Iranian Journal of Microbiology

Volume 17 Number 6 (December 2025) 961-965
DOI: http://doi.org/10.18502/ijm.v17i6.20364

ORIGINAL ARTICLE

The etiology of acute infectious febrile illnesses at a tertiary care hospital: an experience from a hilly region of Uttarakhand

Yogita Rawat, Shekhar Pal, Arti Negi, Uneza Husain*, Rahul Nath, Nidhi Negi

Department of Microbiology, Government Doon Medical College, Dehradun, Uttarakhand, India

Received: June 2024**, Accepted:** November 2025

ABSTRACT

Background and Objectives: The differential diagnosis of acute febrile illness (AFI) is influenced by the regional distribution of prevalent diseases. Hence, in our hospital-based data analysis, we evaluated the AFI cases presented to our center to raise awareness among clinicians and microbiologists regarding the percentage positivity of the prevailing diseases in the context of AFI based on serology, in and around the city of Dehradun.

Materials and Methods: A total of 38,869 suspected AFI patients were enrolled in the study, and their specimens were analysed for infectious etiologies, including dengue, malaria, enteric fever, and scrub typhus by antigen-antibody based detection methods.

Results: Data analysis conducted from September 2021 to December 2022 among patients with AFI revealed that enteric fever, dengue, scrub typhus, and malaria accounted for 12.65%, 7.37%, 1.44%, and 0.18% of cases, respectively.

Conclusion: Since enteric fever followed by dengue was found to be contributing the maximum, mass education regarding safe drinking water, hygiene, sanitation, and strengthening of vector control measures is the need of the hour.

Keywords: Acute febrile illness; *Salmonella*; Fever; Scrub typhus; Malaria

INTRODUCTION

Acute febrile illnesses (AFI) are responsible for the majority of outpatient visits in hospitals. Any fever of up to two weeks' duration, rapid in onset, caused by diverse pathogens, and without any evidence of organ or system-specific etiology, is defined as AFI. The various differentials of AFI in India include dengue, typhoid fever, chikungunya, malaria, leptospirosis, and rickettsial infections (1-3). Dengue, one of the most important contributors of AFI, is transmitted by the bite of infected mosquitoes such as *Aedes aegypti* or *Aedes albopictus.* The incidence of the disease has increased enormously (up to 30-fold) during the past five decades (4). Typhoidal Salmonellae such as *Salmonella typhi* and *Salmonella paratyphi* are transmitted through contaminated food or water, and hence enteric fever is a major public health concern in developing countries. The incidence rate of malaria (transmitted by being bitten by an infected female *Anopheles* mosquito) has subsided over the years, while scrub typhus, which is caused by chigger bites harboring *Orientia tsutsugamushi*, has increased in India (5-7). For dengue and scrub typhus, serology and Polymerase Chain Reaction (PCR) constitute the major investigations. For malaria, various diagnostic options include microscopy, rapid diagnostic tests, and PCR, while the commonly used tests for the detection of enteric fever in most of the laboratories are culture, the Widal test (tube/slide), and IgM/IgG rap-

*Corresponding author: Uneza Husain, MD, Department of Microbiology, Government Doon Medical College, Dehradun, Uttarakhand, India. Tel: +135-2722829 Email: uneza47@gmail.com

Copyright © 2025 The Authors. Published by Tehran University of Medical Sciences.
This work is licensed under a Creative Commons Attribution-Non Commercial 4.0 International license (https://creativecommons.org/licenses/by-nc/4.0/). Noncommercial uses of the work are permitted, provided the original work is properly cited.

id point-of-care tests. Timely use of diagnostic tests supporting the presence of infection is extremely helpful and often acts as a lifesaver for patients. In hospital settings, rapid diagnostic tests give the result in minutes or hours, giving the clinicians enough time to manage the patient in a focused manner rather than thinking broadly, keeping all the differentials in mind, and getting confused. Empirical treatment should be kept limited as far as possible. The present study aims to evaluate the suspected cases of acute febrile illnesses based on seropositivity to ascertain the burden of the various diseases that are attributed to such illnesses in patients presenting at our center in Uttarakhand. In addition, knowledge of the exact etiology is essential nowadays due to the incorporation of various antimicrobial stewardship programs that teach us to treat according to pathogen-specific guidelines to combat antimicrobial resistance.

MATERIALS AND METHODS

Study design. It is a descriptive cross-sectional study.

Study participants. In the present study, all the suspected cases of acute febrile illness presenting in outpatient departments (OPD) and/or indoor patients of a tertiary care hospital in Dehradun were included. A total of 38869 patients were enrolled in the study.

Study duration. The study was done between September 2021 and December 2022.

Procedure. Several rapid detection tests were used. Malaria was detected using the Standard Q Malaria P.f/Pan antigen test (S D Biosensor Healthcare Pvt. Ltd.). For enteric fever, the Typhoid IgG & IgM antibody test (BIOGENIX Inc Pvt. Ltd.) and the slide Widal test (ARKRAY Healthcare Pvt. Ltd.) were used. Scrub typhus was detected with the TRUSTline IgG & IgM antibody test (Athenese-Dx Pvt. Ltd.), and dengue was tested using the Q-Line/Standard Q Dengue Ag +Ab kit (Q-Line Biotech Pvt. Ltd. / S D BIOSENSOR Healthcare Pvt. Ltd.) for NS1 antigens and IgM/IgG antibodies. The age, sex, and seasonal distribution of the cases were also assessed.

Statistical analysis. The adequate sample size was found to be 381 using the following formula:

$n= [z^2 p(1 - p) / e^2] / [1 + \{(z^2 p (1 - p) / e^2)-1/N\}]$

n = sample size

N =population size

z =standard normal variate based on the confidence coefficient

p = estimate for population proportion

e = specified margin of error

All the relevant data collected from the laboratory information system were entered in a Microsoft Excel (Microsoft Corporation, Redmond, Washington, United States) spreadsheet. In the present study, descriptive statistics were applied. Categorical data were presented in the form of frequency or proportions.

Ethical approval. The study was done after approval by the research review board and Institutional Ethics Committee (IEC Ref No: GDMC/IEC/2023/46).

RESULTS

Out of 38,869 enrolled patients with suspected AFI, serological methods detected dengue in 7.37% (800/10,852), malaria in 0.18% (15/8,138), enteric fever in 12.65% (1,970/15,568), and scrub typhus in 1.44% (62/4,311) of cases. The total prevalence of a confirmed infective etiology was 7.32% (2,847/38,869), as shown in Table 1. Of these seropositive cases, 1,378 were male and 1,469 were female, yielding a male-to-female ratio of 0.9:1 (Table 2). Maximum AFI cases with infective etiology were reported in the age group of 20-29 years, followed by 30-39 years. The 20-29 years age group was the most common among patients with dengue, typhoid, and malaria. In contrast, scrub typhus was most frequent in the 20-29 and 50-59 year age groups in equal numbers (Fig. 1). Seasonal distribution in 2022 showed the maximum number of cases in September-October for typhoid and dengue, while the peak occurred in October-November for malaria and scrub typhus, as shown in Table 1.

DISCUSSION

Acute infectious febrile illnesses pose a significant public health concern worldwide, particularly in tropical and subtropical regions. Vector-borne infectious diseases such as malaria, dengue, chikun-

Table 1. Month-wise distribution of dengue cases, scrub typhus, malaria, and enteric fever cases (expressed as number and percentage)

Month	Dengue		Scrub Typhus		Malaria		Enteric fever	
	Total positive [(N (%)]	Total tested (N)	Total positive [(N (%)]	Total tested (N)	Total positive [(N (%)]	Total tested (N)	Total positive [(N (%)]	Total tested (N)
2021								
September	31 (6.3%)	496	23 (10.1%)	227	5 (0.9%)	565	68 (8.5%)	802
October	70 (12.6%)	557	0 (0 %)	259	1 (0.3%)	381	100 (14.2%)	703
November	58 (10.5%)	553	5 (2.1%)	234	1 (0.3%)	384	103 (16.1%)	638
December	49 (9.5%)	514	4 (1.8%)	219	0 (0 %)	309	93 (15.3%)	606
2022								
January	0 (0 %)	75	0 (0 %)	54	0 (0 %)	76	26 (12%)	216
February	0 (0 %)	34	1 (3.4%)	29	0 (0 %)	60	39 (18.3%)	213
March	0 (0 %)	77	1 (1.2%)	84	1 (0.7%)	148	41 (9.2%)	446
April	1 (0.8%)	125	3 (3.9%)	76	0 (0 %)	188	35 (7.5%)	468
May	1 (0.6%)	175	1 (0.6 %)	155	0 (0 %)	232	34 (5.9%)	574
June	0 (0 %)	196	1 (0.7%)	143	0 (0 %)	243	13 (1.7%)	768
July	2 (0.7%)	286	0 (0 %)	228	0 (0 %)	351	88 (9.3%)	943
August	10 (1.6%)	621	0 (0 %)	293	0 (0 %)	509	156 (12.8%)	1216
September	154 (6.7%)	2295	4 (0.5 %)	766	0 (0 %)	1625	267 (10%)	2670
October	291 (9.7%)	3012	9 (0.96 %)	942	5 (0.3%)	1983	666 (20.7%)	3224
November	122 (8.5%)	1436	8 (1.8 %)	439	2 (0.3%)	794	203 (13.2%)	1534
December	11 (2.8%)	400	2 (1.2%)	163	0 (0 %)	290	38 (6.9%)	547
Total	800 (7.37%)	10852	62 (1.44%)	4311	15 (0.18%)	8138	1970 (12.65%)	15568

Table 2. Gender-wise distribution of dengue, scrub typhus, enteric fever, and malaria cases (expressed as number and percentage)

Disease	Male [(N (%)]	Female [(N (%)]
Dengue	469 (58.6%)	331 (41.4%)
Scrub Typhus	30 (48.4%)	32 (51.6%)
Malaria	6 (40%)	9 (60%)
Enteric fever	873 (44.3%)	1097 (55.7%)
Total	1378 (48.4%)	1469 (51.6%)

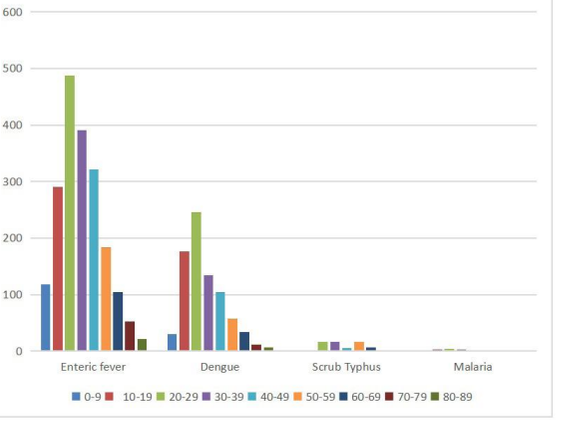

Fig. 1. Age-wise (years) distribution of dengue, scrub typhus, malaria, and enteric fever cases (expressed as a number)

gunya, and scrub typhus contribute significantly to the etiology of AFI in India (8). There has been a resurgence of scrub typhus (a re-emerging rickettsial disease) in the recent past (5, 9). The increased availability of molecular methods and growing clinician awareness have led to enhanced testing, making scrub typhus one of the top causes of AFI. Previously published data suggested that scrub typhus shows variable presentation in the form of fever, nausea/vomiting, shortness of breath, cough, headache, and altered sensorium (10). Eschar may not be visible in cases of scrub typhus; hence, serology plays an important role. In a study done by Shelke et al., among 270 patients with a history of acute undifferentiated febrile illness (AUFI) who were analyzed for various etiologies, 47% (127) were of scrub typhus, 12% (33) were malaria cases, 17.40% (47) were dengue,

4% (12) were enteric fever, 2% (5) were leptospirosis, undiagnosed was 6.66% (18), while other infections such as viral, upper and lower respiratory tract infection, urinary tract infection, and acute gastroenteritis constituted 10.37% (28) cases (2). In a retrospective study done by Rani et al. from Tamil Nadu, among 200 patients with acute febrile illness (AFI), dengue was the most common cause, detected in 27% of cases (54). Other causes included typhoid (3%; 6 cases), malaria (2%; 4 cases), and rickettsial infections (1%; 2 cases) (1). In the present study, data analysis of AFI patients showed that enteric fever, dengue, scrub typhus, and malaria accounted for 12.65%, 7.37%, 1.44%, and 0.18% of cases, respectively (as detected by serology). Enteric fever (the leading contributor of AFI in our study) remains a major global health issue, especially in areas with poor sanitation and limited access to clean water. The classic symptoms include sustained fever, headache, malaise, abdominal pain, diarrhea or constipation, and sometimes rash. Bone marrow culture (though seldom used) is the gold standard test for the diagnosis of enteric fever. It is considered more sensitive than blood culture, as a larger number of microorganisms exist in the bone marrow (11). Apart from bacterial culture, serology and molecular methods like PCR are becoming increasingly popular. The simplicity of lateral flow tests and the extent of information that can be derived from a small quantity of readily obtainable biological samples currently position serology as the most probable immediate diagnostic option (12). Differentiating scrub typhus from enteric fever is very challenging, and clinicians always face a dilemma in framing the actual diagnosis until the laboratory investigation reports mention the exact etiology. Hence, rapid point-of-care tests provide a great rescue for the clinician starting pathogen-directed therapy. The present study data, based on the percentage positivity of etiology of AFI, will be helpful for clinicians for early diagnosis and prompt management. The study was associated with a few limitations. As our study included only symptomatic patients (either admitted or outpatient) from our hospital, we could not evaluate the spectrum of these diseases amongst those patients not turning up in our hospital. A limited number of etiological agents responsible for causing AFI were investigated due to limited resources, which included laboratory diagnostic capacity. Use of the Widal test for the diagnosis of enteric fever may have missed a few early cases of enteric fever. ELISA or CLIA (Chemiluminescence immunoassay)-based tests were not used for the diagnosis of dengue.

CONCLUSION

Enteric fever and dengue are still important differentials of AFI in Uttarakhand, as can be inferred from the data of our center. Hence, preventive measures like mass education regarding the use of safe drinking water, hygiene, sanitation, and strengthening of vector control measures should be implemented to avoid the clustering of cases and associated complications. Further research and development in the context of entomological studies can augment existing investigations and aid in better understanding the current burden of AFI in Uttarakhand.

REFERENCES

1. Wangdi K, Kasturiaratchi K, Nery SV, Lau CL, Gray DJ, Clements ACA. Diversity of infectious aetiologies of acute undifferentiated febrile illnesses in south and Southeast Asia: a systematic review. *BMC Infect Dis* 2019; 19: 577.
2. Shelke YP, Deotale VS, Maraskolhe DL. Spectrum of infections in acute febrile illness in central India. *Indian J Med Microbiol* 2017; 35: 480-484.
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: 114-117.
4. Tissera H, Samaraweera P, de Boer M, Gandhi S, Malvaux L, Mehta S, et al. The Burden of Acute Febrile Illness Attributable to dengue virus infection in Sri Lanka: A Single-Center 2-Year Prospective cohort study (2016-2019). *Am J Trop Med Hyg* 2021; 106: 160-167.
5. Devasagayam E, Dayanand D, Kundu D, Kamath MS, Kirubakaran R, Varghese GM. The burden of scrub typhus in India: A systematic review. *PLoS Negl Trop Dis* 2021; 15(7): e0009619.
6. Husain U, Kalyan RK, Jahan A, Gupta KK, Verma SK. Scrub Typhus and its co-infection with Leptospirosis at a tertiary care hospital in Uttar Pradesh. *Trop Doct* 2022; 52: 302-303.
7. Panda S, Swain SK, Sarangi R. An epidemiological outbreak of scrub typhus caused by Orientia tsutsugamushi - A comprehensive review. *J App Biol Biotechnol* 2022; 10: 76-83.

8. Robinson ML, Kadam D, Khadse S, Balasubramanian U, Raichur P, Valvi C, et al. Vector-Borne disease is a common cause of hospitalized febrile Illness in India. *Am J Trop Med Hyg* 2018; 98: 1526-1533.
9. Chakraborty S, Sarma N. Scrub Typhus: An Emerging Threat. *Indian J Dermatol* 2017, 62: 478-485.
10. Varghese GM, Trowbridge P, Janardhanan J, Thomas K, Peter JV, Mathews P, et al. Clinical profile and improving mortality trend of scrub typhus in South India. *Int J Infect Dis* 2014; 23: 39-43.
11. Bhandari J, Thada PK, Hashmi TM, DeVos E (2024). Typhoid Fever. In: StatPearls. Treasure Island (FL): StatPearls Publishing, Available from: https://www.ncbi.nlm.nih.gov/books/NBK557513/
12. Baker S, Blohmke CJ, Maes M, Johnston PI, Darton TC. The current status of enteric fever diagnostics and implications for disease Control. *Clin Infect Dis* 2020; 71(Suppl 2): S64-S70.