Original Article

Clinical spectrum and aetiology of patients with acute febrile illness: experience at a tertiary level hospital in Dhaka, Bangladesh

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ABSTRACT

***Background**: In developing countries like Bangladesh, etiologies of acute febrile illness (AFI) remain largely unknown due to limited diagnostic facilities. AFI is often associated with high morbidity and mortality, due to high prevalence of local individual diseases. The prioritization of the differential diagnosis of a clinical syndrome of AFI is needed. Aim of this study was to evaluate the etiology and clinical spectrum of AFI of the patients attending a tertiary level hospital in Dhaka.*

***Methods**: This cross-sectional study was carried out in the Department of Internal Medicine of BIRDEM General Hospital, Dhaka during the period of July 2019 to June 2020. Patients with AFI, defined as fever for less than 2 weeks duration, were approached for this study. In this study all the diagnosed cases of AFI were taken, to evaluate their etiology, clinical and laboratory parameters. Informed written consent were obtained. Data were collected by convenient sampling in a preformed structured data sheet containing history, clinical finding, laboratory investigation and imaging studies. Collected data were analyzed using the statistical software SPSS 22.*

***Results:** Total patients were 344, mean age of the study participants was 43.47 (±14.78) (range 19 to 63) years with a majority in age group 51-60 years (25.30%). Female predominance was observed (58%). Fever pattern was intermittent in 52% patients and continued in 48% patients. Presenting clinical features were body ache, abdominal pain, rash, arthralgia, vomiting, cough, respiratory distress, tachypnea, chest pain, diarrhea, weakness, headache and myalgia. Frequency of clinical features varied with diagnosis. Urinary tract infection (UTI) was the commonest (37.80%) etiology followed by dengue (33.70%), pneumonia (10.50%), typhoid (9%), typhus (5.20%), acute gastroenteritis (2.90%) and leptospirosis (0.90%). The co-morbidities among patients were diabetes mellitus (39.50%), hypertension (27.90%), ischemic heart disease (4.65%) and chronic kidney disease (2.90%).*

***Conclusion:** In this study UTI was the commonest etiology of AFI followed by dengue, pneumonia, typhoid, typhus, acute gastroenteritis and leptospirosis.*

***Key words:** acute febrile illness, etiology, clinical spectrum, Bangladesh.*

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INTRODUCTION

Acute febrile illness (AFI) or acute fever or short febrile illness is traditionally defined as any illness associated with fever of 2 weeks or shorter duration, rapid in onset, caused by diverse pathogens. The clinical signs and symptoms of most of the infections are similar and the correct diagnosis is only possible by using pathogen specific diagnostic test.[1]

AFI is associated with significant morbidity and mortality in developing countries. In developed countries AFI is often due to viral etiological agents, whereas in the developing countries, the etiologies of AFI include

dengue, malaria, enteric fever, chikungunia, leptospirosis, brucellosis, rickettsia infection and other undiagnosed infection.[2-5]

In addition to great diversity of the pathogens, the burden of AFI is compounded by limited resources, low immunization rates and poor public health control measures. Further, AFI having non-specific signs and symptoms without any focal point of infection makes its diagnosis and management a very challenging affair.[6] Although the clinical management guideline for AFI are available, these are rarely supported by knowledge of the locally prevalent causative agents. The infectious agents causing AFI varies by different regions suggesting that diagnosis and management needs to be based on a methodical evaluation of area specific etiologies.

The use of laboratory-based syndrome surveillance can alert clinicians and also provide the knowledge of common infectious etiologies circulating in the given region during a specific time period.[7] Thus, it is important to maintain a proper epidemiological data of AFI which helps us in generating an evidence-based diagnosis and effective treatment guidelines as most of them are treatable. This study was carried out to investigate the causes of AFI and their clinical spectrum.

METHODS

This cross-sectional study was carried out among patients with fever of less than 2 weeks duration admitted in the Department of Internal Medicine, BIRDEM General Hospital, Dhaka, Bangladesh from July 2019 to June 2020. After fulfilment of the eligibility criteria, data were collected from the patients in a preformed structured data sheet, containing history, clinical finding, laboratory investigation and imaging studies. Convenient sampling was done. The objective of the study was discussed in details with the patients before enrollment. A total 344 patients were included in the study according to inclusion and exclusion criteria. Every ethical issue was discussed with the patients or guardian (in case of inability of the patients to give information), regarding the study and informed written consents were obtained. Data were analyzed by statistical package for the social science (SPSS) version 22. Results were presented in tables and figures. Ethical approval was obtained from the Institutional Review Board (IRB) of BIRDEM Academy. It was ensured that all information and record were kept in private. Inclusion criteria were (a) patients more than 18 years of age, (b) irrespective of gender and (c) patients with fever less than 2 week. Exclusion criteria were (a) patients with diagnosed case of infection before admission and (b) patients is already on antibiotic.

RESULTS

Total patients were 344 with mean age of 43.47 (±14.78) (range 19 to 63) years), majority (25.30%) being in age group 51-60 years (Figure 1). There was female predominance (58%). Fever pattern was intermittent in 52% patients and continued in 48% patients. Presenting clinical features were body ache, abdominal pain, rash, arthralgia, vomiting, cough, respiratory distress, tachypnea, chest pain, diarrhea, weakness, headache and myalgia. Frequency of clinical features varied with diagnosis. Urinary tract infection (UTI) was the commonest (37.80%) cause followed by dengue (33.70%), other are shown in Figure 2. Diabetes mellitus (39.50%) was the commonest comorbidity and other are shown in Table I.

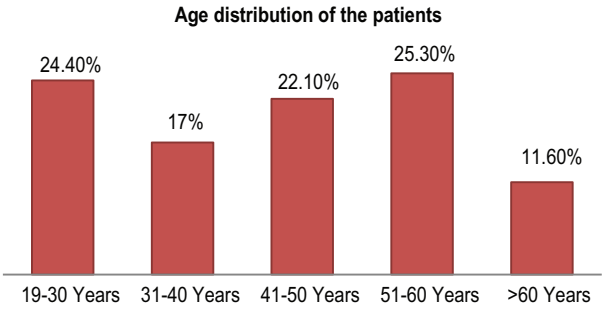

Figure 1. Age distribution of the patients with acute febrile illness (N = 344)

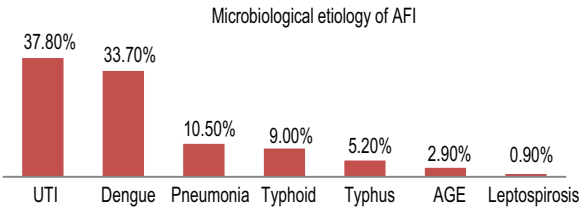

Figure 2. Aetiology of patients having acute febrile illness (N = 344)

Table I. Co-morbidities of the patients with acute febrile illness (N = 344)

Co-morbidities	Number	Percentage
Diabetes Mellitus (DM)	136	39.50
Hypertension (HTN)	96	27.90
Ischemic heart disease (IHD)	16	04.70
Chronic Kidney Disease (CKD)	10	02.90

Clinical features of AFI

UTI: Among 130 UTI patients, after fever, abdominal pain (93.10%) was the commonest symptom followed by burning micturition (86.90%), supra-pubic pain (82.30%), urgency (64.60%), frequency (55.40%), vomiting (30.80%) and incontinence (10.80%).

Dengue: Among 116 dengue patients, body ache (91.40%) was the commonest symptom after fever, then were vomiting (85.20%), rash (39.17%) and gum bleeding (12.90).

Pneumonia: Among 36 pneumonia patients, cough, respiratory distress, chest pain were present 100%, 100% and 22.20% cases respectively.

Enteric fever: Among 31 enteric fever cases, abdominal pain was commonest symptom (71%) after fever; other symptoms were body ache (61.30%), diarrhoea (38.70%) and vomiting (35.50%).

Typhus: Among the 18 typhus fever cases, body ache (50%) and abdominal pain (50%) were the two most common symptom, followed by rash (33.30%), arthralgia (27.80%) and vomiting (16.70%).

Acute gastroenteritis (AGE): Among 10 AGE cases, abdominal pain, vomiting and diarrhoea were present in 100%, 80% and 70% cases respectively.

Leptospirosis: Among the 3 leptospirosis cases weakness, headache and myalgia were present in 100%, 100% and 100% cases.

Laboratory finding of acute febrile illness

UTI: Median total white cells (WBC), platelet and urinary pus cell were 13,640/mm^3, 3,42,000/mm^3 and 11/high power field respectively. *E. coli* was the commonest organism (64.60%) followed by *Klebsiella* (15.40%), *Acinetobacter* (10%), *Staphylococcus* (6.2%) and *Citrobactor* (3.80%).

Dengue: Median platelet and WBC count was 49,500/mm^3 and 4,850/mm^3 respectively, median ALT and AST were 65.50 IU/L and 73 IU/L respectively; leucopenia, thrombocytopenia and elevated ALT and AST were observed 19%, 74.10% and 79.30% cases respectively. NS_1 Ag was positive 31% and IgM antibody was positive 80.20% cases.

Pneumonia: Median WBC count was 12,920/mm^3, leucocytosis, renal impairment and elevated AST were observed in 52.78%, 2.78% and 2.78% cases. *Klebsiella* was commonest microorganism followed by *Staphylococcus* and *Streptococcus*. In chest X-rays, consolidation was observed among 66.70% cases.

Enteric fever: Median WBC was 9,410/mm^3, median ALT and AST was 60 IU/L and 66 IU/L. *Salmonella typhi* was isolated 61.30% cases and *Salmonella paratyphi* was isolated 38.70% cases. In ultrasonography splenomegaly was observed in 48.39% cases.

Typhus: Median WBC and platelet was count 8,275/mm^3, 4,05,500/mm^3, leucocytosis, elevated ALT and AST was observed 16.70%, 83.30% and 83.30% cases respectively. All the 18 cases were diagnosed by rising (4 fold) titre in Weil Felix test (OX:K > 1:320).

AGE: Median WBC and platelet was 18,175/mm^3 and 3,69,000/mm^3, presence of pus cell and RBC in stool was 60% and 40% cases. In stool culture, *Salmonella paratyphi* was isolated 20% cases.

Leptospirosis: Median WBC and platelet counts were 18,420/mm^3 and 3,85,250/mm^3, all the leptospirosis cases were diagnosed by positive anti-leptospira antibody (IgM).

DISCUSSION

Mean age of our patients was over 43 years with one-fourth in age group 51-60 years and nearly two-thirds were females. Similar study was done in India showed the mean age of AFI cases (37.40+ 20) years.[5,9] Most of their study subject were male.

UTI was the commonest etiology that was present in this study followed by dengue, pneumonia, typhoid, typhus, AGE and leptospirosis. Previous researcher reported that scrub typhus was the commonest etiology of AFI in India followed by malaria and dengue.[9] However, other researcher found scrub typhus was the leading etiology of AFI and dengue was the second

leading cause of AFI.[5] A systematic review conducted by Wangdi et al. Described dengue as the commonest etiology of AFI in South East Asian Countries.[12]

Clinical and laboratory findings of our dengue cases were comparable to another study conducted by Prashanth et al. who found body ache, vomiting, abdominal pain and rash among their 83.50%, 50.40%, 31.40% and 20.70% cases respectively.[13] Laul et al. and Azad et al. found almost similar findings regarding clinical features of dengue in their respective study.[14,15] ALT and AST level was higher the upper limit of normal value which are consistent to the finding of this study.[15]

Study conducted by Iqbal et al. also found abdominal pain (71%) as the commonest feature of typhoid other than fever.[16] They also noted diarrhea, vomiting, hepatomegaly and splenomegaly among their 43%, 29%, 14% and 14% cases respectively. Study conducted by Sur et al. and Gupta et al. also noted *Salmonella typhi* as the main organism responsible for typhoid fever.[17,18] In our series, *Salmonella typhi* was more common and the clinical and laboratory features were comparable with previous reports.

The clinic-pathological findings of our cases with typhus are nearly similar to the findings of Bhat et al. and Choi et al. Bhat et al. who found mean ALT level 77±12 IU/L and mean AST level 124±16 IU/L and both are also higher than upper limit of normal value.[19,20]

Cough and respiratory distress were found in all cases of pneumonia. The median WBC count was higher than upper limit of normal value. Consolidation was observed in two-thirds cases. And all of these findings are nearly concordant to the findings of Abdullah et al., Tamunosiki et al. *and* Htun et al. *Klebsiella* was the commonest organism. However, study conducted by Para et al. and Tamunosiki et al. found *Streptococcus pneumonia* as the most common organism responsible for pneumonia in their respective study.[24]

According to Schmutz et al. and Uhnoo et al., fever, abdominal pain, diarrhea and vomiting were the common clinical presentations of AGE.[25] Consistent to those studies this study also noted abdominal pain, vomiting and diarrhea in 100%, 80% and 70% of AGE cases respectively. Positive stool culture was found in 50% cases and *Salmonella* was the most common organism that was isolated from stool culture. Study conducted by Stroni et al. and colleagues also found *Salmonella* as the most common pathogen responsible for AGE.[26]

All of the leptospirosis cases had weakness, headache and myalgia. The median WBC count was higher than upper limit of normal value. Diagnosis was established by presence of leptospira Ig M antibody in all three cases. Study conducted by Holla et al. also noted myalgia, headache and generalized weakness as most common clinical features of leptospirosis besides fever. They also observed leucocytosis among their study subjects which is also consistent to the finding of this study.[27]

Small sample size was the limitation of this study. This study was conducted in one center which is not representing our whole population. A multi-center research in future will aid in the identification of etiology and clinical spectrum of AFI.

This study showed that UTI, dengue, pneumonia, typhoid, typhus, AGI and leptospirosis were identified etiologies of AFI.

Authors' contribution: MSH, MRR, JUA planned research. MSH collected data, drafted manuscript. All authors read and approved final version for submission.

Conflict of Interest: Nothing to declare.

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