

The utility of the sequential organ failure assessment score in predicting mortality in critically ill obstetric patients admitted to a high dependency unit in Uganda

Abstract

Background: Most maternal deaths result from severe maternal morbidity (SMM with subsequent organ/system dysfunction and organ failure. The objective was to assess the performance of Sequential Organ Failure Assessment (SOFA) score in cases of SMM admitted to the high dependency obstetric unit.

Methods: Organ/system dysfunction and failure were assessed according to the maximum score for the six components (respiratory, neurological, renal, hepatic, cardiovascular and coagulation system). The total maximum SOFA score was estimated using the worst result each component on a single day. The distribution of SOFA scores was assessed for normality by using the Shapiro Wilk Test, [$p=003$]. The mean maximum SOFA scores for each organ/system were computed according to according to outcome (survival or death), using the Mann-Whitney test. The sensitivity, specificity, and the area under the curve (AUC) for each organ/system were evaluated. A Receiver Operator Characteristic (ROC) curve was fitted using maximum likelihood estimates for the total maximum SOFA score, in order to assess the sensitivity, specificity and discriminatory abilities of the maximum SOFA scores.

Results: Of the 425 patients with SMM, 345(81.2%, 95%CI 71.8-82.4) survived while 80(18.8%, 95% CI: 12.9, 22.6) did not survive. All the non-survivors and 64(18.5%) of the survivors presented with multiple organ/system dysfunction. Non-survivors were more likely to present with more severe and with multiple organ/system dysfunction. The maximum total SOFA score had good discrimination in the respiratory, cardiovascular and neurological systems, but poor discrimination in the renal, hepatic and coagulatory systems. The total maximum SOFA score displayed an area under the curve (AUC) of 0.83(95% CI: 0.56, 1.00), with a cutoff value of at least 8.0 sensitivity of 86.7%, and specificity of 90.0%.

Conclusion: The total maximum SOFA score showed good predictive and discriminative abilities for maternal mortality in women with severe maternal morbidity.

Keywords: sofa score, severe maternal morbidity, maternal near miss

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Abbreviations: AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; AUC, area under the roc curve; HELLP syndrome, syndrome of hemolysis elevated liver enzymes and low platelets; HDU, high dependency obstetric unit; ICU, Intensive CARE UNIT; REC, Research and Ethics Committee; ROC, curve-receiver operator characteristic curve; SOFA, sequential organ failure assessment; SD, standard deviation; SMM, severe maternal morbidity; WHO, world health organization

Introduction

Obstetric complications are a major cause of maternal morbidity and mortality, where maternal death is a final point on a continuum between severe (though non-life-threatening) and fatal obstetric complications.^{1,2} On this continuum are patients with severe obstetric complications, severe maternal morbidity (SMM), who develop organ or system dysfunction.^{3,4} Some of these are referred to as maternal near miss in case they narrowly survive death from such severe

complications.⁵⁻⁶ Both early recognition, detection and referral of potentially life threatening severe obstetric complications, and prompt access to safe, affordable basic and emergency obstetric care, are essential to reduce maternal morbidity and mortality.³⁻⁶

The challenge of predicting severe morbidity and mortality is that different obstetric patient populations tend to develop different patterns of organ system dysfunction.⁸⁻¹⁰ An ideal scoring system should allow both quantification of the severity of illness and estimation of the probability of mortality during hospitalization.⁸⁻¹¹ The ideal scoring system would have the following characteristics:⁸⁻¹¹ should be based on routinely collected data or variables, should be sensitive enough to identify all cases or possibly potential cases of organ/system dysfunction, and should be specific enough with a high level of discrimination. In addition, it should be objective, reliable, show abnormality in only one direction, and should be applicable to diverse obstetric population settings. Also, it should be reproducible, therapy independent and reflect acute rather than chronic organ

dysfunction, with ability to predict quality of life and functional status for survivors beyond hospitalization. No scoring system is ideal.

The SOFA^{7,8} score was developed by a group from the European Society of Intensive Care Medicine to describe the degree of organ dysfunction associated with sepsis. It employs parameters from six organ systems-respiratory, cardiovascular, central nervous systems, renal, coagulation, and liver which are weighted (each 1-4) to give a final score [6-24 (maximum)]. The SOFA score has since then been validated to describe organ dysfunction in diverse patients with obstetric complications unrelated to sepsis⁹⁻¹¹ and has been validated to quantify the severity and extent of organ dysfunction and to predict prognosis for severely ill patients.¹²⁻¹⁵ As the organ system functioning worsens, the score increases. SOFA scores can therefore assess individual or multiple organ dysfunction or failure.

Studies that have evaluated SMM in intensive care units (ICU) have reported that the degree of organ dysfunction, the number of failing organs, and the duration of the condition are directly related to higher maternal mortality.¹²⁻¹⁵ Prior studies have revealed high maternal morbidity and mortality related to severe obstetric complications in our setting.^{16,17} While withholding treatment in cases requiring ICU care increases maternal morbidity and mortality, unnecessary admissions lead to wastage of scanty resources and deny those who qualify the opportunity to receive necessary prompt care.^{18,19} However, there is little information from Uganda the patterns of organ dysfunction based on SOFA scores in severely ill obstetric patients. We hypothesized that scores that indicated organ/system dysfunction were correlated with mortality. If they were, the SOFA scores would be useful and reliable as proxy indicators of maternal near miss.

Methods

This study was conducted in Mulago hospital, the national referral hospital for Uganda. The detailed methods have been described elsewhere.¹⁶ Briefly the study involved women with severe maternal morbidity (SMM) admitted to the high dependency obstetric unit (HDU), between March 1, 2013 and January 28, 2014. Data was collected on age, parity, obstetric complication, management received, investigations done for organ/system dysfunction, referral for more specialized care (such dialysis for acute kidney injury (AKI), death and survival. Those patients who survived death (maternal near miss) after manifesting organ/system dysfunction were classified as maternal near miss.

With modification of the procedure described by Moreno et al.²⁰ the maximum SOFA score was determined for each of the six organ systems- respiratory, coagulation, hepatic, cardiovascular, neurologic and renal to reflect the worst score during the entire duration of hospitalization in the ICU or HDU. Since arterial blood gas analysis was not routinely performed, most patients did not have records of the partial pressure of oxygen (PaO₂), and therefore the oxygen saturation level with a pulse oximeter or monitor was used as a proxy. Likewise, renal dysfunction is derived from serum creatinine levels, which were not routinely available on all days of hospitalization for all admitted patients. Diagnosis of renal dysfunction relied on the worst level of urine output, serum urea or serum electrolytes as surrogate markers of renal dysfunction. For all organ/systems, a maximum SOFA score of ≥ 1 was used to define organ/system dysfunction, while a score of ≥ 3 was used to diagnose organ/system failure. The aggregate total maximum SOFA score (range 0-24) was derived from the maximum SOFA score for each individual organ. Thus the maximum score was the worst score during the period of hospitalization.

For data analysis, the mean and standard deviation or medians with interquartile ranges were computed for numerical variables, while frequencies and percentages were computed for categorical variables. The distribution of SOFA scores was assessed for normality by using the Shapiro Wilk Test, [p=003]. The SOFA scores were not normally distributed. The median maximum SOFA scores for each organ/system evaluated were computed according to according to outcome (survival or death), using the Mann-Whitney nonparametric test for independent samples. For each system assessed, sensitivity, specificity, and the area under the curve (AUC) were evaluated, together with their respective 95% confidence intervals (95% CI). Assuming a binormal distribution, a Receiver Operator Characteristic (ROC) curve with confidence bands was fitted using maximum likelihood estimates for the total maximum SOFA score, in order to assess the sensitivity, specificity and discriminatory abilities of the maximum SOFA scores to predict survival.

This research was part of a post-doctoral research project of the last author (DKK) entitled: "Evaluation and surveillance of the impact of maternal and neonatal near-miss morbidity on the health of mothers and infants in Jinja and Mulago hospitals". Ethical approval to conduct the study was obtained from the Ethics and research committees of Mulago hospital (REC 310-2012), the School of Medicine, Makerere University College of Health Sciences (REC 2012-172) and from Uganda National Council for Science and Technology. Permission to conduct the study was obtained from the department of Obstetrics and Gynaecology, Makerere University, and from Mulago National Referral Hospital and Jinja Hospital.

Participants gave written informed consent to be enrolled in the study and for their data to be included in the study. The languages used in the informed consent were English and the local languages (Luganda and Lusoga for Mulago and Jinja hospitals respectively). Participants included minors (aged 14-17years), as Uganda national guidelines for human subject research allow research on mature and emancipated minors in certain situations (such as in pregnancy), with prior approval of an institutional review board.

For those with very severe morbidity, consent was obtained retrospectively when they recovered, or consent was obtained from the next of kin to involve the patients' in the study and/or to include the patients' information in our data. Participants and their next of kin received assurances that participation was voluntary, and that participants were free to stop participation at any time without their decision affecting the care they were entitled to. All those with complications, and their newborns, were provided free medical care or, where necessary, were offered additional counseling or referred to get other support services not available at the two health facilities. Permission was obtained from the management of the two referral hospital (and from the study participants) to review the participants' records.

Results

The study included 425 women with severe obstetric complications, admitted to the high dependency unit of Mulago hospital, from March 1, 2013 to February 28, 2014). The maternal characteristics of the 425 women have been presented in Table 1. The mean duration of stay in the HDU was 2.45 (2.12) days and it ranged from 1 to 13days. Of the 425,345(81.2%, 95%CI 71.8-82.4) survived while 80(18.8%, 95% CI: 12.9, 22.6) did not survive. All the non-survivors presented with multiple organ/system dysfunction, while 64(18.5%) of the survivors presented with multiple organ dysfunction. Table 2 shows a comparison of the maximum and total SOFA scores for women who

survived with SMM and women who did not survive, showing that non-survivors were more likely to present with more severe and with multiple organ/system dysfunction.

Table 1 Socio-demographic characteristics and clinical diagnoses of the admitted severely ill patients

Characteristics	Number (percentage) Maternal Deaths n=80 N %	Number (percentage) Maternal Near Miss n=345 N %
Age Category		
18 years or less	7 (8.5)	29 (8.2)
19-24 years	30 (36.9)	125 (36.1)
>=24 years	43 (54.6)	191 (55.4)
Gravidity		
1	18 (22.3)	71 (20.5)
4-Feb	38 (47.7)	195 (56.4)
5 and more	24 (30.0)	79 (23.2)
Education level		
None or primary level	45 (56.3)	154 (44.7)
Secondary level	31 (38.2)	164 (47.5)
Post-secondary (tertiary)	4 (5.5)	27 (6.6)
Obstetric haemorrhage		
Antepartum	4 (5.4)	37 (10.8)
Postpartum	22 (26.9)	85 (24.7)
Ruptured uterus	17 (20.8)	58 (16.5)
None	37 (46.2)	180 (52.2)
Abortion-related		
Hemorrhage	5 (6.3)	12 (3.3)
Postabortion sepsis	0 (0.0)	3 (0.9)
Septic abortion	1 (1.3)	5 (1.4)
Not abortion related	76 (89.4)	325 (94.4)
Hypertensive disorders		
Severe Preeclampsia	3 (3.8)	84 (24.3)
Eclampsia	8 (10.0)	62 (18.0)
Chronic Hypertension	0 (0.0)	4 (1.2)
HELLP Syndrome	2 (1.5)	7 (2.0)
Not hypertension related	67 (84.0)	195 (56.4)
Pueperal sepsis		
Present	9 (10.8)	42 (11.2)
Not related to sepsis	71 (89.2)	303 (89.8)
Obstructed labor		
Present	12 (14.6)	82 (22.7)
Not related to obstructed labor	68 (85.4)	263 (77.8)

Table 3 & Table 4 show the ability of the maximum SOFA score, evaluated for each of the individual organ/system, to predict or discriminate between survivors and survivors. The maximum total SOFA score had good discrimination in the respiratory, cardiovascular and neurological systems, but poor discrimination in the renal, hepatic and coagulatory systems. Table 5 shows the ability of the total SOFA score to predict or discriminate survival in critically ill obstetric patients. The total maximum SOFA score displayed an area under the curve (AUC) of 0.83 (95% CI: 0.56, 1.00), with a cutoff value of at least 8.0 sensitivity of 86.7%, and specificity of 90.0%.

Table 2 Comparison of the maximum SOFA scores between survivors and non survivors admitted with severe maternal morbidity for different organ/system dysfunction

System involved	Maternal death (Mean ± SD)	Maternal near miss (Mean ± SD)	p-value (Wilcoxon rank test)
Respiratory	5.0 (3.3)	1.5 (0.8)	<0.001
Coagulation	1.6 (1.3)	1.5 (1.0)	0.448
Hepatic	2.9 (1.2)	2.0 (1.4)	<0.001
Cardiovascular	3.2 (0.7)	1.9 (1.2)	<0.001
Neurologic	2.4 (0.7)	1.8 (2.0)	0.009
Renal	1.4 (0.7)	0.8 (1.0)	< 0.001
Total maximum SOFA Score	515.7 (5.8)	4.8 (1.8)	<0.001

Table 3 Sensitivity, specificity and area under the curve (AUC) for the receiver operator characteristic (ROC) curve of individual SOFA scores in prediction of survival

Score	Sensitivity	Specificity	Area under the ROC curve
Respiratory system			
≥1	100	56.8	0.90 (95% CI: 0.82, 1.00)
≥2	100	69.9	
≥3	80	78.3	
≥4	80	94.2	
Neurological system			
≥1	60	71.88	0.70 (95% CI: 0.42, 0.99)
≥2	40	89.06	
≥3	40	98.44	
≥4	40	100s	
Cardiovascular system			
≥2	40	89.06	0.65 (95%CI 0.40, 0.90)
≥3	40	96.88	
≥4	20	100	

Table 4 Sensitivity, specificity and area under the curve (AUC) for the receiver operator characteristic (ROC) curve of individual SOFA scores that did not predict survival

Score	Sensitivity	Specificity	Area under the ROC curve
Hepatic system			
≥1	60	55.6	0.56 (95% CI: 0.28, 0.80)
≥2	20	64.3	
≥3	20	86.5	
≥4	0	98.8	
Renal system			
≥1	40	70.31	0.58 (95% CI 0.30, 0.72)
≥2	40	87.5	
≥3	0	98.44	
Coagulation system			
≥1	80	29.69	0.46 (95% CI: 0.26, 0.65)
≥2	60	43.75	
≥3	0	73.44	

Table 5 Sensitivity and Specificity of total SOFA scores in predicting maternal morbidity in women with SMM (Area under the curve 0.83 (95% CI: 0.56, 1.00))

Total maximum SOFA Score	Sensitivity	Specificity
≥1	100	7.81
≥2	100	12.5
≥3	80	23.44
≥4	80	32.81
≥5	80	48.44
≥6	80	60.94
≥7	60	78.13
≥8	60	84.38
≥9	60	90.63
≥10	60	98.44
≥12	60	98.44
≥14	20	100

Discussion

The study shows that the total maximum SOFA score had good predictive and discriminative abilities for survival or death in critically ill obstetric patients. Assessment of organ/system dysfunction is essential in the management of severe maternal morbidity (SMM).^{6-8,21-24} SMM refers to women with severe obstetric complications, some of whom die and others narrowly survive death (maternal near miss).²⁵ Scores based on criteria of organ/system dysfunction or failure, such as SOFA scores, have greater discriminatory power in cases of SMM.^{6,7,9,14,21} Consequently, women who survive SMM after presenting with high SOFA scores may be classified as maternal near miss, as the high SOFA scores

represent severe organ/system dysfunction or failure^{1,11-15} during their hospitalization.

In this study, the modified maximum SOFA score enabled analysis of the pathophysiologic process of SMM, as the aggregated score reflects most severe degree of organ/system dysfunction. Apparently, the maximum SOFA score performs better than a score for each individual organ/system dysfunction. This could be explained by the interdependence of organ/system function and the fact that several organ/systems are simultaneously or consequently involved during critical obstetric illness.¹⁶ Such multiple organ/system involvement may be subtle or unrecognized.

The commonest clinical diagnoses Most patients in our study participants were severe preeclampsia and eclampsia, obstetric hemorrhage, ruptured uterus and severe obstructed labor. These diagnoses may differ in different countries. This constitutes a challenge in predicting survival and mortality as different obstetric patient populations may develop different patterns of organ/system dysfunction.⁸⁻¹⁰ This challenge necessitates identification and validation of population-specific scores for organ/system dysfunction in patients with obstetric morbidity. The SOFA score offers several advantages:²⁶⁻³⁰ it uses variables that can be easily measured without the need of very complex resources, proxy measures could be used in cases where complex or expensive variables cannot be measured, measurements can easily be standardized, and scores have high predictive and discriminatory ability in SMM. As in other studies,^{12-14,21-24,26} the maximum aggregated SOFA scores were prognostic, though in retrospect. In our study, the 95% confidence limits of the point estimates for the area under ROC curves of nearly all the systems showed that upper limits were >0.75 for all organs, indicates that severe obstetric morbidity is associated with multiple organ/system dysfunction. Indeed values of ≥10 or ≥12 significantly increase the probability of maternal deaths.^{12-14,21-24}

This study evaluated the performance of total maximum SOFA score for cases of SMM and shows that the score has good performance. Assessment of the SOFA scores has potential utility in cases of SMM.^{5,10,11,13} The total SOFA score may be used to develop a cut off for referring obstetric patients with severe morbidity to referral units or to the HDU or ICU. Any score >0 as a cut-off point may be used for referral from a primary care centre, while an individual organ score of ≥1 should referral to HDU or ICU. Individual organ SOFA scores ≥1 or total SOFA score is ≥3 indicates possibility of multiple organ dysfunction. Very high scores are suggestive of very severe organ/system dysfunction.

Organ-specific-based scoring systems such as the SOFA are superior to diagnosis-based systems for several additional reasons.⁸⁻¹⁰ Many patients have simultaneous multiple organ/system dysfunction or failure during the course of severe obstetric illness, as demonstrated in our participants. Secondly, as shown by the reason for admission, obstetric patients may have multiple clinical diagnoses, either at admission or during their hospitalization. For instance, some patients admitted with postpartum hemorrhage later developed hypotension, shock, acute kidney injury or disseminated intravascular coagulopathy. Also, all patients with HELLP syndrome developed thrombocytopenia and acute kidney injury (AKI). Furthermore, severity scoring systems such as the SOFA allow generation of a score that reflects the severity of the condition that necessitates admission for critical care, thereby enabling comparison of patients with differing diagnoses as long as

the scores are standardized.^{8–10} If serial SOFA scores are generated over time, they could be used to monitor the patients' prognosis and response to therapy. In addition, the SOFA could be used as a tool to audit the quality of care.^{8–10}

Nevertheless, SOFA score as evaluated in this study have some limitations. Their main purpose is to describe the sequence of complications (in SMM) and not to predict mortality, much as there is a relationship between organ/system dysfunction, failure and death.³¹ Some of the patients with multiple organ dysfunction in our study survived, yet others with lesser organ involvement did not. In addition, some laboratory-based variables were not routinely available on a daily basis. In spite of this, our findings are in agreement with previous research that SOFA scores have good discrimination between survivors and non-survivors.³² In addition, as in prior research,^{33–36} multiple organ dysfunction evidenced by high SOFA scores are associated with higher mortality. The use of proxy variables for SOFA scores has been validated in prior research. For instance, pulse oximetry as a measure of oxyhemoglobin saturation has been validated as a reliable alternative to measurement of PaO₂ in calculation of the SPO₂/FiO₂.³⁶ Also, respiratory SOFA scores obtained using the SF ratio and the score calculated with the PF are well correlated.³⁷ Another limitation of our study is that only the worst scores were used, yet in the course of critical illness, the severity of organ/system dysfunction may change over time.³⁸ Likewise, dynamic assessment of the SOFA score is superior at predicting 28-day survival/mortality.^{39–41} Furthermore, modifications of the SOFA score^{42–46} have been shown to have good discrimination of development of more severe morbidity.

Conclusion

Our results show that the total maximum SOFA score showed good and acceptable performance in patients with severe maternal morbidity admitted to the high dependency unit. The modified SOFA score was able to evaluate, though retrospectively, the severity and prognosis of morbidity by discriminating between survivors and non-survivors. The discriminatory power of the modified SOFA score seems this unaffected by the physiological changes that occur in pregnancy or the diversity of pregnancy complications that are associated with severe morbidity. Maximum values of the modified SOFA score may be used to conceptually define a maternal near miss. The results of the modifications of the SOFA score show the feasibility of using the SOFA scores in low resources settings.

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Competing interests

The authors declare that they have no competing interests.

Availability of data and materials

Data from is available on request from Makerere University research repository, through the authors.

Consent for publication

No individual identifier information is included in the manuscript. So consent for publication is not applicable.

Ethics approval and consent to participate

Ethical approval to conduct the study was obtained from the ethics and research committees of Mulago hospital (REC 310-2012), the School of Medicine, Makerere University College of Health Sciences (REC 2012-172) and from Uganda National Council for Science and Technology. Permission to conduct the study was obtained from the Department of Obstetrics and Gynaecology, Makerere University, and from Mulago National Referral Hospital and Jinja Hospital. Participants gave written informed consent to be enrolled in the study and for their data to be included in the study.

Author's contributions

DKK conceptualized the study as part of his post-doctoral research project. DKK collected the data, led the analysis, and wrote the text of the paper. SNM gave advice on the data analysis, presentation of the results, reviewed and edited the text and approved the final manuscript.

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