Acute Undifferentiated Febrile Illness (AUFI) in adult hospitalized patients: An experience from a tertiary care hospital of western Uttar Pradesh region from North India

Dr. Jyoti Goyal[1§], Dr Mamta Sharma[2], Dr. R.K. Mani[3], Dr. Paramjeet Bhatia[4], Dr. Karunesh[4], Dr. Ankita Chourasia[6]

[1]Head of Department, Department of Internal Medicine, Nayatimedicity, Mathura (UP) India.
[2]Consultant, Community Medicine & Biostatistics, Nayatimedicity, Mathura (UP) India
[3]CEO and Chairman, Critical care and Pulmonary Medicine, Nayatimedicity, Mathura (UP) India
[4]Senior Consultant, Department of Internal Medicine, Nayatimedicity, Mathura (UP) India
[5]Senior Resident, Department of Internal Medicine, Nayatimedicity, Mathura (UP) India
[6]Consultant, Community Medicine & Biostatistics, Nayatimedicity, Mathura (UP) India

Abstract— *Acute undifferentiated febrile illness (AUFI) is a common occurrence in low and middle income groups countries like India and constitutes heavy burden on healthcare industry especially from month of June to September. AUFI includes various diseases which are very difficult to differentiate. So this study was conducted on 504 AUFI cases to present an etiological profile of these AUFI cases. It was found that among these 504 AUFI cases, 6.54% were Malaria, 15% Typhoid, 14% Dengue, 3.17% Chickenguniya, 4.56% were mixed infections and 60.7% were undiagnosed.*

Keyword: Acute Undifferentiated Febrile Illness (AUFI), Malaria, Undiagnosed Undifferentiated Febrile Illness (UUFI), Dengue, Chikungunia .

I. INTRODUCTION

Acute undifferentiated febrile illness (AUFI) is considered to be a febrile illness of < 3 weeks duration without any localized symptoms and specific signs.[1] A number of diseases were included in this category. Most of these illnesses have nonspecific symptoms and signs and it is difficult to differentiate among them clinically. A huge gap is existing in understanding of specific clinical characteristics and diagnostic lab parameters to identify a specific illness. Even a very astute physician faces a big diagnostic challenge while managing these illnesses. Local pattern of febrile illness in a specific geographical area influences the differential diagnosis and laboratory workup for AUFI.

AUFI is a common occurrence in low and middle income groups countries like India and constitutes heavy burden on healthcare industry especially from month of June to September 12. During this season, these diseases form the main bulk of hospital admissions and OPD visits.[2,3,4]

AUFI can be caused by bacterial, viral, rickettsial or protozoal organisms. Being situated in the tropical region, India is endemic for range of tropical infections like Dengue, Chikungunya, enteric fever, viral hepatitis, malaria, leptospirosis, Japanese encephalitis, meningitis, influenza etc.[5] Though data from western UP region is lacking.

Numerous laboratory investigations are done to diagnose aetiologies of AUFI, but despite of that some still may remain undiagnosed and are known as undiagnosed undifferentiated febrile illness (UUFI), though exact definition of UUFI is missing. This short term undiagnosed undifferentiated febrile illness (UUFI) closely resembles PUO. PUO in contrast to AUFI is a well-defined and widely studied problem. A very clearly defined protocols and guidelines for diagnosis and management of PUO are

existing. PUO and UUFI can be differentiated from each other by the duration of fever and their different aetiologies. Most of the fevers caused by AUFI recover within 3 weeks' time, either with treatment or spontaneously. If fever persists for more than 3 weeks' time, it comes under the class of PUO. [6]

Diagnosed AFI can be malarial acute febrile illness or non-malarial acute febrile illness (NMAFI).Though availability of rapid card test and peripheral smear for malaria makes early and definitive diagnosis of this illness with very few exceptions none the less it is important to have a clear guideline and training for diagnosis and treatment of malaria. Indiscriminate use of antimalarial especially for treatment of non-malarial acute febrile illness (NMAFI) has potential to create resistance for antimalarial drugs.[6]

AUFI has high prevalence, lacks specific clinical features and needs early empiric treatment, thereby creating chances of indiscriminate use of antibiotics and antimalarials. Though protocols and guidelines are available for evaluation and management of AUFI, they are generalised in nature and have found limited applications. Further strategies for managing AUFI need to be customized depending on geography, availability of resources and cost. We have studied the distribution of etiological profile of AUFI and also the percentage of UUFI in our study.

Present study aims to determine the distribution of etiological profile of AUFI patients admitted in Mathura and proportion of UUFI among them.

II. METHODOLOGY

A cross-sectional study was conducted over a period of 6 months from 1 June 2016 to 1 Dec 2016. All 15 to 85 years aged admitted cases with history of fever over 38.3 degrees C for < 3 weeks of duration without any specific localizing signs or symptoms were enrolled for the study. All critically ill patients requiring direct admission to ICU, cases of localized infection like pneumonia, abdominal infections, meningitisetc., patients of severe sepsis with septic shock, haematological malignancies, autoimmune disorders, those on immunosuppressant, fever > 3 weeks' time (PUO) were excluded from the study

Following information was retrieved: demographic data including age, sex and clinical hospitalization data including rash, vomiting, headache, joint pain, diarrhoea. Relevant biochemical, haematological and serological data were also retrieved for eg. Dengue NS1 Ag/IgM antibody, material parasite slide/card, IgM antibody for chikungunya, typhidot assay.

Laboratory results were interpreted as per standard diagnostic criteria's for different etiologies of AUFI.

Data thus collected were incorporated in to Microsoft excel sheet and analysed using IBM SPSS version 20 software (trial version).

III. RESULTS

A total of 625 patients were admitted during study period of 6 months. Out of these, 504 were enrolled in study and 121 were excluded as per exclusion criteria. Among these 504 study participants, etiologically 6.54% were diagnosed as Malaria, 15% as typhoid, 14% as dengue, 3.17% as chickenguniya, 4.56% as mixed infections and 60.7% remains undiagnosed. (Figure 1&2).

Figure 1

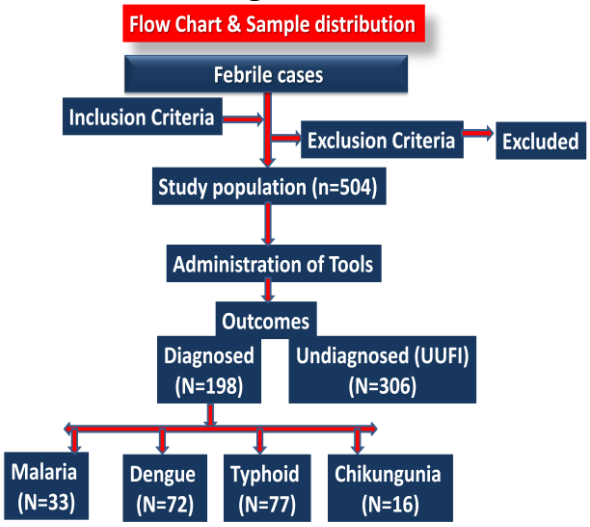
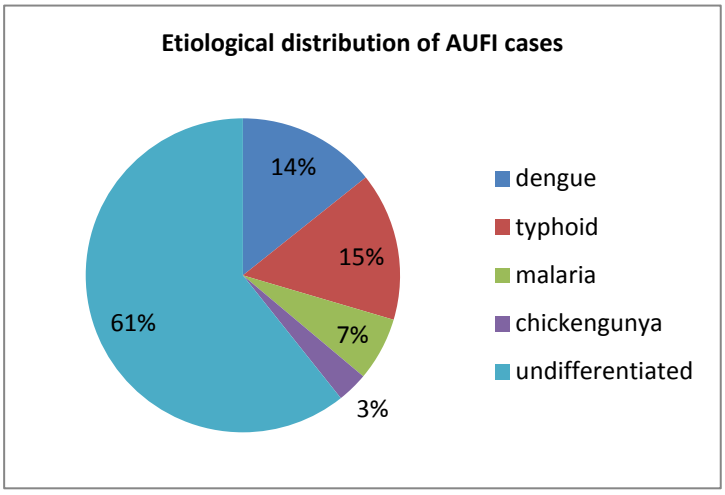


Figure 2



Most common mixed infections were of Dengue- typhoid in 73% and 27 % were confections of malaria - dengue and malaria - typhoid.

Majority of the patients were young in their second, third and fourth decades of life with 40.67% of patients between 25 to 45 years of age. 1.78% of patients were above age of 80 years. Males (65.07%) were more commonly affected in comparison to females (34.9%). (Figure 3)

Symptoms associated with fever were vomiting (34.5%), joint pain (33.0%), headache (30 %), rashes (3.6%) and diarrhoea (2.97%). (Figure 4)

Figure 3

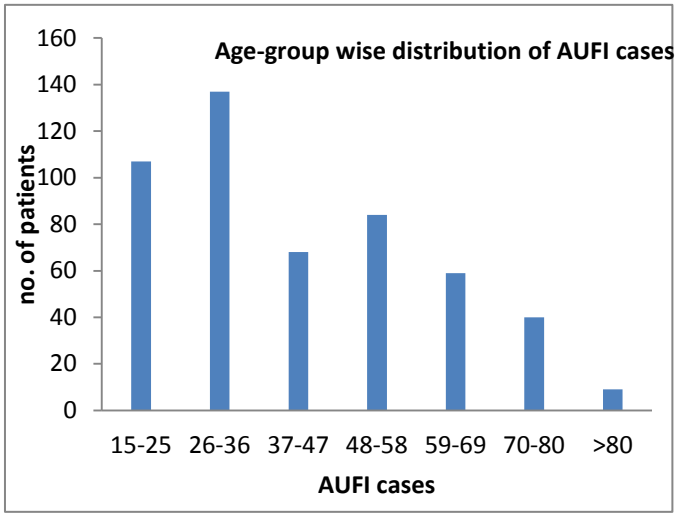
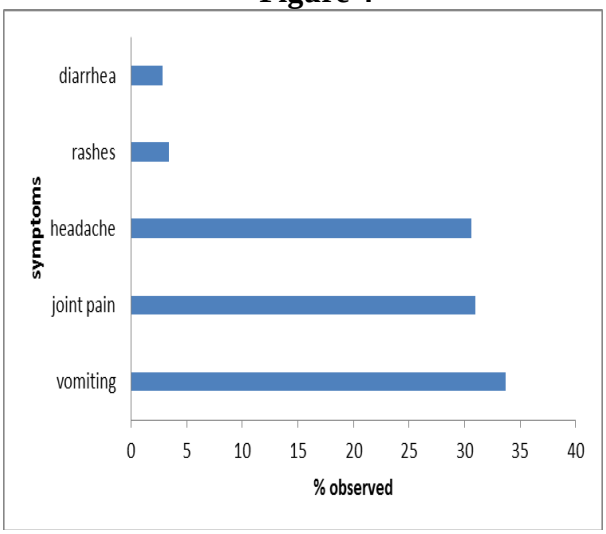


Figure 4



Severe thrombocytopenia (<50,000) was seen in 22.61% patients.

History of hypertension, diabetes, cardiovascular diseases and COPDs was asked. These all co-morbidities, combined together were present in 9.1 % of patients.

Average length of stay for majority was between 3 to 5 days with mean length of stay was 4.36 days.

IV. DISCUSSION

In present study 60.7% of AUFI cases remain undiagnosed (UUFI) whereas 15% were diagnosed as typhoid, 14% as Dengue, 6.54% as Malaria, 3.1% as Chikungunia and 4.56% as mixed infection. Literature also reported that AUFI cases includes malaria, dengue, leptospirosis, rickettsial infections especially scrub typhus, typhoid fever, Japanese encephalitis, influenza and many undiagnosed organisms.[7] Similar findings were made by other authors[2,3,4,8,9] who conducted studies in India and other parts of Southeast Asia. UUFI. Abhilash etal reported Scrub typhus as most common cause of AFI (35.9%) followed by dengue (30.6%), malaria (10.4%), enteric fever (3.7%), and leptospirosis (0.6%).

Malaria positive cases and enteric cases were found 6.54% and 15% respectivlely in present study which was comparable to a study done by Balvinder etal in which was reported 4.7%. & 10.9% respectively.[9] In this study most common mixed infections were Dengue- typhoid (73%). Co-infections of malaria dengue and malaria typhoid combined together constituted 27%. Mixed infection proportion is quite variable in different studies ranging from7-78.9 %. Proportion of mixed infections is quite high in north India. [10-13]

Most common age group affected in this study was between 25-45 years of age, reflecting young economically active people are affected more with these illnesses which were also supported by literature.[14] Increased outdoor exposure to mosquitoes and ticks, use of contaminated water may be factor responsible for this.

Males predominate over female in this study. Similar observation was made by other study conducted in northern India.[15] It can also be explained with more outdoor activities and more risk of exposure for mosquito bite among males.

Comorbidities like HTN, DM2, CAD, COPD combined together were present in 9.1% of patients in these studies. Low incidence of comorbidity may be explained by relatively younger people getting affected from the illness, as these comorbidities are usually associated with the advanced age. Present epidemiological evidence of association of comorbidities with severity of illness is limited and only suggestive. However it is important to identify these comorbidities early and patient should be kept in close observation if needed to improve outcome and avoid complications.[16]

Proportion of UUFI (60.7%) is almost similar to study done in North Queens land Australia (56.8 %)[17] and Thailand (61.3 %)[8] but in an another study done by Abhilash etal only 18.8 % cases were diagnosed with UUFI.[4] High incidence of UUFI in our study may be because of undiagnosed cases of scrub typhus and Leptospira infection. Etiologic profile for AUFI is diverse and varies with geographical prevalence and diversity. Many unidentifiable causes like Bartonella, Tick borne diseases, viral URI may alsocontribute for the aetiology of UUFI category.

In this study, rashes, joint pain, diarrhoea, headache, vomiting were common symptoms found and vomiting and headache were the most common symptom. A study done in Thailand also reported common symptoms of AUFI as headache, myalgia, nausea and vomiting.[8]

Mean duration of the stay found 4.39 days in this study which was well in resonance with to a study done in Singapore.[18]

V. CONCLUSION

It is important to know the various aetiologies responsible for AUFI. In present study, 60.7% of AUFI cases remain undiagnosed (UUFI) whereas 15% were diagnosed as typhoid, 14% as Dengue, 6.54% as Malaria, 3.1% as Chikungunia and 4.56% as mixed infection. It will not only help stakeholders for choosing preventive measures but will guide clinicians to make appropriate clinical judgement for diagnosing and treating these illnesses. UUFI formed the main category in this study, reflecting the need of broader diagnostic approach to identifying a broad range of infectious agents. A protocol based approach for diagnosing and managing AUFI will reduce the cost, burden on healthcare professional and help in selective use of antibiotics and antimalarials. Hence, need of protocol is well understood and it is to be established by each institute depending on their local prevalence and pattern of the illness.

LIMITATION OF STUDY

Data to differentiate vivax from falciparum and serial platelet counts could not be collected in this study. Enteric fever cases would have been diagnosed better if tests for blood culture and Widal test data could have been correlated. Though sensitivity and specificity of the serological testing for various aetiologies are not 100% and chances of over or under diagnosis is there. However, this number should not be large enough to interfere with the purpose of the study

CONFLICT OF INTEREST

None declared till now.

REFERENCES

[1] Joshi R, Kalantri SP. 1. Acute Undifferentiated Fever: Management Algorithm. Update on Tropical Fever.2015; 1-14.

[2] Chrispal A, Boorugu H, Gopinath KG, Chandy S, Prakash JA, Thomas EM, 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

[3] Murdoch DR, Woods CW, Zimmerman MD, Dull PM, Belbase RH, Keenan AJ, et al. The aetiology of febrile illness in adults presenting to Patan Hospital in Kathmandu, Nepal. Am J Trop Med Hyg. 2004; 70(6):670-5.

[4] KundavaramPaul PrabhakarAbhilash, Jonathan Arul Jeevan, ShubhankerMitra. Undifferentiated Febrile Illness in Patients Presenting to a Tertiary Care Hospital in South India: Clinical Spectrum and Outcome J Glob Infect Dis. 2016 Oct-Dec; 8(4): 147–54

[5] T. Dikid, S.K. Jain, A. Sharma, A. Kumar, J.P. Narain. Emerging & re-emerging infections in India: An overview. Indian J Med Res 138, July 2013, pp 19-31

[6] Abba K, Deeks JJ, Olliaro P, Naing CM, Jackson SM, Takwoingi Y, et al. Rapid diagnostic tests for diagnosing uncomplicated P. falciparum malaria in endemic countries. The Cochrane database of systematic reviews. 2011(7):CD008122

[7] 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):719-26

[8] Leelarasamee A, Chupaprawan C, Chenchittikul M, Udompanthurat S. Aetiologies of acute undifferentiated febrile illness in Thailand. J Med Assoc Thai. 2004; 87:464-72.

[9] Balvinder Singh Arora, Monika Matlani,KarnikaSaigal. Major aetiologies of acute undifferentiated fever in 2013 and 2014: an experience in retrospect Int J Adv Med. 2017 Apr; 4(2):568-572

[10] S. Ahmed,M. Dhar G. Mittal, N. K. Bhat N. Shirazi V. Kalra H. C. Sati V. Gupta A comparative hospital-based observational study of mono- and co-infections of malaria, dengue virus and scrub typhus causing acute undifferentiated fever European Journal of Clinical Microbiology & Infectious Diseases. April 2016; 35 (4):705–71.

[11] Mushtaq MB, Qadri MI, Rashid A. Concurrent Infection with Dengue and Malaria: An Unusual Presentation. Case Reports in Medicine. 2013, doi:10.1155/2013/520181 (cited 2013 Mar 10)

[12] Suresh V, Krishna V, Raju CHN, Teja PS, Usha V. A rare case of triple infection with dengue, malaria and typhoid. Int J Res Dev Health. 2013; 1(4):200-03.

[13] Sharma A, Raina R, Dhiman P, Adarsh, Madhabhavi I, Panda P. Rare Coinfection of Scrub Typhus and Malaria in Immunocompetent Person. Online J Health Allied Scs. 2012; 11(2):12

[14] MA Andrews, Aleena Elizabeth, PraveenlalKuttichira. Clinical profile of acute undifferentiated febrile illness in patients admitted to a teaching hospital in Kerala. Health Sciences 2014;1(3):JS001D.

[15] Garima Mittal ,Sohaib Ahmad, R K Agarwal, MinakshiDhar, Manish Mittal, and Shiwani Sharma. Aetiologies of Acute Undifferentiated Febrile illness in Adult Patients – an Experience from a Tertiary Care Hospital in Northern India. J ClinDiagn Res. 2015 Dec; 9(12): 22–24

[16] Pang J, Salim A, Lee VJ, Hibberd ML, Chia KS, Leo YS, et al. Diabetes with hypertension as risk factors for adult dengue haemorrhagic fever in a predominantly dengue serotype 2 epidemic: a case control study. PLoSNegl Trop Dis. 2012; 6(5):e1641.

[17] SusilawatiTN, McBride WJ. Undiagnosed undifferentiated fever in Far North Queensland, Australia: a retrospective study. International journal of infectious diseases:IJID: official publication of the International Society for Infectious Diseases. 2014; 27:59-64

[18] Tun ZM, Moorthy M, Linster M, Su YC. Characteristics of acute febrile illness and determinants of illness recovery among adults presenting to Singapore primary care clinics. BMC Infect Dis. 2016 Oct 28; 16(1):612.