

## Acute Febrile Illnesses – Clinico-epidemiological Pattern in a Remote Geographical Location of North-eastern India

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**Background:** Acute undifferentiated febrile illness (AUF / AFI) is a common cause for patients seeking hospital care in tropical countries like India. Non-specificity of symptoms and lack of appropriate diagnostics pose a challenge, especially in resource-limited settings. Investigation into the etiology and trends of AUF provide valuable public health data to target clinical workup and guide optimal treatment. **Method:** A record-based descriptive study was conducted on all AFI cases presented to a Government tertiary care centre in a tribal hilly state of Northeast India in the year 2021. **Result:** Under five children were the most affected and respiratory infections were the most common cause of fever. Enteric fever and scrub typhus were the most common cause of undifferentiated fever. However, it was a remarkable finding that no case of malaria or dengue was reported from this region. Fevers remained undetermined in 28% of cases. Undetermined fevers and scrub typhus had higher occurrence during winters while no seasonality was observed with enteric fever. The majority of the patients recovered and were discharged. The case fatality rate was 0.35%.

**Conclusion:** The local epidemiology of AUF can help guide presumptive diagnosis and deliver optimal patient management in these settings. Typhoid and scrub typhus are to be considered differentials for AUF in this region.

**Keywords:** Acute febrile illness (AFI), Acute undifferentiated febrile illness (AUF), Epidemiology, Northeast India

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<p>Michi Monya, General Duty Medical Officer, , Chera Talo District Hospital, Kurung Kumey, Arunachal Pradesh, India. Email: <a href="mailto:michie2707@gmail.com">michie2707@gmail.com</a></p>	<p>Michi Monya, Acute Febrile Illnesses – Clinico-epidemiological Pattern in a Remote Geographical Location of North-eastern India. Int J Med Res Rev. 2023;11(4):82-88. Available From <a href="https://ijmrr.medresearch.in/index.php/ijmrr/article/view/1429">https://ijmrr.medresearch.in/index.php/ijmrr/article/view/1429</a></p>	

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## Introduction

Fever in the tropics is a nebulous terminology. Due to the myriad of clinical manifestations of fever, it is often broadly classified based on the duration of symptoms.[1] Unlike fever of unknown origin (FUO), which has a standard definition, “acute febrile illness” (AFI), “short febrile illness” or “acute fever” lacks an international consensus definition. Since FUO requires the duration of a fever to be longer than three weeks, some authors have defined AFI as a fever lasting less than three weeks. [2] AFI has been used synonymously with acute undifferentiated febrile illness (AUI) in several publications. [2-4]

Acute febrile illness is a common cause among patients seeking healthcare in India. [5] Most febrile illnesses of duration less than a week are due to viral infections which subside without 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 cases like respiratory infection, gastrointestinal infection, skin infections etc. the etiology and site of infection can be localized from history and clinical examination, but in other cases lacking any localizable organ-specific signs or symptoms, investigations are required. [6] Common causes of undifferentiated febrile illnesses in tropical countries like India include dengue, malaria, leptospirosis, enteric fever, chikungunya, rickettsia and Japanese encephalitis. [7]

Non-specificity of symptoms and signs poses a diagnostic and therapeutic challenge to healthcare workers, especially in resource-limited settings. [2] In such situations, knowledge of the local prevalence of infections is critical to target clinical workup and treatment. A better understanding of causes geographically would help in narrowing down the vast diagnostic workup needed to pinpoint the etiological agent and guide to an optimal treatment to avoid unwanted usage of antibiotics and antimalarials. [8]

Despite considerable heterogeneity of AUI etiology by population, region, and time, there is limited published literature detailing these findings, both by geographic location and period. Hence, this study was undertaken to describe the trends and etiology of AFI reported in a government tertiary care centre in the year 2021.

## Material and Methods

A record-based descriptive study was conducted in a Government Tertiary Care Centre in Kurung-Kumey district of Arunachal Pradesh which is a hilly tribal area in the north-eastern part of India.

A universal sample of all patients with fever > 38.3° C (101.0° F) of less than 21 days duration, presenting in OPD or ED between January 2021 to December 2021 was taken for the study.

Exclusion criteria: Previously diagnosed cases of,

Collagen vascular disorders

Endocrine disorders

Malignancies

Fever of duration ≥21 days

## Results

The age range of the participants was quite wide ranging from 15 days to 80 years of age. However, the mean age was at the lower end (11.60 ± 13.84 years) indicating the higher occurrence of AFI in the younger age group. Under five age group was found to be the most affected. 23.88% of the participants were adults but did not know their exact age who were marked as ‘a’ and were categorized as ‘Adult unspecified’. Distribution among genders was almost equal. The majority of the patients were recruited from the outpatient department (OPD). (Table 1)

**Table 1: Baseline parameters of AFI cases, Govt. Tertiary care centre, Arunachal Pradesh, 2021**

Parameters	Category	N	Percentage
Age (Years)	Under 5	418	36.41
	6-12	186	16.20
	13-18	75	6.53
	19-59	183	15.94
	>60	12	1.04
	Adult unspecified	274	23.88
Gender	Male	544	47.39
	Female	604	52.61
Site of patient recruitment	OPD	939	81.79
	ED	209	18.21

**Etiology Of Afi:** The majority of the AFI cases reported in our study were localizable to one of the organ systems whereas 38.07% of cases

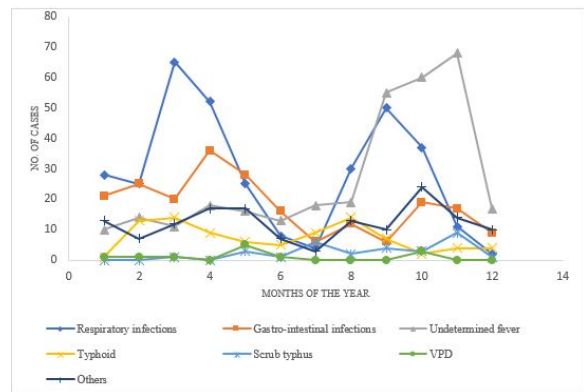
Presented with fever with no localizing source. Among the localized infections, respiratory infections were the most common. Among the undifferentiated fevers, the majority were undetermined followed by enteric fever and scrub typhus. It is interesting to note that there were no cases of mosquito-borne diseases identified during the year. (Table 2)

**Table 2: Etiology of AFI cases, Govt. Tertiary care centre, Arunachal Pradesh, 2021**

Etiology		N (1148)	Percentage	Percentage out of total AFI cases
Acute	Total	711	100	61.93
	Localized Infection			
	Respiratory infections	339	47.68	29.53
	Gastro-intestinal infections	215	30.24	18.73
	ENT infections	86	12.10	7.50
	UTI	32	4.50	2.79
	CNS infections	10	1.41	0.87
	Mixed organ infections	14	1.97	1.22
	Chicken pox	8	1.12	0.67
	Mumps	4	0.56	0.35
	Syphilis	2	0.28	0.17
	Hepatitis B	1	0.14	0.09
Acute Undifferentiated Febrile Illness	Total	437	100	38.07
	Undetermined	319	73.00	27.79
	Typhoid	88	20.14	7.67
	Scrub Typhus	30	6.86	2.61

**Seasonal Trend in AFI:** To study the trend of AFI cases, the cases were grouped into five different categories. Chicken pox and mumps were included in the category named Vaccine preventable diseases (VPD). Influenza-like illness (ILI) and other respiratory infections were included in the category of respiratory infections. Acute gastroenteritis and dysentery were included in gastrointestinal infections. Typhoid and Scrub typhus were analysed separately due to their higher prevalence. Diseases like hepatitis, syphilis, mixed organ infections, urinary tract infections and infections of the Ear Nose Throat and CNS were included in the category named "others". The AEFI cases which could not be diagnosed were termed undetermined fever.

We document a bimodal trend in the occurrence of AFI over the year with peaks during spring and pre-winter seasons. Respiratory infections showed a typical bimodal presentation. Gastrointestinal infections were more prevalent during the summer. Undetermined fevers and scrub typhus had a higher occurrence in the winter period. Enteric fever and fever due to vaccine-preventable diseases were present similarly throughout the year. (Figure 1)



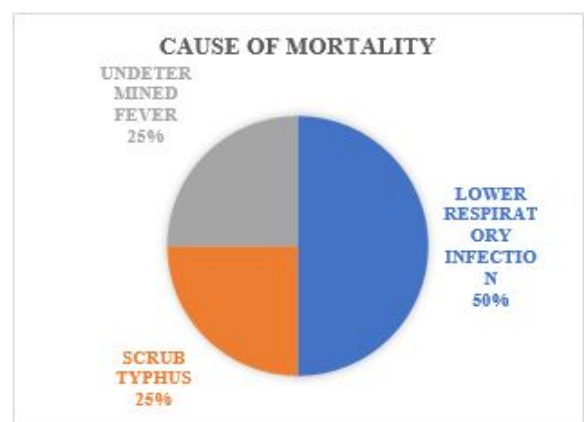
**Figure 1: Seasonal trend of AFI cases, Arunachal Pradesh, 2021**

**Outcome Of the Disease:** The outcome of the illness was computed using patients admitted to the wards. The majority of the patients with AFI recovered and were discharged. (Table 3) There were 4 cases of mortality making the case fatality rate in our study 0.35%. All the deaths were seen among children under 15 years. Two of the deaths were due to respiratory infection both of whom were infants, 1 death was due to scrub typhus in an 11 years old child and 1 mortality was in a case of undetermined high-grade fever without any localizing signs and symptoms in 14 years old. (Figure 2)

**Table 3: Disease outcome, AFI cases, Govt. Tertiary care centre, Arunachal Pradesh, 2021**

Outcome	N (209)	Percentage
Recovered	178	85.17
DAMA*	13	6.22
Referred	14	6.70
Death	4	1.91

\*Discharge Against Medical Advice



**Figure 2: Causes of mortality, AFI cases, Govt. Tertiary care centre, Arunachal Pradesh, 2021**

## Discussion

Acute febrile illness is a common cause among patients seeking healthcare in India. The etiologies of febrile illness can vary region wise suggesting that diagnosis, treatment and control programs need to be based on a methodical evaluation of area-specific etiologies.[9]

This study aimed to establish the clinical-epidemiological profile of acute febrile illness in the tribal hilly setting of northeastern India.

A total of 1148 patients presenting with AFI in a Government tertiary care centre during the study period of one year were evaluated. Participants consisted of a wide age range from 15 days to 80 years. Similarly in a previous study in Uganda, participants ranged in age from 5 months to 95 years and in another study among hospitalized patients in Indonesia, the age range was 1 to 98 years. [10, 11] Under five age group was the most affected in our study which was on par with a previous study conducted in Kerala.[12]

Distribution among genders was almost equal with females being only marginally higher. A similar finding was noted in a previous study on AFI from a tertiary care centre in Puerto Rico.[13] However, this was in contrast to several other studies where males were affected more than females.[2,11,16]

The majority of the patients in our study were recruited from the outpatient department (OPD) and only 18.21% of patients were admitted indicating major presentation as mild to moderate disease. This finding was consistent with another study where only 19% of enrolled patients were admitted. [13]

The most common cause of fever presentation in our study was respiratory infections. Similarly in a previous study, acute respiratory infections accounted for 50-75% of febrile presentations at outpatient clinics.<sup>14</sup> It is noteworthy that there were a bulk of cases which were un-diagnosed and classified as undetermined fever, which made the second largest group in our study. This reflects the need for improvement in clinical and diagnostic modalities in diagnosing cases of AFI. A similar finding was noted in an earlier study from Pondicherry.[2]

Among the confirmed cases, enteric fever was the most common followed by scrub typhus. In a previous study from Sikkim, Scrub typhus was observed to be the most common cause of acute febrile illness followed by dengue, malaria and typhoid.[7] Another study from Pondicherry revealed the most prevalent etiologies as scrub typhus, dengue and enteric fever.[2] In a study from Vellore scrub typhus, malaria, enteric fever and dengue were the most common of all acute febrile illnesses.[4]

However, a study from Kerala revealed dengue as the most common AFI.[12] In a systematic review conducted by including many independent studies from South and South Eastern Asia, dengue was found to be the most common etiology for AFI in this part of the world.<sup>15</sup> Similarly in another study from Himachal heavy burden of tropical infections were dengue, enteric fever, scrub typhus and malaria in that order of occurrence.[16]

It is remarkable that in contrast to these studies from several parts of India, there were no cases of dengue or malaria in our study.

The state of Arunachal along with Nagaland and Manipur has reported to show a steady decline in malaria cases from 2009 until 2018.[17] In a report published in 2022 on the number of malaria cases across Arunachal Pradesh India 2014-2021; a significant decline was noted in malaria cases reported from the state with 6082 cases in 2014 to only 7 cases in 2021.[18] In fact, on the occasion of world malaria day 2022, Arunachal was felicitated as one of the best-performing states in the country in terms of malaria elimination by the Union Ministry of Health and Family Welfare. [19]

A dengue outbreak had been reported from the region of Pasighat of East Siang district in Arunachal Pradesh in 2012; [20] yet NVBDCP records a dramatic decrease in dengue cases in the state since 2015; from 1933 cases and 1 death in 2015 to 17 cases and no death till May 2022. [21]

Identification of mumps in 3 subjects, all under the age of 9 years and chicken pox in 6 subjects, including adults, highlights the need for comprehensive vaccination in India. In a previous study in Indonesia measles was identified in several subjects, including adults.[11]

Mixed organ infections were found in 1.22% of AFI cases in our study. This was similar to a meta-analysis where 2.2% of patients were found to have co-infection.<sup>22</sup> Contrarily, the majority of patients (51.7%) had multi-organ clinical manifestations in a study in Indonesia.<sup>[11]</sup> Mixed infections can result in an illness with overlapping symptoms, resulting in a situation where the diagnosis and management pose a challenge to the treating physician.<sup>[16]</sup>

We document a bimodal trend in the occurrence of AFI over the year with peaks during spring and pre-winter seasons. In a study in Himachal, AEFI occurred mostly during the months of monsoon and post-monsoon period. <sup>[16]</sup> This difference could be due to the non-availability of mosquito-borne diseases like dengue and malaria in our study which are known to have a seasonal trend during monsoon.

Undetermined fevers and scrub typhus had a higher occurrence in the winter period in our study. Scrub typhus is classically known as a post-monsoon disease; however, another study has documented the prolonged occurrence of scrub typhus extending well into December. <sup>[23]</sup> The continuation of the rainy season till late November could have a bearing on the prolonged outbreak of this disease.

In our study, enteric fever was present almost throughout the year. Similarly, no significant seasonal variation in enteric fever was documented in a study from Mumbai.<sup>[24]</sup> Another study gave similar results, where scrub typhus peaked during the monsoon season and the cooler months, whereas no seasonality was observed with enteric fever and malaria. <sup>[25]</sup>

Respiratory and gastrointestinal infections were highest among the under-5 age group. This finding was consistent with the previous study.<sup>[14]</sup> Typhoid fever was seen more in adults whereas the majority of scrub typhus cases (90%) were seen in children under 13 years of age in our study. This was in contrast to studies which indicated that children are at risk of developing typhoid fever and that the seroprevalence of scrub typhus steadily rose with age.<sup>15</sup> This could be due to the higher involvement of children in outdoor activities in the regions of the study.

The case fatality rate in our study is 0.35%. This was similar to a systematic review conducted in the South East Asian region where the case

Fatality rate was 0.5%.<sup>15</sup> Higher mortality of 5.9% was documented among hospitalised patients with AFI in Indonesia. <sup>[11]</sup>

Lower respiratory infections were the major cause of death followed by scrub typhus and undetermined fever in our study. All the deaths were seen among children under 15 years. Similarly lower respiratory infections were the leading cause of death and mostly among children in a study in Nagpur.<sup>9</sup> After lower respiratory infection, undetermined fever and scrub typhus constituted an equal proportion of causes of death emphasizing the lack of diagnostic modalities in undetermined fevers and problems of late diagnosis and treatment in case of scrub typhus. In a study on hospitalized patients with AFI, the three most common microbiologic etiologies identified in the fatal cases were *M. tuberculosis* (8/89, 8.9%), *R. typhi* (7/89, 7.8%), and *Salmonella* spp. (5/89, 5.6%). <sup>[11]</sup>

## Conclusion

This study highlights the clinical-epidemiological pattern and antibiotic trend of AFI in this part of India. Under five children were the most affected with a slightly higher female representation. The majority presented in the outpatient department connoting higher occurrence of mild to moderate disease. Respiratory infections were the most common cause of fever. Approximately 28% of participants in this study remained without a diagnosis. Improved and better availability of diagnostics may lead to more appropriate management and treatment of cases, leading to a reduction in overall mortality.

Enteric fever and scrub typhus were the most common cause of undifferentiated fever. However, it was a remarkable finding that no case of malaria or dengue was reported from this region. Scrub typhus was a substantial cause of morbidity and mortality indicating the importance of high clinical suspicion, early diagnosis and treatment.

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