Content available at: https://www.ipinnovative.com/open-access-journals

IP International Journal of Medical Paediatrics and Oncology

Journal homepage: https://www.ijmpo.com/

Original Research Article

A study on acute undifferentiated febrile illness in children (Age 2 Months to 18 Years)

Chirag Mittal[1], Bhupesh Jain[1,*], Suresh Goyal[1]

[1] *RNT Medical College, Udaipur, Rajasthan, India*

ARTICLE INFO

Article history:
Received 28-02-2023
Accepted 05-04-2023
Available online 03-05-2023

Keywords:
Acute undifferentiated febrile illness
Fever with short duration
Fever without focus

ABSTRACT

Introduction: Acute Undifferentiated Febrile Illness (AUFI) is a common cause of patients seeking healthcare in India. Appropriate diagnosis is essential for proper management of children, since failure to identify the nature of the causative pathogen results in increased morbidity and mortality due to diseases either being untreated or treated with inappropriate antimicrobials, Also there is waste of medicines and increased resistance to antimicrobials, which has a major public health threat worldwide.
Aims and Objectives: To study clinical profile of children admitted with AUFI and to find out common causes of AUFI in Children (2 months to 18 years of age) and their seasonal trends.
Materials and Methods: A prospective study was carried out over 200 children of age 2 months to 18 months admitted in Balchikitsalaya MBGH Hospital with Acute Undifferentiated Febrile Illness of less than 7 days duration over a period of 12 months from November 2021 to October 2022.
Results: Majority of the patients were in the age group of 10-15 years (32.5%). Out of 200 AUFI patients, majority had undifferentiated illness (53%) followed by Malaria (16.5%), UTI (12.5%), Dengue(11%), Scrub Typhus(5%) and Enteric Fever(2.5%). Higher incidence of AUFI was seen from August to November.
Conclusion: More than 50% cases of Acute Febrile Illness were due to Undifferentiated Illnesses, hence it can be concluded that provided the cause of undifferentiated illness is found, the irrational use of antibiotics and antimalarial should be prevented.

1. Introduction

Acute Undifferentiated Febrile Illness (AUFI) is a common cause of patients seeking healthcare in India. Unlike Pyrexia of Unknown Origin (PUO), which enjoys a standard definition, “Acute Undifferentiated Febrile Illness” or “short febrile illness” or “acute fever” lacks an international consensus definition. Since PUO requires duration of fever to be longer than three weeks, some authors have defined Acute Undifferentiated Febrile Illness, as fever that resolves within three weeks.[1] Some studies have also taken AUFI as fever less than 7 days of duration.[2]

Acute Undifferentiated Febrile Illness poses a diagnostic and therapeutic challenge to the health workers, particularly in limited resource settings. A number of viruses, bacteria, protozoa and rickettsia can cause fever. The non-specificity of symptoms and signs and lack of availability of accurate diagnostics often leads to irrational use of antibiotics and antimalarial drug. The cause of Acute Undifferentiated Febrile Illness is driven by the regional disease burden, seasonality of infectious diseases, spectrum and severity of disease, availability of diagnostics and access to health care facilities.

Etiology of Acute Undifferentiated Febrile Illness varies according to climate, season, age of patient etc. In our

* *Corresponding author*.
E-mail address: drbhupeshudr@gmail.com (B. Jain).

https://doi.org/10.18231/j.ijmpo.2023.003

country common causes of Acute Undifferentiated Febrile Illnesses are Malaria, Scrub typhus, Dengue fever, Typhoid Fever, Chikungunya, Urinary Tract Infections etc.

Acute Undifferentiated Febrile illness can be potentially fatal if the aetiology is not recognised and if not treated early. In low income countries, many preventable deaths occur because of delayed or lack of correct diagnosis. Hence there is an urgent need of a guided diagnostic approach which can only happen if there is enough evidence for the diseases prevalent in the region.

This study was conducted with aim to study clinical profile of children admitted with Acute Undifferentiated Febrile Illness. And to find out common causes of Acute Undifferentiated Febrile Illness in Children (2 months to 18 years of age) and their seasonal trends.

2. Materials and Methods

A prospective study was carried out over 200 children of age 2 months to 18 months admitted in Balchikitsalaya MBGH Hospital with Acute Undifferentiated Febrile Illness of less than 7 days duration over a period of 12 months from November 2021 to October 2022. Ethical clearance was taken from the Institute Ethical Committee.

Each selected child with AUFI was examined in detail and was investigated to find the cause. A detailed history was recorded with general demographic details of the patient; like Age, Sex, Address, Socioeconomic Status etc. was recorded on a prestructured proforma. Each patient was examined thoroughly, Anthropometry (height, length, weight, BMI, MUAC etc.), vital parameters and detailed Systemic examination was performed and positive findings were recorded. All the selected children have undergone following investigation to reach to the etiology of AUFI ; CBC, PBF, Urine Routine & Microscopy, Malarial Parasite Antigen Card Test, ELISA for Dengue, ELISA for Scrub, Blood Sugar, SGOT, SGPT, Chest X-ray, Blood Culture, Urine culture etc. All the children included were of age 2 month to 18 years admitted in Balchikatsalya MBGH Hospital with Acute Undifferentiated Febrile Illness of less than 7 days of duration & consenting to participate in the study. Patients having Fever with Diarrheal, Respiratory, CNS causes or Organ specific illnesses or with any chronic illness; known case of CHD (Congenital Heart Disease), RHD (Rheumatic Heart Disease), Birth Asphyxia, CRF (Chronic Renal failure) or CKD (Chronic Kidney Disease), Chromosomal / Congenital malformation or the child with immunodeficiency; HIV, on immunosuppressant, Surgery or immediate Post Operated cases etc were excluded from the study.

3. Results

During the study total number of patients enrolled were 200, who fulfilled the inclusion criteria and gave their consent to participate. Patients mainly enrolled were found in age groups of 10-15 Years (32.5%) (Figure 1). The possible reason for more preponderance in this age group could be more outdoor activity done by children of these ages.

Malaria and UTI were seen mostly in patients of 1-5 years of age, Enteric Fever and Undifferentiated illness patients were seen in 5-10 years age and Scrub typhus and Dengue Fever patients were mainly seen in 10 to 15 years of age group (Table 1).

Males (58.5%) were more commonly affected than Females (41.5%), the ratio was 1.4:1. One of the possible reasons for having male predominance in vector borne diseases could be more outdoor activity done by male subpopulation.

In our study out of 200 AUFI patients, Majority of patients (53%) had Undifferentiated illness, 16.5% had Malaria, 11% had Dengue Fever, 2.5% had Enteric Fever, 5% had Scrub Typhus and 12.5% had UTI (Table 2).

In our study, on clinical examination, it was found that majority of the patients (151, 75.5%) had no specific clinical findings except fever. Remaining patients had Pallor (41, 20.5%), Splenomegaly (27, 13.5%), Icterus (6, 3%), Rashes (7, 3.5%) and Hepatomegaly (10, 5%) as clinical signs (Table 3).

On basis of laboratory parameters in our study we found that among patients of AUFI, average Hemoglobin level was found above 10gm/dl, but in patients diagnosed of Malaria, Hemoglobin level was found significantly low. Among the patients with AUFI, WBC count in most patients were between 4000/uL to 11000/uL. But WBC count in Dengue Fever and UTI Group was significant. Platelet count in Dengue Fever was significantly low. The CRP level in patients with Malaria was found to be significantly higher. In Peripheral Blood film examination, Microcytic hypo chromic anemia was mainly seen in patients with Malaria (78.8%). Majority of patients with elevated SGPT were having Scrub Typhus. The mean and median SGPT level in Scrub Typhus patient was 550 mg/dl and 83.5 U/L respectively (Table 4).

In our study, high incidence of AUFI were seen from August to November months, of which maximum cases were seen in September (16.5%) and October (16.5%) months. The post-monsoon surge is attributed to the influence of rainfall on the breeding of vectors and transport and dissemination of infectious agents. This fact points to the need for implementation of preventive steps, public education, and physician awareness during this season (Figure 2).

36.4% participants had E.coli in Urine Culture followed by Acinetobactor (31.8%), Klebsiella (18.2%) and Enterobacter (13.6%).

Table 1: Association between age group and etiology parameters

Parameters	Age Group						p value
	2 Months-1 Year (n = 15)	1-5 Years (n = 50)	5-10 Years (n = 60)	10-15 Years (n = 65)	>15 Years (n = 10)	Total (n = 200)	
Final Diagnosis: Malaria (Yes)	2	11	8	10	2	33	0.774[2]
Final Diagnosis: Dengue Fever (Yes)	1	7	2	12	0	22	0.054[2]
Final Diagnosis: Enteric Fever (Yes)	0	1	2	2	0	5	1.000[3]
Final Diagnosis: Scrub Typhus (Yes)	0	3	2	4	1	10	0.694[3]
Final Diagnosis: UTI (Yes)	1	9	6	7	2	25	0.577[2]
Final Diagnosis: Undifferentiated Illness (Yes)* **	11	20	40	29	5	105	0.039[2]

Table 2: Distribution on basis of etiology and number of cases

Etiology	Number of cases
Dengue Fever	22 (11.0%)
Malaria	33 (16.5%)
Enteric Fever	5 (2.5%)
Scrub Typhus	10 (5.0%)
UTI	25 (12.5%)
Undifferentiated Illness	105 (52.5%)

Table 3: Distribution of participants in terms of clinical examination

Examination	Cases (200)
Pallor	41 (20.5%)
Splenomegaly	27(13.5%)
Hepatomegaly	9(4.5%)
Rashes	7(3.5%)
Icterus	6(3%)
NAD	151(75.5%)

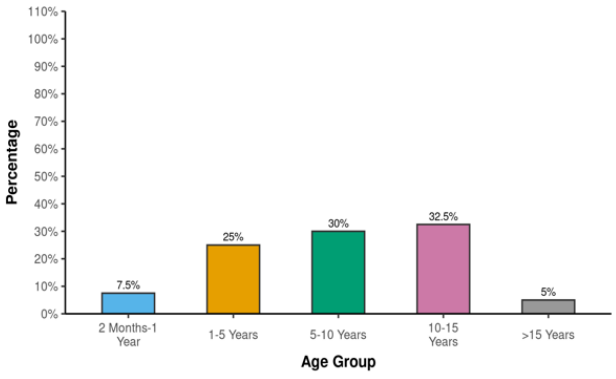

Fig. 1: Distribution of the participants in terms of 'age group'

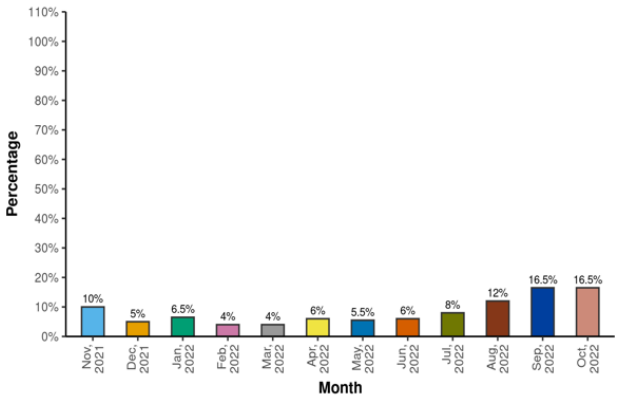

Fig. 2: Distribution of the participants in terms of seasonal variation (months)

4. Discussion

Most of the participants had Age Group: 10-15 Years (32.5%), followed by 5-10 years (30%), 1-5 years (25%),

Table 4: Distribution of participants in terms of laboratory parameters.

Parameters	Hb (gm/dL)	p value	WBC TLC (10^3/uL)	p value	Platelet Count (Lacs/mcL)	p value	CRPQ (mg/dL)	p value	PBF: Microcytic Hypochromic Anisopoikilocytosis	p value	SGPT (U/L)	p value
Final Diagnosis: Dengue Fever* **		0.025[3]		<0.001[3]		<0.001[3]		0.336[3]		0.176[3]		0.041[3]
Yes	11.82 ± 1.71		3.90 ± 1.77		1.03 ± 0.71		4.81 ± 4.83		2 (4.8%)		101.9 ± 205.6	
No	10.76 ± 1.95		8.45 ± 4.37		2.47 ± 1.37		18.30 ± 51.69		20 (12.7%)		73.81 ± 267.2	
Final Diagnosis: Malaria* **		<0.001[3]		0.092[3]		0.318[3]		<0.001[3]		<0.001[2]		<0.001[3]
Yes	8.08 ± 2.10		8.27 ± 2.34		2.23 ± 1.69		49.49 ± 91.16		26 (61.9%)		55.36 ± 26.67	
No	11.43 ± 1.36		7.96 ± 4.64		2.33 ± 1.33		10.36 ± 31.89		7 (4.4%)		81.16 ± 285.2	
Final Diagnosis: Enteric Fever		0.625[3]		0.055[3]		0.070[3]		0.197[3]		1.000[3]		0.128[3]
Yes	11.42 ± 1.81		11.90 ± 4.85		3.01 ± 2.46		8.04 ± 3.95		1 (2.4%)		61.40 ± 40.74	
No	10.86 ± 1.96		7.91 ± 4.30		2.26 ± 1.33		17.04 ± 49.56		4 (2.5%)		77.30 ± 264.1	
Final Diagnosis: Scrub Typhus		0.447[3]		0.585[3]		0.092[3]		0.718[3]		0.441[3]		0.002[3]
Yes	10.57 ± 1.83		9.26 ± 5.98		1.61 ± 0.67		36.09 ± 101.21		3 (7.1%)		550.0 ± 994.1	
No	10.89 ± 1.96		7.95 ± 4.25		2.35 ± 1.41		15.80 ± 44.89		7 (4.4%)		52.01 ± 110.1	
Final Diagnosis: UTI* **		0.032[3]		<0.001[3]		0.313[3]		0.010[3]		0.006[2]		0.006[3]
Yes	11.08 ± 1.13		12.84 ± 3.87		2.25 ± 1.19		11.86 ± 9.71		0 (0.0%)		29.08 ± 15.50	
No	10.71 ± 1.98		7.32 ± 3.96		2.22 ± 1.40		17.53 ± 52.19		25 (15.8%)		83.74 ± 278.2	
Final Diagnosis: Undifferentiated Illness		0.118[3]		0.066[3]		0.226[3]		<0.001[3]		<0.001[2]		<0.001[3]
Yes	11.25 ± 1.24		7.90 ± 4.11		2.23 ± 1.21		8.29 ± 25.14		11 (26.2%)		45.82 ± 111.0	
No	10.48 ± 2.44		8.87 ± 4.44		2.19 ± 1.56		25.87 ± 64.31		95 (60.1%)		111.9 ± 359.6	

Hb column - ***Significant at p<0.05, 1: Spearman Correlation, 2: Kruskal Wallis Test, 3: Wilcoxon-Mann-Whitney U Test
WBC TLC column - ***Significant at p<0.05, 1: Spearman Correlation, 2: Kruskal Wallis Test, 3: Wilcoxon- Mann-Whitney U Test
Platelet count column - ***Significant at p<0.05, 1: Spearman Correlation, 2: Kruskal Wallis Test, 3: Wilcoxon- Mann-Whitney U Test
CRPq Column - ***Significant at p<0.05, 1: Spearman Correlation, 2: Kruskal Wallis Test, 3: Wilcoxon- Mann-Whitney U Test
PBF Microcytic Hypochromic - ***Significant at p<0.05, 1: Wilcoxon-Mann-Whitney U Test, 2: Chi-Squared Test, 3: Fisher's Exact Test, 4: t-test
SGPT Column ***Significant at p<0.05, 1: Spearman Correlation, 2: Kruskal Wallis Test, 3: Wilcoxon-Mann-Whitney U Test

2 Months to 1 Year (7.5%) and remaining participants had Age Group: >15 Years (5.0%). Most common age group of AUFI was 6 -12 years (55.9%) in a study done by Prabha S et al,[3] while Desari R et al[4] found that most common age group affected was 3-5 years (31.3%) in their study. The possible reason for more preponderance in 10 -15years of age group could be more outdoor activity done by children of these ages.

In our study Malaria was prevalent in all age groups, but most commonly present (33.3%) among children of 1 to 5 years of age groups. In the study done by Kumar A et al[5] showed that malaria was most common in age group 5-10 years(37%). Dengue Fever (54.5%) cases were prevalent in all age groups, but maximum cases were seen in 10 to 15 years of age groups. Similarly in the study of Mishra S et al,[6] the maximum numbers of Dengue Fever cases were seen in the group >11 years of age (34.02%) and the least affected age group was that of infants. Enteric Fever (40% each) was mainly seen in age groups 1 to 5 years and 5 to 10 years. These findings were in correlation with the study done by Behera J et al,[7] where they found that 75% of the children with Enteric Fever belonged to the 6 to 14 years age group. Scrub Typhus was most prevalent in 10 to 15 years of age groups. In the study done by KumarBhat N et al,[8] they found that patients of Scrub Typhus were mainly below 12 years age. UTI was most prevalent in 1 to 5 years of age groups. In study done by Bhonsle K et al[9] the majority of the cases of UTI were in children of 0-5 year of age, the higher prevalence in this pediatric age group may be due to excessive or unhygienic use of diapers and improper cleaning of urogenital area of children. . Undifferentiated illness or undiagnosed fever (37%) cases were mainly seen in 5 to 10 years of age groups.

On Gender basis it was found that, out of 200 patients enrolled, 117{58.5%} were Males and 83{41.5%} were Females (ratio M:F =1.4:1). In a study done by Nagar R et al[10] found that out of 200 cases, 132 (66%) were Males and 68 (34%) were Females (ratio M: F=1.9:1). One of the possible reasons for having male predominance in vector borne diseases could be more outdoor activity done by male subpopulation.

High incidence of AUFI were seen from August to November months and maximum incidences were seen in September (16.5%) and October (16.5%) months. Similarly, the study done by Walia M et al[2] observed a seasonal trend in the incidence of non- respiratory non-diarrheal AFI had peak in post-monsoon season (42%) The post-monsoon surge is attributed to the influence of rainfall on the breeding of vectors and transport and dissemination of infectious agents. This fact points to the need for implementation of preventive steps, public education, and physician awareness during this season.

On clinical examination, out of 200 patents enrolled in our study, 151 (75.5%) patients had no specific clinical findings except fever, 41(20.5%) patients had Pallor, 27(13.5%) had Splenomegaly, 6(3%) patients had Icterus, 7(3.5%) patients had Rashes and 9(4.5%) had Hepatomegaly as clinical signs. In study done by Nagar R et al,[10] found that 28% cases had Pallor and 35% cases had Splenomegaly. In another study done by Desari R et al,[4] found 3.1% had Splenomegaly. In the study done by Prabha S et al[3] found Rashes in 2.3 % cases. In Study by Desari R et al[4] found Hepatomegaly to be present in 3.7% cases, which were similar to our study findings.

On basis of laboratory parameters in our study we found that among patients of AUFI, average Hemoglobin level was found above 10gm/dl, but in patients diagnosed with Malaria, Hemoglobin level was found significantly low with p value <0.05. The mean Hemoglobin in patients of Malaria were found to be 8.08 ± 2.1gm/dl. Decreased level of Hemoglobin along with Pallor, Anemia and Splenomegaly were found more associated with P.falciparum than P.vivax. These findings were in correlation with the Study of Kumar A et al[5] and study done by Nagar R et al[10] who had shown similar findings.

Among the patients with AUFI, WBC count in most patients were between 4 (*10^3/uL*) to 11 (*10^3/uL*). But WBC count in Dengue Fever and UTI Group was significant with p value of <0.001. Mean WBC count in Dengue Fever was 3.90 ± 1.77 (10^3/uL). Similarly in the study done by Nagar R et al,[10] 46% Dengue Fever patients had leucopenia (low WBC count). In the study done by Prabha S et al[3] found 34% of patients of Dengue Fever had leucopenia. In our study mean WBC count in UTI patients was 12.84 ± 3.87 (10^3/uL). Similarly in the study done by Prabha S et al[3] found that majority of the patients of UTI had Leucocytosis (75 %). Platelet count in Dengue Fever was significantly low with p value of <0.001. In patients of Dengue Fever the mean Platelet count was 1.03 ± 0.71 (Lacs/mcL) and 68.2% patients had thrombocytopenia, These findings were in correlation with the findings of Mishra S et al,[6] who in their study found 78.57% patient with Dengue Fever had thrombocytopenia.

Majority of patients with UTI had Urine culture positive. E. coli (36.4%) was found to be the most common cause of UTI, followed by Acinetobactor (31.8%), Klebsiella (18.2%) and Enterobacter (13.6%). In Study done by Bhonsle K et al[9] the most common organism responsible to cause UTI was found to be E. Coli (60 % cases) followed by Klebsiella 10.8%.

Majority of patients with elevated SGPT were having Scrub Typhus. The median SGPT level in Scrub Typhus patient was 83.5 U/L. In a study done by Das P et al they found that liver enzymes transaminases AST and ALT were elevated and median SGPT level was found to be 102 U/L.

5. Conclusion

As Acute Febrile illness accounts for the majority of outpatient visits and inpatient admissions in India. The causes for the same are variable and need a systematic approach to identify the cause for appropriate therapy. Acute Undifferentiated Febrile illness can be potentially fatal if the etiology is not recognised and treated early. In low income countries, many preventable deaths occur because of delayed or lack of correct diagnosis. In the resource-limited settings, the impact of diagnostic tests that can be provided at immediate point-of-care is potentially great. As can be noted in this study, more than 50% cases of Acute Febrile Illness were due to Undifferentiated Illnesses, hence it can be concluded that provided the cause of undifferentiated illness is found, the irrational use of antibiotics and antimalarials should be prevented.

6. Ethical Standards

All procedures performed in studies involving human participants were in accordance with ethical standards of international committee and with Helsinki Declaration of 1964 and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors.

7. Source of Funding

None.

8. Conflicts of interest

There are no conflicts of interest.

References

1. Susilawati TN, Mcbride WJ. Undiagnosed undifferentiated fever in far North Queensland, Australia: a retrospective study. *Int J Infect Dis*. 2014;27:59–64. doi:10.1016/j.ijid.2014.05.022.
2. Walia M, Rauf A, Singhi S, Nallasamy K, Ray P. Non-respiratory and non- diarrheal causes of acute febrile illnesses in children requiring hospitalization in a tertiary care hospital in North India: A prospective study. *Am J Trop Med Hyg*. 2018;99(3):783–8. doi:10.4269/ajtmh.18-0056.
3. Prabha S, Barathy C, Sriram P, Raja A. Aetiology and clinical spectrum of acute undifferentiated febrile illness in hospitalized children. *Int J Pediatr Res*. 2017;4(11):636–43.
4. Dasari R, Reddy K, Nimmagadda A, Kuruvada S, Sneha N, Srikrishna S, et al. Clinico - Etiological profile of acute undifferentiated fever in children 6 months - 15 years. *IP Int J Med Paediatr Oncol*. 2021;7(1):1–5.
5. Kumar A, Ahmar R, Kishore S. Clinical profile of malaria in children at a tertiary care hospital of Bihar and evaluation of parasite LDH based rapid diagnostic test for malaria. *Panacea J Med Sci*. 2021;11(1):106–10.
6. Mishra S, Ramanathan R, Agarwalla S. Clinical Profile of Dengue Fever in Children: A Study from Southern Odisha, India. *Scientifica (Cairo)*. 2016;p. 6391594. doi:10.1155/2016/6391594.
7. Behera J, Rup A, Dash A. Clinical and laboratory profile of enteric fever in children from a tertiary care centre in Odisha, Eastern India. *Cureus*. 2021;13(1):12826. doi:10.7759/cureus.12826.
8. Bhat NK, Dhar M, Mittal G. Scrub typhus in children at a tertiary hospital in north India: clinical profile and complications. *Iran J Pediatr*. 2014;24(4):387–92.
9. Bhonsle K, Vyas A, Vyas H, Ramchandani A, Hemwani K. Prevalence, identification and frequency of uropathogens causing urinary tract infection in children in Ujjain (M.P.). *Indian J Microbiol Res*. 2022;9(2):131–4.
10. Nagar R, Nagar P, Verma M, Sharma R. Etiological profile of children admitted with fever without focus for less than 7 days duration at tertiary care center. *Asian J Pharm Clin Res*. 2021;15(1):119–21.

Author biography

Chirag Mittal, Resident

Bhupesh Jain, Associate Professor

Suresh Goyal, Senior Professor

Cite this article: Mittal C, Jain B, Goyal S. A study on acute undifferentiated febrile illness in children (Age 2 Months to 18 Years). *IP Int J Med Paediatr Oncol* 2023;9(1):13-18.