Original Article

Individual organ dysfunction in case of acute febrile illness

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Abstract

Objective: 1) To document proportion of single organ dysfunction or combination of organ dysfunction in acute febrile illness cases. 2) To asses demographic profile, etiology, severity of illness (by SOFA score) in these patient. **Material and Methods:** It is a cross sectional observational study in a tertiary care centre in Mumbai. All the patients admitted to hospital with acute febrile illness with organ dysfunction will be noted and those admitted to MICU with inclusion criteria mentioned above will be included. **Results**: Our study which was an observational study was done in a tertiary care centre in Mumbai over a period of 1 year. Overall admissions in Medical ward during this period were 18513. Out of these patients, all patients those having AFI were screened and statistical analyses were done. Total 2560 patients were diagnosed as AFI, which was 13.83% of total admissions. Maximum number of AFI patients with organ failure was young adults predominantly male. Dengue, malaria and leptospirosis are the commonest amongst etiology. Out of these 8.20% were AFI with organ failure and 36 patient required ICU (17.14%). Sizable number of AFI patients develops organ failure (8.20%). Coagulation failure is commonest followed by ARF, Hypotension, Hepatitis, Hypoxia and CNS involvement. **Conclusion:** AFI is a common cause of organ dysfunction requiring ICU care.
Keywords: Acute Febrile Illness, MODS, prognosis.

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INTRODUCTION

Acute febrile illness (AFI) is a common cause for patients seeking healthcare in India, especially between June and September[1,2]. Unlike fever of unknown origin (FUO), which enjoys a standard definition, AFI (acute febrile illness), or Acute Febrile Illness (AFI), lacks an international consensus definition. Since FUO requires duration of fever to be longer than three weeks, some authors have defined AFI as fever that resolves within three weeks[3]. More traditionally however, AFI has been defined as fever of two weeks or shorter in duration[4]. Thus the term AFI is used to denote fevers that typically do not extend beyond a fortnight, and lack localizable or organ-specific clinical features.[5] Fevers with proven diagnosis are known as diagnosed-AFIs; those that defy diagnosis are called undiagnosed AFI[3]. Because malaria is an important and treatable cause of AFIs in the tropics and ranks number one in the differential diagnosis of acute fevers, patients who test negative for malaria are assigned a diagnosis of non-malarial AFIs[6]. Many UAFIs often resolve either on their own or in response to empiric therapies. Those AFIs which persist, and total duration of illness becomes longer than three weeks are classified as FUO. AFI like Malaria, Leptospirosis, Dengue fever etc frequently cause MODS. Quantification of degree of organ dysfunction is done using SOFA score (SEQUENTIAL ORGAN FAILURE ASSESSMENT SCORE). It is a good predictor of mortality in critically ill patients with a good SOFA score meaning good prognosis. The mortality of patients with multiple organ dysfunctions can range from 10% to 100%, depending upon factors like number of failing organs, severity of organ failure and duration of organ failure[7]. Present study was conducted to analyses cases presenting to tertiary

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centre and identify risk factors for need of organ support, mortality and morbidity in these patients so that future epidemics can be managed in more systematic manner considering limited resources available.

MATERIAL AND METHODS

Place of study

A general medical wards and Medical intensive care unit.

Study design

It is a cross sectional observational study in a tertiary care centre in Mumbai. All the patients admitted to hospital with acute febrile illness with organ dysfunction will be noted and those admitted to MICU with inclusion criteria mentioned will be included.

Inclusion Criteria

1. All admitted patients with acute febrile illness with at least one organ/organ system dysfunction/failure namely Respiratory system, Coagulation system, Liver, Cardiovascular system, Central Nervous System and Renal.
2. Age > 12 years of either sex.
3. Patients willing to give consent.
4. Patient hospitalized for at least 24 hour.

Exclusion Criteria

1. Patients with pre-morbid severe end stage disease- CKD (chronic kidney disease), Advanced AIDS, End stage liver disease, COPD (chronic obstructive pulmonary disease), Malignancy.
2. Patients admitted as Acute Febrile Illness but later on proved to have Sepsis (blood culture sensitivity+), Pneumonia, Pylonephritits, Meningitis, Brain abscess, liver abscess, tuberculosis, Tropical Pyomyositis.

Study Procedure

All indoor patients admitted to hospital over a period of one year with acute febrile illness (AFI) will be screened for presence of organ dysfunction. Patients requiring admission in medical ward OR Medical Intensive Care Unit care and satisfying inclusion criteria will be studied in details. Detailed history and clinical examination will be noted which will include history, duration and pattern of fever, associated symptoms like breathlessness, bleeding, oliguria, altered sensorium, convulsion jaundice etc. Their detailed systemic examination was carried out. SOFA score was used as an objective assessment of severity illness. Treatment received was noted like antibiotics, anti malarials, supportive treatment like transfusions, Haemodialysis, ionotropes etc. Routine haematological and biochemical investigations were carried out which included complete blood count, liver function test, renal function test, X ray chest. Special tests to determine etiology like peripheral smear for malaria parasite (PSMP), malarial antigen test, tests for dengue, leptospirosis etc were done.. Tests like CT, MRI, Cerebrospinal fluid examination (CSF), 2D-echocardiography, etc were carried out only when indicated. Patients severity index will be calculated using SOFA score- Patients were followed up till discharge, transfer to other ward or death, Autopsy findings will be noted in cases whenever performed Statistical analysis was done by using Students t test for numerical data and Chi square test for qualitative data.

OBSERVATIONS AND RESULTS

Our study which was an observational study was done in a tertiary care centre in Mumbai over a period of 1 year. Overall admissions in Medical ward during this period were 18513. Out of these patients, all patients having fever were screened. 2560 patients were diagnosed as fever which was 13.83% of Total admissions. Out of these 8.20% were AFI with organ failure and 36 patient required ICU (17.14%). Out of 217 patients who diagnosed as AFI with organ failure total 7 patients were excluded from the study. Two patients were suffering from terminal malignancy. And two were having underlying chronic kidney disease. Three were having disseminated tuberculosis. Following this exclusion, remaining 210 patients were studied in detail further.

Table 1: Distribution of study group as per Diagnosis

DIAGNOSIS	Frequency	Percent
UAFI	53	25.24%
Dengue	70	33.33%
P.Vivax	47	22.38%
P.Falciparum	7	3.33%
Mixed Malaria	10	4.76%
Leptospirosis	23	10.95%
Total	**210**	**100.00%**

As shown in above table Dengue was detected in 33.33% (70) patients, followed by malaria in 30.48 % (64), leptospirosis in 10.95 % (23) and undifferentiated fever in 25.24 % (53). Duration of hospital stay for AFI patients varied from 1 to 18 days with maximum number of patients required hospital stay for 4 to 6 days. Leptospirosis patients required more hospital stay as compare to malaria, Dengue and UAFI. Maximum number of leptospirosis patients required ICU care 14/36(38.88%), with mean ICU stay of 5.21 days, Dengue 25%, UAFI 19.44% and Malaria 16.66%. Apart from fever which was present in all patients Dyspnoea is most come symptom observed in 37 patients followed by bleeding[26], oliguria[12] and alt sensorium[10]. Jaundice is most common sign observed in 36 patients followed by rash[32], pallor[22], subconjunctival haemorrhage[12] and haemoptysis[9].

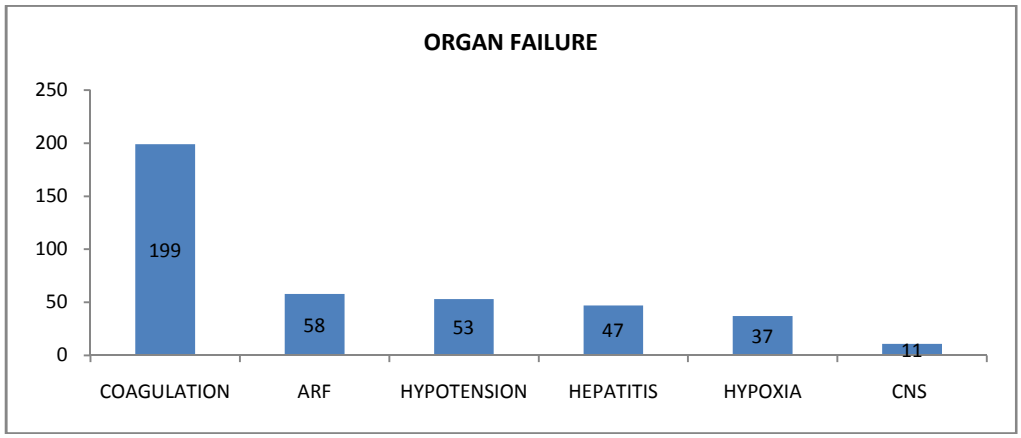

Figure 1: Number of patiens with individual organ failure

As shown in above Figure coagulation was the most common organ failure observed followed by ARF, Hypotension, Hepatitis, Hypoxia, CNS involvement. Out of 210 patients 7 (3.33%) expired and 203 survived there were 6 male and 1 female. Following is the detail of supportive treatment received by AFI patients during their hospital stay.

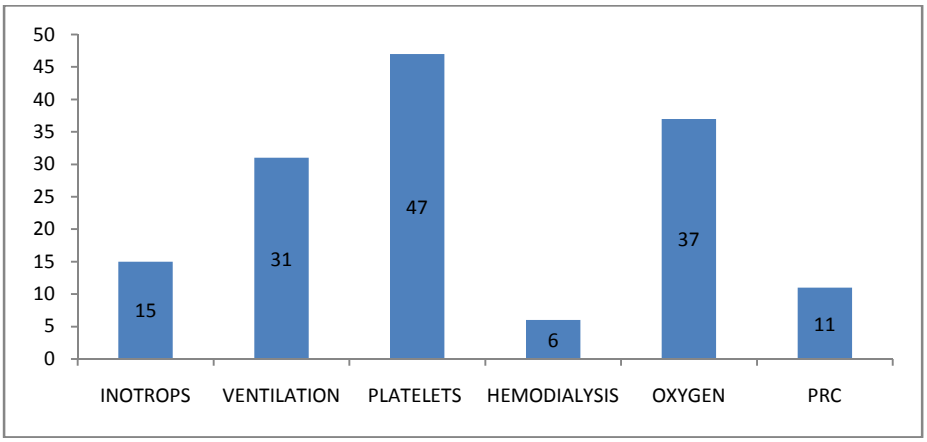

Figure 2: Organ support given

As shown in above analysis organ support in form of Platelets transfusion was required in maximum number of patients 47(22.38%) followed by Oxygen and Mechanical ventilation in 37(17.62%) and 31(14.76%) patients respectively, Inotropic support was given to 7.14% patient, blood transfusion given to 11(5.24%) patients, only 6(2.86%) patients received Haemodialysis.

Table 2: Number of patients with thrombocytopenia and platelet transfusion

	NO OF PATIENTS(210)	PLATELETS TRANSFUSION(47)	P VALUE	Association is
UAFI	53	8	0.141028	not sig
DENGUE	70	25	0.001045	Sig
MALARIA	64	5	0.000798	Sig
LEPTOSPIROSIS	23	9	0.041117	Sig

As shown in above data platelet transfusion given to 47 patients with thrombocytopenia (199), out of which maximum number of dengue patients (25/70) given platelet transfusion followed by leptospirosis (9/21).Out of 70 dengue patients 35.70% patients required platelets and in 21 leptospirosis patients 42.90% given platelets in malaria 8.65% (5/53) and in UAFI 16% (8/42). Result is statistically significant in case of dengue, malaria and leptospirosis.

Table 3: Number of patients with aki and hemodialysis given

	NO OF PATIENTS(210)	HEMODIALYSIS	P VALUE	Association is
UAFI	53	0		
DENGUE	70	1	0.379581	not sig
MALARIA	64	0		
LEPTOSPIROSIS	23	5		

As shown in above data 58 (27.62%) patients developed AKI. Leptospirosis responsible for maximum number of AKI patients 23 (39.66%), followed by Dengue 13 (22.41%), malaria 12(20.69%) and UAFI 10 (17.24%). Maximum number of patients with leptospirosis received hemodialysis 5/6.

Table 4: Number of patints with hypoxia and ventilator support given

	NO OF PATIENTS(210)	M.VENTILATION	P VALUE	Association is
UAFI	53	6		
DENGUE	70	8	0.000097	
MALARIA	64	4		SIGNIFICANT
LEPTOSPIROSIS	23	13		

As shown in above analysis Leptospirosis was responsible for maximum number patients with Hypoxia 37.83% (13/37) followed by Dengue 24.32%, Malaria and UAFI 18.91% each. out of 37(17.62%) patients with hypoxia 31 patients required mechanical ventilation out of which 13 patients were leptospirosis followed by dengue[8],UAFI[6], and malaria[4].NIV given to 16/31 patients and IPPV given to 15/31 patients. P value is statistically significant. Total 210 patients 53 (25.24%) patients developed hypotension. Out of which 15 (28.30 %) required inotropic support. Dengue responsible for maximum number of patients with hypotension followed by UAFI[12], malaria[11] and leptospirosis[5]. P value statistically is significant. Following is analysis of mortality with requirement of organ support.

Table 5: Comparison of mortality with ventilatory support

VENTILATORY SUPPORT (NIV/IPPV)		SERVIVAL/DEATH		Total
		DEATH	DISCHARGE	
Yes	No.	7	24	31
	%	22.60%	77.40%	100.00%
No	No.	0	179	179
	%	0.00%	100.00%	100.00%
Total	No.	7	203	210
	%	3.30%	96.70%	100.00%
Chi-Square test	Value	df	P Value	Association is
Pearson Chi-Square	41.813	1	<0.001	Sig
Fisher's Exact Test			<0.001	Sig

As shown in above data all patients who died required mechanical ventilation (22.60%), out of 31 patients on ventilator 77.40 % survived. Association is statistically significant with P value is <0.001. All patients who died required blood products transfusion (12.70%), and out of 55 patients required transfusion 87.30% survived. Association is statistically significant. Inotropic support given to 15 patients - 8 survived and 7 expired. P value is significant in this association. Haemodialysis was given to 7 patients out of which one expired and 6 survived. P value is statistically not significant in this association. Hepatitis developed in 47 patients out of which 6 died and 41 patients who had hepatitis survived. Out of 11 patients with CNS involvement 5 patients died and 6 patients survived. SOFA score is significantly high in case of leptospirosis with mean of 10 compared to malaria, dengue and UAFI with mean of 4. Leptospirosis responsible for maximum number of deaths (42.85%) followed by dengue and malaria (28.57%). Autopsy was done in 2 patients out of 7 who died. Cause of death given in one case was acute renal failure due to acute tubular necrosis with interstitial pneumonitis with hepatitis with acute respiratory distress syndrome in case of leptospirosis. In another case cause of death was given was acute tubular necrosis with mild hepatitis in case of dengue fever.

DISCUSSION

Our study which was an observational study was done in a tertiary care centre in Mumbai over a period of 1 year. As data reveals that total 210 patients were studied. Out of which 75.24% are male and 24.76% was female. An average age was 28 years. Male and female ratio is

3:1.Similar study done in Uttarakhand by Ragini sing *et al*[8] A total of 1141 patients were found to AFI, 54.2% were male and 45.8% were female. Male female ratio was 1:1. Maximum numbers of patients (49.05%) requiring hospital stay for the period of 4 to 6 days. Symptom duration was 2 to 5 days observed in 73% of patients in our study. In study done in Mumbai by Bajpai *et al*[9] also the symptom duration was 2 to 4 days in 65% of patients. Dengue was detected in 33.33% (70) patients, followed by malaria in 30.48% (64), leptospirosis in 10.95% (23) and undifferentiated fever in 25.24%(53). In Bajpai *et al*[9] study cause of fever could not be determined in 53.75% deaths, whereas in 22.5%, it was malaria, 21.88% was leptospirosis, and in 1.88% it was dengue. In Chavla V *et al*[10] Out of 834 total admissions 60 (7.2%) patients suffered from leptospirosis. This lower number of patients with UAFI in present study may be because of better diagnostic facility available now compare to 10 years back. In Chavla V *et al* (10) male predominance might be because of it was study of leptopirosis which is common in patients who wades through flooded water. Fever was found in almost all patients which were the most common symptom followed by dyspnoea, bleeding, oliguria, and altered sensorium. Jaundice was the most common sign observed followed by rash, pallor, subconjunctival haemorrhage, and hemoptysis. In study done by MamathaB patil *et al*[11] bleeding manifestation were seen in 45% of patients of which petechiae and/or purpura were the commonest (85%). In a study by Shruti K Bharala *et al*[7] common bleeding manifestations were gum bleed, purpura, petechial rash, and bruising. Hypotension was observed in 25.24%of patients. Hepatitis was developed in 22.38% of patients. In Kothari *et al*[12] a study published from Mumbai, hepatic failure occurred in 26% of patients with 49% mortality. Out of 210 patients 7 expired (3.33%) - males 85.71% had higher mortality than females (14.28%). In study by Bajpai *et al*[9] also very high percentage of males (81%) died as compared with females (19%). Leptospirosis responsible for maximum number of deaths (42.85%) followed by dengue and malaria 28.57% each. In Chavla V *et al*[10] total mortality in leptospirosis patients was 52% which was much higher compared to the total MICU mortality (31.4%). In present study also maximum number of deaths seen in leptospirosis patients. SOFA score is significantly high in case of leptospirosis with mean of 10 compared to malaria, dengue and UAFI with mean of 4. As mentioned in Abhinandan KS *et al*[13] SOFA score was very high among non survivors as compared to survivors. The trend of SOFA score was progressively declining in survivors while non-survivors had stable higher score during the first week. Organ support in form of platelets transfusion was required in maximum number of patients 22.38 % (47) followed by Oxygen (37) and Mechanical ventilation (31) in 17.62% and14.76% respectively. Inotropic support was given to 7.14%[15] patient and only six (2.86%) patients received Haemodialysis. Complication like thrombocytopenia found in maximum numbers of patients that in 94.76%. Very sever thrombocytopenia (<20000) observed in 69 (32.86%) patients. Platelets transfusion was given to 47(22.38%) patients out of 199 patients with thrombocytopenia, out of which maximum number of patients had dengue (25/70), followed by leptospirosis (9/21). In study by Mamatha B Patil *et al*[11] infection was the commonest cause of thrombocytopenia and dengue fever was the most common among the infections. In study by Paramjit Kaur *et al*[14] conducted in four tertiary level hospitals of Delhi observed that 73.5% of patients with dengue hemorrhagic fever and 48.7% of dengue fever classified as per WHO guidelines were given platelet transfusions. All patients who died required blood products transfusion (12.70%), and out of 55 patients required transfusion 87.30% survived. Association is statistically significant. Acute kidney injury was observed in 27.62 % (58) of patients of which 10.34%[6] required haemodialysis, leptospirosis responsible for maximum number of AKI patients (39.66%), followed by Dengue (22.41%), Malaria (20.69%) and UAFI (17.24%). Maximum number of patients with leptopirosis (5/6) received haemodialysis. Only one patient requiring haemodialysis died. In study by Gopal Basu *et al*[15] incidence of AKI in AFI was 41.1% which was very high as compare our study of which 7.9% required dialysis. Incidence of AKI was highest with falciparum malaria (63.2%), followed by mixed malaria (54.2%), leptospirosis (50.0%) and least with enteric fever (6.3%). AKI was observed at an average rate of 35–40% among other acute febrile illnesses. As compare to this study the incidence of AKI in our study was low. In Kothari *et al*[12] a study from Mumbai showed that 70% of patients with severe leptospirosis had renal failure. Hypoxia developed in 17.62% of patients and ARDS developed in 26 patients (12.38%). Leptospirosis was responsible for maximum number patients with Hypoxia 37.83% (14/37) followed by Dengue 24.32%, Malaria and UAFI 18.91% each. Out of 37 (17.62%) patients with hypoxia 31 patients's required mechanical ventilation. Non invasive ventilation (NIV) was given to 16/31 patients and invasive ventilation (IPPV) given to 15/31 patients. P value is significant in all cases. All patients (10/37) with Pao2/Fio2<200 required mechanical ventilation. All patients who died required mechanical ventilation (22.60%), out of 31 patients on ventilator 77.40 % (24/31) survived. In study by RR Bhadade *et al* (16), factors attributable for ALI/ARDS were: Malaria in 16

patients (27.6%), leptospirosis in 12 (20.7%), malaria with dengue in 3 (5.2%), undiagnosed fever in 16 (27.6%), pneumonia in 8 (13.8%), urinary tract infection in 2 (3.4%), and pancreatitis in one (1.7%) patient. Our study results were similar with this study. Hypotension was observed in 25.24%of patients. Dengue fever responsible for maximum number of patients with hypotension followed by UAFI > malaria > leptospirosis and 28.30 % required inotropic support. All patients who died required initropic support, and out of 15 (7.14%) patients on inotropic support 53.30% survived. Leptospirosis patients required more hospital stay as compare to malaria, dengue and UAFI. Maximum number of leptospirosis patients required ICU care 14/36 (38.88%), with mean ICU stay of 5.21 days followed by Dengue 25%, AFI 19.44% and Malaria 16.66%. Overall AFI constitute a significant number of patients requiring hospitality. Dengue, malaria and leptospirosis contribute sizable number of AFI patients who go to develop organ failure. However with specific therapy and appropriate organ support many of patients can be salvageable. Oxygen, mechanical ventilation, blood products transfusion and dialysis are important supportive therapy required to these patients.

CONCLUSION

1. Sizable number of AFI patients develops organ failure (8.20%). Coagulation failure was commonest followed by ARF, Hypotension, Hepatitis, Hypoxia, CNS involvement.
2. Maximum number of AFI patients with organ failure was young adults predominantly male. Dengue, malaria and leptospirosis were the commonest amongst etiology. However sizable number of patients remains undifferentiated despite of extensive investigation, Maximum derangement of SOFA score seen in leptospirosis.
3. In addition to specific treatment for etiology these patients requires various therapy for organ support commonest being platelets transfusion followed by oxygen, mechanical ventilation, inotropic support, haemodialysis.
4. Amongst AFI patients with organ failure maximum number of mortality seen in patients with leptospirosis. Amongst organ failure hypotension, coagulopathy and acute kidney injury associated with maximum mortality followed by ARDS, hepatitis and CNS involvement.

LIMITATIONS

1. This study was done on AFI patients who were admitted in hospital (Indoor patients), however sizable number of AFI patients received treatment on OPD basis only. Hence this data can not be representative of disease in community.
2. Sometimes facilities like ICU care, mechanical ventilation, platelets transfusion, blood transfusion are subjected to availability.
3. Empirical treatment can cure many patients of so-called AFI even if they have specific cause like pneumonia, meningitis etc which may not have been diagnosed on admission.

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