

Acute Undifferentiated Febrile Illness Progressing to Multi Organ Dysfunction Syndrome: A Diagnostic Dilemma in Critical Care

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Abstract

Objective: There has been a recent surge in patients presenting to critical care units with acute undifferentiated febrile illness (AUFI) rapidly progressing to multi organ dysfunction syndrome (MODS). There has been paucity of literature on these patients in Northern part of India. We studied the clinical presentation, complications, and outcome of these patients in a tertiary care hospital in north India.

Materials & Methods: A retrospective observational study of patients admitted in Medical ICU of Fortis Hospital, Mohali with AUFI & MODS over July 2012 to October 2012. Detailed history, examination, laboratory parameters, complications and outcomes were studied.

Results: A total of 40 cases were studied. The final diagnosis were leptospirosis (35%), Scrub typhus (27.5%), Dengue (17.5%), Influenza A (2.5%) and unknown etiology (17.5%). Mean age of patients was 44.5 years (22 years to 67 years) and males (65%) outnumbered females (35%). There was no correlation with common sources like working in farm lands, contact with animals and other epidemiological risk factors. Primary symptoms at the time of presentation were fever (100%), flu like symptoms (87.5%) and altered sensorium (48.5%). All patients progressed to MODS requiring intensive care and were further complicated with secondary nosocomial infections in ICU. Respiratory complications were most common in our study (100%). Several cases presented with severe icteric disease and renal failure (74.5% & 60.5% respectively). Coagulation disorders (84%) especially thrombocytopenia was common. Neurological manifestations were seen in 35% of our cases, three of these patients (7.5%) were diagnosed to have intracranial bleed. Recovery was observed in 28 of 35 patients (80%), as five patients went against medical advice. Seven patients died, giving mortality of 20%.

Conclusion: Disease-specific clinical profiles with vigilant monitoring and proactive care is the key for early diagnosis and salvaging these patients. Even rare/uncommon diagnosis should be considered in differentials to avoid delay in management. Reporting of these cases in national data base will increase awareness among physicians, thus decreasing mortality and morbidity.

Key Words: "AUFI "(Acute undifferentiated febrile illness; "MODS"(Multi organ dysfunction syndrome).

Introduction

Fever is a common presenting complaint in the developing world and is the most common presentation in most of the healthcare delivery systems in India. Febrile illness can be localized to organ systems or non localized, commonly referred to as acute undifferentiated febrile illness (AUFI). However, in the developing world, the self limiting fever is no more restricted to general wards and clinics.

There has been a recent surge in patients presenting to critical care units with AUFI rapidly progressing to multi organ dysfunction syndrome (MODS). India, being a tropical nation, is a fertile nest for potentially lethal illnesses such as malaria, dengue fever, enteric fever, leptospirosis, rickettsiosis and influenza A.¹ There is a paucity of literature on the appropriate evaluation, presentation and outcomes of adult fever patients progressively worsening on a short notice in our ICU's.²

In the absence of established protocols, patients may be subjected to unnecessary investigations at considerable cost and the inappropriate prescribing of antimicrobial therapy.³

Objective

The aim was to study the presentation, epidemiological shifts, complications, and outcomes of patients presenting to the critical care unit with fever as their chief complaint with rapid progression to MODS. The accumulation of data on a multicentre basis can standardize the approach to such patients in a way that will reduce unnecessary testing and inappropriate use of antibiotics. In addition aim was to stress on the intensive care with aggressive proactive measures which can improve the mortality data of any critical care unit.

Study Design

Detailed history was recorded and detailed clinical examination was done in all the patients who presented with fever and MODS. Investigations done included: hemogram, metabolic profile, chest radiography, and electrocardiogram. Peripheral smear for malarial parasite was examined in all the patients. Samples for blood cultures and urine cultures were collected and any clinically obvious site of sepsis was investigated. Most of these patients underwent computed tomography (CT) of the thorax. Serological tests for other etiologies like influenza, dengue, scrub typhus and leptospirosis were also done.

Methods

All patients between 14 and 70 years of age, admitted to the Department of Critical Care, Fortis Hospital, Mohali who had had a febrile illness for 5-21 days, with no evident focus of infection following initial clinical evaluation and who required hospitalization, were enrolled into the study. Patients were excluded if they declined to participate in the study.

Results

From July 2012 to October 2012, 40 patients were enrolled. All patients enrolled met the criteria of fever (> 38.0°C). The mean age of enrolled patients was 44.5 years (interquartile range [IQR] 22-67 years of age) (Fig.1) and males (65%) outnumbered females (35%) (Fig.2).

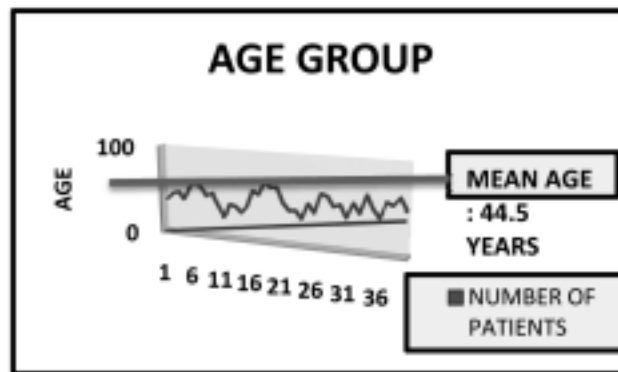


Fig.1 Mean age of the enrolled patients

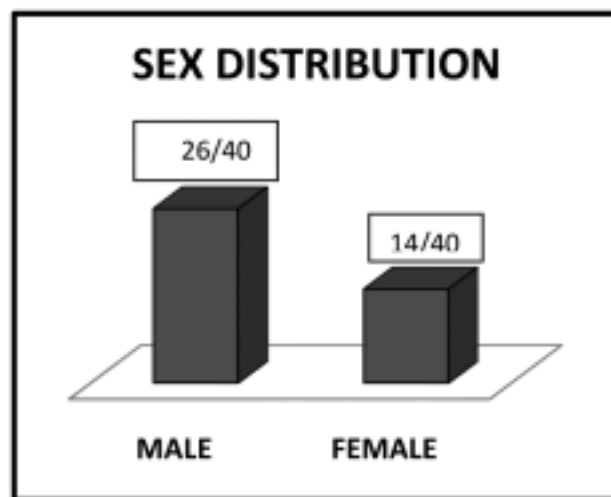


Fig.2 Sex distribution of the study group

The patients came from the northern Indian states of Punjab (60.5%), Haryana (31.8%) and Himachal Pradesh (7.7%). There was no correlation with common sources like working in farm lands, contact with animals and other epidemiological risk factors.

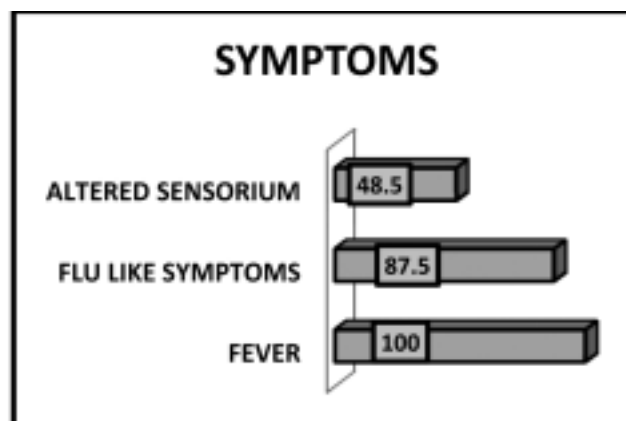


Fig.3 Symptoms on presentation to ICU

AFI predominantly occurred during the monsoon and subsequent months between July to October. The mean time from onset of symptoms to presentation was 9.7 days. The most common symptoms reported by enrolled patients included fever (100%), flu like symptoms (87.5%) and altered sensorium (48.5%) (Fig 3).

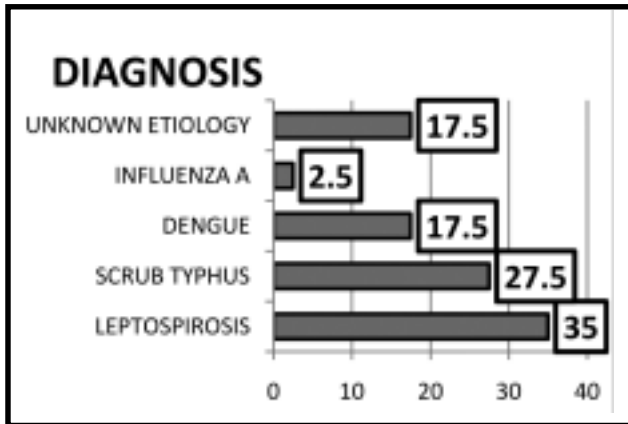


Fig.4 Distribution as per diagnosis

Laboratory testing was performed for agents believed to be endemic to the region in addition to a variety of emerging pathogens. The final diagnosis were leptospirosis (35%), Scrub typhus (27.5%), Dengue (17.5%), Influenza A (2.5%) and unknown etiology (17.5%) (Fig.4). All of these patients deteriorated and developed MODS. Respiratory complications were most common in our study (100%). Several cases presented with severe icteric disease and renal failure (74.5% & 60.5% respectively). Coagulation disorders (84%) especially thrombocytopenia was common.

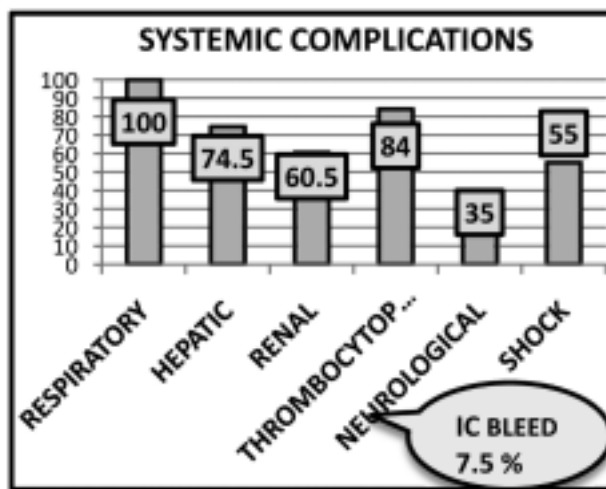


Fig.5 Systemic complication during ICU stay

Neurological manifestations were seen in 35% of our cases, three of these patients (7.5%) were diagnosed to have intracranial bleed. 55% cases were in shock during some point of time in their ICU course (Fig 5).

Outcome analysis revealed complete recovery in 28 of 35 patients (80%). However five patients left against medical advice (LAMA) and hence outcome could not be assessed in them. Seven patients died, giving a mortality rate of 20% in the remaining 35 patients.(Fig.6)

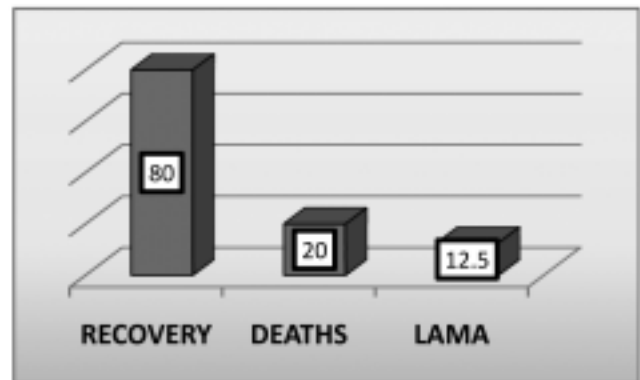


Fig.6 Outcome analysis

Discussion

The agents of human febrile illness can vary by region and country suggesting that diagnosis, treatment, and control programs need to be based on a methodical evaluation of area-specific etiologies. Limited resources and the great diversity of acute febrile illness (AFI) etiologies in India challenge diagnosis, treatment, and public health responses to endemic and epidemic diseases. Further confounding this is the fact that a majority of the patients present with non-descript symptoms (e.g., low-grade fever, general malaise, headache, and muscle ache) and usually no focal point of infection initially but deteriorate rapidly. Health care providers lacking proper knowledge are usually unable to determine specific etiologies, seriousness and often lead to misuse of useful diagnostic tests and antibiotics. In this study, we identified influenza, leptospira, dengue and scrub typhus as the most frequently identified pathogens associated with AFI. Although recently leptospirosis is being increasingly reported from the north Indian subcontinent, the actual incidence is unknown.⁴ Our study showed a high scrub typhus and dengue proportion, probably due to low disease awareness and, consequently,

a higher referral rate. Dengue fever incidence has been estimated at 14% among AFIs in a rural population-based southern Indian study and 48% in a hospital-based study in urban northern India.³

Respiratory disease

Respiratory symptoms, signs and abnormal chest radiography were the most common manifestation in our study group. Pulmonary involvement, commonly interstitial pneumonitis with possible vasculitis, leading to acute respiratory distress syndrome (ARDS), was reported in up to 55% of scrub typhus patients.⁵ A much higher incidence of ARDS in scrub typhus was documented in our cohort. Influenza associated ARDS is documented in 2.1-11.4% of Indian in-patients, the risk being higher among pregnant and non-immune individuals.⁶

The pathophysiology of ARDS in dengue is the result of endothelial injury, increased alveolar permeability and fluid overload.

Hepatic and renal disease

Majority of patients had injury to liver sinusoidal epithelial cell resulting in elevations in hepatic transaminase levels (74.5% in our study), with relatively mild elevations in alkaline phosphatase and bilirubin. Hepatic injury in leptospirosis causes marginal rise in hepatic transaminases with significant mixed hyper bilirubinaemia due to intravascular haemolysis, hepatocyte dysfunction and bile stasis. In contrast, studies (including ours) have shown that significantly elevated hepatic transaminase levels are common in dengue infections. Normal serum aspartate transaminase (AST) levels are a strong negative predictor for dengue haemorrhagic fever (DHF).⁷ Renal failure was seen in 60.5 % of the study group; most commonly in leptospirosis (33%) followed by scrub typhus (16%), dengue (11.9%) and Influenza A (5.6%).

Haematological involvement

Most common haematological abnormality was in the form of thrombocytopenia (80%). Thrombocytopenia was known as integral to the presentation of dengue, with up to 70% of patients with dengue exhibiting this.⁸ Marked thrombocytopenia, overt bleeding and haemo concentration secondary to plasma leak favors DHF/dengue shock syndrome (DSS). But in our study leptospirosis (56%), Scrub

typhus (38%) and influenza A (13.8%) were also major contributors. Thrombocytopenia in scrub typhus is generally mild.

Central nervous system (CNS) and cardiovascular system (CVS) involvement

In this study, 55% of patients presented to us with shock which was refractory in a few (11%). Though neurological involvement was the least common presentation, altered sensorium, including coma, mainly occurred in scrub typhus (53.6%). Most common presentation in our study was in the form of intracranial bleed. CNS involvement, commonly encephalitis presenting with altered sensorium and seizures, was uncommon in our cohort.

Conclusion

Disease-specific clinical profiles provide a useful methodology to systematically identify and document causes of acute fever. Clinical manifestations and laboratory abnormalities were inconstant; severe complicated disease with respiratory failure, severe hepatic dysfunction, and renal failure was also observed. The increased awareness among physicians of protean clinical manifestations of AEFI and early laboratory diagnosis will help reduce morbidity and mortality associated with disease. It is imperative to maintain a sound epidemiological database of AEFIs. Region-specific epidemiological databases of AFI need to be created so that evidence-based diagnostic criteria and treatment guidelines can be developed.

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