

Aetiologies of Acute Undifferentiated Febrile illness in Adult Patients – an Experience from a Tertiary Care Hospital in Northern India

GARIMA MITTAL¹, SOHAIB AHMAD², R K AGARWAL³, MINAKSHI DHAR⁴, MANISH MITTAL⁵, SHIWANI SHARMA⁶

ABSTRACT

Introduction: Acute undifferentiated febrile illness (AUI) is a common clinical entity in most of the hospitals. The fever can be potentially fatal if the aetiology is not recognized and appropriately treated early.

Aim: To describe the aetiology of fever among patients in a tertiary care hospital in Northern India.

Materials and Methods: A one-year retro-prospective, observational study was conducted in adults (age>18years) presenting with undifferentiated febrile illness (of duration 5-14 days). Diagnosis was confirmed by suitable laboratory tests after exhaustive clinical examination.

Results: A total of 2547 patients with AUI were evaluated. Of these, 1663 (65.3%) were males and 884 (34.7%) were females. Dengue (37.54%); enteric fever (16.5%); scrub typhus (14.42%); bacterial sepsis (10.3%); malaria (6.8%); hepatitis A (1.9%); hepatitis E (1.4%); leptospirosis (0.14%); were the main infections while no specific diagnosis could be delineated in 11%. Mixed infections were noted in 48 (1.9%) patients.

Conclusion: A good clinical acumen supported by the basic investigations can help diagnose the cause of fever with reasonable certainty.

Keywords: Dengue, Malaria, Scrub typhus, Typhoid

INTRODUCTION

Infectious diseases are leading causes of morbidity and mortality in tropical countries. The term acute undifferentiated febrile illness (AUI) connotes fever of <14 days duration without any evidence of organ or system specific aetiology [1]. In resource limited settings fever may be treated empirically or self treated due to lack of access to diagnostic tests. Thus, knowledge of local prevalence of infections is critical in order to target clinical work up and treatment [2]. There are only a limited number of studies from Northern India reporting on the aetiology of fever and reliable surveillance data are not available [3]. The main objective of this study was to describe the aetiology of fever among patients in a tertiary care hospital in Northern India.

MATERIALS AND METHODS

This was conducted as a retrospective, observational study over a period of 12 months between December 2012 to November 2013 at Himalayan Institute of Medical Sciences, Swami Rama Himalayan University, Dehradun, India. The study included patients (age>18years) presenting with AUI with oral temperature over 38.3°C within last 24 hours, duration of fever ranging from 5-14 days, no specific single organ involvement by history taking and physical examination, normal or non-specific results of the following investigations: complete blood count, thick film for malaria, urinalysis and chest roentgenogram. Diagnosis was confirmed by suitable laboratory tests after exhaustive clinical examination. Patients suffering from more than one infective aetiology were considered as mixed infection.

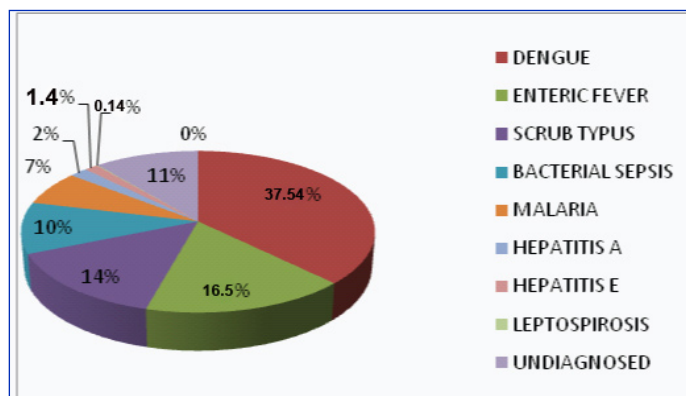
Laboratory tests

Tests had been ordered according to the discretion of the treating physicians and no additional tests were conducted for the purposes of the study. Blood cultures were processed through automated "Bactec 9120" (BD Diagnostics). Malaria was diagnosed with microscopy slides stained with Leishman stain (Fisher scientific) and/or antigen detection by rapid diagnostic kits (QDX). Further

the following microbiological tests were used: Scrub typhus Detect IgM ELISA (InBios International, Inc, USA), Dengue Duo NS1/ IgM Cassette (SD Bioline), Leptospira IgM Cassette (SD Bioline), Widal Ag kit with titres of O₂≥80, H₂≥160 or four fold rise in titres (Febrile Antigen set, Span Diagnostics Ltd., Gujarat, India), Anti HEV IgM EIA (Diasorin, Italy) and Anti HAV IgM EIA (Diasorin, Italy).

RESULTS

A total of 2547 patients with AUI were evaluated. Of these, 1663(65.3%) were males and 884(34.7%) were females. Dengue (37.54%); enteric fever (16.5%); scrub typhus (14.42%); bacterial sepsis (10.3%); malaria (6.8%); hepatitis A (1.9%); Hepatitis E (1.4%); leptospirosis (0.14%); were the main infections while no specific diagnosis could be delineated in 11% as shown in [Table/Fig-1]. Mixed infection was noted in 48(1.88%) patients. Most common mixed infections were Dengue with scrub typhus (15 cases), Malaria with scrub typhus (11 cases) and malaria with dengue (8 cases). Three patients were diagnosed to be suffering from malaria with dengue with scrub typhus. Rest was one case each of different combination of urinary tract infection, malaria, dengue, enteric fever and hepatitis A infection.



[Table/Fig-1]: Aetiological pattern of febrile patients (total no. =2547)

Month	Dengue	Enteric Fever	Scrub Typhus	Malaria	Total (%)
DEC'12	16	14	14	10	54(2.12)
JAN'13	1	4	3	0	8 (0.3)
FEB'13	1	15	5	0	21 (0.8)
MAR'13	1	18	0	1	20 (0.81)
APR'13	2	20	2	7	31 (1.2)
MAY'13	2	30	1	16	49 (1.3)
JUN'13	0	26	2	23	51 (2)
JUL'13	30	25	3	15	73 (2.9)
AUG'13	34	50	71	13	168 (6.5)
SEP'13	94	72	80	90	336(13.19%)
OCT'13	631	108	140	0	879 (34.5)
NOV'13	144	42	46	0	232 (9.1)
TOTAL	956 (37.54%)	424 (16.64%)	367 (14.42%)	175 (6.8%)	1922

[Table/Fig-2]: Month wise distribution of adult febrile patients along with their aetiologies of common causes of fever

Parameters	Dengue (n=956)	Enteric fever (n=424)	Scrub Typhus (n=367)	Malaria (n=175)
Days of hospitalization*	5.4 ± 2.2	3.7 ± 1.4	8.5 ± 3.7	6.5 ± 5.4
Clinical				
Fever	92.7	100	100	100
Abdominal pain	5.4	83.9	8.1	14.2
Altered bowel habits	2.9	70.7	4.0	11.4
Bleeding	5.7	0	0.8	0
Lymphadenopathy	6.0	0	10.0	0
Icterus	1.5	0	15.8	20
Splenomegaly	0.2	20.2	9.8	58.2
Hepatomegaly	16.6	9.9	19.6	61.7
Rash	83.6	0.2	6.2	0
Haematological				
Anaemia	1.0	7.5	86.1	89.1
Leucopenia	92.9	60.3	12.2	65.7
Thrombocytopenia	92.0	28.7	29.9	54.2
Biochemical				
ALT	57.0	59.9	51.4	31.4
AST	70.9	44.3	27.2	26.2
ALP	1.8	3.3	42.5	7.4
Bilirubin	15.1	2.8	48.2	8.0
Albumin	9.9	52.8	48.2	71.4
Azotemia	4.7	2.3	21.5	20.0

[Table/Fig-3]: Clinical and laboratory parameters associated with common aetiological agents of AUI

NOTE: All figures except * are mentioned in percentages; * mentioned as mean ± SD

In our study, AUI occurred most commonly during the months of August, September and October (56.1%) as shown in [Table/Fig-2]. These are the months of monsoon and post monsoon period.

The most common signs and symptoms, deranged laboratory parameters and duration of hospital stay of these febrile illnesses according to their aetiological agents are depicted in [Table/Fig-3].

DISCUSSION

The study revealed the heavy burden of tropical infections such as dengue, enteric fever, scrub typhus and malaria. Previous studies in Northern and Southern parts of the country have shown the similar results [1,4,5]. A similar study conducted by Singh R et al., [6] from the region of Uttarakhand also showed that dengue, malaria, typhoid and enteric fever are the most common aetiological agents of acute febrile illness.

Males were affected twice as that of females. This may be due to their easy exposure to mosquitoes and mites because of their outdoor activities. In our study, AUI occurred most commonly during monsoon and post monsoon seasons (56.1%) as shown in [Table/Fig-2]. For, mosquitoes and mites to breed and thrive, monsoon period is considered the best time. Drinking water is also contaminated during rainy season. All these factors lead to increase in above mentioned causes of fever in these particular months. Seasonal upsurge in fever is also a well known documentation in other studies [5,7,8].

Dengue, malaria, scrub typhus, enteric fever and leptospirosis have been identified as major causes of AUI in Thailand, Malaysia and Nepal [7-11]. Various studies conducted particularly in South India by Chrispal et al., [5], Gopalakrishnan et al., [12], and Kashinkunti et al., [13] have also showed similar results.

In a cohort study by Abrahamsen et al., [14] from Southern India, bacterial infections (38%) and TB (19%) were the most common aetiological agents of fever. Another study from east India [15] reported that TB (53%), neoplasms (17%) and collagen vascular disorders (11%) were the dominant causes.

Mixed infection with more than one aetiological agent can result in an illness with overlapping symptoms, resulting in a situation where the diagnosis and management of such a patient could be challenging for the treating physician [16-20]. Symptoms of one disease may mimic with other disease which are also prevalent in this area. So, patients presenting with acute febrile illness should not be presumed to be suffering from single infection alone. The clinician should investigate thoroughly to look for other causes of fever.

LIMITATIONS

Limitations of the study were that it did not make an exhaustive search into all the causes of fever since viral studies are not available in our institute and it would have increased the cost to the patient. Secondly, the study included only adult patients while children would expect to have different fever aetiologies due to exposure and immunity. Hence, the pattern of fever aetiology found in this study would not be representative for the causes of fever in general population. Further, studies are needed, both community and hospital based including the adult as well as paediatric population in order to provide more evidence based information about the prevalence of aetiologies of fever in tropical country like India.

CONCLUSION

Our study clearly identified the major aetiologies of AUFI in this part of India. Dengue was the commonest cause of AUFI followed by enteric fever, scrub typhus and malaria. Active fever surveillance is necessary as clinical diagnosis is not always sufficient to detect all febrile cases. Laboratory confirmation is essential to refine disease burden estimates of common causes of AUFI. We would recommend establishing accurate epidemiologic database of different aetiologies of fever in every region to anticipate epidemic preparedness in terms of resources and health care delivery.

REFERENCES

- [1] Joshi R, Colford JM, Reingold A. Nonmalarial acute undifferentiated fever in a rural hospital in central India – Diagnostic uncertainty and overtreatment with anti malarial agents. *Am J Trop Med Hyg.* 2008;78(3):393-99.
- [2] Chaturvedi HK, Mahanta J, Pandey A. Treatment-seeking for febrile illness in north-east India: an epidemiological study in the malaria endemic zone. *Malar J.* 2009;8(1):301.
- [3] John TJ, Dandona L, Sharma VP, Kakkar M. Continuing challenge of infectious diseases in India. *Lancet.* 2011;377(9761):252–69.
- [4] Thangarasu S, Natarajan P. A protocol for emergency department management of acute undifferentiated febrile illness in India. *Int Journal of Emer Med.* 2011;4:57.
- [5] 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):230-34.
- [6] 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(6):MC01-03.
- [7] Jena B, Prasad MNV, Murthy S. Demand pattern of medical emergency services for infectious diseases in Andhra Pradesh – A geo-spatial temporal analysis of fever cases. *Indian Emergency Journal.* 2010;1(5):821.
- [8] 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):670–75.
- [9] Sripandikulchai R, Lumbiganon P. Aetiology of obscure fever in children at a university hospital in northeast Thailand. *Southeast Asian J Trop Med Public Health.* 2005; 36:1243–46.
- [10] Leelarasamee A, Chupaprawan C, Chenchittikul M, Udompanthurat S. Aetiologies of acute undifferentiated febrile illness in Thailand. *J Med Assoc Thai.* 2004;87:464–72.
- [11] Ellis RD, Fukuda MM, McDaniel P, Welch K, Nisalak A, Murray CK, et al. Causes of fever in adults on the Thai-Myanmar border. *Am J Trop Med Hyg.* 2006;74:108-13.
- [12] Gopalakrishnan S, Arumugam B, Kandasamy S, Rajendran S, Krishnan B. Acute undifferentiated febrile illness among adults - A hospital based observational study. *J Evolution Medical Dental Sciences.* 2013;2(14):2305-19.
- [13] 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(2):3399-402.
- [14] Abrahamsen SK, Haugen CN, Rupali P, Mathai D, Langeland N, Eide GE, et al. Fever in the tropics: aetiology and case fatality – a prospective observational study in a tertiary care hospital in south India. *BMC Infectious Diseases.* 2013;13:355.
- [15] Kejarawal D, Sarkar N, Chakraborti SK, Agarwal V, Roy S. Pyrexia of unknown origin: a prospective study of 100 cases. *J Postgrad Med.* 2001;47(2):104-07.
- [16] Pradutkanchana J, Pradutkanchana S, Kemapanmanus M, Wuthipum N, Silpajajakul K. The aetiology of acute pyrexia of unknown origin in children after a flood. *Southeast Asian J Trop Med Public Health.* 2003;34:175–78.
- [17] 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).
- [18] 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.
- [19] Singhsilarak T, Phongtananant S, Jenjittikul M, Watt G, Tangpakdee N, Popak N, et al. Possible acute coinfections in Thai malaria patients. *Southeast Asian J Trop Med Public Health.* 2006;37:1-4.
- [20] 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. (cited 2012 Jul 25).

PARTICULARS OF CONTRIBUTORS:

1. Assistant Professor, Department of Microbiology, Himalayan Institute of Medical Sciences, SRH University, Jolly Grant, Dehradun, Uttarakhand, India.
2. Associate Professor, Department of Medicine, Himalayan Institute of Medical Sciences, SRH University, Jolly Grant, Dehradun, Uttarakhand, India.
3. Professor and Head, Department of Microbiology, Himalayan Institute of Medical Sciences, SRH University, Jolly Grant, Dehradun, Uttarakhand, India.
4. Associate Professor, Department of Medicine, Himalayan Institute of Medical Sciences, SRH University, Jolly Grant, Dehradun, Uttarakhand, India.
5. Associate Professor, Department of Neurology, Himalayan Institute of Medical Sciences, SRH University, Jolly Grant, Dehradun, Uttarakhand, India.
6. Postgraduate, Department of Microbiology, Himalayan Institute of Medical Sciences, SRH University, Jolly Grant, Dehradun, Uttarakhand, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Garima Mittal,
Assistant Professor, Department of Microbiology, Himalayan Institute of Medical Sciences, SRH University,
Jolly Grant, Dehradun, Uttarakhand, India.
E-mail: garimamittal80@gmail.com

Date of Submission: **Sep 09, 2014**
Date of Peer Review: **Dec 16, 2014**
Date of Acceptance: **Jan 30, 2015**
Date of Publishing: **Dec 01, 2015**

FINANCIAL OR OTHER COMPETING INTERESTS: None.