Clinical and Etiological Profile of Acute Febrile Illness in Children Admitted to A Tertiary Care Hospital In Eastern India

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Abstract

Background: Febrile illness in children is an important cause of morbidity and mortality and often present with diagnostic challenge. Clinical management guidelines for acute febrile illness (AFI) are available, but knowledge of the locally prevalent causative agents is lacking behind.
Objectives: Objective of this study was to evaluate the clinical and etiological profile of AFI patients admitted to a tertiary care teaching Institute, in the eastern part of India.
Patients and methods: This cross sectional study was conducted on children aged from 3 months to 12 years, with history of fever of 4-7 days duration and satisfied the inclusion – exclusion criteria. Period of study was from February 2020 to July 2021.
Results: Among 100 patient in this study, females were 51 and males were 49. Patients with age age>5 years comprised 41 %. Etiologies of AFI were undifferentiated fever in 24%, pneumonia (12%), dengue (8%), acute gastroenteritis (7%), bronchiolitis (7%), Multiple Inflammatory Syndrome in Children (MIS-C) (6%), Scrub (6%) and other infections. Gastrointestinal, central nervous and respiratory systems were involved in 73%, 46% and 38% respectively. Infectious causes (92%) were significantly higher than non-infectious causes (8 %). Complications were present in 27 % of patient. Survival rate was 90 %. Among the risk factors, living in congested area and incomplete immunization were most important .
Conclusion: Etiology in many of AFI remain undifferentiated. Further research and active surveillance on this field will promote appropriate management and improve the survival of patients.

Keywords: Acute febrile illness; Children; Etiology; Eastern India.
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Introduction

Febrile illness in children is an important cause of morbidity and mortality and often present with diagnostic challenge. Infectious diseases are the leading causes of febrile illness in tropical countries (**Jayashree and Singhi, 2017**) Febrile illnesses are caused by diverse pathogens and often present with nonspecific symptoms to healthcare facilities (**Peacocket and Newton, 2008; Deen etal., 2012**) . Such illnesses are a public health challenge as the empirical diagnosis or treatment is a common practice and diagnostic facilities are scarce due to lack of access or inadequate diagnostic capacity (**Chaturbedi etal., 2009**). The World Health Organization (WHO) reported that, the infectious diseases, namely pneumonia, diarrhea, HIV/AIDS, malaria, tuberculosis and neonatal infections, cause death between 0.40 to 1.05 million per year in low income countries (**Abrahansen et al., 2013)**.

Infections are frequently aggravated or compounded by low rates of immunization, co-morbidities, late presentations, climate variation, over population and urbanization in developing countries and tropical regions (**Peacock et al.,2008; Deen et al., 2012; Singhet al .,2014**).

Clinical management guidelines for acute febrile illness (AFI) are available, but the knowledge of the locally prevalent causative agents is inadequate (**WHO 2005; WHO2005; Singhi et al., 2014**). It is difficult to take any uniform strategy to determine the underlying etiology, as the epidemiology of fever is changing over time (**Dinarello and Porat, 2015**).

There is paucity of data available with respect to etiology and epidemiology of these infections in children (**John et al., 2011**). We carried out this study with the objective to find out the clinical and etiological profile of AFI in children admitted to our tertiary care teaching hospital in Kolkata, in eastern part of India.

Patients and methods

Study setting: This was a hospital based observational and cross sectional study. It was done in the Department of Pediatrics of a tertiary care teaching Institute in Kolkata, in eastern part of India.

Period of study: February 2020 to July 2021.

Study population: Children of 3 months to 12 years of age, admitted with fever of 47days duration and fulfilled the inclusion and exclusion criteria.

Sample size: 100 patients.

The estimation of sample size N was calculated as per the formula

$N=\{(Z\alpha/2)^2 * p*(1-p)\} / (ME)^2$

$N= \{(1.96)^2 *.50*.50\}/(0.1)^2=96.04$

$Z\alpha/2$= 1.96 in case of 95% CI. P=prevalence of acute febrile illness in paediatric age group.

As there was no such direct data available on the prevalence of acute febrile illness in this age group, the prevalence was assumed as 50%

ME= Margin of Error =10%

The required sample size was 96.04 , which was converted to a round figure and the total sample size was taken as 100.

Definition of problem: Fever was defined as rectal temperature of 38°C (100.4°F) or more.

Inclusion criteria:

1. Acute febrile illness of 4-7days duration.
2. Age between 3 months to 12 years.
3. Available adequate medical records supplemented with history from reliable source.

Exclusion criteria: post-surgical febrile patients, patients with chronic disease, congenital heart disease, any underlying malignancy.

Ethical clearance: Ethical clearance was taken from the Institutional Ethics

Committee. Written informed valid consent was taken from each parent.

Data collection: Detailed history of fever and other symptoms were taken, general and systemic examination were done. The information was recorded in a predesigned proforma. Various tests were done as needed for diagnosis. Investigations included: Complete blood count, peripheral blood smear for malaria parasite, rapid malaria antigen detection test, scrub typhus IgM ELISA, leptospira IgM ELISA, Chikunguny IgM ELISA, dengue NS1 antigen ELISA and IgM ELISA, blood culture, urine culture, nasopharyngeal and oropharyngeal swab for viral component detection with PCR.

Outcome definition: To establish the etiology of fever and to assess the risk factors.

Statistical analysis

Data was collected, recorded and compiled on Microsoft Excel data sheet. Statistical methods and software were used to analyze the data. Categorical variables were expressed as number of patients and percentage of patients. Statistical analysis was performed with help of Epi Info (TM) 7.2.2.2 software. Descriptive analysis was performed to calculate the mean and standard deviations (S.D.). Chi-square (x^2) test was performed to find the associations, and Fisher Exact test was used when indicated. An alpha level of 5% had been taken, $p<0.05$ was taken as statistically significant.

Results

Among 100 patient in this study, females were 51 and males were 49. The median age was 3.58 years, and mean age was 4.26±3.53 years (range 3 months - 12 years). Maximum patients were in age group >5 years (41 %).Patients with 1- 5 years aged were 30% and <1 year of age were 29%. In establishing the diagnosis based on clinical and laboratory findings, causes of fever were undifferentiated viral fever (24%), Pneumonia (12%), Dengue (8%), acute gastroenteritis(AGE) (7%), Bronchilotis (7%), Scrub (6%), Multiple Inflammatory Syndrome in Children(MIS-C) (6%) and, Meningitis(5%) , Sepsis(5%), urinary tract infection (UTI) (5%), n Covid 19 (4%) and Typhoid (3%).(**Fig1**).

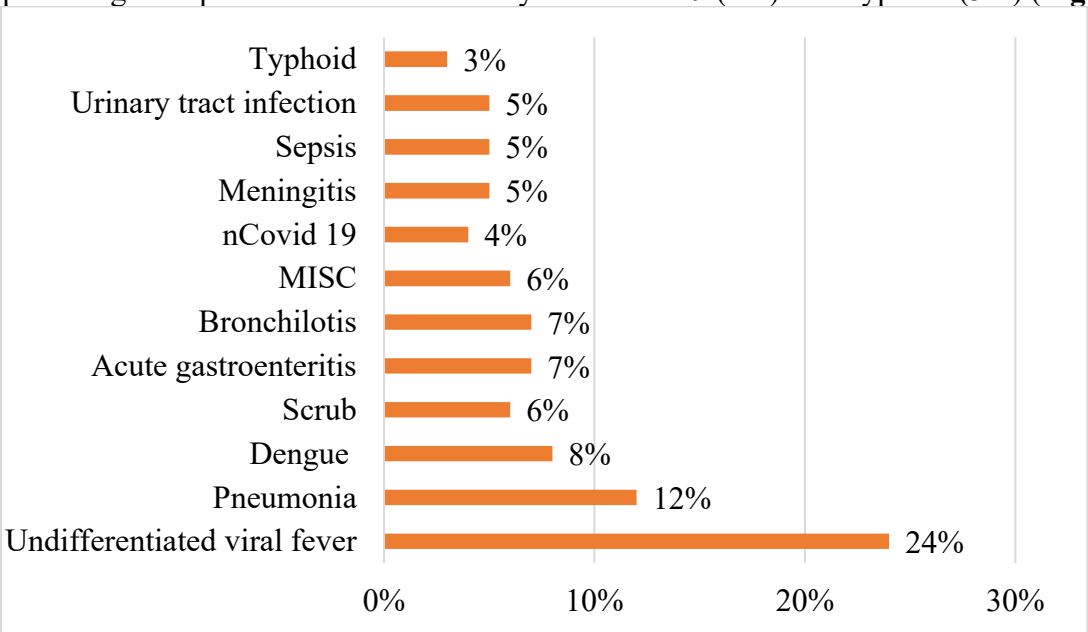

Fig 1. Distribution of etiologies in patients

Significant association noted with the age of the patients and the diagnosis (p=0.0023) in this study. Bronchiolitis, sepsis and pneumonia were mostly seen in patients with <1 year age. Scrub typhus infection and dengue were more common in >5 years of age. In regards to clinical presentation, gastrointestinal involvement in the form of vomiting, pain abdomen, refusal to feed, diarrhoea, were seen in (n=73) 73% patients. Respiratory system was involved in (n=38) 38% patients and central nervous system in (n=46) 46 % patients. (**Fig.2**). Microbiological agents were detected in 23% (n=23) patients. (**Table.1**). Urine culture was done in 5 patients, positive growth were for *E. coli* (n=3, 3%) and *Klebsiella* (n=1,1%). Blood C/S was done in 33 cases, pathogens isolated were *staphylococcus aureus* (n=2, 2%) . *Acinetobacter baumanii* (n=1,1%) and *E. coli* (n=1,1%). CSF culture was done in the patients presented with features of neuro-infections, and *Group b streptococci* (n=1,1%) and *streptococci pneumonia* (n=1,1%) were detected in them. Viral panel on nasopharyngeal /oropharyngeal swab was done in 20 cases and virus was identified in 8 of them : *RSV virus* (n=3,3%), influenza virus (n=2,2%), *adeno virus* (n=2,2%), and *parainfluenza* (n=1,1%). Hematological alterations seen in our cohort as: leukocytosis in 44%, leucopenia in 3%, low hemoglobin levels in 43%, hyperbilirubinemia in 24%, and raised liver enzymes (ALT and AST) in 66% and 35%respectively.

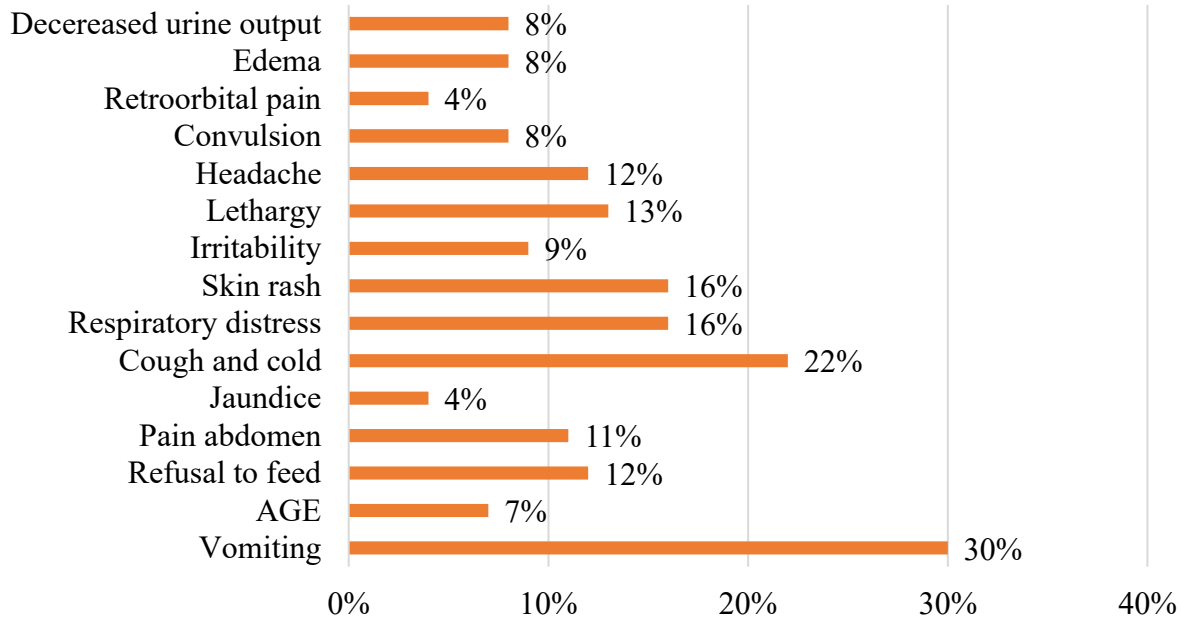

Fig.2.Clinical presentations

Table.1. Microbial agents detected among cases

Microbial agent	Number
n COVID 19 virus	4
E. Coli	4
Influenza Virus	3
RSV virus	3
Adeno virus	2
Group-B Streptococci	2
Staphylcoccus Aureus	2
Acinetobacter baumanni	1
Klebsiella Pneumoniae	1
StreptococciPneumoniae	1
Total	23

There were complications seen in our cohorts in (n=27) 27 %: hypovolemic shock (10 %) , cardiogenic shock (4%), generalized tonic-clonic seizure (GTCS) (3%) raised intracranial pressure (3%), and acute respiratory distress syndrome (ARDS) (3%), (**Fig.3**).

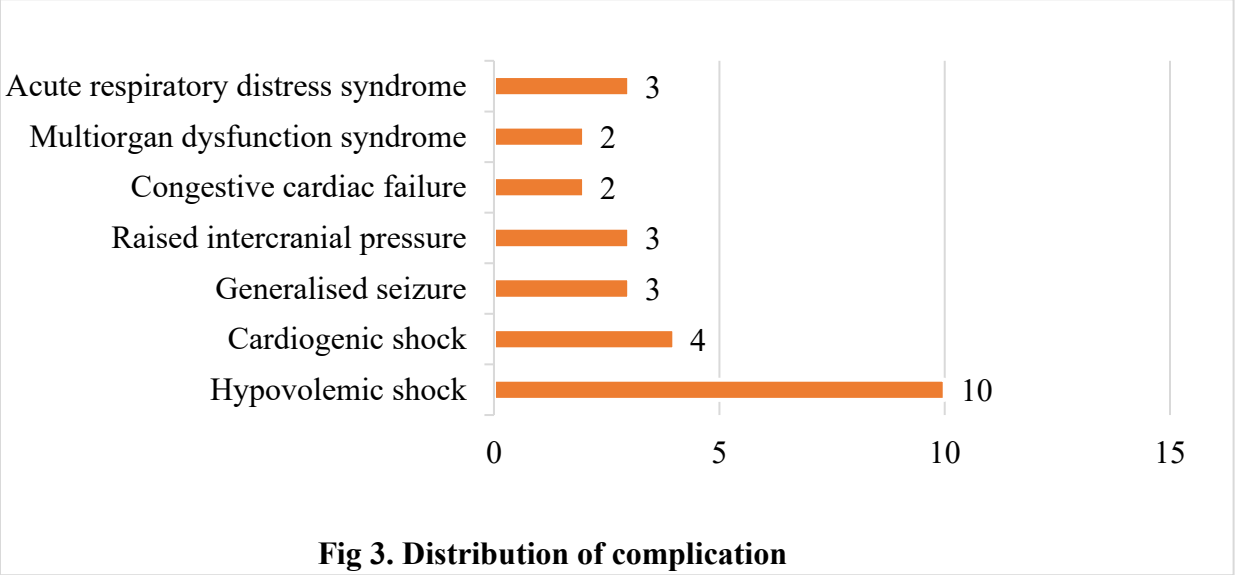

Fig 3. Distribution of complication

Eight (8%) of our cohort did not show any evidence of infection. They had immunological / rheumatological disorder as the primary etiology. Infectious causes (n=92, 92%) were significantly higher than noninfectious cause in this study. Survival rate was 90 % and death rate was 10% in our study. Death rate was higher in patients presented with pneumonia, dengue and MIS-C. Risk factors detected in our study were: living in congested area (26.83%), incomplete immunization (24.39%), and presence of contact history (21.95%) (p=0.0083). (**Table 2).**

Table 2. Risk factors

Risk factor determination	Numbers	Percentage
Living in congested area	11	26.83%
Not immunized up to date	10	24.39%
Contact history present	9	21.95%
Congenital heart disease	4	9.76%
Previous hospitalization	4	9.76%
Ingestion of street food	3	7.32%

Discussion

Infectious diseases affect all age group, particularly in those living in tropical regions. Fever is the main clinical symptom of various infections. Acute undifferentiated fever (AUF) or acute febrile illness (AFI) is characterized as rectal temperature ≥ 38 °C and its of duration of 2–14 days, with nonspecific symptoms and signs: loss of appetite, malaise, myalgia etc (**Matlani et al.,2021;Chheng et al.,2013**,). AUF prevalent in tropical and subtropical regions are collectively termed as tropical fever (**Singhi et al.,2014**).

AFIs are responsible for a huge burden of morbidity and mortality .Tropical infections also responsible for loss of Disability Adjusted Life Years (DALY)s (**Murray et al.,2012**).

Diversity exists in the trends and occurrence of AUF or tropical fevers in different regions. They are greatly influenced by season and geography, some are perennial while others exhibit seasonal variations. AUF may have overlapping clinical presentations and diverse etiologies **(Dinarello and Porat, 2015).** The etiological agents commonly detected in febrile patients in the South Asian region including India are dengue, malaria, scrub typhus, typhoid, and leptospira (**Matlani et al.,2021**). Among 100 patient in our study, causes of AUF observed mainly were undifferentiated viral fever (24%), pneumonia (12%), dengue (8%), Scrub (6%),acute gastroenteritis (7%), MISC (6%), nCovid 19 infection in 4%.

Matlani M et al in their study from north India on children found dengue (55.5 %) , malaria (19%) and scrub (19%) as etiological factors (**Matlani et al .,2021**). Dengue (16.2%) and scrub (7.8%) were the main causative agents in the study conducted by Cheng K et al from Combodia (**Chheng et al., 2013**). In contrast, Simelis T et al from Ethiopia , found urinary tract infection (18.4%) , bacteremia (6.4 %) and malaria (3.2 %) in their study (**Shimelis et al., 2020**).

Morch K et al from south India in patients >5 years of age and with history of fever of 2-14 days, reported malaria (17%), dengue (16 %) scrub (10%) , and bacteremia (8%) in their study (**Mørch et al.,2017**). Abrahamsen S K et al reported tuberculosis (19%), respiratory tract infection (11%) and urinary tract infection(10%) in their study on adult population from south India (**Abrahansen et al.,2013**)

In this study, females were 51 and males were 49. Maximum patients were in age group >5 years (41%).The median age was 3.58 years, and mean age was 4.26±3.53 years (range 3 months - 12 years). In a study by Simelis T et al, median age was reported as 20 months (range 2 months - 12 years), male were 59%, female 41% (**Shimelis et al., 2020**) . In a study by Cheng K et al , median age was 2.0 (0.8-6.4) years and 69% of children were < 5 years of age (**Chheng et al.,2013**).

However, study conducted by Matlani M et al , mean age was 6.94 years, male were 63%% , female were 37 % (**Matlani et al.,2021**).

In eight (8%) of our cohort we could rule out infection. They had immunological/rheumatological disorder as the primary etiology. Abrahansen S K et al, reported 15% patients fever had noninfectious etiology on adult population from south India (**Abrahansenet al., 2013**).

Out of 100 patients in our study, survival rate was 90% and death rate was 10%. Death rate was 5.6% in the study done by Chheng K et al (**Chheng et al., 2013**). Infectious diseases, namely malaria, infective hepatitis or leptospira were not evident in our study. There were incidences of COVID 19 infection during our study period. Our hospital was not a dedicated COVID hospital and most of the fever diagnosed with COVID-19 infection were transferred out to dedicated COVID 19 hospital.

Limitations :There are limitations in this study. It was a single centric study and conducted in a setting where the patients primarily belonged to the lower or middle socioeconomic strata. Sample size was small for studying of any individual etiology. Gold standard tests for some AUF could not be performed due to limitation of resources and economic constraints.

Conclusion

It is essential that the local epidemiology/ etiology of infections and AUF should be known to the treating physician for appropriate management. There is dearth in literature of studies on AUF in children from this part of India.

This study highlights the emerging problems of scrub typhus, Covid-19 infection and MIS-C in our setup. The present study may contribute in filling the knowledge gap on this important public health issue from this region of our country. Multicenter study from this region of India with larger sample size would validate this issue in a better way in developing relevant action plan

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Conflicts of interest: None declared

Author's contributions

Roshni Mondal – conceptuatization, methodology, formal analysis, writing of original draft Sarbani Misra (Roy) - formal analysis, writing original draft, reviewing, editing. Sumana Datta(Kanjilal), Dipankar Gupta, Mrinal Kanti Das- formal analysis, writing- reviewing, editing.

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