

# Organ Dysfunction and Organ Failure as Predictors of Outcomes of Severe Maternal Morbidity in an Obstetric Intensive Care Unit

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## ABSTRACT

**Background:** Most of the maternal deaths are preceded by severe maternal morbidity (SMM). Organ dysfunction and organ failure may occur as part of the pathophysiologic spectrum in SMM.

**Aim:** To determine the predictive and discriminative abilities of the Sequential Organ Failure Assessment (SOFA) scores to determine outcomes in pregnant women with SMM, who were admitted to a maternal ICU.

**Materials and Methods:** A retrospective study design was used to ascertain the diagnostic effectiveness of Sequential Organ Failure Assessment (SOFA) scores. Maximum individual SOFA scores and total maximum SOFA score were compared between women with and without SMM, and in women with SMM who survived or did not survive. Primary outcome measure of interest was maternal mortality.

**Results:** A majority (n=73, 85.88%) of the 85 women in the study had obstetrics related causes. The total maximum SOFA score was significantly higher in women with SMM as compared to that in women without SMM ( $p < 0.001$ ). The total maximum SOFA score showed ability to discriminate pregnant women with SMM who would not survive (AUROC 0.77, 95% CI: 0.46, 1.00). The positive likelihood ratios and accuracy for total SOFA scores of  $\geq 10$  and  $\geq 12$  were 19.20 and 38.40, and 94.20% and 95.65% respectively. The post-test probabilities for maternal deaths in women with SMM for SOFA scores  $\geq 10$  and  $\geq 12$  were 60.01% and 75.01% respectively.

**Conclusion:** The total maximum SOFA score showed good predictive and discriminative abilities for maternal mortality in pregnant women with SMM, who were admitted to ICU.

**Keywords:** SOFA scores, Severe Maternal Morbidity, Organ Dysfunction, Organ Failure, ICU

## INTRODUCTION

Reducing maternal deaths is an important objective of the Millennium Development Goals that aims to reduce the maternal mortality ratio by three quarters between 1990 and 2015 [1]. The World Health Organization estimated that nearly 99% of maternal deaths occurred in low or middle income countries [2]. Maternal death is often preceded by a severe maternal morbidity (SMM), that includes organ dysfunction and organ failure [3,4]. A pregnant woman maybe considered to have SMM if she has a potentially life threatening condition or a maternal near miss [5]. Early recognition and management of potentially life threatening maternal morbidity and access, availability and affordability of basic and emergency life-saving skills, is essential to reduce maternal mortality. The Sequential Organ Failure Assessment (SOFA) score is a validated score which is used to quantify organ dysfunction and to predict prognosis for severely ill persons in the ICU [6-9]. There is little information from India on the patterns of organ dysfunction in severely ill pregnant women and its potential association with maternal mortality, although a previous study has reported on the use of acute physiology score II (APACHE II) in an obstetric intensive care unit [10]. The current study aimed to determine whether the SOFA scores could be used to predict or discriminate maternal mortality in pregnant women with SMM.

## MATERIALS AND METHODS

A retrospective study design was used to retrieve information on pregnant women who were admitted to the maternal ICU of a maternal and new-born tertiary care centre in south India, during the period from January 2011 to December 2012. The study included all pregnant women who were admitted to the ICU during the study period and excluded women admitted to the ICU who were not

pregnant. Details including age, body mass index, prior obstetric history, associated medical and surgical co-morbidities, cause of ICU admissions, details of management, duration of ICU stay and organ dysfunction or failure were abstracted from the medical records database.

A maximum SOFA score was determined (range 0-4, with 4 being the worst score) for each of the six organ systems- respiratory, coagulation, hepatic, cardiovascular, neurologic and renal- which was used to derive SOFA score [11]. The maximum SOFA score reflected the worst score for the woman during the entire duration of stay in the ICU and it did not reflect a snap shot of a single particular day [11]. A maximum SOFA score of  $\geq 1$  and  $\leq 2$  was used to define organ dysfunction and a score of  $\geq 3$  was considered to define organ failure [11]. An aggregate total maximum SOFA score (range 0-24) was derived from the maximum SOFA score for each individual organ [11].

The extracted data were first entered into a de-identified Microsoft Office Excel spreadsheet that conformed to the Declaration of Helsinki protocol and was then exported into a statistical software for analysis (STATA Version 9, College Station, Texas, USA). The distribution of SOFA scores was assessed for normality by using the Shapiro Wilk Test ( $p = 0.0004$ ). The SOFA scores for each organ were compared between mothers who survived and non-survivors by using the non-parametric Wilcoxon ranksum test, as the SOFA scores were not normally distributed. The predictive and discriminatory abilities of the SOFA scores for identifying survivors among women with SMM were ascertained by using tests of diagnostic effectiveness, including sensitivity, specificity and area under the Receiver Operator Characteristic (ROC) curve. Statistical significance was pre-defined as a value  $< 0.05$ .

## RESULTS

The study included 85 women with a mean (SD) age of 27.02 (4.25) years (range 20 to 38 years). Seventy three (85.88%) of these 85 women were admitted for obstetrics related conditions. The maternal characteristics of the 85 women have been presented in [Table/Fig-1]. The mean duration of stay in the maternal ICU was 2.45 (2.12) days and it ranged from 1 to 13 days. Sixty nine (81.18%, 95% CI: 71.82, 81.44) women had SMM and 5 (5.88%, 95% CI: 2.19, 12.55) of the 85 women did not survive. All the 5 women who did not survive had SMM. Two of the five women who did not survive had single organ involvement, while one woman each had 2, 4 and 6 organ involvements respectively.

The maximum and total SOFA scores were compared between women with SMM and those without it (see [Table/Fig-2]) and between women who survived with SMM and women who did not

Characteristic	n%
Primigravid	38 (44.71%)
Nulliparous	45 (52.94%)
Hypertension	36 (42.35%)
Diabetes Mellitus	8 (9.41%)
Thyroid disorders	12 (14.12%)
Body Mass Index $\geq$ 30	7 (8.23%)
Caesarean Section	67 (78.82%)
Spontaneous Vaginal Delivery	10 (11.76%)
Ventilatory Support	19 (22.35%)
Vasopressors used	8 (9.41%)
Inotropes used	7 (8.23%)
Vasodilators used	8 (9.41%)
Blood Transfusion	48 (56.47%)
Postpartum hemorrhage	20 (23.53%)
Sepsis	22 (25.58%)
Single organ involvement	43 (50.59%)
Two organ involvement	14 (16.47%)
Three organ involvement	17 (20.00%)
> Three organ involvement	5 (5.88%)

**[Table/Fig-1]:** Maternal characteristics of the 85 women included in the study n:numbers

Numbers	Women with SMM (n=69)	Women without SMM (n=16)	p-value (Wilcoxon ranksum test)
Respiratory System	1.21 (1.50)	0.13 (0.50)	0.003
Coagulation	1.59 (1.28)	0.5 (1.09)	0.001
Hepatic	0.99 (1.19)	0.38 (0.89)	0.05
Cardiovascular	0.32 (0.86)	0 (0.00)	0.13
Neurologic	0.51 (0.93)	0.31 (0.70)	0.39
Renal	0.46 (0.78)	0.19 (0.40)	0.26
Total SOFA Score	5.07 (3.33)	1.5 (1.82)	<0.001

**[Table/Fig-2]:** Comparison of mean SOFA scores between women with severe maternal morbidity and women without severe maternal morbidity admitted to the maternal ICU

Numbers	Survivors (n=64)	Non-Survivors (n=5)	p-value (Wilcoxon ranksum test)
Respiratory System	1.02 (1.37)	3.6 (0.89)	0.0006
Coagulation	1.61 (1.31)	1.4 (0.89)	0.73
Hepatic	0.98 (1.20)	1.00 (1.22)	0.82
Cardiovascular	0.25 (0.73)	1.2 (1.79)	0.05
Neurologic	0.41 (0.73)	1.8 (2.05)	0.06
Renal	0.44 (0.75)	0.8 (1.09)	0.45
Total SOFA Score	4.70 (2.81)	9.80 (5.85)	0.05

**[Table/Fig-3]:** Comparison of SOFA scores between survivors and non survivors admitted to the ICU with severe maternal morbidity

survive with SMM (see [Table/Fig-3]). The ability of the maximum SOFA score which was evaluated for each of the individual organs to predict or discriminate maternal mortality in women with SMM has been presented in [Table/Fig-4]. The ability of the total SOFA score to predict or discriminate maternal mortality in women with SMM has been presented in [Table/Fig-5]. The positive likelihood ratios for total SOFA scores of  $\geq$ 10 and  $\geq$ 12 were 19.20 and 38.40 respectively and the accuracies for total SOFA scores of  $\geq$ 10 and  $\geq$ 12 were 94.20% and 95.65% respectively. Considering that the pre-test probability for maternal deaths in women with SMM was

	Sensitivity	Specificity	Area Under ROC Curve
<b>Respiratory System</b>			0.92 (95% CI: 0.82, 1.00)
$\geq$ 1	100.00	57.81	
$\geq$ 2	100.00	68.75	
$\geq$ 3	80.00	78.13	
$\geq$ 4	80.00	93.75	
<b>Coagulation</b>			0.46 (95% CI: 0.26, 0.65)
$\geq$ 1	80.00	29.69	
$\geq$ 2	60.00	43.75	
$\geq$ 3	0.00	73.44	
$\geq$ 4	0.00	92.19	
<b>Hepatic</b>			0.53 (95% CI: 0.28, 0.78)
$\geq$ 1	60.00	54.69	
$\geq$ 2	20.00	62.50	
$\geq$ 3	20.00	85.94	
$\geq$ 4	0.00	98.44	
<b>Cardiovascular</b>			0.65 (95% CI: 0.40, 0.91)
$\geq$ 2	40.00	89.06	
$\geq$ 3	20.00	96.88	
$\geq$ 4	20.00	100.00	
<b>Neurologic</b>			0.70 (95% CI: 0.42, 0.99)
$\geq$ 1	60.00	71.88	
$\geq$ 2	40.00	89.06	
$\geq$ 3	40.00	98.44	
$\geq$ 4	40.00	100.00	
<b>Renal</b>			0.58 (95% CI: 0.30, 0.86)
$\geq$ 1	40.00	70.31	
$\geq$ 2	40.00	87.50	
$\geq$ 3	0.00	98.44	

**[Table/Fig-4]:** Sensitivity, specificity and area under receiver operator characteristic curve of individual sofa scores to predict maternal death in women with severe maternal morbidity admitted to the maternal ICU

	Sensitivity	Specificity	Area under ROC curve
$\geq$ 1	100.00	7.81	0.77 (95% CI: 0.46, 1.00)
$\geq$ 2	100.00	12.50	
$\geq$ 3	80.00	23.44	
$\geq$ 4	80.00	32.81	
$\geq$ 5	80.00	48.44	
$\geq$ 6	80.00	60.94	
$\geq$ 7	60.00	78.13	
$\geq$ 8	60.00	84.38	
$\geq$ 9	60.00	90.63	
$\geq$ 10	60.00	96.88	
$\geq$ 12	60.00	98.44	
$\geq$ 14	20.00	98.44	
$\geq$ 17	20.00	100.00	

**[Table/Fig-5]:** Sensitivity, Specificity and area under receiver operator characteristic curve of total SOFA scores to predict maternal death in women with Severe Maternal Morbidity admitted to the maternal ICU

7.25%, the post-test probabilities for maternal deaths in women with SMM were estimated for the cut off values with the highest accuracies (SOFA score  $\geq 10$  and  $\geq 12$ ) were 60.01% and 75.01% respectively.

## DISCUSSION

Previous studies done on populations which were admitted to ICUs have reported maternal mortality rates that ranged from 2.3% to 27% [12-15]. Several studies have reported that the major causes of admissions to ICUs, amongst pregnant women, were obstetrics related [12,13,16]. Several studies have also reported a 40-65% rate of organ failure among pregnant women with SMM, who were admitted to ICU [17,18]. Consistent with these studies, we found a maternal mortality rate of 5.88 % (7.25% in women with SMM), that nearly 86% of the admissions to the ICU were done for obstetrics related causes and that nearly 51% of pregnant women who were admitted to ICUs had at least one organ involvement. Assessment of organ dysfunction and organ failure is essential in the management of SMM. Several scales or scores are used to assess severity and predict outcomes in an ICU, including the APACHE II or the SAPS II scores [12-15,17,18]. The SOFA score offers several advantages, including the use of variables that can be easily measured without the need of very complex resources and the ease of standardizing these variables. Consistent with other studies, respiratory failure was significantly associated with prognosis in this study [12,13,18]. However, a closer look at the 95% confidence intervals around the point estimates for the area under ROC curves showed that upper limits were  $>0.75$  for all organs, except coagulation. This suggested that the SOFA scores for all organs except coagulation could help in discriminating prognosis in pregnant women with SMM. A lack of association with coagulation has been reported earlier and it maybe related to the transitory nature of thrombocytopenia and its reversibility [11,19]. The use of the total SOFA scores was found to be a good indicator of prognosis in this population, with a value of  $\geq 10$  or  $\geq 12$ , which significantly increased the probability of maternal deaths in pregnant women with SMM.

The use of the SOFA scores, and the total SOFA score in particular, offers several opportunities for the obstetric community to attempt to reduce maternal mortality by targeting SMM. The total SOFA score may be used as a cut off for referring pregnant women with SMM to higher centres. The referral may pragmatically be made from a secondary care centre to a tertiary care centre or from a tertiary care centre to a dedicated ICU. The use of the SOFA scores has to be considered pragmatically at a primary care centre, given the resources which are available. However, a cut off of  $>0$  may be considered to be pragmatic for referral from a primary care centre. At the secondary levels, an individual organ score of  $\geq 1$  should alert the obstetrics team to the possibility of organ dysfunction. It might be prudent for secondary care centres to refer pregnant women with SMM if the individual organ SOFA scores are  $\geq 1$  or total SOFA score is  $\geq 3$ , especially when one considers that organ dysfunction and failure may involve multiple organs, that the SOFA score may not be able to identify early organ dysfunction, and the availability and accessibility to maternal ICU centres in India. Most obstetric units are already using modified early obstetric warning scores (MEOWS) [20]. An evaluation of organ dysfunction and calculation of SOFA

score should be triggered when there are four yellow or two red of any parameters in the MEOWS.

## LIMITATIONS

The retrospective nature of data collection and the representativeness of the study population maybe considered as a limitation.

## RECOMMENDATIONS

Further studies, including those done in more diverse ICU settings, will help in determining the replication and generalizability of results. The SOFA scores can be used to ascertain organ dysfunction and failure and they can form the basis for referrals to higher centres.

## CONCLUSION

The SOFA scores are useful for determining prognoses of pregnant women with SMM and they will help in identifying pregnant women with SMM, who may develop worse outcomes.

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