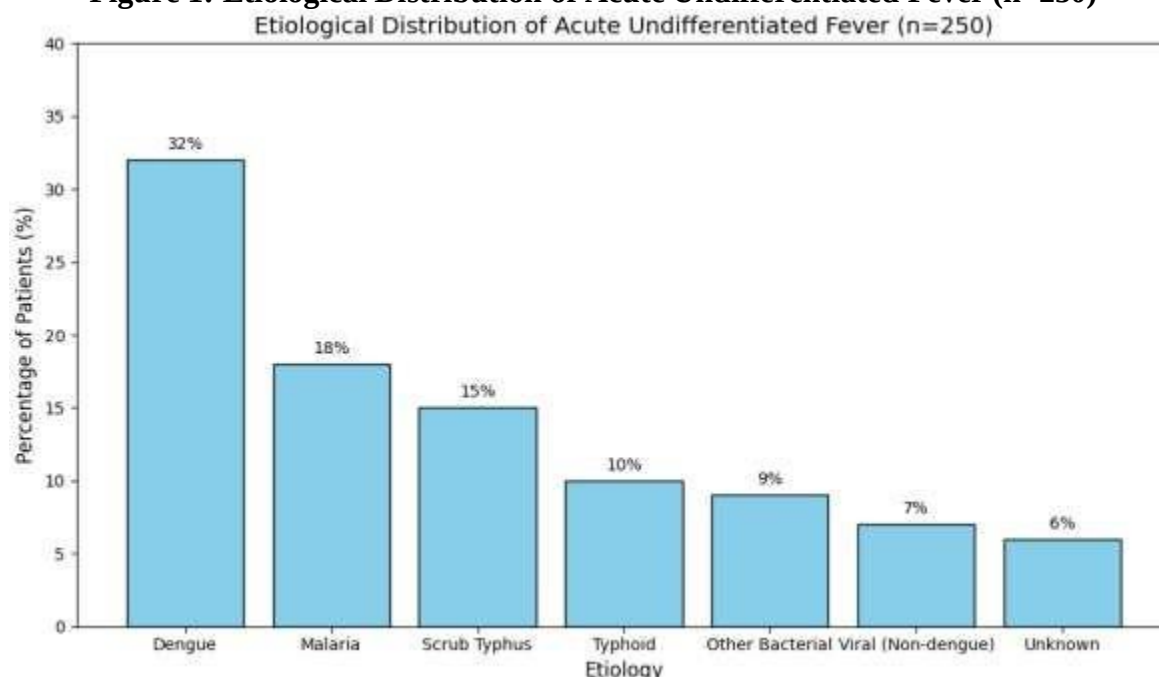
Laboratory Parameter	Abnormal Cases	Percentage (%)
Thrombocytopenia	95	38%
Leukopenia	62	25%
Elevated AST/ALT	75	30%
Elevated Creatinine	30	12%

In 210 patients (84%), an etiological diagnosis was made. Dengue fever (32%), malaria (18%), scrub typhus (15%), typhoid (10%) and other bacterial infections (9%) were the common causes. Other viral infections (besides dengue) were responsible for 7% and unknown cause in 16 patients (6%) (Table 4).

Table 4: Etiological Profile of Acute Undifferentiated Fever

Etiology	Number of Patients	Percentage (%)
Dengue	80	32%
Malaria	45	18%
Scrub Typhus	38	15%
Typhoid	25	10%
Other Bacterial	22	9%
Viral (Non-dengue)	18	7%
Unknown	16	6%

A graphical representation shows the frequency of major etiologies among patients (Figure 1), highlighting dengue as the leading cause of acute undifferentiated fever.

Figure 1: Etiological Distribution of Acute Undifferentiated Fever (n=250)

In total, 85% of patients were successfully treated in the ED or admitted for observation, and 15% were admitted to the ICU for treatment of severe dengue, malaria complications and/or sepsis. Mortality rate was 2% (mainly in patients with multi-organ dysfunction or delayed presentation).

DISCUSSION

Acute undifferentiated fever is a big clinical dilemma in the emergency departments because of its non-specific clinical presentation and wide spectrum of possible causes. In this study, done at Medicine Department, Saidu Group of Teaching Hospital, we noticed that dengue fever was the most common cause, followed by malaria, scrub typhus and typhoid. The results are in line with previous observations in India where patients with thrombocytopenia were found to have dengue or malaria or other viral diseases, highlighting the need for timely diagnosis in emergency situations (1). In areas of limited resources and in tropics, acute febrile illnesses often have similar clinical features, making rapid diagnosis difficult. In a study conducted at University of Gondar Hospital in Ethiopia, researchers found that fever of unknown origin (FUO) frequently led to the diagnosis of malaria, bacterial infection and viral diseases, similar to what we found in Karachi (2). Children are especially vulnerable, and may have nonspecific symptoms including poor feeding, lethargy, or gastrointestinal symptoms, so early evaluation is important (3).

Multi-organ dysfunction in patients with acute undifferentiated fever requires careful monitoring. Sharma et al. reported cases developing renal, hepatic or neurologic involvement, thus highlighting the importance of careful triage and risk stratification in the emergency department (4). In the same way, laboratory parameters that were associated with mortality in the rural hospitals in India were delayed presentation, thrombocytopenia and organ dysfunction, highlighting the importance of the laboratory evaluation at the earliest stage (5). Management is more than a symptomatic approach. Linking diagnosis to local epidemiology, vector exposure and seasonality enables specific interventions, including the use of anti-malarials, antibiotics or supportive care, to improve outcomes and minimize unnecessary drug use (6). In children under 5 years, there is a special risk of bacteremia, as its early symptoms may be overlooked, and excessive antibiotic use may lead to antimicrobial resistance (7). In our study, 9% of patients were found to have bacterial infections which needed prompt intervention.

This study showed that the burden of acute febrile illnesses was seasonal in Karachi. Epidemiological information reveals the highest prevalence in the summer and monsoon periods, which is related to

higher vector activity and environmental conditions that favour the transmission of dengue, malaria and leptospirosis (8). The cornerstone of the triaging of patients and guiding investigations is comprehensive clinical assessment, which involves detailed history and physical examination (9). Stepwise diagnostic algorithms support emergency physicians in making timely and evidence-based decisions and reduce the number of missed diagnoses and unnecessary tests (10). Scrub typhus is an underdiagnosed cause of undifferentiated fever in South Asia. The absence of a pathognomonic eschar and atypical presentations are a problem with delayed diagnosis, which can result in serious complications if not treated early, as emphasized by Khairkar et al. (11). Serology, culture, and molecular testing are the methods for microbiological confirmation, which is the only definitive diagnosis, especially in tertiary centers such as ours, and is important for accurate epidemiological surveillance (12).

The range of etiologies is further affected by regional variation. In Bhutan, frequent prolonged fevers were reported to be caused by rickettsial infections and bacterial pathogens, highlighting the importance of location-specific data to guide clinical decisions and resource allocation (13). Moreover, with the concurrent epidemics like dengue and COVID-19, there is a challenge of overlapping symptoms and careful evaluation is required to avoid misdiagnosis or delayed care (14). Seasonality is important, as is the correlation between monsoon periods and increased vector-borne infections. In Western Maharashtra, Singh et al. showed that monsoon months were associated with an increase in the number of dengue and scrub typhus cases, which is similar to what was observed in Karachi (15). The history of travel is also important in determining risk, because imported or unusual infections may present in patients who have returned from endemic areas, and a detailed travel history is important (16). Lastly, the epidemiology of acute undifferentiated fever is influenced by demographic and regional factors such as age, sex, place of residence and occupation. These factors affect the spread and severity of the disease, and Sharma et al. pointed out that these factors can help prioritize patients for earlier interventions (17). Our study validates the importance of structured assessment, seasonally adjusted diagnostic protocols and rapid supportive care in the tertiary emergency setting to benefit the patient.

CONCLUSION

Acute undifferentiated fever is a common and potentially serious presentation in the emergency department, especially in tropical and subtropical countries. In this study conducted at Medicine Department, Saidu Group of Teaching Hospital, dengue, malaria, scrub typhus and typhoid were found to be the most important causes, while other bacterial or viral infections accounted for a smaller proportion. Prompt diagnosis and management depend on early recognition, careful clinical evaluation and appropriate laboratory investigations. More severe outcomes were related to thrombocytopenia, multi-organ involvement, and delayed presentation, thus the need for risk stratification in the emergency setting. Etiologies vary widely depending on season, travel history, and demographic, and incorporating these data into clinical practice could enhance patient care. In conclusion, a structured evaluation and evidence-based management of AUDF can help to reduce morbidity, prevent complications, and help to optimize the use of resources in tertiary care centers.

REFERENCES

1. Dev A, Kumar A, Kumar S, Gunjan G, Singh S, Arun N. Clinical and Etiological Profile of Acute Undifferentiated Fever With Thrombocytopenia in an Emergency Department. *Cureus*. 2023 Sep 5;15(9).
2. Akelew Y, Pareyn M, Lemma M, Negash M, Bewket G, Derbew A, et al. Aetiologies of acute undifferentiated febrile illness at the emergency ward of the University of Gondar Hospital, Ethiopia. *Trop Med Int Health*. 2022;27(3):271–279.
3. Dasari R, Reddy KS, Nimmagadda A, Kuruvada SS, Sneha N, Srikrishna S. Clinico–Etiological profile of Acute Undifferentiated fever in children 6 months–15 years. *Headache*. 2023;159:54–58.

4. Sharma S, Gupta M, Lehl SS, Singla N. Acute undifferentiated fever presenting as multi-organ dysfunction: Narrowing the differential diagnosis. *J Prim Care Spec.* 2023;4(2):62–66.
5. Mørch K, Manoharan A, Chandy S, Singh A, Kuriakose C, Patil S, et al. Clinical features and risk factors for death in acute undifferentiated fever: A prospective observational study in rural community hospitals in six states of India. *Trans R Soc Trop Med Hyg.* 2023;117(2):91–101.
6. Barathan M. From fever to action: diagnosis, treatment, and prevention of acute undifferentiated febrile illnesses. *Pathog Dis.* 2024;82:ftae006.
7. Ogunkunle TO, Adedoyin TO, Ernest SK, Hassan-Hanga F, Imam A, Olaosebikan R, et al. A prospective cohort study of the clinical predictors of bacteremia in under-five children with acute undifferentiated fever attending a secondary health facility in northwestern Nigeria. *Front Pediatr.* 2022;9:730082.
8. Khan NU, Khan UR, Soomar SM, Ahmed N, Dhalla Z, Subhani F, et al. Epidemiology of patients presenting to the emergency department with acute febrile illness in the summer months in Karachi, Pakistan: a cross-sectional study. *Ann Med Surg.* 2023;85:2409–2413.
9. Kumar VS, Kumar KH, Priya RV, Mounika K, Sabeeha M. Clinical assessment on acute febrile illness—A comprehensive review. 2024.
10. Mehta KK, Jayalal JA, Lele J, Joshi P, Rekha S, Vora A, John B. A Stepwise Guide for Differential Diagnosis and Management of Acute Fever in Primary Care: An Indian Perspective. *Evaluation.* 2022;120(4).
11. Khairkar M, Vagha S, Deotale V. Review on scrub typhus: an important etiology of acute undifferentiated fever illness. *Cureus.* 2023;15(10).
12. Priya AS, Sangeetha ST, Priya AS. Clinical and microbiological study of patients with acute febrile illness at a tertiary hospital.
13. Tsheten T, Lhendup K, Dorji T, Wangdi K. Aetiologies and risk factors of prolonged fever admission in Samtse Hospital, Bhutan, 2020. *Int J Environ Res Public Health.* 2022;19(13):7859.
14. Wee LE, Conceicao EP, Sim JX, Aung MK, Oo AM, Yong Y, et al. Dengue and COVID-19: managing undifferentiated febrile illness during a “Twindemic”. *Trop Med Infect Dis.* 2022;7(5):68.
15. Singh SK, Arora R, Menon AS, Gupta A, Vashisht R, Prasad R, et al. Clinical Features and Etiological Profile of Acute Undifferentiated Febrile Illness in Western Maharashtra: A 2024 Monsoon Observational Study. *J Clin Infect Dis Soc.* 2025;3(2):45–51.
16. Srirama S, Sihag KK, Chandrasekaran AK, Latha NP, Arif W, Kumar BS, Devaraju P. Acute undifferentiated febrile illness in a traveler returning from Burkina Faso, West Africa to Puducherry, India—a case report. *BMC Infect Dis.* 2025;25(1):912.
17. Sharma S, Gupta M, Singla N, Lehl SS, Gaba S. Seasonal, Regional and Demographic Trends in Patients with Acute Undifferentiated Fever in Northern India. *J Indian Med Assoc.* 2022;120(5):33–38.