Original Article

Clinical, Biochemical, and Hematological Pointers toward Dengue Infection in Patients with Acute Undifferentiated Fever

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Abstract

Background: Acute undifferentiated fever (AUF) is fever of < 3 weeks duration with no organ-specific disease features. Dengue infection occurs throughout the year and accounts for about 5% of the cases of AUF. The prompt and appropriate diagnosis will help avoid the use of antibiotics and antimalarials. The tests for carrying out screening for dengue infection are not universally available and are expensive. Hence, the need for appropriate clinical, biochemical, and hematological pointers toward the diagnosis of dengue and it's complications.

Materials and Methods: It is a prospective observational study at MIMS, Mandya. The patient's data, platelet count, mean platelet volume (MPV), platelet distribution width (PDW), biochemical parameters, and clinical characteristics were selected using standard pro forma.

Results: Out of 162 patients with an acute differentiated fever, 15 patients had dengue fever, A headache was present in all patients with dengue fever and was statistically significant. Thrombocytopenia, decreased MPV and PDW, was associated with dengue fever and was statistically significant.

Conclusion: The hematological parameters like reduced platelet count, MPV and PDW in patients with AUF significantly points toward possibility of dengue fever.

Key words: Acute undifferentiated fever, Dengue fever, Mean platelet volume, Platelet count, Platelet distribution width

INTRODUCTION

Acute undifferentiated fever (AUF) is fever of <3 weeks duration with no organ-specific disease features. AUF accounts for vast majority of outpatient visits and inpatient admissions in India.[1] The causes for the same are variable and a systematic approach to identify the cause is necessary, for appropriate therapy. Most of the cases of dengue infection occur during the post-monsoon period.[2] However, dengue infection occurs throughout the year and accounts for about 5% of the cases of AUF.[3] The prompt and appropriate diagnosis will help avoid the use of antibiotics and antimalarials.[1] It also helps in the early recognition of complications and their management. The tests for carrying out screening for dengue infection are not universally available and are expensive. Hence, the need for appropriate clinical, biochemical, and hematological pointers toward the diagnosis of dengue and it's complications.

Aims and Objectives
- To identify clinical features, biochemical and hematological parameters in patients with AUF, which are suggestive of dengue infection.
- To identify clinical features, biochemical and hematological parameters which help in assessment of severity of dengue infection.

MATERIALS AND METHODS

The patients presenting with fever of <15 days with no localizing symptoms and signs were included in the study.

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The clinical features of the patient were noted. The routine biochemical (renal function tests and liver function tests) and hematological parameters done as a part of the fever workup was collected. The patients were screened for dengue infection using NS1 antigen and IgM antibodies. The data were collected in specially designed pro forma and analyzed. A platelet counts <1,50,000 cells/mm,[3] mean platelet volume (MPV) <9 fl and platelet distribution width (PDW) <13 were taken as reduced.

Study Site
Mandya Institute of Medical Sciences, Mandya.

Source of Data
Outpatients attending the Medical out-patient department and inpatients admitted in medical wards and MIMS, Mandya.

Study Design
Prospective observational study.

Inclusion Criteria
Patients over the age of 14 years admitted with fever of <15 days duration with no localizing features.

Exclusion Criteria
- Fever of more than 15 days duration
- Age <14 years
- Retroviral positive disease
- Localized causes of fever like abscess, pneumonia, meningitis, etc.

The statistical significance was assessed by measuring P value. A $P < 0.05$ was considered statistically significant.

RESULTS

This is an interim report after 4 months a 1 year study. The study screened a total of 162 patients with AUF. A total of 15 patients were diagnosed with dengue infection (11 NS1 positive and 4 IgM reactive).

The presence of headache, thrombocytopenia, decreased MPV and PDW had statistically significant association with dengue fever in patients with AUF. A headache was present in all patients with dengue fever. The presence of myalgia and arthralgia were much common in patients with dengue fever but was not statistically significant.

DISCUSSION

Dengue infection is an acute infection caused by single-stranded RNA virus belonging to genus Flavivirus. There are four serotypes of dengue virus. The infection is transmitted by the bite of Aedes mosquitoes. The incubation period ranges from 4 to 10 days. The illness progresses through three phases, febrile phase, critical phase, and recovery phase. Symptomatic dengue infection is grouped by the WHO and divided into three categories.[4]
- Undifferentiated fever
- Dengue fever
- Dengue hemorrhagic fever.

Plasma leakage, hemoconcentration, and abnormalities in homeostasis characterize severe dengue. The mechanisms leading to severe illness are not well defined but the immune response, the genetic background of the individual and the virus characteristics may all contribute to severe dengue. With appropriate initiation of therapy, the case fatality rate is <1%.[4]

The cause of the AUF varies depending on the season and the geographic location. Various studies have reported diagnosis of malaria in 5-50% cases, scrub typhus/Rickettsia fevers in 4-49% cases, enteric fever in 7-30% cases, dengue in 4-19% cases, leptospirosis in 3-10% cases, and influenza in 8-12% cases.[1]

The API guidelines[1] for the management of AUF recommends screening for malaria in all cases by microscopy or rapid diagnostic tests (RDT). The microscopy has sensitivity and specificity of 99.6% and 100% respectively for diagnosis of malaria.[5] If negative for malaria, the patient should be screened for dengue fever. NS-1 antigen-based test is the first step for detection for dengue fever. NS-1 antigen positivity appears on the first day of fever, and may last till ninth day. When NS-1

Table 1: Characteristics of dengue and non-dengue acute febrile illness

Characteristic	Dengue fever (%)	Non-dengue acute febrile illness (%)	P value
Gender			
Male	11 (66.7)	118 (80.3)	0.51
Female	4 (33.3)	29 (20.7)	
Clinical features			
Headache	15 (100)	23 (15.7)	0.0001
Myalgia	12 (80)	88 (59.9)	0.1668
Arthralgia	13 (86.7)	92 (62.6)	0.0877
Sore throat	2 (13.3)	63 (42.9)	0.0146
Lymphadenopathy	0 (0)	16 (10.9)	0.3661
Laboratory investigations			
Increased AST	4 (33.3)	33 (22.4)	0.7486
Elevated creatinine	1 (6.7)	13 (8.8)	1.0000
Leukocytosis	8 (53.3)	79 (53.7)	0.5828
Thrombocytopenia	11 (66.7)	17 (11.6)	0.0001
Decreased MPV	13 (86.7)	9 (6.1)	0.0001
Decreased PDW	12 (80)	18 (12.2)	0.0001
Total	15	147	

MPV: Mean platelet volume, PDW: Platelet distribution width

antigen based rapid test is combined with IgM ELISA, the sensitivity of diagnosis of early dengue reaches 93% and the specificity hovers around 83%. RDT for IgM antibody detection against dengue is useful after the 5th day of fever, as the test is negative early in the course of disease.[6] IfNS-1 or IgM based RDT for dengue is positive, patients must receive guideline-based care for dengue.[5]

In a study conducted in Srilanka by Reller *et al.*,[7] a headache was the most frequent (75.9%) symptom, and lethargy and muscle and joint pain were also reported by >50% of patients with dengue; however, these symptoms were just as frequent in patients without dengue. These findings are similar to our study. Patients with dengue were less likely than those without it to report a cough and sore throat and to have lymphadenopathy, and same was observed in the study.

In a study conducted by Kashikunti *et al.*,[8] leukocytosis, acute respiratory distress syndrome, aseptic meningitis, mild serum transaminase elevation, and hypoalbuminemia, in AUF were associated with scrub typhus and dengue. In a study conducted on children with AUF between the ages of 6 months with 12 years, young age, rash, and raised alanine transaminase (ALT) were significant independent pointers to dengue.[3]

Bashir *et al.*[9] observed that low platelet count, MPV and platelet distribution width PDW may be used as probable indicators for dengue in an endemic area. MPV <9 fl and PDW >13 fl shows considerable sensitivity for the diagnosis of dengue fever. Similar observations were drawn from this study.

CONCLUSION

The hematological parameters like reduced platelet count, MPV and PDW in patients with AUF significantly points toward possibility of dengue fever.

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