Original Article

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Study of Aetiology and Outcome in Acute Febrile Illness Patients with Multiple Organ Dysfunction Syndrome

Internal Medicine Section

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ABSTRACT

Introduction: Acute febrile illness with Multi Organ Dysfunction Syndrome (MODS) carries significant morbidity and mortality despite standard therapy in intensive care settings. Infections are the most common cause of MODS followed by polytrauma. Present study was undertaken in medical intensive care units of a tertiary hospital to study the aetiology and outcome among patients with acute febrile illness developing MODS.

Aim: 1) To study the aetiology of acute febrile illness in patients developing MODS.

2) To study the final outcome among these patients.

Materials and Methods: The present study was conducted at a tertiary care hospital in Mysuru, Karnataka, India, over a period of 6 months from July 2013 to December 2013. The Institutional Ethics Committee Approval (IEC) was obtained before the commencement of the study. A total of 213 cases admitted in intensive care unit with acute febrile illness with two or more organ dysfunction were screened for the inclusion and exclusion criterias.

Results: A total of 213 cases of acute febrile illness with one or more organ dysfunction were screened. Of the screened patients 75 patients were finally included in the study out of which 46 (61.3%) patients were males and 29 (38.7%) patients were females. Aetiology for acute febrile illness with MODS could be established in 49 (65.3%) patients and it was obscure in 26 (34.7%) patients despite repeated investigations. Dengue infection (29.3%) was the commonest cause of febrile illness with MODS followed by leptospirosis (22.7%). Majority of these patients had haematological derangements (78.7%) and liver function test abnormalities (68%). Out of these 75 cases, 54 (72%) patients recovered completely and 21 (28%) patients died. Among males (N=46), 35 (76.1%) patients recovered and 11 (23.9%) patients died where as among females (N=29), 19 (65.5%) patients recovered and 10 (34.5%) patients died. Mortality was proportionate with the number of organ dysfunction, especially Central Nervous System (CNS) involvement.

Conclusion: Incidence of febrile illness with MODS is more prevalent in males but the outcome appears poorer among females. The diagnosis remained obscure in a sizable proportion of these patients. Prognosis was inversely dependent on the number of organs involved especially with CNS manifestations.

Keywords: Dengue illness, Leptospirosis, Malaria, Sepsis

INTRODUCTION

Febrile illness with multi organ dysfunction is a well recognized clinical entity in medical Intensive Care Units (ICU) with high morbidity and mortality especially in developing countries like India. It is also one of the leading causes for critical care admissions with significant financial burden [1]. Despite the advancement in investigations, better resuscitative measures, organism specific antibiotics and advanced organ support methods the mortality rates due to febrile illness with MODS remains high.

Infectious diseases, especially gram negative organisms are the commonest causes of these MODS followed by poly trauma. The pathogenesis of MODS is incompletely understood but hypothesized to result from a combination of impaired inflammatory response and immune dysfunction, maldistribution of microcirculatory blood flow and or ischemic-reperfusion injury [2]. This contributes to sequential involvement of various organs with mortality rate ranging from of 27%-100% depending on the number of organs involved [3,4]. Several scoring systems have been described to diagnose and quantify these organ dysfunctions [5].

The present study was undertaken to study the aetiology and outcome of acute febrile illness patients developing MODS.

MATERIALS AND METHODS

A prospective study was undertaken for a period of 6 months from July 2013 to December 2013 at a tertiary care hospital in Mysuru, Karnataka, India. A total of 213 cases of acute febrile illness with MODS were screened, out of which 75 cases fulfilling the inclusion/exclusion criteria were finally included into the study. The data was collected based on a pretested proforma which included detailed history and clinical examination followed by investigations like complete blood picture, urine routine, serum electrolytes, Renal function test, Liver function test, ECG, arterial blood gas, chest X-ray, ultrasound of the abdomen etc. Depending on the clinical suspicion patients were also investigated for IgM dengue, NS1Ag, IgM leptospira antibodies by ELISA, Weil Felix test, HIV by ELISA, QBC for malarial parasites, and bacteriology assessment of relevant body fluids for gram stain, culture and sensitivity. Any documented organ dysfunction or development of new organ dysfunction was regularly assessed by clinical and biochemical testing every 24 hours. Patients were followed up till their organ dysfunction improved or the patient died due to the illness. Cases in which no aetiological factor was found were considered as -Sepsis with MODS due to undiagnosed aetiology. Institutional ethics committee approval was obtained before commencement of the study. Data was analysed using SPSS software (version 16.0) and Minitab (version 11.0) with statistical parameters like frequency procedure, Chi-square test and Cross tab procedure.

Inclusion Criteria

1. Age more than 18 years
2. Patient in critical care setting
3. Documented or history of fever
4. Dysfunction and/or failure of two or more organs
5. Organ dysfunction persisting for more than 24 hours

Exclusion Criteria

1. Pregnancy
2. Associated with less than two organ dysfunction
3. Organ dysfunction lasting less than 24 hours
4. Chronic illness like diabetes, malignancies, ischemic heart disease etc.
5. Postoperative, posttraumatic or any surgical cases
6. Not able to give informed consent.

RESULTS

A total of 75 patients with acute febrile illness developing multiorgan dysfunction were included in the study out of which 46(61.3%) were males and 29 (38.7%) were females. Most of these patients were in the age group of 26-35 years (30.7%) followed by 15-25 (28%) and 36-45 (18.7%) years [Table/Fig-1]. Fever being universal (100%) among these patients, other common presenting symptoms included vomiting/loose stools (45%) and yellowish discoloration of eyes (30.6%) [Table/Fig-2]. Laboratory evaluation revealed involvement of haematopoietic system in 78.7% of patients followed by hepatobiliary (68%) and renal system (52%). Most common aetiology for acute febrile illness with MODS was dengue fever in 22 (29.3%) patients followed by leptospirosis in 17(22.7%) patients [Table/Fig-3]. Bacterial cause for febrile illness with MODS was identified in only 7 (9.3%) patients with commonest bacteria isolated being *acinetobacter* (N=5) followed by *pseudomonas* (N=2). However, in about 26 (34.7%) patients the diagnosis couldn't be established despite repeated investigations.

Out of these 75 patients, 54(72%) recovered completely and 21(28%) patients succumbed to the illness. Recovery was highest in bacteriological sepsis patients (85.7%) followed by dengue illness (81.8%) [Table/Fig-4]. Mortality was highest in undiagnosed cases (42.3%) followed by malarial infection (33.3%). Among male patients (N=46), 35 (76.1%) of them recovered completely and 11 (23.9%) patients died where as among females patients (N=29), 19 (65.5%) of them recovered completely and 10 (34.5%) patients died. The outcome was better in the age group of 15-25 years (95%) and worse among 55-65 years age group (75%). The prognosis was poor among patients with central nervous system involvement (N=6 patients, 100% mortality) followed by lung involvement in the form of respiratory distress syndrome (N=15, 53.6% mortality) [Table/Fig-5]. Mortality (%) was proportionate with the number of organ involvement (N) {(N=4, 55.6% mortality), (N=3, 35.5%), (N=2, 11.8%)}. In general, poor predictors of outcome at the time of admission seems to be the patients who had low platelet count, raised creatinine levels, lung and central nervous system involvement [Table/Fig-6].

Sex	No. of Patients	Percent (%)
Males	46	61.3
Females	29	38.7
Age Distribution (years)		
15-25	21	28.0
26-35	23	30.7
36-45	14	18.7
46-55	6	8.0
56-65	8	10.7
66-75	1	1.3
>76	2	2.7

[Table/Fig-1]: Demographic characteristics of acute febrile illness patients with MODS.

Clinical Manifestations	Numbers	Percent (%)
Vomiting/loose stools	34	45.4
Bleeding manifestation	14	18.6
Cough	15	20.0
Oliguria	12	16.0
Dyspnoea	20	26.6
Icterus	25	33.3
Pallor	15	20.0
Oedema	15	20.0
Lymphadenopathy	7	9.3
Hepatomegaly	38	50.6
Splenomegaly	27	36.0

[Table/Fig-2]: Clinical features in acute febrile illness patients with MODS.

Aetiology	No. of Patients	Percent (%)
Dengue fever	22	29.3
Leptospirosis	17	22.7
Bacterial septicaemia	7	9.3
Malaria	3	4.0
Undiagnosed infection	26	34.7

[Table/Fig-3]: Aetiology for acute febrile illness with MODS.

Aetiology	Recovered (%)	Died (%)
Dengue fever	18 (81.8)	4 (18.2)
Leptospirosis	13 (76.5)	4 (23.5)
Bacterial septicaemia	6 (85.7)	1 (14.3)
Malaria	2 (66.7)	1 (33.3)
Undiagnosed infection	15 (57.7)	11 (42.3)

[Table/Fig-4]: Aetiology and outcome in acute febrile illness patients with MODS.

Organs Involved	Recovered (%)	Died (%)	p-value
Blood N=59 (78.7%)	40 (67.8%)	19 (32.2%)	0.120
Vascular system N=20 (26.7%)	14 (70%)	6 (30%)	0.816
Liver N=51 (68%)	37 (72.5%)	14 (27.5%)	0.877
Lungs N=28 (37.3%)	13 (46.4%)	15 (53.6%)	0.000
Kidney N=39 (52%)	31 (79.5%)	8 (20.5%)	0.133
CNS N=6 (8%)	0 (0%)	6 (100%)	0.001

[Table/Fig-5]: Organ involvement and outcome in acute febrile illness patients with MODS.

Parameters	Recovered (%)	Died (%)
1. Platelet count on admission (cumm)		
> 1lakh	14 (82.4%)	3 (17.6%)
50,000-1 lakh	8 (57.1%)	6 (42.9%)
< 50,000	32 (72.7%)	12 (27.3%)
2. Breathlessness		
Absent	44 (80%)	11 (20%)
Present	10 (50%)	10 (50%)
3. Serum creatinine		
≤ 1.4	22 (68.8%)	10 (31.3%)
≥ 1.4	32 (75%)	11 (28%)
4. CNS involvement		
Normal	54 (78.4%)	15 (21.7%)
Comatose	0	4 (100%)
Disoriented	0	2 (100%)

[Table/Fig-6]: Comparison with various parameters and outcome in acute febrile illness patients with MODS.

DISCUSSION

Acute febrile illness with obscure aetiology, also described as acute undifferentiated fever, poses a burgeoning problem in clinical practice [6]. In the routine evaluation of these cases of acute febrile

illness, more commonly diagnosed diseases will be dengue fever, malarial infection, leptospirosis, rickettsial fever especially scrub typhus, salmonellosis, bacterial septicaemia [7]. If resources are available, hanta fever, High Fever Severe Thrombocytopenia (HFST) virus and Crimean Congo virus infection can be additionally diagnosed with the work up of febrile illness cases [8]. However, significant proportion of these cases still remain undiagnosed whose prevalence can vary from 8-80% [9]. This non identification could be due to regional and seasonal distribution of the cases, non availability of additional serological markers and lack of knowledge about the prevailing regional infections or absence of standard working protocol. In developing countries like India, it is even worse due to limited accessibility and facility of medical services, social and financial constraints [10,11].

In the present study, out of 75 cases included males outnumbered females and most of these patients are in the productive age group of 15-45years [Table/Fig-1]. All these patients presented with fever followed by vomiting and loose stools with hepatosplenomegaly [Table/Fig-2]. This is because most of the cases were diagnosed with dengue illness followed by leptospirosis [Table/Fig-3]. This is in accordance with other studies wherein the commonest diagnosis was dengue fever, leptospirosis or malaria [9]. Alarmingly in our study in nearly 35% of patients the diagnosis could not be established which in many other studies varied from 8-80%. This was due to non availability of additional serological markers for influenza, hanta, HFST virus and Crimean Congo virus [8]. All the 75 patients (with or without diagnosis) developed multi organ dysfunction during follow up. Despite standard ICU care, proportion of mortality was more in undiagnosed cases when compared to the patients with one or the other diagnosis (44% vs. 20%) [Table/Fig-4]. Early involvement of lungs (respiratory distress syndrome), altered renal parameters, severe thrombocytopenia in patients with or without diagnosis portends poor prognosis during follow up [Table/Fig-5,6]. Patients with central nervous involvement predict highest mortality which was 100% in our study. Although various scoring system are already in vogue for the prognostication in the event of MODS, in our literature search there are no parallel comparisons of prognostication amongst acute febrile illness with and without diagnosis developing MODS [11]. Studies conducted so far have highlighted more on aetiological evaluation than the protocol development for the diagnostic work up of undiagnosed cases of acute febrile illness [9,12]. Hence, there is need of a large scale study across the globe to establish the prevalence of geographic trends about the diseases and to formulate the region based standard working protocol, with additional cost effective serological markers in evaluating these undiagnosed acute febrile illness cases [13].

LIMITATION

Our study has some limitations: 1) patients are from single institution and small in number. This was because we had excluded patients with associated co-morbid illness and non-ICU cases; 2) Additional serological markers couldn't be done due to logistical reasons.

CONCLUSION

Aetiology of acute febrile illness can be influenced by regional and seasonal trends. The sizeable proportion of these cases remains undiagnosed with high mortality when compared to patients with established aetiology. Overall, early involvement of lungs, kidney and haematopoietic system portends bad prognosis in the setting of multiorgan dysfunction. Central nervous system involvement could be an independent clinical predictor of poor prognosis. There is an urgent need of developing standard protocol and cost effective additional serological markers to evaluate undiagnosed cases of acute febrile illness for early diagnosis and prognostication.

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