

Trends in Acute Undifferentiated Febrile Illness in Patients Seeking Treatment from a Tertiary Care Hospital of Central Kerala

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ABSTRACT

BACKGROUND

Acute undifferentiated febrile illness (AUI / AFI) is one of the most common reasons for people seeking medical care globally. Investigation into the aetiology and trends in AUI cases are valuable public health data source. Absence of such evidence-based data may result in unintended public health consequences. Present study was undertaken to address the gap in period specific trends in AUI cases reported from the region.

METHODS

A record based descriptive study was done in patients treated with AUI from January 1st, 2015 to December 31st, 2019 in Government Medical College, Ernakulam. Universal sampling technique was adopted, and the data was entered in Microsoft Excel and analysed using Epi-Info software. Line diagram was constructed to obtain the trends in AUI cases over the five-year period. Chi-square test was applied to find out the association between age group (paediatric and others) and causative agents of AUI.

RESULTS

A total of 7998 AUI cases were included in this study. Highest number of AUI cases (1986) was reported in the year 2017. Under five age group was the most common, 1564 (19.6 %). Majority of the AUI were reported among males, 4947 (61.9 %). Undetermined fever was found to be the most common AUI, 2188 (27.4 %). Dengue fever, 1993 (24.9 %) was the most diagnosed AUI. Viral aetiology was found to be the most common, 3895 (48.7 %) in both paediatric and other age groups. No statistically significant association was found between (P-value = 0.22) age group and organisms causing AUI. There were 121 (1.5 %) deaths reported among the AUI cases during the five-year period. It was seen that the case fatality due to AUI was highest (2.41 %) in the year 2019.

CONCLUSIONS

A lack of consistent pattern in the aetiology of AUI cases reported over the five-year study period, calls for persistent vigil by the public health surveillance system in the region, to identify any impending infectious disease outbreak at the earliest. As this study is based on hospital-based surveillance record it can underestimate the disease incidence.

KEYWORDS

Acute Undifferentiated Febrile Illness (AUI), Trends, Dengue, Acute Febrile Illness

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BACKGROUND

The term acute undifferentiated febrile illness (AUI) connotes fever of less than 14 days duration without any evidence of organ or system specific aetiology at the onset.¹ These types of fever are commonly reported from the tropical and subtropical regions of the world.² Most of these cases present with similar symptoms with lack of focal signs, making it a challenge for the clinician to diagnose and treat the illness appropriately. Owing to scarce diagnostic facilities available in the resource poor settings, presumptive treatment is given to manage such cases. This can increase the morbidity and mortality.³

AUI cases are the most common among all the in patients being treated in the medicine wards of tertiary care hospitals across India.⁴ In a multi centric study from North India, Malaria was reported to be the most common AUI,⁵ whereas a systematic review from South East Asia revealed viral causes to be the most common.⁶ One of the studies from South India reported, Dengue as the most common AUI.⁷ In another ten year descriptive study done in rural Kerala, South India, most common laboratory confirmed illness was Leptospirosis.³ This indicates that there may be a regional variations in the distribution of pathogenic agents causing AUI.

The recent pandemic of COVID-19 sheds light on the fact that, if timely warning and containment measures are not undertaken at the early stages of an outbreak the emerging infectious diseases can spell havoc on the health care system. Emerging and re-emerging infectious diseases are a matter of concern to the public health system.⁸ In spite of considerable heterogeneity of AUI aetiology by population, region, and in time, there is limited published literature detailing these findings, both by geographic location and time period. Emerging infectious diseases continue to loom as a threat throwing up multitude of challenges in front of the public health system in India. Majority of the tropical diseases causing AUI have similar presentations at the onset, this remains an issue in case of developing countries. These countries do not have enough facilities and multiplex tests which will aid the physician in diagnosing a case of AUI at the earliest.

This delay can result in an increase in preventable deaths among AUI cases in resource limited settings. A prominent sequential trend of specific AUI s in a particular region can enable the public health surveillance system to stay vigil and take timely and appropriate preventive measures to combat emerging infectious diseases. Hence, this study was undertaken to describe the trends and aetiology of AUI reported from Government Medical College Ernakulam during the last five years (2015 - 2019). This study also sheds light on the common aetiological trends of AUI in this part of the world.

METHODS

A record based descriptive study of acute undifferentiated febrile illness of patients treated in Government Medical

College, Ernakulam during January 1st 2015 to December 31st 2019 was undertaken in the months of October and December 2020. The college is situated in Central Kerala and caters to patients from three different districts of Kerala state namely Ernakulam / Cochin, border areas of Alappuzha and Idukki districts. Topographically these three districts are unique as Ernakulam has predominately urban population, whereas Alappuzha is a coastal belt and Idukki high range, hence the cases reported and treated in this medical college can be taken as a representative population of Kerala state as a whole.

Study Population and Sampling

Patients treated with AUI during January 1st 2015 to December 31st 2019 in Government Medical College Ernakulam were included in this study. The term acute undifferentiated febrile illness (AUI) connotes fever of less than 14 days duration without any evidence of organ or system specific aetiology at the onset.¹ Universal sampling technique was adopted. There was a total of 7998 study subjects satisfying the inclusion criteria of AUI. All of them were included in this study.

Data Collection

Data regarding the study variables were collected from the Regional-Prevention of epidemic and infectious diseases (RPEID) cell records maintained in the department of Community Medicine, Government medical college, Ernakulam. This is a retrospective study based on the data available from the records to understand the trends in AUI in the region. RPEID cell has been established in all Government Medical colleges and few Private medical colleges in Kerala. The major objective of this cell is to supplement the data regarding communicable diseases reported through the IDSP (Integrated Disease Surveillance Programme) portal of Government of India. This cell undertakes active surveillance and outbreak response activities in case of public health emergencies in the region catered by the medical college. Principal of the concerned medical college is the chairman and senior most Associate Professor in the Department of Community Medicine is the Coordinator of the RPEID cell. Institutional RPEID cell records are maintained in the form of a soft copy, permission to access the same was obtained from the concerned authorities and the relevant data (which included age, gender, clinical / laboratory diagnosis, date of admission, date of discharge and outcome of the cases which satisfied the eligibility criteria of AUI) were collected.

Statistical Analysis

Data was entered in an Excel sheet and all the qualitative variables were analysed and expressed in proportions and percentages. Line diagram was constructed using the Microsoft Excel sheet to obtain the trends in AUI cases over the five-year period. Chi-square test was applied to find out the association between age group (paediatric and others)

and causative agents of AUFI, this was done using Epi-Info software.

Ethics

Ethics clearance was obtained from Human Ethics Committee (HEC) of Government Medical College, Ernakulam (IEC No 31 / 2020) before commencement of this study.

RESULTS

A total of 7998 subjects were included in this study. The total number of AUFI cases reported year wise from January 1st 2015 to 31st December 2019 is depicted in a bar diagram (Figure 1). The highest number 1986 (24.9 %) of AUFI cases were reported in the year 2017. All cases reported with AUFI in the institution were included in this study irrespective of their age (Table 1). Under five age group was found to be the most common, 1564 (19.6 %). Majority of the AUFI cases were males 4947 (61.9 %). Undetermined fever was the most common, 2188 (27.4 %) followed by Dengue fever, 1993 (24.9 %), (Table 2). The AUFI cases which did not have a specific diagnosis were termed as undetermined fever. In order to study the trend in AUFI cases reported over a period of five years from 1st January 2015 to 31st December 2019, the cases were grouped into six different categories and a line diagram was constructed using the Microsoft excel spread sheet (Figure 2). Chicken pox, diphtheria, mumps and measles were included in the category named Vaccine preventable diseases (VPD). Influenza like illness (ILI) and other respiratory infections were included in the category respiratory infections (respiratory infection). Dengue and malaria were included in the third category which was termed as arthropod borne diseases, fourth category was termed zoonoses in which Acute encephalitis syndrome and leptospirosis were included. Diseases like hepatitis, urinary tract infections (UTI) and enteric fever were included in the category named "others". The AUFI cases which could not be diagnosed were termed as undetermined fever. Highest number of Vaccine preventable diseases (VPD) were reported in the year 2015 (177) the number declined to below 100 in the year 2016, whereas no case of VPD was reported in the year 2019. The number of respiratory illness (respiratory infection) reported from the institution was almost consistent over the five-year period with a slight increase during 2017. The maximum number (798) of arthropod borne diseases were reported in the year 2017, following which there was a consistent dip in the number of cases reported in the subsequent (2018 - 19) years. The number of cases reported with zoonoses in the institution remained consistent over the five-year period, except for a slight increase in the years 2018 and 2019. There were 102 cases of zoonoses reported in the year 2018 and 94 cases in the year 2019. The maximum number (789) of undetermined fever cases were reported in the year 2018, following which the number decreased to less than half (303) in the year 2019 when compared to the previous year (2018).

Age Group (yrs.)	Number (%)
Under five	1564 (19.6)
6 - 18	1363 (17)
19 - 25	958 (12)
26 - 35	807 (10.1)
36 - 45	899 (11.2)
46 - 55	939 (11.7)
56 - 65	769 (9.6)
Above 65	699 (8.7)
Total	7998 (100)

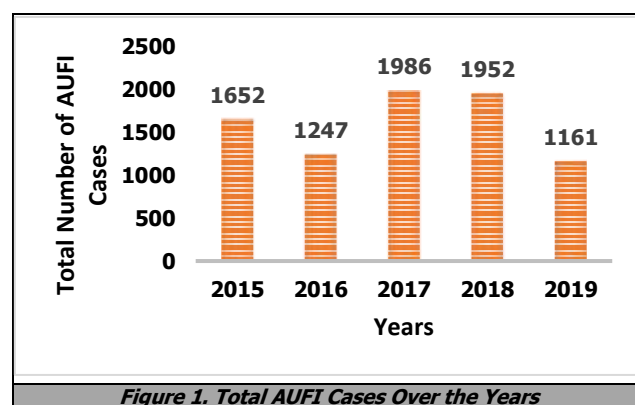
Table 1. Age Distribution of the Study Subjects

Aetiology	Number (%)
Undetermined fever	2188 (27.4)
Dengue	1993 (24.9)
Influenza like illness (ILI)	1318 (16.6)
Respiratory infections	508 (6.4)
UTI	587 (7.3)
Chicken pox	459 (5.7)
Hepatitis	376 (4.7)
Leptospirosis	217 (2.7)
Malaria	135 (1.7)
Enteric fever	94 (1.2)
Acute encephalitis syndrome (AES)	52 (0.7)
Mumps	42 (0.5)
Measles	24 (0.3)
Diphtheria	05 (0.1)
Total	7998 (100)

Table 2. Aetiology of the Cases

Aetiology	Total Patients	Deaths (N = 121) (% of Total Deaths)
Influenza like illness	1318	48 (39.6 %)
Dengue	1993	21 (17.3 %)
Leptospirosis	217	19 (15.7 %)
Hepatitis	376	11 (9.0 %)
Respiratory infection	508	10 (8.2 %)
Undetermined fever	2188	8 (6.6 %)
Acute encephalitis syndrome	52	2 (1.6 %)
Enteric fever	94	2 (1.6 %)

Table 3. Outcome



Age Group	Viral (%)	Bacterial (%)	Protozoal (%)	Undetermined (%)
Paediatric age group	1206 (30.9)	532 (29.8)	43 (31.8)	719 (32.9)
Others	2689 (69.1)	1248 (70.2)	92 (68.2)	1469 (67.1)
Total	3895 (100)	1780 (100)	135 (100)	2188 (100)

Table 4. Association between Age Group and Causative Organisms of AUFI

Chi-square = 4.33
Df = 3
P-value = 0.22

Diseases like hepatitis, urinary tract infections and enteric fever were included in the category termed "others" showed a slight increase from 228 cases in the year 2015 to 330 cases in the year 2017, following which there was a dip in the reported cases in the years 2018 and 2019, only forty cases were reported in the year 2019 (Figure 2). There was a total of 121 deaths among the AUFI cases reported during this period (Table 3). We also calculated the case fatality

rate for each year for the five-year period. It was seen that case fatality due to AEFI was highest (2.41 %) in the year 2019 (Figure 3). Case fatality rate is an indicator which helps in the assessment of killing power or virulence of an organism. As per this study majority of the deaths were due to influenza like illness (ILI), 48 (39.6 %) followed by dengue fever 40 (17.3 %). Chi square test was applied to find the association between age group and causative organisms of AEFI (Table 4). Viral aetiology was found to be the most common 3895 (48.7 %) in both paediatric and other age groups. We did not get a statistically significant association between (P-value = 0.22) age group and organisms causing AEFI.

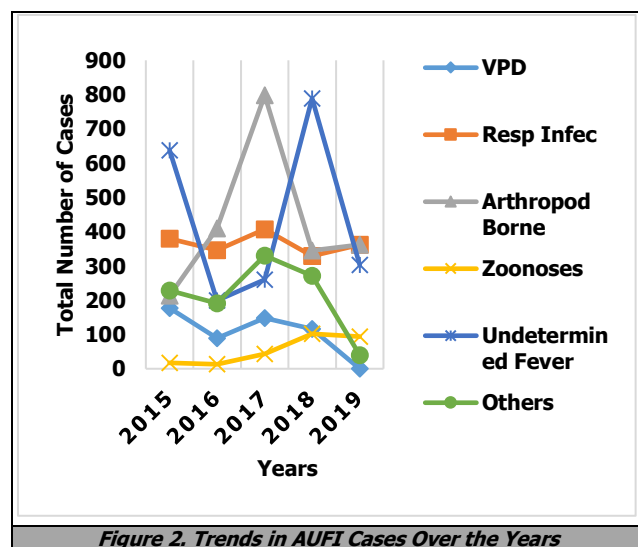


Figure 2. Trends in AEFI Cases Over the Years

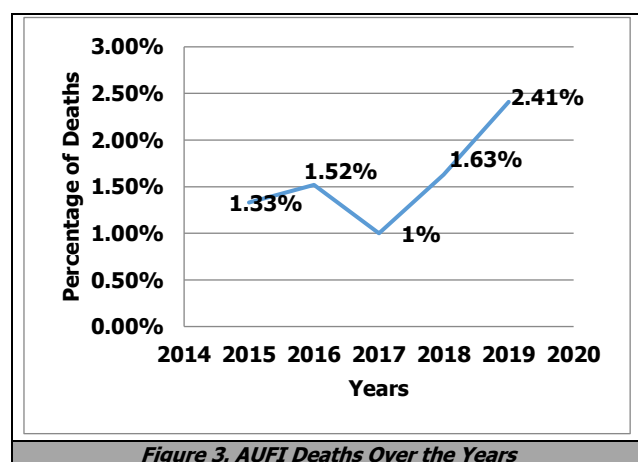


Figure 3. AEFI Deaths Over the Years

DISCUSSION

Acute undifferentiated febrile illness can have a varied trend and regional difference in its presentation. This could be due to various factors like environment, host defence and difference in distribution of infectious agent in that particular region.² A sound knowledge of local causes and trends in AEFI can help in guiding the treating physician to apply this for appropriate empiric treatment and case management. In the present study AEFI cases belonging to all ages reported in the institution during the five-year study period were included, under five was the most common age group. In

most of the studies on AEFI / AFI conducted across the world paediatric age group has been excluded. This could be due to the fact that most of these studies were conducted either in the internal medicine or the infectious disease departments of health care institutions. Most studies that have included paediatric age groups have excluded adults from the study, hence we could not compare the age groups reported among various studies with the present study. However, we tried to find out the association between causative organisms of AEFI and the age group, but we did not get a significant association between the two. Viral organisms were found to be the most common AEFI causing organisms across all ages, in this study. Many other studies done in India and abroad also reveal similar findings.^{4-7,9-11} Current study had a preponderance of male sex among the reported cases of AEFI, this is in line with various other studies conducted across the world.^{6,7,9,12} Among the laboratory confirmed causes, dengue was the most common AEFI as per the present study. Many other studies from India also reveal similar findings.^{5,7} In a systematic review conducted by including many independent studies from South and South Eastern Asia, dengue was found to be the most common aetiology for AEFI in this part of the world⁶. In our study those AEFI cases which did not have a clinical or laboratory diagnosis were included in the category of undetermined fever. In spite of advances in medical science various studies report, 8 % - 80 % of AEFI cases to be undiagnosed.^{7,13}

A study from a tertiary care hospital in North India reported that 60.7 % of the AEFI cases could not be diagnosed.¹⁴ There exists a paucity of available technology for early diagnosis of AEFI cases, even in Tertiary care settings of resource limited country like India. This fact can be substantiated by the high percentage of undiagnosed (undetermined fever) AEFI cases in the present study. The trend of undiagnosed AEFI cases showed varying frequency over the five-year study period, most of the undetermined cases were reported in the year 2018, when Kerala was stuck by a major disaster in the form of floods. All three districts namely Ernakulam / Cochin, Thrissur and Alappuzha which are the catchment area of the medical college, were badly affected by this natural disaster. Most number of AEFI deaths from the institution were also reported in the same year. Majority of the deaths in the study were due to influenza like illness (ILI). Whereas another study from South India reports leptospirosis to be the most common infection leading to death.⁷ Though the study was undertaken to find out the trends in AEFI cases over the five year period, we did not find a consistent pattern in the aetiology of the reported cases during this period. Lack of such pattern emphasise the need for continuous monitoring of changing trends in AEFI cases being reported from the region. The Division of Global Health Protection, centre for Global Health states that "AEFI has no current consensus standardized approach when considered as a syndromic case definition for public health surveillance or research, especially in global settings where AFI treatment is performed with limited diagnostic availability."¹⁵ Etiologic AFI investigations are thought to be a valuable public health data source, which contribute necessary information on

disease prevalence, and helps to inform estimates of morbidity and mortality. Many of the tropical diseases causing AEFI have similar presentations at the onset, with the twin burden of endemic diseases and emerging infectious diseases the onus is on the public health system to tackle this menace. Patients in both public and private sector are made to undergo various investigations which invariably delay the treatment and increase the cost. Despite recurring epidemics, scientific data about these epidemics remain scanty. In low- and middle-income countries, many preventable deaths occur owing to delay in diagnosis. Availability of multiplex tests which can quickly identify a pathogen from a group of pathogens that causes similar symptoms is of paramount importance. This study is an attempt to systematically assess the trends in AEFI occurring in a particular region which will help tackle this public health catastrophe effectively. Though this study could not find a consistent pattern in occurrence of AEFI over the five-year period, the authors are of the opinion that if a scientific protocol is used for diagnosis and treatment of AEFI, the percentage of undetermined fever can be brought down significantly over the years. Hence, further research and development of a region-specific standard protocol for diagnosis and treatment of AEFI is called for.

CONCLUSIONS

Diagnosis of acute undifferentiated febrile illness remains a challenge even in a tertiary care centre like ours. Variation in trends of AEFI and lack of consistent pattern over a period of time even in the same region calls for strengthening of the ongoing public health surveillance, so as to take timely and appropriate preventive measures to combat potential outbreaks of infectious diseases. Though this study could not find a consistent pattern in occurrence of AEFI over the five-year period, the investigators are of the opinion that a region-specific scientific protocol for the diagnosis and treatment of AEFI will help in bringing down the percentage of undetermined fever over the years. Therefore, further research and development of a region-specific standard protocol for diagnosis and treatment of AEFI is the need of the hour.

Limitations

It is a hospital-based surveillance record which underestimates the disease incidence. The true burden of disease cannot be well characterised as all patients do not seek medical attention at a hospital.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

Financial or other competing interests: None.

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REFERENCES

- [1] Leelarasamee A, Chupaprawan C, Chenchittikul M, et al. Etiologies of acute undifferentiated febrile illness in Thailand. *J Med Assoc Thai* 2004;87(5):464-472.
- [2] Climate change and Health. <https://www.who.int/news-room/fact-sheets/detail/>.
- [3] Ittyachen AM, Ramachandran R. Study of acute febrile illness: a 10-year descriptive study and a proposed algorithm from a tertiary care referral hospital in rural Kerala in southern India. *Trop Doct* 2015;45(2):114-117.
- [4] Mørch K, Manoharan A, Chandy S, et al. Acute undifferentiated fever in India: a multicentre study of aetiology and diagnostic accuracy. *BMC Infect Dis* 2017;17(1):1-11.
- [5] Mittal G, Ahmad S, Agarwal RK, et al. Aetiologies of acute undifferentiated febrile illness in adult patients – an experience from a tertiary care hospital in Northern India. *J Clin Diagnostic Res* 2015;9(12):DC22-DC24.
- [6] Wangdi K, Kasturiaratchi K, Nery SV, et al. Diversity of infectious aetiologies of acute undifferentiated febrile illnesses in south and Southeast Asia: a systematic review. *BMC Infect Dis* 2019;19(1):1-17.
- [7] Andrews MA, Ittyachen AM. Aetiology of acute febrile illness: a multicentre study from the province of Kerala in Southern India. *Trop Doct* 2018;48(4):322-325.
- [8] Celik I, Saatci E, Onereyuboglu F. Emerging and re-emerging respiratory viral infections up to Covid-19. *Turk J Med Sci* 2020;50(SI-1):557-562.
- [9] Kasper MR, Blair PJ, Touch S, et al. Infectious etiologies of acute febrile illness among patients seeking health care in South-Central Cambodia. *Am J Trop Med Hyg* 2012;86(2):246-253.
- [10] Capeding MR, Chua MN, Hadinegoro SR, et al. Dengue and other common causes of acute febrile illness in asia: an active surveillance study in children. *PLoS Negl Trop Dis* 2013;7(7):e2331.
- [11] Thangarasu S, Natarajan P, Rajavelu P, et al. A protocol for the emergency department management of acute undifferentiated febrile illness in India. *Int J Emerg Med* 2011;4:57.
- [12] Veligandla G, Vanan E, Padmavathi E, et al. Etiological spectrum and prevalence of Acute Undifferentiated Febrile Illness (AEFI) in fever cases attending our tertiary care centre. *Int J Curr Microbiol Appl Sci* 2017;6(5):954-962.
- [13] Susilawati TN, McBride WJ. Acute undifferentiated fever in Asia: a review of the literature. *The Southeast Asian Journal of Tropical Medicine and Public Health* 2014;45(3):719-726.
- [14] Goyal J, Sharma M, Mani R, et al. Acute Undifferentiated Febrile Illness (AEFI) in adult hospitalized patients: an experience from a tertiary care hospital of western Uttar Pradesh region from North India. *Int Multispecialty J Heal* 2017;3(6):186-191.

- [15] Rhee C, Kharod GA, Schaad N, et al. Global knowledge gaps in acute febrile illness etiologic investigations: a scoping review. *PLoS Negl Trop Dis* 2019;13(11):1-16.