

**Original Research Article****The Etiology of Fever in Adults Presenting in Department of General Medicine in IGIMS**

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**Abstract**

*In India, febrile illness is one of the most common reasons for seeking medical attention, but there is limited information on the frequency of specific infections.*

**Aim:** *To evaluate the causes of fever in patients.*

**Method:** *300 patients presented with fever seen between October 2019 to March 2020 were included in study.*

**Results:** *In our study most common disease associated with fever was upper respiratory tract infection; 28.8% male and 26.8% female were diagnosed with URTI respectively. Second most common disease associated with fever was enteric fever; 20.3% male and 15.4% female were diagnosed with enteric fever. Dengue fever was the third most common disease associated with fever in our study; 16,3% male and 13% female had dengue fever. Urinary tract infection (UTI) and malaria were the fourth and fifth most common disease found in our study.*

**Conclusion:** *Among febrile illness, URTI, enteric fever, dengue fever and malaria were the most common in this study. Scrub typhus should be considered in the differential diagnosis of patients with acute febrile illness. Tuberculosis needs to be considered in the diagnosis of febrile illnesses*

**Keywords:** *Febrile illness, Upper respiratory tract infection, Enteric fever, Malaria, Dengue fever, Scrub typhus.*

**Introduction**

The infectious causes of febrile illness remains poorly characterized in many parts of world, largely due to limited diagnostic facilities. Infectious disease are the leading causes of death in tropical countries. The world Health

Organisation (WHO) reports that each of the main infectious aetiologies (that is pneumonia, diarrhoea, HIV/AIDS, malaria, tuberculosis (TB), and neonatal infections), cause between 1.05 and 0.24 million deaths respectively per year in low income countries.<sup>1</sup>

Sentinel hospital based studies performed over defined periods of time have provided useful clinical and public health information in countries that lack resources for long term routine diagnostic testing.<sup>2</sup>

In India, febrile illness is one of the most common reasons for seeking medical attention, but there is limited information on the frequency of specific infections. While the burden of some infections (e.g malaria, enteric fever, dengue, Tuberculosis) is believed to be substantial, the importance of others (e.g leptospira and rickettsial) is lacking.<sup>3- 5</sup>

In resource- limited settings fever may be treated empirically or self-treated due lack of access to diagnostic tests.<sup>6</sup> However, clinical algorithms in order to differentiate malaria, for instance, from other causes of fever are not specific.<sup>7 - 8</sup>

Nonmalarial acute undifferentiated fever refers to a febrile illness with no indication of an organ-specific disease after diagnosis of malaria has been excluded. This term often refer to self-limiting viral illness are major public health problem.<sup>9 - 11</sup>

Fever was attributed to infection in 37% to 74% of patients, whereas a non-infectious aetiology was identified in 3% to 52 % of patients.<sup>12</sup>

In the past 30 years, the most common identifiable fever of unknown origin aetiologies in adults changed from infectious to inflammatory diseases or unknown causes.<sup>13</sup>

Nevertheless, there are only a limited number of studies from India reporting on the aetiology of fever, and reliable surveillance data are not available.

### **Aims and Objectives**

- 1) To evaluate the causes of fever in patients.
- 2) To look for common types of fever.

### **Material and Methods**

This observational, prospective, non-interventional study includes patients with fever, who were willing to be enrolled from OPD and Indoor from department of Medicine, Indira

Gandhi Institute of Medical science, Patna, Bihar, between October 2019 and March 2020 after approval from ethics committee.

300 patients coming with fever is to be selected.

### **Inclusion Criteria**

- 1) Male and female patients with fever
- 2) Age  $\geq$  18 years
- 3) Patients willing to give informed consent for study.

### **Exclusion Criteria**

- 1) Age  $\leq$  18 years
- 2) Pregnant female
- 3) Unwilling or unable to comply with protocol

Detailed history is to be taken and examination done from each patient. Most febrile illnesses of duration less than a week are due to viral infections which subside without any specific treatment and hospitalization. However, when the duration of fever is more than seven days, etiology can be varied and usually patients are admitted for evaluation. In certain infections like upper respiratory tract infection, lower respiratory tract infection, gastrointestinal tract infection and skin infection the etiology and site of infection is evident from history and clinical examination itself, but in some cases investigations are required.<sup>14</sup> Laboratory investigations done as per need, that is complete blood count, Liver function test, kidney function test, Blood sugar, Typhi dot, widal test, Leptospira Ig M ELISA, Dengue NS1 antigen, Dengue IgM/IgG antibody, Scrub Typhus IgM ELISA, Quantitative buffy coat(QBC), Malaria microscopy, HIV, HBsAg, Anti-HCV, Blood culture, Urine culture, ANA/ENA test, Biopsy, stool microscopy, CSF examination, Sputum (Routine, culture, Gene Xpert) and radiological investigation that is Chest X-ray, Abdominal ultrasound, CT scan, MRI done.

Diagnostic criteria for malaria: Peripheral smear showing malarial parasite or pLDH/ HRP2 antigen positive (Rapid test for Pv /Pf, ZEPHYR Biomedicals Goa, INDIA).

Diagnostic criteria for enteric fever: Blood culture positive for Salmonella typhi or para typhi or WIDAL positive done by slide agglutination and tube agglutination method more than 1:160 titre (TYDAL Widal Antigen Set/Antigens for Slide and Tube Tests, TULIP DIAGNOSTICS (P) LTD, Goa, INDIA).

Diagnostic criteria for dengue: IgG/ IgM Antibodies to dengue virus by rapid immune chromatographic test Dengue NS1Ag and Ab J Mitra and CO. Pvt. Ltd., OKHLA NEW DELHI, INDIA.

Diagnostic criteria for scrub typhus: Eschar or IgM Elisa positive or Weil Felix test positive (OX K titre >80), SD scrub IgG/IgM(STANDARD DIAGNOSTIC INC, REPUBLIC OF KOREA).

Diagnostic criteria for leptospirosis: Positive for IgM antibodies to leptospira (SD Leptospira IgG/IgM, STANDARD DIAGNOSTIC Republic of korea)

Diagnostic criteria for Kala-Azar: Bone marrow for LD, Rapid test (kalazar Detect rapid test, In Bios International , seattle , USA)

When more than one diagnosis explaining fever had been noted, than the most probable etiology (based on available clinical information) was registered as main etiological diagnosis.

**Results**

A total of 300 patients coming with fever was selected for study. Among them 177 were male and 123 were female.

**Table- 1**

Characteristics	Patients ( n = 300)
<b>Age ( yrs)</b> Mean	36.4
<b>Gender</b> Male Female	177 (59%) 123 (41%)
<b>Fever duration (Weeks)</b> < 1 week 1 – <4 weeks 4- <12 weeks >12 weeks	(105)35% (90)30% (81) 27% (24)8%
<b>Comorbidity</b> Hypertension Type 2 Diabetes HIV	(39)13% (36)12% (6)2%

Mean age of patients was 36.4 years, 59% were male and 41% were female. In most of patients fever were of duration less than 1 week( 35%), Next common duration of fever were 1 - <4 weeks.27% of patients had fever duration of 4 - <12 weeks and 8% had fever duration of >12 weeks. 39(13%) patients had comorbidity of hypertension; 36(12%) had type2 diabetes and 6(2%) had HIV.

**Table-2:** Etiology and Sex distribution

	Male n=177	%	Female n=123	%	Total
Malaria	14	7.9%	6	4.8%	20
Enteric fever	36	20.3%	19	15.4%	55
Dengue fever	29	16.3%	16	13%	45
Scrub typhus	3	1.6%	1	0.8%	4
Leptospirosis	3	1.6%	0	0%	3
Kala-Azar	4	2.2%	2	1.6%	6
Liver abscess	4	2.2%	1	0.8%	5
URTI	51	28.8%	33	26.8%	84
Pneumonia	3	1.6%	2	1.6%	5
UTI	6	3.3%	18	14.6%	24
Pulmonary TB	8	4.5%	2	1.6%	10
Extra pulmonary TB	2	1.1%	2	1.6%	4
HIV	5	2.8%	1	0.8%	6
Connective tissue disorder	1	0.5%	11	8.9%	12
Malignancy	5	2.8%	4	3.2%	9
Undiagnosed	3	1.6%	5	4%	8

URTI-Upper respiratory tract infection, UTI-Urinary tract infection

In our study most common disease associated with fever was upper respiratory tract infection; 28.8% male and 26.8% female were diagnosed with URTI respectively. Second most common disease associated with fever was enteric fever; 20.3% male and 15.4% female were diagnosed with enteric fever. Dengue fever was the third most common disease associated with fever in our study; 16,3% male and 13% female had dengue fever. Urinary tract infection (UTI) and malaria were the fourth and fifth most common disease

found in our study. Pulmonary and extra pulmonary tuberculosis was also diagnosed in 10 and 4 patients respectively. 12 patients were diagnosed with connective tissue disorder in which male to female ratio was 1:11. Few cases of scrub typhus(4), leptospirosis(3), Kala-azar(6), liver abscess(5), pneumonia(5) and HIV(6) were also diagnosed as cause of fever in our study. 9 cases diagnosed as malignancy for cause of fever. In 8 patients cause of fever were not diagnoses.

**Table- 3:** Etiological distribution of Patients across various age group (n=300)

	18 - <30yr	30-<45yr	45- <60yr	>60yr
Malaria	9	7	2	2
Enteric fever	27	18	7	3
Dengue fever	19	16	6	4
Scrub typhus	2	2	0	0
Leptospirosis	2	1	0	0
Kala-Azar	3	2	1	0
Liver abscess	1	2	2	0
Upper respiratory tract infection	30	25	11	18
Pneumonia	1	1	2	1
Urinary tract infection	2	8	12	2
Pulmonary TB	4	3	1	2
Extra pulmonary TB	0	2	2	0
HIV	0	3	3	0
Connective tissue disorder	3	7	2	0
Malignancy	0	2	3	4
Undiagnosed	4	3	1	0
Total	107	102	55	36

In our study most of patients with fever were young. Age groups 18- <30 years were most commonly affected (107).URTI, enteric fever, dengue fever and malaria were common disease associated with fever in 18-<30 years groups.

Second most common group was of 30- <45 years (102). In these groups most common disease associated with fever were; URTI, enteric fever, dengue fever, malaria and UTI.

55 patients were in the age group 45- <60 years, and most common etiology in these age group was UTI (12), followed by URTI(11) .

In the age group >60 there were 36 patients. Most of patients were diagnosed with URTI in these age groups, next most common etiology were malignancy and dengue fever.

## Discussion

Among the 300 patients selected for study 177(59%) were male and 123(41%) were female, with mean age of patients was 36.4 years. In most of patients fever were of duration less than 1 week( 35%), Next common duration of fever were 1 - <4 weeks.27% of patients had fever duration of 4 - <12 weeks and 8% had fever duration of >12 weeks. 39(13%) patients had comorbidity of hypertension; 36(12%) had type2 diabetes and 6(2%) had HIV.

In our study most common disease associated with fever was URTI; 28.8% male and 26.8% female were diagnosed with URTI respectively. Second most common disease associated with fever was enteric fever; 20.3% male and 15.4% female were diagnosed with enteric fever. Dengue fever was the third most common disease associated with fever in our study; 16,3% male and 13% female

had dengue fever. A study conducted by Singh et al, from north India had shown that dengue, malaria and enteric (Typhoid) fever are the most common etiological agent of acute febrile illness.<sup>15</sup> Urinary tract infection (UTI) and malaria were the fourth and fifth most common disease found in our study. Pulmonary and extrapulmonary tuberculosis was also diagnosed in 10 and 4 patients respectively. 12 patients were diagnosed with connective tissue disorder in which male to female ratio was 1:11. 4 cases of scrub typhus, 3 cases of leptospirosis, 6 cases of Kala-azar, 5 cases of liver abscess, 5 cases of pneumonia and 6 cases of HIV were also diagnosed as cause of fever in our study. 9 cases diagnosed as malignancy for cause of fever. In 8 patients cause of fever were not diagnoses.

In our study most of patients with fever were young with age groups 18- <30 years. URTI, enteric fever, dengue fever and malaria were common disease associated with fever in 18-<30 years group.

URTI was the most common etiology in all the age groups except in 45-<60 years age groups; where UTI was the most common etiology found in our study.

### Conclusion

Among febrile illness, URTI, enteric fever, dengue fever and malaria were the most common in this study. Scrub typhus should be considered in the differential diagnosis of patients with acute febrile illness. Tuberculosis needs to be considered in the diagnosis of febrile illnesses. The treating physician has to keep in mind the comprehensive list of differential diagnosis for patients with febrile illness due to varied etiologies.

The provision of accurate epidemiologic data for common pathogens will enable resources to be directed towards key areas and will be of practical importance to clinicians.

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**Conflict of Interest:** None

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