Clinical Profile and Outcome of Multiple Organ Dysfunction Syndrome (MODS) in a Tertiary Care Centre of Manipal, Karnataka

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ABSTRACT

BACKGROUND

To study the clinical profile and outcome of multiple organ dysfunction syndrome (MODS) in previously healthy adult patients and to assess the correlation between sequential organ failure assessment (SOFA) score at admission and mortality in these patients.

METHODS

This study was conducted at a tertiary care hospital attached to a medical college of south India. This was a prospective observational study. All adult patients presenting with multiple organ dysfunction syndrome between October 2010 and June 2012 were selected for the study. SOFA score was recorded for all the patients at the time of admission. Patients were followed up till the time of death or discharge.

RESULTS

In this study, majority of the cases were males and belonged to middle age group. Epidemic diseases such as scrub typhus and leptospirosis were the most common causes of MODS. Fever was the most common presenting symptom of MODS. Majority of patients recovered. Higher SOFA score at admission is associated with increased mortality, duration of hospital stay, requirement of ventilatory support, haemodialysis, and central venous access.

CONCLUSIONS

Infectious diseases are responsible for most cases of MODS. Higher SOFA score at admission is associated with increased morbidity and mortality. Majority of people recover with appropriate treatment.

KEYWORDS

MODS, Clinical Profile, SOFA Score, Outcome

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DOI: 10.18410/jebmh/2021/643

How to Cite This Article:
Marijayanth M, Horatti A, Tandure V, et al. Clinical profile and outcome of multiple organ dysfunction syndrome (MODS) in a tertiary care centre of Manipal, Karnataka. J Evid Based Med Healthc 2021;8(41):3547-3552. DOI: 10.18410/jebmh/2021/643

Submission 21-10-2019,
Peer Review 29-10-2019,
Acceptance 23-10-2021,
Published 30-10-2021.

BACKGROUND

Multiple organ dysfunction syndrome is a clinical syndrome characterized by the development of progressive and potentially reversible physiologic dysfunction in 2 or more organs or organ systems that is induced by a variety of acute insults, including sepsis.[1] Organ dysfunction is a common event among intensive care patients, with almost all critically ill patients having some degree of organ dysfunction during their hospital stay. Alteration in organ function can vary widely from a mild degree of organ dysfunction to completely irreversible organ failure. The degree of organ dysfunction has a major clinical impact.[2-3] Morbidity and mortality in MODS increases as the number and severity of organ failure increases.

Major risk factors for MODS include sepsis and the systemic inflammatory response syndrome (SIRS), shock and prolonged periods of hypotension, trauma, bowel infarction, hepatic dysfunction, increased age, and alcohol abuse. MODS appears to result from a cascade of organism-related factors, inflammatory mediators, endothelial injury, disturbed haemostasis, and microcirculatory abnormalities. MODS is currently recognized as a major cause of mortality in SIRS, trauma, sepsis and other critical illnesses.[4] Primary MODS is the direct result of a well-defined insult in which organ dysfunction occurs early and can be directly attributable to the insult itself.

Secondary MODS develops as a consequence of a host response and is identified within the context of systemic inflammatory response syndrome. Several studies[5–7] indicated that mortality in severe sepsis is a function of the number of failing organ systems and the severity of dysfunction within the system.

In fact, MODS is now regarded as the most common cause of death among patients in non-coronary critical care units.[8]

The prognosis of patients with severe sepsis is related to the severity of organ dysfunction at the time of admission to the intensive care unit (ICU).[9]

Specific scoring systems have been used to quantify the level of organ dysfunction and have been primarily used in the evaluation of various investigational agents. Scoring systems such as the sequential organ failure assessment are useful tools for assessing and quantifying organ dysfunction and failure over time. In the SOFA system, organ system dysfunction is used to evaluate morbidity in critically ill patients.[10]

Additionally, the SOFA score is a good indicator of mortality. Many studies[11,12] have found that patients with the highest SOFA score during the first 48 hours of care in the intensive care unit had increased mortality rate.

However there is scarcity of literature addressing the clinical profile, correlation between SOFA score at admission and outcome of MODS among previously healthy patients.

Hence, the present study was undertaken to assess these points in previously healthy adult patients with MODS.

METHODS

This was a prospective observational study, conducted at a tertiary care hospital attached to a medical school of south India between October 2010 and June 2012. Necessary ethical clearance was obtained from the Institutional Ethical and Research Committee.

A total of 172 adult patients (age more than 18 years) presenting with MODS and satisfying the study criteria were studied.

The following groups of patients were excluded

- Patients having documented pre-existing organ dysfunction.
- Patients on drugs which may cause organ dysfunction.
- Patients with conditions causing immunosuppression or on drugs causing immunosuppression.
- Pregnant patients.
- Patients with diabetes mellitus.
- Patients with hypertension.

Demographic data such as age and sex were recorded. Patients or their caregivers were interviewed for the clinical history and clinical signs. Thorough clinical examination was conducted for all patients. Findings were recorded in a predesigned and pretested proforma. Further, these patients were subjected to investigations. Renal function tests (RFT), liver function tests (LFT), complete blood counts (CBC), arterial blood gas analysis were among other investigations requested by the treating physicians. Other investigations done were blood culture, quantitative buffy coat study for malarial parasite and serological studies (acute sera and where necessary convalescent sera were studied).

Final diagnosis was made on the basis of clinical features and the results of lab investigations. In cases where a specific diagnosis was not reached, the patients were included among the category "Undiagnosed".

SOFA Score	0	1	2	3	4
Respiration PaO_2/FIO_2(mm Hg) SaO_2/FIO_2	> 400	< 400221 – 301	< 300142 – 220	< 20067– 141	< 100 < 67
Coagulation Platelets $10^3/mm^3$	> 150	< 150	< 100	< 50	< 20
Liver billirubin (mg/dL)	< 1.2	1.2 1.9	2.0 – 5.9	6.0 – 11.9	> 12.0
Cardiovascular hypotension	No hypotension	MAP < 70	Dopamine </= 5µg/kg/min or dobutamine (any dose)	Dopamine > 5µg/kg/min or Epi/ Nor epinephrine </= 0.1µg/kg/ min	Dopamine > 15µg/kg/min or Epi/ Nor epinephrine > 0.1µg/kg/ min
CNS Glasgow coma score	15	13 – 14	10 – 12	6–9	<6
Renal creatinine (mg/dL) or urine output (mL/d)	< 1.2	1.2 – 1.9	2.0 – 3.4	3.5 – 4.9 or < 500	> 5.0 or < 200

Table 1. Assessment of SOFA Score

Based on these variables, the SOFA score was determined and patients were graded for the severity of the condition as below;

- Score ≤ 6
- Score 7 to 12
- Score 13 to 18
- Score of > 18

The data obtained was coded and entered into Microsoft Excel worksheet. The categorical data was expressed as rates, ratios and proportions and comparison was done using chi-square test. The continuous data was expressed as mean ± standard deviation (SD) and the comparison was done using student 't' test. A probability value ('p' value) of less than or equal to 0.05 was considered as statistically significant.

RESULTS

The present hospital based cross sectional study was conducted in the Department of Medicine, Kasturba Medical College, Manipal over a period of two years. A total of 172 patients presenting with multiple organ dysfunction syndrome were studied.

The data obtained was coded and entered into Microsoft Excel worksheet. The data was analysed and the final results and observations were tabulated as below. A total of 172 patients presenting with multiple organ dysfunction syndrome were studied. Out of these, 115 patients (66.86 %) were males and 57 (33.14 %) were females. Highest number of patients (N = 78, 45.35 %) were between 31 to 45 years. The mean age of the study population was 42.83 ± 13.38 years with range being 18 to 75 years.

In the present study, 43.02 % patients had SOFA score between 13 to 18 followed by 37.21 % between 7 to 12. However, 11.05 % patients had SOFA score of < 7 and 8.72 % patients had SOFA score of more than 18.

The presenting clinical symptoms/signs of the patients studied are shown in table 2. Majority of the patients presented with fever (94.77 %), hepatomegaly (79.65 %), and myalgia (74.42 %).

Presentation	Distribution (n = 172)	
	Number	Percentage
Fever	163	94.77
Headache	116	67.44
Cough	96	55.81
Breathlessness	118	68.60
Jaundice	95	55.23
Diarrhoea	22	12.79
Oliguria	94	54.65
Myalgia	128	74.42
Lymphadenopathy	25	14.53
Tachypnoea	124	72.09
Crepitations	127	73.84
Hepatomegaly	137	79.65
Splenomegaly	45	26.16

Table 2. Presenting Complaints

The most common diagnosis was scrub typhus (24.42 %). The next common diagnosis was leptospirosis (22.09 %).

Diagnosis	Distribution (n = 172)	
	Number	Percentage
Acute gastroenteritis	5	2.91
Acute pancreatitis	4	2.33
Dengue	10	5.81
Sepsis E. Coli	10	5.81
Falciparum malaria	8	4.65
H1N1	13	7.56
Leptospirosis	38	22.09
Pneumonia	9	5.23
Scrub typhus	42	24.42
Snake bite	6	3.49
Malaria (vivax)	13	7.56
Undiagnosed	14	8.14
Total	**172**	**100.00**

Table 3. Diagnosis

In the present study, 96 (55.81 %) patients required invasive mechanical ventilation and 14 patients (8.14 %) required non-invasive ventilation. 62 (36.05 %) patients did not require mechanical ventilation. Haemodialysis was required for 82 (47.77 %) patents. Central line access was required in 105 (61.05 %) patients. Mean SOFA scores in patients who had central venous access were significantly high (15.00 ± 3.47; p < 0.001). In this study, almost half of the patients (49.42 %) had hospital stay between 8 to 14 days. In 26.16 % and 20.93 % patients, it was less than 8 days and 15 to 21 days and 3.49 % patients required hospitalization of more than 21 days. The mean duration of stay was 11.23 ± 4.28 days with range being 2 to 24 days.

Majority (79.07 %) of the patients improved whereas 15.70 % expired. However, 5.23 % patients were discharged against medical advice and were not available for follow up. There was a positive association of SOFA score with increasing age (p = 0.003). Higher mean SOFA scores were observed in patients who were intubated (15.09 ± 3.40) and who underwent non-invasive ventilation (9.92 ± 4.83) compared to those who did not require ventilatory support (8.74 ± 3.51) suggesting a strong association of higher SOFA scores with ventilatory support (p < 0.001). The mean SOFA score in patients who underwent dialysis were high compared to those who did not require dialysis (15.85 ± 2.82 versus 9.15 ± 3.59) and this difference was statistically significant (p < 0.001). The mean SOFA scores in patients who had central venous access were significantly high (15.00 ± 3.47; p < 0.001). There was also increasing trend of mean SOFA scores with increased duration of hospital stay which was statistically significant (Table 4).

Hospital Stay (Days)	Mean SOFA Score	
	Mean	SD
< 8	11.55	6.05
8 to 14	11.89	4.17
15 to 21	14.38	3.26
> 21	23.00	1.10

Table 4. Mean SOFA Score and Length of Hospital Stay

ANOVA test F=13.84, DF=171, p=<0.0001

Outcome	Mean SOFA Score	
	Mean	SD
Improved	10.96	4.06
Expired	17.63	2.84
Discharged against medical advice	18.11	1.17

Table 5. Mean SOFA Scores and Outcome

ANOVA test F = 45.27, DF = 171, p = <0.0001

The mean SOFA scores in patients who expired (17.63 ± 2.84) and those who were discharged against medical advice (18.11 ± 1.17) were high compared to those who

improved (10.96 ± 4.06) and this difference was statistically significant (p < 0.001).

SOFA Score Range	Improved (n = 136)		Expired (n = 36)		Total (n = 172)	
	No	%	No	%	No	%
up to 6	19	100.00	0	0.00	19	11.05
7 to 12	62	96.88	2	3.13	64	37.21
13 to 18	54	72.97	20	27.03	74	43.02
> 18	1	6.67	14	93.33	15	8.72
Table 6. Overall SOFA Score and Mortality						
Chi square test x^2 = 66.50, DF = 3, p =< 0.0001						

Among the 19 patients with SOFA scores up to 6, all (100 %) improved whereas of the 15 patients with SOFA scores of > 18, 93.33 % patients expired and 6.67 % patients improved and this difference between the higher SOFA score in patients with mortality was statistically significant (p < 0.001). Out of 115 male patients, 18 (15.65 %) expired whereas out of 57 females 18 (31.58 %) expired. This difference of outcome between the sexes was statistically significant (p = 0.016). Out of 36 patients who expired, 12 (54.55 %) were aged more than 60 years whereas among the patients aged between 18 to 30 years, 2 (6.25 %) expired. This difference of outcome among different age groups was statistically significant. In the present study, among the patients with 18 to 30 years the mean SOFA scores were 11.13 ± 4.52 whereas in those who were aged more than 60 years the mean SOFA scores were 15.41 ± 4.01 suggesting positive association of SOFA score with increasing age (p = 0.003).

DISCUSSION

Scoring systems can be useful to predict the severity and prognosis of critically ill patients and also to guide the therapy. Commonly used outcome prediction scores taken during the first 24 hours of intensive care unit (ICU) admission includes systems such as acute physiology and chronic health evaluation (APACHE) II and III, simplified acute physiology score (SAPS) II and Mortality Probability Models (MPM) II. The SOFA score was developed during a consensus conference organized by the European Society of Intensive Care and Emergency Medicine. Originally termed the "sepsis-related" organ failure assessment, it can be applied equally to all ICU patients. Initial validation was performed on a heterogeneous group of 1,449 critically ill patients. The MODS and the SOFA allow the calculation of a summary value for the degree of dysfunction for six organs (respiratory, hematologic, liver, cardiovascular, central nervous system and renal). Four levels of dysfunction are identified for each of the organ systems for both the MODS and the SOFA score. Although MODS is readily recognized by experienced clinicians, there is no clear consensus with respect to systems whose function is deranged, descriptors that best measure the derangement, or the degree of derangement that constitutes organ dysfunction or failure. Given the difficulties with accepted definitions, it is not surprising that the actual incidence of MODS/MOF is unknown. In part, this uncertain incidence is related to lack of a uniformly accepted definition, but there also is uncertainty concerning how to factor in pre-existing organ dysfunction/failure. Nevertheless, scoring systems such as APACHE and SOFA have been proven to be good predictors of outcome in critically ill patients and provide an objective way of assessing the severity of illness.

In this study, majority of patients were males. Most of them had fever as the presenting complaint. Infectious diseases were the most common cause of MODS especially scrub typhus and leptospirosis. These two infections i.e. scrub typhus and leptospirosis are common in people who work outside and come in contact with vegetation and water contaminated with rat urine. This can explain the high incidence of these two infections among males who traditionally go out for work and get exposed to organisms causing these two infections. In the present study, majority (79.07 %) of the patients improved whereas 15.70 % expired. 5.23 % patients were discharged against medical advice. This indicates that with early diagnosis and effective treatment, most of the patients can improve. Almost half of the patients (49.42 %) had hospital stay between 8 to 14 days. 3.49 % patients required hospitalization of more than 21 days. The mean length of stay was 11.23 ± 4.28 days with range being 2 to 24 days. Longer duration of stay was associated with higher SOFA score. There was a strong association between higher SOFA score and mortality. Higher mean SOFA scores were also observed in patients who were intubated (15.09 ± 3.40) and in those who underwent non-invasive ventilation (9.92 ± 4.83).

Vincent et al.[11] in 1998 working on "sepsis-related "problems published the first evaluation of the SOFA score. The main outcome measures included incidence of dysfunction/failure of different organs and the relationship of this dysfunction with outcome. In this cohort of patients, the median length of ICU stay was 5 days, and the ICU mortality rate was 22 %. They found that infected patients had more severe organ dysfunctions compared to those without infection. The evaluation of a subgroup of 544 patients who stayed in the ICU for at least 1 week showed that survivors and non-survivors followed a different course. In this subgroup, the total SOFA score increased in 44 % of the non-survivors but in only 20 % of the survivors which was statistically significant. Conversely, the total SOFA score decreased in 33 % of the survivors compared with 21 % of the non-survivors. A study by Antonelli et al.[12] in 1999 found that the non-survivors were significantly older than the survivors (51 years +/-20 vs 38 +/-16 years, p < 0.05) and had a higher global SOFA score on admission (8 +/-4 vs 4 +/- 3, p < 0.05) and throughout the 10-day stay. On admission, the non-survivors had higher scores for respiratory (> 3 in 47 % of non-survivors vs 17 % of survivors), cardiovascular (> 3 in 24 % of non-survivors vs 5.7 % of survivors), and neurological systems (> 4 in 41 % of non-survivors vs 16 % of survivors); although the trend was maintained over the whole study period, the differences were greater during the first 4 - 5 days. After the first 4 days, only respiratory dysfunction was significantly related to outcome. A higher SOFA score, admission to the ICU from the same hospital, and the

presence of infection on admission were the three major variables associated with a longer length of stay in the ICU. Because the total maximum SOFA score can be easily calculated daily for the patient, no restriction based on the patients' ICU length of stay is necessary. In our study, the mean SOFA scores increased as the duration of hospital stay increased. This increasing trend of mean SOFA score with increased duration of hospital stay was statistically significant. All these findings concur with the results of previous studies

The mean SOFA score in patients who underwent dialysis was high compared to those who did not have dialysis (15.85 ± 2.82 versus 9.15 ± 3.59) ($p < 0.001$). The mean SOFA score in patients who had central venous access was significantly high (15.00 ± 3.47; $p < 0.001$). The mean SOFA score in patients who expired (17.63 ± 2.84) and those who were discharged against medical advice (18.11 ± 1.17) was high compared to those who improved (10.96 ± 4.06) ($p < 0.001$). It was observed that, the mean SOFA scores in patients who succumbed were significantly high compared to those who improved in all the age groups ($p < 0.05$). Among the 19 patients with SOFA scores up to 6, all (100 %) improved whereas of the 15 patients with SOFA scores of > 18, 93.33 % patients succumbed and 6.67 % patients improved and this difference between the higher SOFA score in patients with mortality was statistically significant ($p < 0.001$).

There were some early published studies that have since examined the utility and accuracy of the SOFA score, which proved that maximum SOFA score and increasing SOFA score are highly prognostic for stratification of critically ill patients including septic patients.[13-15] Lithuania[16] et al. observed that SOFA score on day 1 and day 3 was significantly higher in non-survivors than those in survivors. In the present study of the 115 male patients, 18 (15.65 %) expired whereas of the 57 females 18 (31.58 %) expired. This difference of outcome between the sexes was statistically significant ($p = 0.016$). Of 36 patients who expired, 54.55 % were aged more than 60 years whereas among the patients aged between 18 to 30 years, 6.25 % expired. This difference of outcome among different age groups was statistically significant.

The MODS and the SOFA have been used in many clinical studies. The reliability of the SOFA score as an outcome predictor has been demonstrated and the correlation between a high degree of organ failure as assessed by the SOFA score and mortality is well established. The results from this study show that the MODS and the SOFA score correlate well with outcome in terms of mortality prediction.

CONCLUSIONS

The present study showed fever as the most common clinical presentation of MODS in previously healthy adult patients. Infectious diseases were the cause of majority of MODS cases. Male patients were more commonly affected and most of the patients belonged to middle age. Increasing age is also associated with higher SOFA score and increased mortality. Increasing organ dysfunction as measured by the SOFA score consistently correlates with increasing mortality. Majority of the patients with MODS improved with appropriate treatment. SOFA score can be used as an alternative to APACHE II score.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.
Financial or other competing interests: None.
Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

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