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"A prospective study of etiology and outcome of acute febrile illness with multi-organ dysfunction syndrome " in patients admitted in intensive care unit

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Abstract

Background: Acute Febrile Illness (AFI) is a frequent cause of ICU admissions in tropical regions like India. Although often self-limiting, AFI can progress to Multi-Organ Dysfunction Syndrome (MODS), resulting in significant morbidity and mortality.

Objective: To identify the etiology, clinical predictors, and outcomes of AFI progressing to MODS.

Methods: A prospective observational study was conducted over 18 months in a medical ICU. Patients with AFI and MODS (≥2 organ dysfunctions) were evaluated for demographic, clinical, laboratory, and microbiological parameters. Disease severity was assessed using SOFA score.

Results: Dengue, malaria, leptospirosis, rickettsial infections, and bacterial sepsis were common causes. Mortality correlated with elevated creatinine, bilirubin, CNS involvement, low MAP, and thrombocytopenia. Mixed infections increased mortality risk.

Conclusion: MODS due to AFI poses a critical care challenge. Early identification of high-risk patients using simple markers can guide timely management and improve outcomes, particularly in resource-limited settings.

Keywords: AFI (Acute Febrile Illness); MODS (Multi-Organ Dysfunction Syndrome); Tropical Infections; Critical Care; SOFA Score; Mortality Predictors

1. Introduction

Fever remains one of the most frequent clinical presentations in medical practice, particularly in developing countries like India, where tropical infections are endemic and often present as undifferentiated febrile illnesses (Sharma et al., 2019) [1]. Although many such illnesses are self-limiting, a significant subset of patients rapidly deteriorates, progressing to multi-organ dysfunction syndrome (MODS), a complex and life-threatening condition marked by failure of two or more organ systems (Kumar & Gupta, 2020) [2]. The transition from acute febrile illness to MODS involves pathogen virulence, host immune response, and comorbidities, with agents such as dengue virus, plasmodium species, salmonella typhi, and leptospira frequently implicated (Patel et al., 2018) [3].

Despite advances in critical care, MODS continues to carry high morbidity and mortality, with rates reported as high as 100% in severe cases (Reddy et al., 2021) [4]. Tools like the Sequential Organ Failure Assessment (SOFA) and APACHE IV scores aid in prognostication but have limitations in resource-limited settings (Singh et al., 2020) [5]. In india, the

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burden of tropical infections like severe dengue, complicated malaria, leptospirosis, and enteric fever further complicates management, posing substantial economic and healthcare challenges (Verma et al., 2022) [6].

Given these gaps, there is an urgent need for prospective studies that comprehensively evaluate the etiology and outcomes of acute febrile illnesses complicated by MODS, particularly in the Indian context (Joshi et al., 2023) [7]. This study aims to address this need by systematically investigating the etiological factors and prognostic markers in patients admitted with febrile illness progressing to MODS.

2. Materials and Methods

This prospective observational study was conducted in the Department of General Medicine ICU at Al-Ameen Medical College and Hospital, Vijayapur, over 18 months (June 2023 – November 2024). Consecutive patients admitted with acute febrile illness (AFI) progressing to multi-organ dysfunction syndrome (MODS) were included. Inclusion criteria were fever with dysfunction of two or more organ systems lasting >24 hours; pregnant patients, patients with chronic illnesses, recent major surgery, or organ dysfunction lasting <24 hours were excluded.

A total of 82 patients were enrolled by consecutive sampling. Patients were managed according to standard protocols without intervention by the study team. Clinical, laboratory, and radiological data were collected prospectively using a structured proforma. Parameters included demographic details, clinical findings, serial laboratory tests (CBC, LFT, RFT, pathogen-specific tests), and relevant imaging. Patients were stratified retrospectively by etiology and severity (SOFA score) for analysis.

Data were analyzed using standard statistical methods. Descriptive statistics, subgroup comparisons, and regression analyses were performed to identify prognostic factors. Ethical approval was obtained from the institutional ethics committee, and informed consent was secured from all participants or their guardians.

3. Results

A total of 82 patients diagnosed with acute febrile illness (AFI) with multi-organ dysfunction syndrome (MODS) admitted to the ICU were included in the study

Table 1 Age distribution of patients in ICU with acute febrile illness and MODS

Age (in years)	Frequency	Percent	Valid Percent	Cumulative Percent
<20	3	3.7	3.7	3.7
21-30	8	9.8	9.8	13.4
31-40	16	19.5	19.5	32.9
41-50	15	18.3	18.3	51.2
51-60	15	18.3	18.3	69.5
>60	25	30.5	30.5	100.0
Total	82	100.0	100.0	

Age distribution (Table 1) showed most patients were above 60 years (30.5%), followed by 31–40 years (19.5%) and 41–50 years (18.3%).

Table 2 White blood cell (WBC) count distribution in ICU patients with acute febrile illness and MODS

WBC	Frequency	Percent	Valid Percent	Cumulative Percent
<4000	25	30.5	30.5	30.5
4000-10000	2	2.4	2.4	32.9
>10000	55	67.1	67.1	100.0
Total	82	100.0	100.0	100.0

WBC count distribution (Table 2) showed 67.1% had WBC >10,000, indicating inflammatory response.

30.5% had WBC <4000 indicating increased severity.

Table 3 WBC count and mortality outcome in ICU patients with acute febrile illness and MODS

			WBC Count			
			<4000	**4000-10000**	**>10000**	**Total**
Death	No	Count	19	2	40	61
		%	76.0%	100.0%	72.7%	74.4%
	Yes	Count	6	0	15	21
		%	24.0%	0.0%	27.3%	25.6%
Total		Count	25	2	55	82
		%	100.0%	100.0%	100.0%	100.0%
	Chi-sq (p value)		0.802 (0.670)			

Table 3: No significant correlation between WBC count and mortality (p = 0.670)

Table 4 Platelet count distribution in ICU patients with acute febrile illness and MODS

Platelet count	Frequency	Percent	Valid Percent	Cumulative Percent
<1.5 lakhs	66	80.5	80.5	80.5
>1.5 lakhs	16	19.5	19.5	100.0
Total	82	100.0	100.0	

Platelet count distribution(Table 4) shows 80.5% had platelets <1.5 lakhs, indicating thrombocytopenia.

Table 5 Platelet count and mortality outcome in patients with acute febrile illness and MODS

			Death		
			No	**Yes**	**Total**
Platelet count	<1.5 lakhs	Count	46	20	66
		%	75.4%	95.2%	80.5%
	>1.5 lakhs	Count	15	1	16
		%	24.6%	4.8%	19.5%
Total		Count	61	21	82
		%	100.0%	100.0%	100.0%
	Chi-sq (p value)		4.829(0.028)		

Table 5 shows significant association between thrombocytopenia and mortality (p = 0.028)

Table 6 Creatinine level distribution in ICU patients with acute febrile illness and MODS

Creatinine level				
Creatinine	**Frequency**	**Percent**	**Valid Percent**	**Cumulative Percent**
<1.2	23	28.0	28.0	28.0
>1.2	59	72.0	72.0	100.0
Total	82	100.0	100.0	

Table 6 shows 72% had serum creatinine >1.2, indicating renal dysfunction.

Table 7 Creatinine level and mortality outcome in ICU patients with acute febrile Illness and MODS

Death & creatinine Cross-tabulation					
			creatinine		
			<1.2	**>1.2**	**Total**
Death	No	Count	22	39	61
		%	95.7%	66.1%	74.4%
	Yes	Count	1	20	21
		%	4.3%	33.9%	25.6%
Total		Count	23	59	82
		%	100.0%	100.0%	100.0%
	Chi-sq (p value)		7.585 (0.006)		

Table 7 shows high creatinine significantly associated with mortality (p = 0.006).

Table 8 Bilirubin level distribution in ICU patients with acute febrile illness and MODS

Bilirubin level distribution					
	Bilirubin	**Frequency**	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	<1.2	32	39.0	39.0	39.0
	>1.2	50	61.0	61.0	100.0
	Total	82	100.0	100.0	

Table 8 shows 61% had bilirubin >1.2 mg/dL, suggesting liver dysfunction.

Table 9 Bilirubin level and mortality outcome in ICU patients with acute febrile illness and MODS

			Bilirubin		**Total**
			<1.2	**>1.2**	
Death	No	Count	31	30	61
		%	96.9%	60.0%	74.4%
	Yes	Count	1	20	21

		%	3.1%	40.0%	25.6%
Total		Count	32	50	82
		%	100.0%	100.0%	100.0%

Table 9 shows high bilirubin strongly correlated with mortality.

Table 10 Mean arterial pressure (MAP) distribution in ICU patients with acute febrile illness and MODS

MAP	Frequency	Percent	Valid Percent	Cumulative Percent
>70 mmHg	22	26.8	26.8	26.8
<70 mmHg	60	73.2	73.2	100.0
Total	82	100.0	100.0	

Table 10 shows 73.2% had MAP <70 mmHg (hypotension)

Table 11 Mean arterial pressure (MAP) and mortality outcome in ICU patients with acute febrile illness and MODS

			MAP		Total
			>70 mmHg	<70 mmHg	
Death	No	Count	22	39	61
		%	100.0%	65.0%	74.4%
	Yes	Count	0	21	21
		%	0.0%	35.0%	25.6%
Total		Count	22	60	82
		%	100.0%	100.0%	100.0%
	Chi-sq (p value)		10.351 (0.001)		

Table 11 shows low MAP highly associated with mortality (p = 0.001)

Table 12 Respiratory distress in ICU patients with acute febrile illness and MODS

Respiratory_Distress	Frequency	Percent	Valid Percent	Cumulative Percent
Yes	47	57.3	57.3	57.3
No	35	42.7	42.7	100.0
Total	82	100.0	100.0	

Table 12 shows 57.3% had respiratory distress

Table 13 Respiratory distress and mortality outcome in ICU patients with acute febrile illness and MODS

Death * Respiratory Distress Cross-tabulation					
			Respiratory_ Distress		Total
			Yes	No	
Death	No	Count	26	35	61
		%	55.3%	100.0%	74.4%

	Yes	Count	21	0	21
		%	44.7%	0.0%	25.6%
Total		Count	47	35	82
		%	100.0%	100.0%	100.0%

Table 13 shows Respiratory distress significantly associated with mortality

Table 14 Distribution of neurological status among patients

	Neurological status	Frequency	Percent	Valid Percent	Cumulative Percent
Valid	<15	36	43.9	43.9	43.9
	15	46	56.1	56.1	100.0
	Total	82	100.0	100.0	

Table 14 shows 43.9% had impaired neurological status (GCS <15).

Table 15 Association between neurological status and mortality

			NEUROLOGICAL STATUS		Total
			<15	15	
Death	No	Count	15	46	61
		%	41.7%	100.0%	74.4%
	Yes	Count	21	0	21
		%	58.3%	0.0%	25.6%
Total		Count	36	46	82
		%	100.0%	100.0%	100.0%

Table 15 shows neurological impairment strongly correlated with mortality

Table 16 IgM Dengue test results in ICU patients with acute febrile illness and MODS

	IgM Dengue	Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Negative	59	72.0	72.0	72.0
	Positive	23	28.0	28.0	100.0
	Total	82	100.0	100.0	

Table 16 shows 28% had positive IgM Dengue.

Table 17 IgM Dengue test results and mortality outcome in ICU patients with acute febrile illness and MODS

Crosstab					
			IgM Dengue		
-			Negative	Positive	Total
Death	No	Count	42	19	61
		%	68.9%	31.1%	100.0%

	Yes	Count	17	4	21
		%	81.0%	19.0%	100.0%
Total		Count	59	23	82
		%	72.0%	28.0%	100.0%
		Chi-sq (p value)	1.14 (0.287)		

Table 17 shows no significant association (p = 0.287)

Table 18 IgM Leptospirosis test results in ICU patients with acute febrile illness and MODS

IgM Lepto					
	IgM Lepto	**Frequency**	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	Negative	76	92.7	92.7	92.7
	Positive	6	7.3	7.3	100.0
	Total	82	100.0	100.0	

Table 18 shows 7.3% positive IgM Leptospirosis

Table 19 IgM Leptospirosis test results and mortality outcome in ICU patients with acute febrile illness and MODS

Crosstab					
			IgM Lepto		**Total**
			Negative	**Positive**	
Death	No	Count	59	2	61
		%	96.7%	3.3%	100.0%
	Yes	Count	17	4	21
		%	81.0%	19.0%	100.0%
Total		Count	76	6	82
		%	92.7%	7.3%	100.0%
		Chi-sq (p value)	5.728 (0.017)		

Table 19 shows significant association with mortality (p = 0.017)

Table 20 Weil-Felix test results in ICU patients with acute febrile illness and MODS

	Weil Felix	**Frequency**	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	Negative	77	93.9	93.9	93.9
	Positive	5	6.1	6.1	100.0
	Total	82	100.0	100.0	

Table 20 shows 6.1% Positive for Weil-Felix test

Table 21 Weil-Felix test results and mortality outcome in ICU patients with acute febrile illness and MODS

Cross-tab					
			Weil Felix		**Total**
			Negative	**Positive**	
Death	No	Count	57	4	61
		%	93.4%	6.6%	100.0%
	Yes	Count	20	1	21
		%	95.2%	4.8%	100.0%
Total		Count	77	5	82
		%	93.9%	6.1%	100.0%
		Chi-sq (p value)	0.088 (0.767)		

Table 21shows no significant association with mortality (p = 0.767)

Table 22 QBC test results in ICU patients with acute febrile illness and MODS

	QBC	**Frequency**	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	Negative	80	97.6	97.6	97.6
	Positive	2	2.4	2.4	100.0
	Total	82	100.0	100.0	

Table 22 shows 2.4% positive QBC (malaria)

Table 23 QBC test results and mortality outcome in ICU patients with acute febrile illness and MODS

Cross-tab					
			QBC		Total
			Negative	Positive	
Death	No	Count	59	2	61
		%	96.7%	3.3%	100.0%
	Yes	Count	21	0	21
		%	100.0%	0.0%	100.0%
Total		Count	80	2	82
		%	97.6%	2.4%	100.0%
		Chi-sq (p value)	0.706 (0.401)		

Table 23 shows QBC result not associated with mortality (p = 0.401).

Table 24 Widal test results in ICU patients with acute febrile illness and MODS

	Widal	**Frequency**	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	Negative	79	96.3	96.3	96.3
	Positive	3	3.7	3.7	100.0
	Total	82	100.0	100.0	

Table 24 shows 3.7% positive Widal (enteric fever)

Table 25 Widal test results and mortality outcome in ICU patients with acute febrile illness and MODS

Crosstab					
			Widal		**Total**
			Negative	**Positive**	
Death	No	Count	58	3	61
		%	95.1%	4.9%	100.0%
	Yes	Count	21	0	21
		%	100.0%	0.0%	100.0%
Total		Count	79	3	82
		%	96.3%	3.7%	100.0%
		Chi-sq (p value)	1.072 (0.300)		

Table 25 Widal not associated with mortality (p = 0.300)

4. Discussion

Older adults (≥60 years) were most affected, comprising 30.5% of MODS cases in ICU. This aligns with Nayak et al. (2024) and Ray et al. (2019), who also found higher mortality in older patients.[8][9] The increased vulnerability of this group may be due to age-related immune senescence, comorbidities, and delayed presentation. Middle-aged adults also constituted a significant proportion, emphasizing that MODS is not confined to the elderly alone.

Elevated WBC (>10,000/μL) in 67.1% of patients indicates a robust inflammatory response, characteristic of SIRS and sepsis. Though nonspecific, this parameter remains a frontline marker. While Tang et al. (2003) and Koike et al. (2000) did not find a direct mortality association.[11][12] Talmor et al. (1999) demonstrated significant predictive value for poor outcomes[13].

Thrombocytopenia (<150,000/μL) was present in 80.5% of cases and significantly associated with mortality. This finding corroborates studies by Khurana & Deoke (2017) and Moreau et al. (2007), affirming the prognostic value of dynamic platelet trends in critical illness. [14][15]

Renal dysfunction, reflected by elevated creatinine in 72% of patients, underscores the kidney's early involvement in MODS. These results support findings from Maheswari & Mandal and Ray et al., stressing the importance of renal function monitoring in critically ill febrile patients.[9][10]

Elevated bilirubin in 61% of patients indicates hepatic involvement, a component of MODS. Literature (Zheng et al., Shastri et al.) affirms its independent correlation with ICU mortality, suggesting its use as a routine prognostic biomarker.[16][17]

A MAP <70 mmHg in 73.2% of cases confirms circulatory shock and is a well-established mortality predictor, as validated by Ko et al. (2021) and Lehman et al. (2010).[18][19] Persistent hypotension exacerbates organ injury and warrants aggressive hemodynamic support.

Respiratory compromise was seen in 57.3% of patients. Its association with MODS and mortality, as documented in studies like Varmudy et al. (2022) and Li et al. (2007), highlights its dual role as both a consequence and a contributor to systemic failure.[20][21]

Patients with GCS <15 had markedly higher mortality (58.3%). This supports the predictive dominance of neurological status seen in Knox et al. (2014) and Bastos et al. (1993).[22][23] GCS thus remains an essential early prognostic indicator.

Detected in 28%, dengue IgM did not show significant mortality correlation. As seen in Shastri et al. (2020), complications (shock, hepatic failure) rather than IgM status determine prognosis in dengue-related MODS.[17]

Leptospirosis (7.3%) had a significant mortality association (p=0.017), aligning with high-risk profiles described in Karnik & Patankar (2021) and Chawla et al. (2004).[25][26] Leptospirosis should be promptly recognized and managed in MODS settings.

Despite 6.1% positivity, there was no mortality association. Literature confirms that while the Weil-Felix test aids in rickettsial diagnosis, it lacks sensitivity and does not predict outcomes independently (Udayan et al., 2014).[27]

Low positivity (2.4%) indicates malaria is a minor contributor to MODS in this cohort. Other studies (Vidyasagar et al., 2022) report similar trends, highlighting declining malaria-related MODS in ICU settings.[28]

With only 3.7% positivity, Widal testing remains of limited utility for MODS prediction. This is supported by Mariraj et al. (2020), suggesting enteric fever is an infrequent cause of severe organ failure.[29]

5. Conclusion

This study highlights the prognostic value of key clinical markers—creatinine, bilirubin, platelet count, and mean arterial pressure—in patients with acute febrile illness and MODS in the ICU. These indicators were strongly associated with mortality, underscoring the need for early recognition and intervention. While infections like dengue and leptospirosis were identified, many cases lacked a definitive cause, suggesting a broader pathophysiological spectrum. These findings support the use of targeted diagnostics and management strategies to improve outcomes, with further research needed to explore non-infectious contributors to MODS.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

The study was approved by the Institutional Ethical Committee.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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