

Original Research Article

<https://doi.org/10.20546/ijcmas.2019.807.147>

## Study of Etiological Pattern in Acute Undifferentiated Febrile Illness in a Tertiary Care Hospital, Bengaluru, India

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### ABSTRACT

Health care providers lacking proper diagnostic tools are usually unable to determine specific etiologies, often diagnosing patients with acute undifferentiated febrile illness (AUF) presumptively based on clinical features and assumptions regarding circulating pathogens. Acute fever can be potentially fatal if the etiology is not recognized and treated appropriately. A cross-sectional study was conducted in a tertiary care hospital, Bengaluru, from July-December 2018. Blood was collected from patients with acute fever for peripheral smear, serological tests. Rapid diagnostic tests were done and later confirmed by ELISA. Negative samples were retested with ELISA for dengue, chikungunya and leptospirosis. A total of 100 patients with AUF were evaluated. Of these, 54% were males and 46% were females. Majority were in the age group of 21-30 years. Typhoid fever (27%), Dengue (19%), Scrub typhus (9%), Malaria (8%), Leptospirosis (1%), Chikungunya (1%) were the main infections detected. Mixed infections were noted in 9% patients. Specific diagnosis could not be delineated in 35% of patients. Implementation of standardized protocol for the assessment of AUF helps in managing the disease with cost effective treatment and reduces antibiotic resistance.

#### Keywords

AUF, Malaria,  
ELISA, Dengue,  
Chikungunya,  
Scrub typhus

#### Article Info

##### Accepted:

10 June 2019

##### Available Online:

10 July 2019

### Introduction

Acute fever or acute undifferentiated febrile illness (AUF) is a rapid onset of fever and symptoms such as headache, chills or muscle and joint pains. It is commonly seen in the tropical and subtropical regions and can be caused by diverse pathogens<sup>[3]</sup>. AUF is defined as any illness associated with fever of 2 weeks or shorter in duration, rapid in onset,

caused by diverse pathogens without any evidence of organ or system-specific etiology<sup>[4]</sup>.

Majority of the patients present with non-specific symptoms (low-grade fever, general malaise, headache, and myalgia) and usually no focal point of infection. Due to this reason, differential diagnosis of these etiologies based on clinical criteria alone is not possible and

the correct diagnosis is only possible by using pathogen specific diagnostic tests<sup>[3]</sup>.

In developing countries like India- Malaria, Dengue, Chikungunya, Scrub typhus, Typhoid, and Leptospirosis presents as Acute Undifferentiated Febrile Illness (AUI). Wide variety of causative agents and limited diagnostic tests to make prompt diagnosis pose major challenge in treating acute febrile illness in tropical countries<sup>[1]</sup> (Fig. 3).

Hence, depending on the cause, guidelines for investigation and antimicrobial therapy can be developed for general physicians to deal with AUI. The aim behind this development of testing and treatment guideline is to manage the etiologies of acute fever and also to eliminate the primary bacteremia with antimicrobial therapy, since it can pose a serious threat to the patient<sup>[8]</sup>.

## **Materials and Methods**

A cross-sectional study was conducted in a tertiary care hospital, Bengaluru, for a period of 6 months from July 2018 to December 2018. All patients with history of acute febrile illness (fever less than 2 weeks) who consent for the study were included. This study was conducted in 100 patients.

### **Sample collection**

Peripheral venous blood was collected in both EDTA and plain collection tubes from each patient, 10ml for adults and 3-5ml for pediatric patients. Blood collected in plain tube was centrifuged at 3000g for 10minutes and serum was separated and stored for serological tests.

### **Processing**

Widal test was performed using serum sample for diagnosis of typhoid. Weil Felix was done

for diagnosis of scrub typhus, and rapid diagnostic tests for dengue, chikungunya. The samples which were positive for Dengue and Chikungunya by rapid tests were confirmed by IgM capture ELISA. The samples which tested negative by rapid diagnostic tests were also retested with ELISA.

Peripheral smear was done from sample collected in EDTA tube to detect malarial parasites. Both thick and thin smear was prepared, dried, fixed and stained with Giemsa stain. To diagnose Leptospirosis, IgM ELISA was done. The study algorithm was followed as mentioned in figure 1.

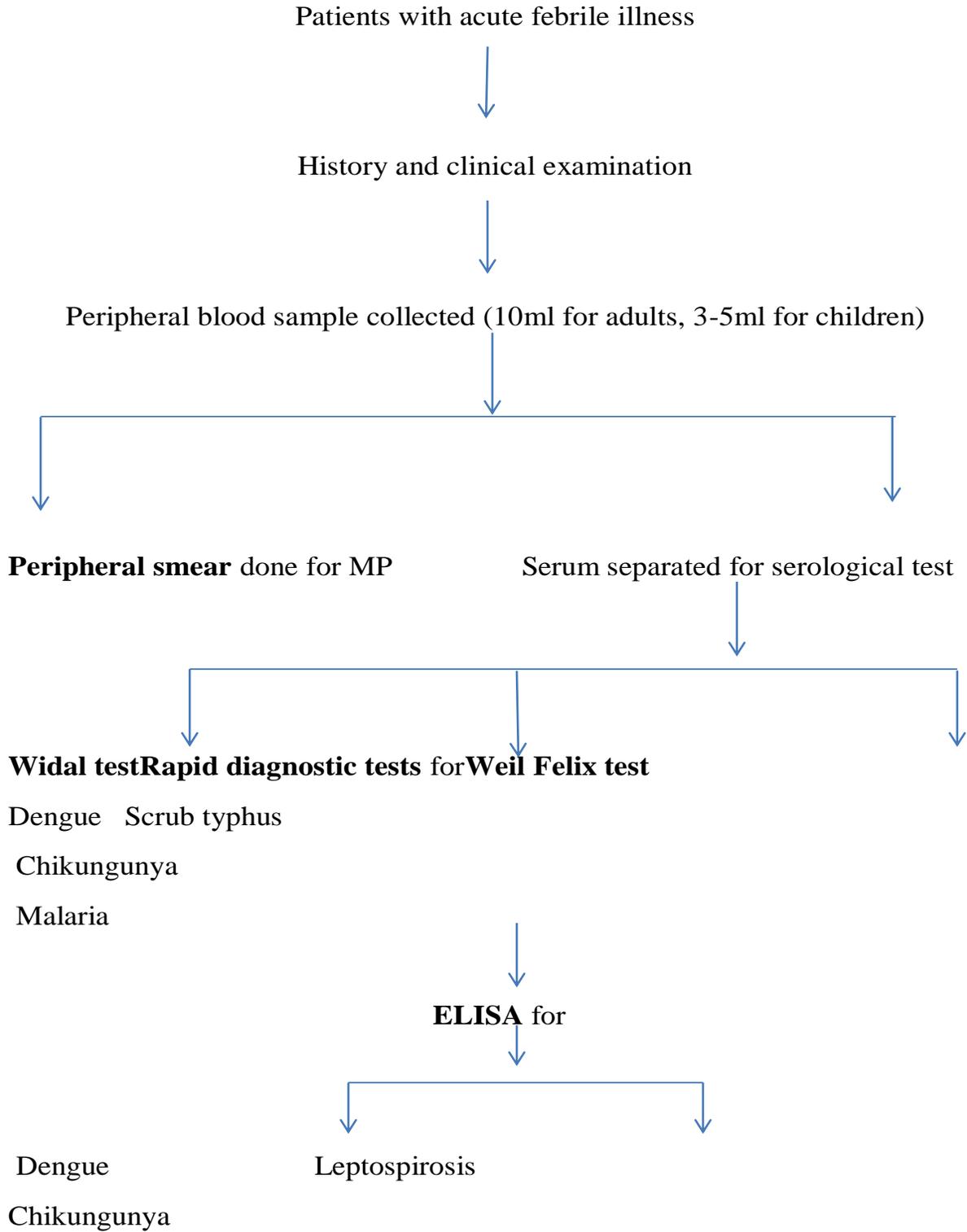
## **Results and Discussion**

A total of 100 samples were included in the study. Of which 54% were males and 46% were females. Most of the patients were in the age group of 21-30 years (34%) followed by 31-40 years (13%). Figure 2 shows the age-wise distribution of all patients. 62% of the cases were from OPD (Outpatient department) and 38% of patients were from IPD (Inpatient department). Majority of them presented with history of 5-7days of fever (57%), followed by 2-3days of fever (21%).

Clinical profile of patients shows they presented with history of fever and malaise (41%), arthralgia (30%), headache (22%). Other associated symptoms were chills and rigors (16%), pain in abdomen (13%), diarrhea (6%), and rash (2%). 5% of the patients had history of travel to endemic areas within past 10 days of onset of fever. History of exposure to plant, shrubs was seen in 3% of patients.

Table 1 and 2 shows the clinical profile of patients presenting with acute fever and epidemiological details respectively.

Out of 100 samples, 27% were diagnosed as typhoid fever by Widal test.



**Fig.1** Study algorithm

Fig.2 Age-wise distribution of patients with acute fever

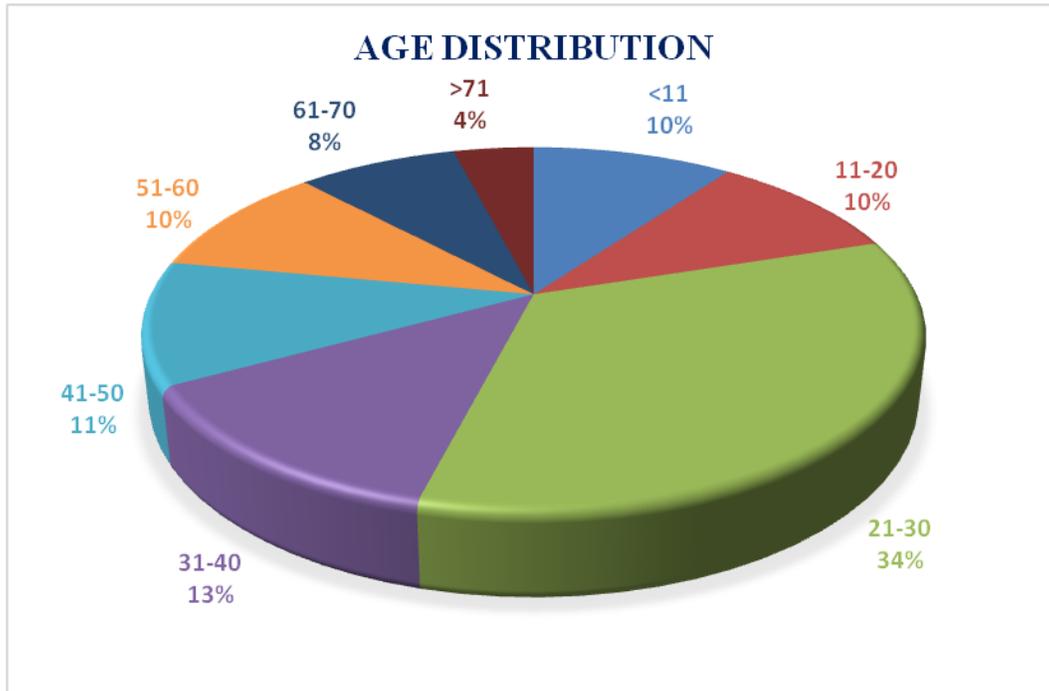
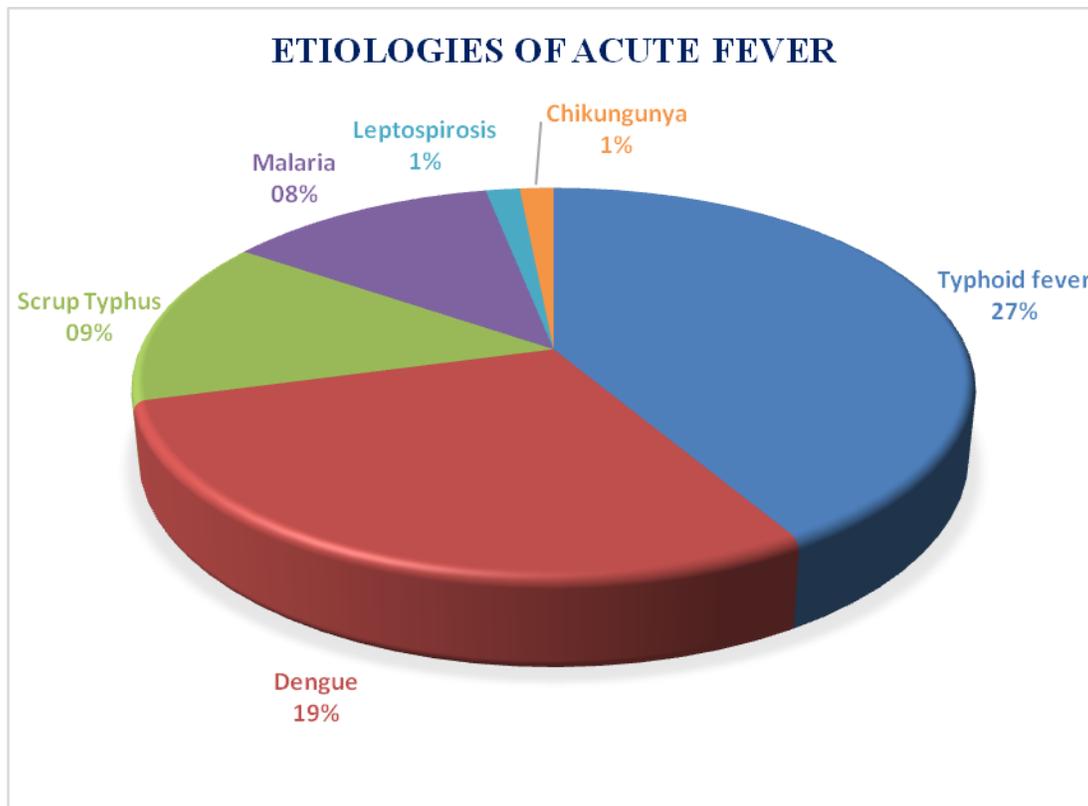


Fig.3 Etiologies of acute fever detected in this study



**Table.1** Clinical profile of patients with acute fever

Sl.no	Associated symptoms	Percentage positive
1	Diarrhea/dysentery	6%
2	Cough/ sore throat/common cold	2%
3	Breathlessness	0
4	Rash (macule/papule/maculo-papular/eschar/pustule/bullae/others)	2%
5	Jaundice	0
6	Headache	22%
7	Malaise	41%
8	Arthralgia	30%
9	Chills and rigors	16%
10	Hemorrhagic manifestations	0
11	Others(Pain abdomen)	13%

**Table.2** Epidemiological details of patients with acute fever

Sl. no	Epidemiological details	Percentage positive
1	Presence of similar case in house	3%
2	Presence of similar case/s in the village or locality	0
3	History of travel in last 10 days	5%
4	History of exposure to plants/shrubs	3%

Rapid diagnostic tests (RDT) showed 15% samples positive for Dengue NS1 antigen. None of the samples were positive for Chikungunya by rapid tests. Dengue samples were confirmed by IgM Capture ELISA. Out of 15 RDT dengue positive samples, 11% were positive for IgM antibodies and 4% showed equivocal results.

Out of the RDT negative samples which were retested with ELISA, 4% isolates were positive for Dengue IgM Capture ELISA and 1% was positive for Chikungunya IgM Capture ELISA.

On examining peripheral smear of EDTA samples, 8% samples were positive for malaria parasites (MP). Of which, 6% was diagnosed as *Plasmodium vivax*, 1% as *Plasmodium falciparum* and 1% as mixed infection having both *P. falciparum* and *P.*

*vivax*. 9% of cases were diagnosed as Scrub typhus by Weil Felix test. 1% was positive for IgM ELISA for Leptospira.

9% of the samples showed co-infection. 3% was MP with Widal, 3% Dengue with Widal, 2% was Scrub typhus with Widal, 1% Dengue with Leptospira.

Out of 100 cases, 35% samples tested negative for all the tests included in this study.

Male predominance was noticed in this study (54%) which was similar to Shelke *et al.*, (2017), 51.11% was males and 48.88% were females. This may be due to the reason that males get more exposed to the outer environment than females.

Majority of the patients were in the age

group of 21-30 years (34%) which was similar to other studies. According to Shelke *et al.*, (2017), nearly 25.95% were belonging to 15–25 years of age group.

The predominant cause of fever in our study was Typhoid fever (27%), followed by Dengue (19%) and scrub typhus (9%). Singh *et al.*, (2014) shows dengue was detected in 71.2 %, malaria 12.8%, typhoid 8.1% and scrub typhus 6.0%. Mixed infection was noted in 1.9%.

According to Mittal *et al.*, (2015), Dengue was predominant (37.54%) followed by enteric fever (16.5%) and scrub typhus (14.42%).

In India, dengue positivity ranged between 8% and 71% among AEFI cases<sup>[7]</sup>. The studies conducted in Tamil Nadu, Dehradun, showed dengue is a prime cause of AEFI cases.

Scrub typhus was the third cause of AEFI cases (9%) in this study. There was no eschar found in cases which tested positive for scrub typhus, a study conducted by Sinha *et al.*, (2014) did not show scrub typhus patients with eschar among 42 positive cases of scrub typhus which was included in their study. Scrub typhus has become one of the most predominant infections in all the regions of India. This may be due to earlier infection used to be unnoticed and now due to the availability of serological tests and polymerase chain reaction (PCR).

In our study Malaria was found in 8% cases. A study conducted by Singh *et al.*, (2014) reported malaria 12.8% and reported as second cause in AEFI cases.

Leptospirosis was diagnosed in 1% of AEFI cases in our study which was similar to the study carried out by Joshi *et al.*, (2008), and

2% in Shelke *et al.*, (2017).

35% of cases could not be diagnosed by the tests used in this study. According to Shelke *et al.*, (2017) 6.6% patients remained undiagnosed.

The limitation of this study was other bacterial infections like brucellosis, urinary tract infection and viral diseases like hepatitis could not be tested.

Scrub typhus and Dengue are emerging as an important pathogen of acute febrile illness in this part of Karnataka. Lack of information about the specific etiologies slows our ability to make the accurate diagnosis, and provide effective treatment. Hence active fever surveillance is necessary as clinical diagnosis is not always sufficient to detect all febrile cases.

### **Acknowledgements**

I express my sincere thanks and gratitude to Dean and Director, Dr. H.S. Satish and Principal Dr. C.R. Jayanthi, BMC&RI, Bengaluru for allowing conducting this study. Dr. Ambica R., M.D., Professor and Head, Department of Microbiology, for her masterly guidance, invaluable advice, and supervision. I thank all my teachers, colleagues, all technical staff and non-teaching staff member of the Department for their help and support.

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**How to cite this article:**

Varsha V. Desai and Ambica, R. 2019. Study of Etiological Pattern in Acute Undifferentiated Febrile Illness in a Tertiary Care Hospital, Bengaluru, India. *Int.J.Curr.Microbiol.App.Sci*. 8(07): 1234-1240. doi: <https://doi.org/10.20546/ijcmas.2019.807.147>