



Original Research Article

Clinico – Etiological profile of Acute Undifferentiated fever in children 6 months - 15 years

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ABSTRACT

Introduction: Acute febrile illness (AFI) is defined as a patient with fever of 38°C or higher at presentation or history of fever that persisted for 2–14 days with no localizing source. Fever is the main clinical symptom of various tropical infectious diseases.

Materials and Methods: Retrospective observational examination was directed after endorsement from the Institutional Ethics Committee in Paediatric division, Apollo General Hospital, AIMSR, Jubilee hills from January 2016 till December 2019.

Inclusion criteria: All the patients who were conceded in the ward or emergency unit complications of intense febrile infections, patients a half year to 15 years old were taken for the investigation.

Exclusion criteria: Patients with associated infections when the complications cannot be attributed to febrile illness or patients with haematological malignancies, autoimmune disorders, and those on immunosuppressant were excluded from the study.

Results : In present investigation, an aggregate of 290 patients with intense identical fever were assessed out of these 157 (63%) were male and 133 (36.6%) were female. In this investigation typhoid fever was the most well-known reason for undifferentiated fever (33.7%) trailed by malaria (25.5%), dengue fever (19.6%), urinary tract disease (8.2%), Acute gastroenteritis (5.5%), Pneumonia (3.1%), Bronchiolitis (2.4%), Hepatitis (1.0%) and Pharyngotonsillitis (0.6%).

Conclusions : It is important to know the aetiology and clinical pattern of acute undifferentiated fever for their proper management and it will help to prevent morbidity and mortality.

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1. Introduction

Acute febrile illness (AFI) is defined as a patient with fever of 38°C or higher at presentation or history of fever that persisted for 2–14 days with no localizing source. Fever is the main clinical symptom of various tropical infectious diseases.¹

Like other developing nations, India with limited resources, is facing lots of health effects due to climate change, including vector borne and water borne diseases such as leptospirosis, dengue and malaria, enteric fever

etc with significant level of morbidity and mortality in the patients suffering during this period. A significant number includes mixed infections with the previously mentioned agents, while a few others still remain unidentified.²

As an initial move towards the improvement of calculations that could control clinical administration of intense febrile ailments, it is essential to decide the study of disease transmission and clinic etiological and lab profile of the intense febrile ailments.

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2. Aim and Objectives

Point of our examination is to decide segment factors, manifestations, signs and etiology of intense undifferentiated fever among hospitalized youngsters matured a half year to 15 years and to depict the exhibition of standard analytic techniques.

3. Materials and Methods

Review observational examination was led after endorsement from the Institutional Ethics Committee in Paediatric division, Apollo General Hospital, AIMSR, Jubilee hills from January 2016 till December 2019.

3.1. Inclusion criteria

All the patients who were conceded in the ward or emergency unit difficulties of intense febrile sicknesses, patients a half year to 15 years old were remembered for the investigation.

3.2. Exclusion criteria

Patients with associated infections when the complications cannot be attributed to febrile illness or patients with haematological malignancies, autoimmune disorders, and those on immunosuppressant were excluded from the study.

3.3. Case definition

Acute febrile illness (AFI) is defined as a patient with fever of 38°C or higher at presentation or history of fever that persisted for 2–14 days with no localizing source

Details of history and results of a thorough physical examination were entered on a standard data collection sheet.

The routine baseline investigations included complete blood count analysis, serum electrolytes, liver and renal function tests.

Reports of thick/thin smear performed to detect malarial parasites, enzyme linked immunosorbent assay (ELISA) tests performed for agents believed to be endemic to the region like dengue IgM ELISA, leptospira IgM ELISA and Widal test or Leptospirosis PCR, Dengue PCR report if available were entered in case record sheet. Blood culture was done by Bactec method.

3.4. Statistical analysis

CHI SQUARE test was utilized to evaluate contrasts between extents.

4. Results

In present investigation, a sum of 290 patients with intense undifferentiated fever were assessed out of these 157 (63%) were male and 133 (36.6%) were female (Table 1).

Table 1: Distribution of gender

Gender	No. of patients	Percentage
Male	157	63.3
Female	133	36.6
Total	290	100

Table 2: Distribution of different age groups of patients

Age	No. of patients	Percentage
6 months-2 years	62	21.3
3-5 years	91	31.3
6-10 years	73	25.1
11-15 years	64	22.0
Total	290	100

In Table 2, in our study, the most of the patients the age group of 3-5 years i.e., 91 out of 290 (21.3%), followed by 6-10 years, i.e., 73 out of 290 (25.1%).

Table 3: Clinical Symptoms and sign.

Clinical Symptoms and sign	No. of patients	Percentage
Pyrexia	290	100
Headache	159	54.8
Rhinitis	136	46.8
Vomiting	117	40.3
Rash	93	32.0
Abdominal Pain	78	26.8
Diarrhoea	57	19.6
Cough	31	10.6
Hepatomegaly	11	3.7
Splenomegaly	9	3.1

In Table 3 out of 290 patients, most common symptom was pyrexia (100%), headache (54.8%), rhinitis (46.8%), vomiting (40.3%), Rash (32%), Abdominal Pain (26.8%), Diarrhoea (19.6%), cough (10.6%), hepatomegaly (3.7%) and splenomegaly (3.1%).

Table 4: Acute febrile illness aetiology

Final aetiology	No. of patients	Percentage
Typhoid	98	33.7
Malaria	74	25.5
Dengue	57	19.6
UTI	24	8.2
Acute Gastroenteritis	16	5.5
Pneumonia	9	3.1
Bronchiolitis	7	2.4
Hepatitis	3	1.0
Pharyngotonsillitis	2	0.6

In Table 4, in this investigation typhoid fever was the most well-known reason for undifferentiated fever (33.7%) trailed by malaria (25.5%), dengue fever (19.6%), urinary tract disease (8.2%), Acute gastroenteritis (5.5%),

Pneumonia (3.1%), Bronchiolitis (2.4%), Hepatitis (1.0%) and Pharyngotonsillitis (0.6%%).

Table 5: Laboratory findings of acute Undifferentiated fever in children

Variable		No. of patients	Percentage
Anaemia (Hb in gm/dl)	Mild (10.1-11)	196	67.5
	Moderate (7-10)	93	32.0
	Severe (<7)	1	0.3
WBC Count (cells/cumm)	(>11,000)	74	25.1
	4000-11,000	21	7.2
	<4000	195	67.2
Platelets count (cells/ml)	1,00,000-1,50,000	77	26.5
	1,00,000-1,50,000	162	55.8
	<50,000	51	17.5
Urine Culture		24	8.2
Blood Culture		3	1.0
Blood widal		98	33.7
Dengue Testing		57	19.6
Bilirubin		3	1.0
SGOT >		91	31.3
ALP		93	32.0
SGPT		86	29.6

In Table 5, regarding the hematological and biochemical boundaries, connection with hemoglobin level was Mild in the vast majority of the cases. The connection with leukopenia if there should be an occurrence of malaria and dengue. We saw between the seriousness of thrombocytopenia and dengue fever. Among the dengue fever patients, raised serum glutamic oxalo-acidic transaminase (SGOT) was the most well-known finding seen in 31.3% of patients while raised antacid phosphatase was seen in generally (32.0%) of the malaria patients. A sum of 29.6% of typhoid patients had raised SGPT.

Table 6: Treatment of Acute Undifferentiated fever in children

Final aetiology	No. of patients	Percentage
Ceftriaxone	98	33.7
Chloroquine	74	25.5
Doxycycline only	53	18.2
Ceftriaxone or Azithromycin	24	8.2
Doxycycline or Azithromycin	93	32.0

In Table 6, treatment-Enteric fever was treated with Ceftriaxone. Chloroquine was utilized for treatment of Malaria. Dengue was dealt with symptomatically and with liquids as per Dengue convention. On the off chance that fever continued even following 6 days of anti-microbials, at that point Azithromycin was added. UTI was treated with Ceftriaxone or Amikacin. In the undiscovered fever class, gotten experimental antibiotics.

5. Discussion

Acute Undifferentiated fever (AUF) is characterized as estimated temperature ≥ 38 °C and history of febrile disease of 2–14 days span, with no confined reason as decided by the treating doctor.³ They can be related with stomach ache, looseness of the bowels, haematochezia, nausea or vomiting, rhinorrhoea, SOB, visual agony, altered sensorium, headache, neck stiffness, rash, joint pain, muscle pain, petechiae, ecchymosis, nose or gum bleeding and jaundice. AUF is not the same as pyrexia of obscure source fever of at any rate 3 weeks with no recognized reason even after examination.⁴

Because of enhancements of lab offices and imaging the rate and etiological profile of fever have radically changed. Appropriate history taking and methodical assessment stays the highest quality level for fever sidestepping determination. Uncommonly for newborn children under one month old enough who are in danger for genuine and quickly reformist bacterial and viral diseases reasonable convention based examination and pre-emptive treatments are required.⁵ A syndromic way to deal with tropical contaminations can help in showing up at an etiology, plan examination board and pick early objective empiric treatment.⁶

Tropical fever can be extensively named 1) Undifferentiated fever (Malaria (*P. falciparum*), scrub typhus, leptospirosis, typhoid, dengue); 2) Fever with rash/thrombocytopenia (Dengue, rickettsial diseases, meningococcal contamination, malaria (*P. falciparum*), leptospirosis, measles, rubella); 3) Fever with ARDS (Scrub typhus, falciparum malaria, flu - H1N1, leptospirosis, hantavirus, meloidosis, *Legionella* spp., *Streptococcus pneumoniae*); 4) Febrile encephalopathy (Herpes simplex infection, Japanese B, *S. pneumoniae*, *Neisseria meningitidis*, *Haemophilus* flu, enteroviruses, scrub typhus, cerebral malaria and typhoid encephalopathy); 5) Fever with multi-organ brokenness (falciparum malaria, leptospirosis, scrub typhus, dengue, hepatitis A or E, Hanta virus infection).⁷

In the present study, male children (63.3%) were more affected than female (36.6%). The most common age group affected in our study was between 3-5 years of age, reflecting active people are affected more with these illnesses which were also supported by literature.⁸ The predominance in males may be due to increased chances of exposure to mosquitoes and contaminated water due to their nature of work. Similar observation was made by other study conducted in northern India.⁹

Complete examination board ought to incorporate tests for normal and uncommon infections. Malaria ought to be precluded by fringe blood smear with Giemsa stain, Immuno-chromatographic test to distinguish lactate dehydrogenase (LDH) for *Plasmodium falciparum* and *Plasmodium vivax* and HRP2 to recognize *Plasmodium*

falciparum. For dengue and chikungunya infection contaminations ELISA with explicit IgM antibodies should be finished. Enteric fever ought to be precluded by compound immunoassay to discover IgM and IgG antibodies. Widal test ought to incorporate agglutinating antibodies against O and H antigens of *S. typhi* and H antigens of *S. paratyphi A*.¹⁰⁻¹²

In our investigation, pyrexia and headache pain were the two main symptoms with which youngsters with AEFI introduced, like that announced by Prabha S.¹³ In their investigation, vomiting & cough were dominating in a specific order. Stomach pain and conjunctival suffusion were fundamentally connected with scrub typhus in our examination while Abhilash noticed breathlessness as noteworthy in Children.¹⁴ Another examination done in Thailand announced normal manifestations of intense undifferentiated fever as headache, myalgia and vomiting.¹⁵

In non-industrial nation like India the symptomatic board for intense undifferentiated fever incorporates first line examinations like Malaria microscopy, blood culture, Dengue rapid NS1 antigen and IgM Combo test, Leptospira IgM ELISA, Scrub typhus IgM ELISA and Chikungunya IgM ELISA. Second line testing incorporates Dengue IgM catch ELISA (MAC-ELISA), Scrub typhus immunofluorescence (IFA), Leptospira Microscopic Agglutination Test (MAT), malaria PCR and malaria immunochromatographic rapid diagnostic test (RDT).¹⁶⁻¹⁸

In present examination typhoid fever (33.7%) was the most common reason for intense undifferentiated fever followed by malaria (25.5%), dengue fever (19.5%), urinary tract infection (8.2%), others too. In the typhoid fever, anaemia, leukopenia, and thrombocytopenia are generally seen because of bone marrow concealment and hemophagocytosis. Thrombocytopenia with sickliness is a significant piece of information to the determination of intestinal sickness in patients with AFI. In instances of confounded falciparum malaria, thrombocytopenia is expected to dispersed intravascular coagulation alongside platelet endothelial activation. In instances of straightforward malaria, for example, *Plasmodium vivax*, etiology is macrophage initiation prompting platelet damage, antiplatelet antibodies, sequestration in non-splenic territories, and mostly due to pseudothrombocytopenia because of platelet cluster development. Leukopenia is believed to be because of the confinement of leukocytes from the peripheral circulation, splenic sequestration, and other marginal pools.¹⁹

In our investigation, among the dengue patients, the most widely recognized introductions were headache, vomiting, and gastrointestinal symptoms, for example, stomach ache and diarrhoea. In a past report, normal clinical introductions involved fever, conjunctival congestion, and myalgia (81.9%).²⁰ Derangement of liver enzymes is regularly seen in AFI. In dengue fever, aspartate aminotransferase has been

found to expand all the more rapidly and will in general top at a more significant level. Lab finding of leukopenia and thrombocytopenia was fundamentally connected with Dengue like that revealed by Kundavaram AP.²¹

An investigation directed by Singh et al from the district of Uttarakhand shows that dengue, malaria and Typhoid are the most widely recognized aetiological specialist of acute febrile illness.²² In nations like Thailand, Malaysia and Nepal - dengue fever, malaria, scrub typhus, leptospirosis and enteric have been distinguished as basic causes of intense undifferentiated fever.²³ Chrispal et al had a perception in their investigation in south India on AFI where most patient had Dengue, Malaria, Leptospirosis and typhoid though concentrate by Neelu sree et al had announced Dengue, Malaria, Scrub typhus and leptospirosis in their examination.^{24,25}

Treatment of AUF needs clinical attentiveness of etiology. Dominant part is treated with observational antimicrobials. Chloroquine might be begun for suspected malaria, Ceftriaxone for Enteric fever. Dengue needs suggestive administration with liquids. Ceftriaxone or Amikacin might be begun for suspected UTI.

The etiology of AEFI stays difficult endeavors much of the time. Vector control measures, drinking water supply and disinfection ought to be improved to forestall vector borne and water borne sicknesses. District explicit epidemiological data set of reasons for AEFI should be made. Level-headed, normalized convention based appraisal and treatment of kids with intense undifferentiated fever can diminish undesirable examinations and antimicrobial use.

6. Limitations in our study

There are sure restrictions in our examination, for example, restricted demonstrative offices. Serology for Leptospirosis, Brucella, Chikungunya and other viral examinations would have expanded the particular analysis that might have been made. Our investigation was restricted as far as test size for singular analysis. The investigation with bigger example size would help in assessing the job of these boundaries in a superior manner.

7. Conclusion

Typhoid, Malaria, Dengue were the main significant reasons for acute undifferentiated fever in our investigation. District explicit mindfulness about aetiologies of acute undifferentiated fever would help in convenient recognition of such cases and subsequently better administration decreasing morbidity and mortality over the long run. The discoveries in our investigation underlines the significance of inferring symptomatic tests in a clinical context along with side effects, clinical discoveries and research center tests.

8. Conflicts of Interest

All contributing authors declare no conflicts of interest.

9. Source of Funding

None.

References

- Mørch K, Manoharan A, Chandy S, Chacko N, Alvarez-Uria G, Patil S, et al. Acute undifferentiated fever in India: a multicentre study of aetiology and diagnostic accuracy. *BMC Infect Dis.* 2017;17(1):665. doi:10.1186/s12879-017-2764-3.
- Srinivasaraghavan R, Narayanan P, Kanimozhi T. Culture proven Salmonella typhi co-infection in a child with Dengue fever: a case report. *J Infect Devel Ctries.* 2015;9(09):1033–5. doi:10.3855/jidc.5230.
- Long SS. Diagnosis and management of undifferentiated fever in children. *J Infect.* 2016;72:68–76.
- Rabindran, and MV. Acute undifferentiated fever in children- an overview. *Int J Pediatr Res.* 2017;4(11):634–5. doi:10.17511/ijpr.2017.i11.01.
- Kulkarni N. Study on the effectiveness of transfusion program in dengue patients receiving platelet transfusion. *Int J Blood Transfus Immunohematol*;2012:11–5.
- Gopalakrishnan S, Balaji A, Kandasamy S, Subramaniam R, Babu K. Acute undifferentiated febrile illness among adults – a hospital based observational study. *J Evol Med Dent Sci.* 2013;2(14):2305–19. doi:10.14260/jemds/533.
- Singhi S, Chaudhary D, Varghese MG. Tropical fevers: Management guidelines. *Indian J Crit Care Med.* 2014;18(2):62–9.
- Frean J, Blumberg L. Brisbane: ACTM Publication; 2005. Tropical fevers part A. *Viral, Bacterial Fungal Infect Primer Trop Med.* 2005;p. 1–18.
- Sharma J, Malakar M. Distribution of typhoid fever in different rural and urban areas of Lakhimpur district of Assam. *Int J Res Dev Health.* 2013;1:109–14.
- Shamikumar RP, Narayan K, Sujatha B, Nair LDV. The diagnosis and outcome of acute undifferentiated febrile illness among children- A hospital based observational study. *Int J Recent Trends Scienceand Technol.* 2016;18(2):323–7.
- Mittal G, Ahmad S, Agarwal RK, Dhar M, Mittal M, Sharma S, et al. Aetiologies of acute undifferentiated febrile illness in adult patients- an experience from a tertiary care hospital in Northern India. *J Clin Diagn Res: JCDR.* 2015;9(12):22–4.
- Krishnan R, Pillai RK, Elizabeth K, Shanavas A, Bindusha S. Pediatric scrub typhus in Southern Kerala: An emerging public health problem. *Clin Epidemiol Global Health.* 2016;4(2):89–94. doi:10.1016/j.cegh.2016.03.003.
- Prabha S, Barathy C, Sriram P, Raja AJ, , and. Aetiology and clinical spectrum of acute undifferentiated febrile illness in hospitalized children. *Int J Pediatr Res.* 2017;4(11):636–43. doi:10.17511/ijpr.2017.i11.02.
- Abhilash KPP, Jeevan JA, Mitra S, Paul N, Murugan TP, Rangaraj A, et al. Acute undifferentiated febrile illness in patients presenting to a Tertiary Care Hospital in South India: clinical spectrum and outcome. *J Glob Infect Dis.* 2016;8(4):147–54. doi:10.4103/0974-777x.192966.
- Veligandla G, Vanan E, Padmavathi E, Bhaskar M. Etiological Spectrum and Prevalence of Acute Undifferentiated Febrile Illness (AUI) in Fever Cases Attending our Tertiary Care Centre. *Int J Curr Microbiol App Sci.* 2017;6(5):954–62. doi:10.20546/ijcmas.2017.605.105.
- Colvin JM, Muenzer JT, Jaffe DM, Smason A, Deych E, Shannon WD, et al. Detection of Viruses in Young Children With Fever Without an Apparent Source. *Pediatr.* 2012;130(6):e1455–62. doi:10.1542/peds.2012-1391.
- Kumar M, Krishnamurthy S, Delhikumar CG, Narayanan P, Biswal N, Srinivasan S, et al. Scrub typhus in children at a tertiary hospital in southern India: Clinical profile and complications. *J Infect Public Health.* 2012;5(1):82–8. doi:10.1016/j.jiph.2011.11.001.
- Mueller TC, Siv S, Khim N, Kim S, Fleischmann E, Arie F, et al. Acute Undifferentiated Febrile Illness in Rural Cambodia: A 3-Year Prospective Observational Study. *PLoS ONE.* 2014;9(4):e95868. doi:10.1371/journal.pone.0095868.
- Karoli R, Fatima J, Siddiqi Z, Kazmi KI, Sultania AR. Clinical profile of dengue infection at a teaching hospital in North India. *J Infect Dev Ctries.* 2011;6(07):551–4. doi:10.3855/jidc.2010.
- Mueller TC, Siv S, Khim N, Kim S, Fleischmann E, Arie F, et al. Acute Undifferentiated Febrile Illness in Rural Cambodia: A 3-Year Prospective Observational Study. *PLoS ONE.* 2014;9(4):e95868. doi:10.1371/journal.pone.0095868.
- Kundavaram AP, Jonathan AJ, Nathaniel SD, Varghese GM. Eschar in scrub typhus: A valuable clue to the diagnosis. *J Postgraduate Med.* 2013;59(3):177–8. doi:10.4103/0022-3859.118033.
- Singh R, Singh SP, Ahmad N. A study of aetiological pattern in an epidemic of acute febrile illness during monsoon in a tertiary health care institute of Uttarakhand, India. *J Clin Diagn Res.* 2014;8:1–3.
- Kashinkunti MD, Gundikeri SK, Dhananjaya M. Acute undifferentiated febrile illness- clinical spectrum and outcome from a tertiary care teaching hospital of north Karnataka. *Int J Biol Med Res.* 2013;4:3399–439.
- Chrispal A, Boorugu H, Gopinath KG, Chandy S, Prakash JAJ, Thomas E, et al. Acute undifferentiated febrile illness in adult hospitalized patients: the disease spectrum and diagnostic predictors – an experience from a tertiary care hospital in South India. *Trop Doctor.* 2010;40(4):230–4. doi:10.1258/td.2010.100132.
- Sree N. Apilot study on Acute undifferentiated fever using certain rapid microbiological and virology tests. *Int J Pharm Bio Sci.* 2015;6:716–23.

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