

Technical and Alarm signs for referral in adult patients with acute febrile illness: A study from a tertiary care hospital in North India

Nitin Gupta¹, Ankit Mittal¹, Sharada V. Kutty¹, Arvind Kumar¹, Naveet Wig¹

¹Department of Medicine, All India Institute of Medical Sciences, New Delhi, India

ABSTRACT

Context: There is a huge burden of patients with acute febrile illness (AFI) during the post-monsoon season in India. It is very important to have a functioning triage system, whereby patients with high likelihood of developing a severe illness are referred to higher levels of care. **Aim:** The objective of this study was to identify the alarm signs which would help in triaging of those patients with AFI without any specific diagnosis. **Methods:** This was a retrospective review of records, whereby clinical and laboratory parameters of patients with AFI admitted in our tertiary care center between July 2016 and October 2016 were reviewed. **Statistical Analysis Used:** Appropriate tests of significance were applied using SPSS 21(Chicago, IL, USA) to find statistically significant differences between those who required mechanical ventilation, intensive care, inotropic support, or higher intravenous antibiotics and those who recovered with minimal supportive care. **Results:** Presence of comorbidities, dyspnea, altered sensorium, features of myocarditis, hypotension, leukocytosis ($>11,000/\mu\text{L}$), and acute kidney injury were significantly associated with requirement of higher levels of care, while presence of arthralgia, serositis, and leucopenia indicated a higher likelihood of recovery with minimal support. **Conclusion:** This article highlights the possibility of identification of simple alarm signs in patients with AFI which would indicate the need for higher levels of care.

Keywords: Chikungunya, dengue, malaria

Introduction

In tropical countries such as India, the months of July–October see a huge upsurge in the number of patient admissions due to acute febrile illnesses (AFIs).^[1] These diseases have varied clinical courses ranging from spontaneous recovery to acute fatality. In a developing country like India, this results in a huge burden on all levels of healthcare. The triage of these patients has always been a challenging task, as there are very few studies on predictors of severe disease in patients with AFI without any specific diagnosis.^[2] Consequently, not all patients admitted in the lower levels of healthcare get timely referral. Even though individual

predictors of severity for certain tropical fevers such as dengue and malaria have been proposed, it requires categorization of patients with AFI into individual diseases.^[3,4] The lack of properly functioning round the clock laboratory services further delays the diagnosis in such cases. The objective of this study was to identify the clinical and laboratory parameters, which are significantly associated with severe disease requiring higher levels of care.

Materials and Methods

This was a retrospective review of records, whereby all records of patients with AFI (fever <15 days) who were admitted between July 2016 and October 2016 in one medical unit of our apex care center (All India Institute of Medical Sciences) were reviewed. The clinical and laboratory parameters, final diagnosis, and

Address for correspondence: Dr. Naveet Wig,

3rd Floor, teaching block, Department of Medicine, AIIMS,
New Delhi - 110 029, India.

E-mail: naveetwig@gmail.com

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outcomes were recorded using a detailed proforma. Data were then entered into an Excel sheet. The patients were then divided into two groups. Group 1 consisted of those people who required mechanical ventilation, intensive care, inotropic support, or higher intravenous antibiotics (betalactam/betalactamase inhibitor combination or carbapenems for more than 10 days). All others were grouped under group 2. Appropriate tests of significance were applied using SPSS 21(Chicago, IL, USA) to find statistically significant differences between the two groups.

Results

A total of 53 patients between the age range of 14 and 77 years with AFI (<15 days of fever) were admitted in our unit between July and October, 2016 (July 5, August 16, September 19, October 13). The patients were referred from various parts of North India (Delhi 37, Bihar 4, Haryana 6, Madhya Pradesh 1, Uttar Pradesh 3, West Bengal 2). Seven patients required care in the intensive care unit (ICU). The stay in ICU ranged between 2 and 23 days with a mean of 6 days. A total of 11 patients required mechanical ventilation. Four of these patients developed ventilator-associated pneumonia. A total of 24 patients needed antibiotics during admissions. Among those who received antibiotics, the average duration of antibiotic administration was 7 ± 6 days. The following antibiotics were used for varying durations:

ceftriaxone ($n = 24$), doxycycline ($n = 13$), levofloxacin ($n = 13$), cefoperazone–sulbactam ($n = 10$), piperacillin–tazobactam ($n = 9$), clindamycin ($n = 9$), azithromycin ($n = 9$), vancomycin ($n = 7$), linezolid ($n = 3$), teicoplanin ($n = 4$), metronidazole ($n = 3$), amoxicillin–clavulanate ($n = 3$), amikacin ($n = 2$), and meropenem ($n = 1$). A total of 16 patients developed hypotension and 12 required inotropic support. A total of 10 patients were either in sepsis at the time of admission or developed sepsis during the course of hospital stay. A total of eight patients died during the hospital stay. Platelet transfusion was required in 20 patients. The use of steroids was required in eight patients. Hematological and biochemical parameters of the patients are summarized in Table 1. The following diagnostic outcomes were observed on the basis of clinical features, microbiological investigations, and response to treatment: dengue ($n = 17$), chikungunya ($n = 13$), malaria ($n = 6$), community-acquired pneumonia ($n = 5$), scrub typhus ($n = 3$), malaria–dengue coinfection ($n = 1$), tubercular meningitis ($n = 1$), urinary tract infection ($n = 3$), dengue–chikungunya coinfection ($n = 1$), chicken pox ($n = 1$), and acute undifferentiated febrile illness ($n = 2$).

The patients were divided into two groups; group 1 had 17 patients, while group 2 had 36 patients. The following parameters were more commonly seen in group 1 than in group 2: presence of comorbidities, dyspnea, altered sensorium, features of myocarditis, hypotension, leukocytosis ($>11,000/\mu\text{L}$), and

Table 1: Clinical and laboratory parameters of patients with acute febrile illness categorized into group 1 and group 2

Parameters	Group 1	Group 2	P
Age, years (mean)	44±19	31±14	0.023
Sex	Male 11 (64%), female 6 (36%)	Male 25 (70%), female 11 (30%)	0.730
Comorbidities	9 (53%)	6 (44%)	0.006
Total duration of fever before admission (mean)	6.24±3	6.17±3	0.590
Myalgia	7 (41%)	22 (61%)	0.174
Headache	5 (30%)	16 (44%)	0.296
Arthralgia	1 (6%)	19 (53%)	0.001
Rash	2 (12%)	5 (14%)	0.831
Dyspnea	12 (71%)	8 (22%)	0.001
Altered sensorium	6 (36%)	1 (3%)	0.001
Abdominal pain	4 (24%)	13 (36%)	0.430
Vomiting	5 (30%)	13 (36%)	0.151
Diarrhea	2 (12%)	3 (8%)	0.638
Myocarditis	5 (30%)	1 (3%)	0.004
Bleeding manifestations	2 (12%)	9 (25%)	0.267
Hypotension	12 (71%)	4 (11%)	0.000
Rash	2 (12%)	5 (14%)	0.831
Icterus	4 (24%)	4 (11%)	0.238
Serositis	2 (12%)	16 (44%)	0.019
Hepatomegaly	2 (12%)	6 (17%)	0.642
Splenomegaly	2 (12%)	5 (14%)	0.831
Anemia	11 (65%)	13 (36%)	0.051
Leucopenia	1 (6%)	14 (39%)	0.013
Leukocytosis	15 (88%)	8 (22%)	0.000
Thrombocytopenia	12 (71%)	31 (86%)	0.051
Transaminitis	14 (82%)	28 (78%)	0.701
Requiring platelet transfusion	3 (18%)	17 (47%)	0.038
Acute kidney injury	13 (76%)	3 (8%)	0.00

acute kidney injury (AKI). The following parameters were more commonly seen in group 2: presence of arthralgia (large and small joint), serositis (pleural effusion or ascites or gall bladder edema) and leucopenia ($<4000/\mu\text{L}$). The mean age was significantly higher in group 1 than in group 2.

Discussion

Patients with AFIs are more likely to encounter primary care physicians at the onset of their illness. Although most of these AFIs are self-limiting, it is important for the primary care physicians to identify the ones that may require higher levels of care. Distinguishing low-risk from high-risk patients can be challenging. However, certain clinical features may point toward disease severity and help the physician promptly refer the patient to a higher center. Although there are studies predicting severity in individual diseases, there are no such studies on alarm signs for referral in adult patients presenting with fever. These alarm features could be useful especially in the months of monsoon in India when there is an outbreak of vector borne diseases (dengue, malaria, chikungunya) every year. Some of the patients at low risk end up being referred to a higher center, whereas some who actually require referral might be missed. In developing settings, the option of triage without the compulsion of diagnosis may avoid overwhelming the health system and help us in rationing the limited resources. The economic burden of dengue itself is huge in most parts of India. In an estimate, the average medical cost of a dengue case in 2012 was \$235.20, if hospitalized.^[5]

Higher age and presence of comorbidities were found to be significant factors indicating a requirement of higher levels of care. In a study from Kerala, age >40 years and presence of comorbidities were associated with higher mortality in dengue patients.^[6] Similarly, in a study from Pakistan, increasing age in dengue was found to be a significant factor associated with prolonged stay.^[7] Clinical features such as dyspnea, altered sensorium, features of myocarditis, and hypotension were indicative of the fact that the patient needed earlier referral. In a study from Taiwan, a lower Glasgow coma score was associated with higher mortality.^[8] In a systematic review and meta-analysis, coma score, hypoglycemia, and shock were significant predictors of mortality.^[9] In a study on adult patients with malaria from India, longer duration of fever, decreased urine output, jaundice, and altered sensorium were predictors of severe malaria.^[10] In a study from Sierra Leone, hypotension was a significant predictor of mortality in all febrile patients.^[11] Leukocytosis ($>11,000/\mu\text{L}$) and AKI were laboratory features that predicted the need for referral. AKI has been shown to be a predictor of mortality in dengue patients in other studies as well.^[8] Acute respiratory distress syndrome and AKI were significant predictors of mortality in patients with scrub typhus in an Indian study.^[12] In a study from Delhi, higher age, dyspnea, altered sensorium, and leukocytosis were significantly associated with severe disease/mortality. Presence of arthralgia and leucopenia was associated with milder variants of disease,

probably because these features are more commonly associated with chikungunya (compared to dengue) which rarely has severe manifestations.^[13]

Conclusion

This article highlights the possibility of identification of simple alarm signs in patients with AFI without a diagnosis. These alarm signs can be used by the primary care physicians to identify the need of higher levels of care in patients with AFIs.

Limitations

This was a retrospective study with a very small sample size. There is a need for multicentric prospective studies with larger sample size study ranging over few seasons.

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Conflicts of interest

There are no conflicts of interest.

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