

**To Evaluate Multiple Organ dysfunction Syndrome And Their Survival Outcome According To Sequential Organ Failure Assessment Score And Simplified Acute Physiology Score Among Patients With Infectious Diseases**

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**Introduction**

Lack of clinical diagnostic criteria, high cost and non availability of isolation techniques results in misdiagnosis and treatment failure. <sup>(1)</sup> Due to improper utilization of resources, etiology remains unestablished during the first crucial 24-48 hours. The European society of intensive care medicine organized a consensus meeting in Paris in October 1994 to create SOFA –a sepsis related organ failure assessment score, to describe quantitatively and the degree of organ dysfunction over the time in groups of patients or even in the individual patients. Six organ functions were assessed using the initial SOFA score. This can be used to characterize the patients at the entry or to evaluate effects of treatment. Lack of clinical diagnostic criteria, high cost and non availability of isolation techniques results in misdiagnosis and treatment failure. <sup>(1)</sup> Due to improper utilization of resources, etiology remains un established during the first crucial 24-48 hours. Later in 1993, it was modified to SAPS II<sup>(2)</sup> which was calculated as the sum of points assigned to each of the 17 variables and age, type of admission and 3 underlying diseases. Assessment of SAPS and SOFA score in ICU, may be helpful in knowing the prognosis of the severity of

organ dysfunction and predicting mortality in the infectious diseases in Indian population.

A study concluded that serial measurement of SOFA score during the first week is a very useful tool in predicting the outcome <sup>(3)</sup>. A study in 2001 analysed serial evaluation of SOFA score as an outcome predictor in critically ill and proved SOFA score during the first few days of ICU admission as a good indicator of prognosis<sup>(4)</sup>.SAPS score showed statistical significance in another studies<sup>(5,6)</sup> but showed no statistical significance in a study done in greek ICU<sup>(7)</sup>.

**Multiorgan Dysfunction Syndrome:** It is defined by simultaneous presence of physiological dysfunction and/or failure of 2 or more organs.

Causes: Severe sepsis, Shock of any kind, severe inflammatory conditions such as pancreatitis, Trauma

Principles of MODS:-Organ failure no matter how it is defined must persist beyond 24 hours. Mortality risk increases with the accrual of failing organs.

## Aims and Objectives

**Aims:** To assess sequential organ failure assessment score (SOFA) and simplified acute physiology score (saps) in the patients with infectious diseases and multiple organ dysfunction syndrome (MODS). To compare sofa score with saps score

**Objective:** To identify whether sofa score is better than saps score. To compare survival outcome by sofa score and saps score in various infectious diseases.

**Duration of study:** -18months

**Study Design:** The present study is an observational study.

## Review of Literature

**Definitions: Bacteremia:** Presence of bacteria in blood as evidenced by positive blood cultures.

**Signs of possibly harmful systemic Response:**Two or more of the following conditions: Fever (oral temperature  $>38^{\circ}\text{C}$  or hypothermia  $<36^{\circ}\text{C}$ ). Tachypnea ( $>24$  breaths/min). Tachycardia (heart rate  $>90$  beats/min). Leukocytosis ( $>12,000/\mu\text{L}$ ), or Leucopenia ( $<4000/\mu\text{L}$ ).

**Sepsis:** The harmful host response to infection, systemic response to proven or suspected infection plus some degree of organ hypofunction. i.e. cardiovascular: arterial systolic blood pressure  $<90$  mm of hg or mean arterial pressure  $<70$  mm of hg that responds to administration of IV fluids

**Renal:** urine output  $<0.5\text{ml/kg}$  per hour for 1 hr despite adequate fluid resuscitation

**Respiratory:**  $\text{pao}_2/\text{Fio}_2 <250$  or if the lung is only dysfunctional organ

**Hematological:** platelet count  $<80,000/\text{micro l}$  or 50% decrease in platelet count from highest value recorded over previous 3 days

**Unexplained metabolic acidosis:** a  $\text{ph}<7.3$  or a base deficit  $>5\text{meq/l}$

**Etiology:** The systemic response to microorganism can be dreadful. Microbial invasion in the bloodstream is not essential as local inflammation can also be elicited by distant-organ dysfunction and hypotension.

**Epidemiology:** Severe sepsis is a contributing factor in  $>200,000$  deaths per year in the United States. The incidence of septic shock and sepsis has increased over the past 30 years, and the annual number of cases is now  $>750,000$  (i.e. 3 per 1000 population)

**Pathophysiology:** Sepsis is triggered most often by pathogens that do not ordinarily cause systemic disease in immune compromise hosts. Lack of molecules that can be recognized by host receptors. Elaborate toxins or other virulence factors.

Having numerous TLR-based receptor complexes allows animals to recognize many conserved microbial molecules; others include lip peptides (TLR2/1, LR2/6) flagellin (TLR5), under ethylated DNA CpG sequences (TLR9), single-stranded RNA (TLR7,8), and double-stranded RNA (TLR3).

Most of the commensal aerobic and anaerobic gram-negative bacteria that triggers severe sepsis and shock (includes E. coli, Klebsiella, and Enterobacter) that make this lipid A structure. When they invade human hosts, often through breaks in an epithelial barrier, they are typically confined up to the sub epithelial tissues by the localized inflammatory response.

**Local and Systemic Host Responses to Invading Microbes:** Recognition of the microbial molecules by the tissue phagocytes that triggers production of numerous host molecules such as (cytokines, prostanoids, chemokines, leukotrienes, etc.) that increases the blood flow to the infected tissue (rubor), enhance the permeability of local blood vessels (tumor), recruits the neutrophils and other cells to site of infections (calor), and

elicits pain (dolor). IL-1 $\beta$  exhibits many of the same activities as TNF- $\alpha$ . TNF- $\alpha$ , IL-1 $\beta$ , interferon  $\gamma$ , IL-12, IL-17, and other proinflammatory cytokines probably interact synergistically with one another and with additional mediators.

**Coagulation factors:** Intravascular thrombosis, a hallmark of local inflammation may help wall off invading the microbes and prevent infection and inflammation from spreading to the other tissues. IL-6 and the mediators which promotes intravascular coagulation initially by inducing the blood monocytes and vascular endothelial cells to express tissue factor.

**Local control mechanism:** Host recognition of invading microbes within sub epithelial tissues typically ignites the immune responses that rapidly kills the invaders and then subsides to allow the tissue recovery.

**Systemic control mechanisms:** Circulating levels of cortisol and anti-inflammatory cytokines (e.g., IL-6 and IL-10) increase even in patients with minor infections. Glucocorticoids inhibit cytokine synthesis by monocytes in vitro; the increase of blood cortisol levels that occur early in the systemic response do presumably plays a similarly inhibitory role.

**Endothelial injury:** Leukocyte-derived mediators and platelet-leukocyte-fibrin thrombi also contributes to the vascular injury, but the vascular endothelium also seems to play active role.

**Septic shock:** Most important sign of septic shock is a decrease in peripheralvascular resistance that occurs despite of increased levels of vasopressor and catecholamines.

**Clinical manifestation:** Hyperventilation, which produces respiratory alkalosis, is often a early sign of septic response. Disorientation, confusion, and other manifestations of encephalopathy may also develop early

on, particularly in the elderly and in individuals with preexisting neurologic impairment. Focal neurologic signs are quite uncommon, although the preexisting focal deficits may somehow become more prominent.

Protein catabolism is often markedly accelerated.

Serum albumin levels decreases as a result of hepatic dysfunction and the movement of albumin in the interstitial spaces.

**Adrenal Insufficiency:** A plasma cortisol level of  $\leq 15$   $\mu\text{g/mL}$  ( $\leq 10$   $\mu\text{g/mL}$  if the serum albumin concentration is  $< 2.5$   $\text{mg/dL}$ ) indicates adrenal insufficiency (inadequate production of cortisol).

**Renal Complications:** Oliguria, azotemia, proteinuria, and nonspecific urinary casts are frequently found. Many patients may be polyuric; hyperglycemia may increase this tendency.

## Material And Methods

**Study Design:** The present study is an observational study.

**Study Set Up:** The study is conducted in the Department of General Medicine, Sri Aurobindo Medical College and Post Graduate Institute, Indore (M. P.).

**Study Duration:** The duration of study was 18 months: December 2016 to may 2018.

Patients (male and female) who were diagnosed to infectious diseases leading to multiorgan dysfunction syndrome were included in this study who was seeking medical attention at Sri Aurobindo Medical College and Post Graduate Institute & Hospital, during the period of study. Patients in intensive care unit were asked for participating in the study. Informed written consent was taken from all the patients or patient's attendant. A prestructured proforma was used to collect the baseline data. Detailed clinical examination and biochemical tests were done on all the patients.

**Inclusion Criteria:** Age (18 yrs to 90 yrs) both male and female. Patients with infectious diseases leading to multiple organ dysfunction syndrome in ICU. All patients giving the written consent for participation in the study

**Exclusion criteria:** Any patient below 18 years.

**Sample size:** Justified the sample size: According to MRD records. Various articles mean of sizes therefore this study was feasible on sample size of 60

**Procedure planned:** All the patients were thoroughly investigated. All the relevant medical, personal and surgical history were obtained.

**Investigations Planned:** Complete blood count, Total Bilirubin, Serum Creatinine, Serum urea, Arterial Blood Gas Analysis, Serum electrolytes

**Data collection and methods:** Specially designed prestructured proforma will be used for collecting the data. The data will also be obtained from blood investigations, which shall be directly transcribed from the reports to the proforma by the investigator.

**Statistical Analysis Plan:** Initial SOFA score and SAPS score will be calculated based on worst values of the first 24 hours of admission. All enrolled patients will be followed during ICU stay and main outcome measure will be survival status at ICU discharge.

**Results**

Discrimination for initial SOFA and SAPS score were fair with area under ROC curve of 0.967 and 0.925. In this study, all the 60 patients met the inclusion as well as exclusion criteria's. The mean age among non survivors was 49.15 yrs and in survivor was 46.5 yrs. Off 60 patient 13 patients expired.

The mean age of non survivor was more than survivors. Independent T test was used to compare SAPS and SOFA score as indicator of survival status, both SAPS and SOFA score were found to be statistically significant as mortality

predictor. The mean initial SOFA score among non survivor was 14.85 and among survivor was 6.32. The mean SAPS score among non survivor was 61.62 and among survivor was 40.83.

**Table: 1 Area Under the curve**

Test Result Variable(s)	Area under the Curve				
	Area	Std. Error <sup>a</sup>	Asymptotic Sig. <sup>b</sup>	Asymptotic 95% Confidence Interval	
				Lower bound	Upper bound
SAPS	.925	.034	.000	.858	.992
SOFA	.967	.021	.000	.926	1.000

The test result variable(s): SAPS has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.

a. Under the nonparametric assumption . b. Null hypothesis: true area = 0.5

SAPS score, area under the curve is 0.925, 95% confidence interval of 0.858-0.992, p=0.001.

SOFA score, area under the curve is 0.967, 95% confidence interval of 0.926-1.00, p=0.001.

**Table: 2 .Association of age, SAPS and SOFA scores with mortality**

Association of age, SAPS and SOFA scores with mortality.

Group Statistics					
Parameters	Mortality Category	N	Mean	Std. Deviation	Std. Error Mean
Age years	Survived	47	46.55	18.393	2.683
	Died	13	49.15	17.435	4.836
SAPS	Survived	47	40.83	12.102	1.765
	Died	13	61.62	9.242	2.563
SOFA	Survived	47	6.32	3.051	.445
	Died	13	14.85	3.262	.905

**Table: 3. Independent Sample Test.**

t-test for Equality of Means								
		T	Diff.	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
Age Years	Equal Variances assumed	-.456	58	.650	-2.601	5.703	-14.016	8.815
SAPS	Equal Variances assumed	-5.734	58	.000	-20.786	3.625	-28.042	13.529
SOFA	Equal Variances assumed	-8.789	58	.000	-8.527	.970	-10.469	-6.585

After applying independent t-test, it suggests that mean SAPS score, and SOFA score were statistically significantly more in patients died than survived.

### Discussion

Both initial SOFA score and SAPS score were significantly higher among non survivors than survivors. Area under ROC curve observed for SOFA score model was 0.967 which was otherwise 0.748 in other study in India.<sup>(8)</sup> Area under ROC curve observed in our study SAPS model was 0.925 which was otherwise 0.742 in other study in India.<sup>(8)</sup> The discrimination of SOFA score model was better than SAPS model in our study and the finding was consistent with NAIR et al study.<sup>(8)</sup> Survivors had lower mean SOFA score compared with non survivors which was statistically significant as observed in other studies. Mortality increased with increasing SOFA score which was also statistically significant. Similar to the study done in 1996, on SOFA score to describe organ dysfunction a study in 2001 analysed serial evaluation of SOFA score as an outcome predictor in critically ill and proved SOFA score during the first few days of ICU admission as a good indicator of prognosis<sup>(4)</sup>, Minne et al. in 2008 evaluated SOFA based models for predicting mortality in ICU which suggested that SOFA based model were comparable with APACHE II/III and were competitive with SAPS in mortality prediction in medical ICU and an another study proved APACHE II and SAPS as prognostic models in surgical ICU.<sup>(9)</sup> We found that many cases were undiagnosed febrile illness without an etiology and SOFA score is an indicator of MODS and mortality in such situations it helps physicians to prioritize patients with regard to further treating patients.

### Conclusion

Mortality of patients was significantly high when initial SOFA and SAPS score were high. Discrimination was fair

for both models, but initial SOFA score was superior to SAPS. Initial SOFA score is a superior mortality predictor in infectious diseases in ICU. It helps physicians to prioritize patients with regard to use of organ support. Initial SOFA score is both sensitive and specific, hence, can be used as a better screening tool to analyze organ dysfunction. Initial SOFA score easily measures the degree of organ dysfunction in Infectious diseases, There by helps physicians to modify therapeutic interventions. It will complement other scoring systems. SOFA score if measured daily monitors progression of the disease, which is more informative and improves accuracy.

### Summary

This study was conducted in the Department of General Medicine, Sri Aurobindo Institute of Medical Sciences and Postgraduate Institute with the aims of to assess sequential organ failure assessment score (sofa) and implified acute physiology score (saps) in the patients with infectious diseases and multiple organ dysfunction syndrome (mods) and to compare sofa score with saps score. Total patients taken in study was 60 out of which 13 patients expired. Discrimination for initial SOFA and SAPS score were fair with area under ROC curve of 0.967 and 0.925. After applying independent t-test, it suggests that mean SAPS score, and SOFA score were statistically significantly more in patients died than survived. In the present study it was observed that the SOFA and SAPS score were found to be statistically significant but SOFA score is better to predict mortality than SAPS score

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