ABSTRACT

Background: Despite advances in care, postpartum hemorrhage has continued to contribute disproportionately to maternal morbidity and mortality in developing countries due to delayed and/or substandard care in the diagnosis and management of hypovolemic shock.

Aim: To compare the performance of the shock index with conventional vital signs for prediction of maternal outcome following postpartum hemorrhage and to establish alert thresholds for use in low-resource settings.

Materials and Method: This is a 7-year retrospective cohort study of 289 women treated for primary postpartum hemorrhage at the Alex Ekwueme Federal University Teaching Hospital, Abakaliki. The data for systolic and diastolic blood pressure, mean arterial pressure, pulse pressure, heart rate, and shock index measured at the time of diagnosis of postpartum hemorrhage were analyzed. Adverse maternal outcomes such as intensive care unit admission, blood transfusion ≥5 units, hemoglobin level <7 g/dL, surgical interventions, end-organ failure, and death were reviewed. The area under the receiver operating characteristic curve (AUROC) for each vital sign was used to predict adverse maternal outcomes. Sensitivity, specificity, and negative and positive predictive values were calculated to determine the thresholds of the best predictor.

Results: Shock index had the highest AUROC to predict invasive surgical procedures (0.70 for SI [95% CI 0.66–0.80] compared with 0.69 [95% CI 0.61–0.76] for pulse rate). Shock index was a consistent superior predictor for other outcomes. Shock index (SI) ≥0.9 had 100% sensitivity (95% CI 74.6–100) and 46.7% specificity (95% CI 34.9–56.5) for prediction of intensive care admission, and SI ≥1.7 had 46.9% sensitivity (95% CI 19.8–62.8) and 98.9% specificity (CI 91.1–100) for prediction of maternal death.

Conclusion: Shock index is a consistent superior predictor of adverse maternal outcomes following postpartum hemorrhage when compared with conventional vital signs. SI <0.9 provides reassurance, whereas SI ≥1.7 indicates a need for urgent intervention to prevent maternal mortality.

Key words: Abakaliki; maternal outcomes; postpartum hemorrhage; shock index; vital signs.

Introduction

Postpartum hemorrhage (PPH) is the leading cause of maternal mortality in low-income countries, contributing to nearly a quarter of maternal deaths globally. About 23% of all maternal deaths between January 1999 and December 2008 were estimated to be due to obstetric hemorrhage in

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a study done in a University Teaching Hospital at Abakaliki, Nigeria.[2]

In poor countries like Nigeria, where women often deliver outside health facilities, with unskilled or no birth attendants, mortality rates are higher and delays are longer because of transportation and referral difficulties.[2] Moreover, women who reached tertiary facility dies as a result of delayed and/or substandard care in the diagnosis and management of hypovolemic shock.[3] The keys to reducing hemorrhage-related adverse maternal outcomes are early recognition, prompt intervention, and timely referral.[4]

Visual estimation of blood loss is routinely used to assess severity and guide resuscitation during obstetric hemorrhage. However, visual estimation of blood loss is often inaccurate and underestimates the actual blood loss.[5] Vital signs monitoring is key to hemodynamic assessment, with thresholds for systolic blood pressure and pulse rate used in the clinical trigger or early warning systems to prompt intervention.[3] Impending shock may be masked by the hemodynamic changes of pregnancy, making conventional vital signs less useful, and signs taken in isolation may miss impending deterioration.[6] Changes in conventional vital signs into the abnormal range are late markers of compromise. Relying solely on changes in blood pressure and heart rate as individual parameters may delay vital interventions in women with postpartum hemorrhage and may contribute to avoidable morbidity and mortality.[7] Shock index (SI), the ratio of pulse rate to systolic blood pressure, has been proposed as an earlier marker of compromise than conventional vital signs in nonpregnant populations. It has been studied in trauma and sepsis.[8] The normal SI range is 0.5–0.7 for healthy adults and an SI of >0.9 has been associated with increased mortality.[8] In an obstetric population, SI has also been proposed as a reliable marker of compromise during obstetric hemorrhage. A small number of studies have evaluated SI within obstetric populations in low-income countries, and further research is necessary to inform the clinical utility of SI as a predictor of adverse outcome during postpartum hemorrhage.[6–8] The aim of this study was to compare the predictive performance of shock index and other vital sign parameters that can best predict the adverse maternal outcomes following postpartum hemorrhage and to develop two threshold points indicating the need for referral to a higher level care facility and to identify patients who require intensive treatment during postpartum hemorrhage.

Materials and Method

This is a 7-year retrospective cohort study of women treated for primary postpartum hemorrhage. The study was undertaken from 1st January 2012 to 31st December 2018 at the Alex Ekwueme Federal University Teaching Hospital, Abakaliki. The case notes of all women treated for PPH within the study period were retrieved from the department of medical records and women with blood loss of 1500 mL or more were identified and included as a study cohort. All blood pressure (BP) and pulse rate (PR) values recorded within the first hour following a diagnosis of PPH were included in the analysis (measured using an automated blood pressure device or auscultatory technique with mercury sphygmomanometer). SI, mean arterial pressure (MAP), and pulse pressure (PP) were calculated from these values. For each woman, values measured at the time of the highest SI were selected for analysis.

Adverse clinical outcomes evaluated include admission to an intensive care unit (ICU), blood transfusion ≥5 units, hemoglobin level <7 g/dL (lowest prior to discharge), and invasive surgical interventions to stop bleeding (hemostatic uterine suturing, uterine tear repair, internal iliac artery clamping, bilateral ligation of internal iliac arteries, aortic artery clamping, hysterectomy, and laparotomy), end-organ system failure morbidity defined as clinically-diagnosed major organ failure (respiratory, renal, neurological, cardiac) lasting for 24 h post-resuscitation and death.

The statistical analysis was done using Epi info version 7.1.5, March 2015 (CDC, Atlanta, Georgia, USA). For SI, HR, SBP, diastolic BP (DBP), MAP, and PP, the area under the receiver operating characteristic curve (AUROC) values and 95% confidence intervals were calculated and compared for each outcome. The best vital sign parameter was selected for further analysis, according to the AUROC values achieved across the outcomes.

Four potential thresholds (two lower thresholds and two higher thresholds) of the best vital sign parameter were selected for further analysis to determine their predictive values. Different methods were used to determine the lower and upper thresholds to test (as the data set comprises only high-risk women with blood loss ≥1500 mL, the majority had at least one adverse outcome). The two lower thresholds were selected based on recommendations of both thresholds in previous studies and the rates of false-negative results for ICU admission and other outcomes below each threshold.[9] The upper two thresholds were derived from the centiles of 95%, 98%, and 99% specificity of each of the six outcomes.

Sensitivities, specificities, and positive and negative predictive values were calculated for each of the four thresholds. Appropriate lower and higher thresholds were selected based
on their performance in predicting ICU admission: the lower threshold selected was based on a maintained high sensitivity with a clinically practical specificity; the higher threshold selected was based on a high positive predictive value without compromising the negative predictive value. For each adverse outcome, logistic regression methods were used to control for potential confounding factors such as age at delivery, body mass index (BMI), height, weight, parity, hypertension in pregnancy, anemia, mode of delivery, and syntometrine for the management of the third stage. All women in our study received resuscitative interventions and therefore resuscitations were not treated as confounding factors in the statistical analysis. P value < 0.05 was considered statistically significant.

Results

A total of 306 women with primary postpartum hemorrhage with estimated blood loss ≥ 1500 mL were identified and 17 women were excluded due to incomplete data on vital signs. Therefore, the number of study cohorts were 289. Table 1 shows the participants characteristics. The mean blood loss among the study cohorts was 2264 ± 1321. Table 2 shows the median (interquartile range) of each vital sign parameter: SI 1.4 (1.3–1.7), pulse rate 119 (112–125) bpm, SBP 83 (71–97) mmHg, DBP 55 (48–56) mmHg, MAP 66.5 (58–69.3) mmHg, and PP 31 (29–38) mmHg.

The performance of each vital sign parameter in predicting each of the six adverse clinical outcomes are shown in Table 3. For ICU admission, SI had the highest AUROC value at 0.83 (0.71–0.99), which was significantly higher than for SBP (P = 0.02), DBP (P = 0.001), MAP (P = 0.001), and PP (P < 0.001). SI was not significantly higher than PR (P = 0.634). For blood transfusion ≥ 5 units, SI had the highest AUROC of 0.77, which was significantly higher than for PR (P = 0.01), DBP (P = 0.003), MAP (P = 0.002), and PP (P = 0.01). It was not significantly higher than SBP (P = 0.682). For hemoglobin level < 7 g/dL, end-organ failure, invasive surgical intervention and death, SI consistently performed higher than other vital sign parameters.

SI was chosen to develop vital sign thresholds because it was the most consistent top vital sign predictor across all the adverse maternal outcomes. To establish a potential lower threshold we selected SI ≥ 0.7, an SI of 0.7 has been identified in the literature as the upper limit of normal SI in a nonpregnant population.\cite{8,9} As an alternative lower threshold the authors selected SI ≥ 0.9, as the suggested upper limit of normal immediately postpartum.\cite{9} The value of SI ≥ 0.7 and SI ≥ 0.9 as early predictors of an adverse outcome are shown in Table 4. At SI ≥ 0.7, sensitivity for all adverse outcomes is very high (ranged 93.5–100) and specificity is very low (range 14–16.2), which shows that all positives are correctly identified as such, while most negatives are identified as false positives. Sensitivities are slightly lower (range 67.3–100.0) and specificities are slightly higher (range 44.6–47.1) at SI ≥ 0.9 compared to SI ≥ 0.7. SI ≥ 0.9 performed better than or similar to SI ≥ 0.7 for all outcomes, thus SI ≥ 0.9 was chosen as the lower of the two action thresholds, indicating the need for referral to tertiary care or intensive monitoring within tertiary care. As all the women in the study had a hypovolemic shock, the high rate of positive test results is clinically acceptable.

Table 1: Participants characteristics (n=289)

| Variables         | Mean (± SD) |
|-------------------|-------------|
| Age (years)       | 26±4.2      |
| BMI               | 22±3.6      |
| Parity            | 3±1.9       |
| Blood Loss (mL)   | 2264±1321   |

Table 2: Distribution of hemodynamic variables at the time of diagnosis of postpartum hemorrhage (n=289)

| Variable                      | Median (IQR) |
|-------------------------------|--------------|
| Shock index                   | 1.4 (1.3-1.7)|
| Pulse                         | 119 (112-125)|
| Systolic Blood Pressure       | 83 (71-97)  |
| Diastolic Blood Pressure      | 55 (48-56)  |
| Mean arterial pressure        | 66.5 (58-69.3)|
| Pulse pressure                | 31 (29-38)  |

Table 3: AUC values (95% CI) of performance of hemodynamic parameters to predict clinical outcome following PPH

| Parameter | ICU admission | Blood transfusion ≥5 units | Hemoglobin <7 g/dL | End-organ failure | Invasive surgical intervention | Death |
|-----------|---------------|---------------------------|---------------------|------------------|-------------------------------|-------|
| SI        | 0.83 (0.71-0.99) | 0.77 (0.65-0.81) | 0.75 (0.65-0.83) | 0.78 (0.68-0.88) | 0.70 (0.66-0.80) | 0.87 (0.80-0.95) |
| PR        | 0.80 (0.75-0.97) | 0.57 (0.51-0.64) | 0.72 (0.66-0.79) | 0.59 (0.43-0.66) | 0.69 (0.61-0.76) | 0.63 (0.55-0.70) |
| SBP       | 0.68 (0.46-0.89) | 0.75 (0.65-0.83) | 0.61 (0.67-0.80) | 0.63 (0.55-0.70) | 0.59 (0.43-0.66) | 0.86 (0.80-0.91) |
| DBP       | 0.65 (0.49-0.87) | 0.65 (0.55-0.70) | 0.51 (0.47-0.55) | 0.59 (0.43-0.66) | 0.63 (0.55-0.70) | 0.63 (0.55-0.70) |
| MAP       | 0.65 (0.49-0.87) | 0.65 (0.54-0.6)  | 0.49 (0.38-0.57) | 0.76 (0.70-0.87) | 0.57 (0.51-0.64) | 0.59 (0.43-0.66) |
| PP        | 0.59 (0.43-0.66) | 0.54 (0.48-0.63) | 0.53 (0.48-0.60) | 0.50 (0.46-0.69) | 0.59 (0.43-0.66) | 0.59 (0.43-0.66) |

SI, Shock index; PR, Pulse rate; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; MAP, Mean arterial pressure; PP, Pulse pressure; AUC, Area under the curve.

In bold: highest two AUC values for each outcome.
The SI centile values at 95%, 98% and 99% specificity are shown in Table 5. Using the mean values for SI from Table 5, the thresholds of SI ≥ 1.5 and SI ≥ 1.7 were used for further analysis. The performance of these thresholds to identify women at highest risk of adverse maternal outcome is shown in Table 6. Comparing SI ≥ 1.5 to SI ≥ 1.7, specificity is maximized for all outcomes at SI ≥ 1.7. (range 84.0–85.4 vs. range 96.0–98.9, respectively) with a corresponding increase in positive prediction (range 13.3–29.3 vs. range 27.7–59.7%, respectively); while sensitivities are lower at SI ≥ 1.7 but with negative predictive values. Similarly, slightly higher negative predictive values are achieved with SI ≥ 1.4 due to the higher sensitivities. The selection of which higher threshold to use according to the data for clinical use will depend on the clinical setting and existing referral pathways, as both thresholds SI ≥ 1.4 and ≥ 1.7 may be important for identifying individuals in need of urgent care and resuscitation.

Discussion

Obstetric hemorrhage remains the single most important cause of maternal deaths worldwide and the majority of these deaths occur in a developing country.\[10-19\] A healthy woman can lose up to 30% of her blood volume before SBP decreases, leading to an assumption of hemodynamic stability and delay in care.\[11-15\] Several studies have shown that this lack of recognition of abnormal vital signs in the majority of women who died secondary to PPH.\[13\]

This study compared the predictive ability of SI and other vital sign variables in PPH according to multiple clinical outcomes. This study found SI to be the most consistent predictor of all severe maternal outcomes in women with hypovolemic shock secondary to primary postpartum hemorrhage.\[14\] For ICU admission, SI and HR were significantly better predictors than all other vital signs. This finding was similar to the findings of a study done by Nathan et al. in the UK.\[15\] In addition, the finding was similar to that of a multicenter study carried out by El Alyadi and his colleagues.\[16\] For maternal death, SI had the highest AUCROC value and followed by SBP. It performed significantly better than HR. Conventional vital signs have shown to be late markers of hemodynamic compromise in nonobstetric and obstetric populations. Monitoring postpartum women with SI may help tailor

Table 4: Performance of SI ≥ 0.7 and SI ≥ 0.9 in predicting adverse clinical outcomes

| Outcomes                  | Sensitivity (95% CI) | Specificity (95% CI) | Positive predictive value (95% CI) | Negative predictive value (95% CI) | Prevalence % (n) |
|----------------------------|----------------------|----------------------|------------------------------------|------------------------------------|------------------|
| ICU admission              |                      |                      |                                    |                                    |                  |
| SI ≥ 0.7                   | 100% (74.6-100)      | 15.1% (11.3-20.8)    | 6.3% (3.3-12.5)                    | 100% (88.3-100)                    | 26.3 (76)        |
| SI ≥ 0.9                   | 100% (74.6-100)      | 46.7% (34.9-56.5)    | 8.9% (4.9-15.1)                    | 100% (96.4-100)                    |                  |
| Blood transfusion ≥5 units |                      |                      |                                    |                                    |                  |
| SI ≥ 0.7                   | 93.7% (75.7-99.2)    | 16.2% (10.4-22.3)    | 18.4% (13.6-25.1)                  | 94.4% (76-99.2)                    | 33.9 (98)        |
| SI ≥ 0.9                   | 84.1% (68.3-92.4)    | 44.6% (37.7-54.4)    | 23.7% (16.9-33.7)                  | 93.5% (87.6-98.6)                  |                  |
| Hemoglobin <7 g/dL         |                      |                      |                                    |                                    |                  |
| SI ≥ 0.7                   | 94% (83.9-98.9)      | 14.7% (10.3-22.4)    | 24.2% (17.9-30.1)                  | 92.6% (76-98.9)                    | 42.2 (122)       |
| SI ≥ 0.9                   | 96.4% (50.9-79.7)    | 45.8% (34.5-49.7)    | 24.7% (16.6-32.5)                  | 84.7% (74-96.2)                    |                  |
| End-organ failure          |                      |                      |                                    |                                    |                  |
| SI ≥ 0.7                   | 94.5% (78.1-99.9)    | 15.6% (10.5-23.9)    | 19.3% (17.5-22.4)                  | 95.5% (76.2-98.7)                  | 11.8 (34)        |
| SI ≥ 0.9                   | 67.3% (76.6-98.7)    | 47.1% (32.4-56.9)    | 26.4% (21.3-29.8)                  | 90.1% (71.4-98.7)                  |                  |
| Invasive surgical intervention |                  |                      |                                    |                                    |                  |
| SI ≥ 0.7                   | 93.5% (69.2-99.7)    | 14.0% (9.5-20.1)     | 6.3% (3.4-12.6)                    | 97.8% (88-99)                      | 23.9 (69)        |
| SI ≥ 0.9                   | 80% (56.5-97.2)      | 46% (33.4-53.3)      | 8.9% (3.7-12.1)                    | 98.9% (90.4-99.8)                  |                  |
| Death                     |                      |                      |                                    |                                    |                  |
| SI ≥ 0.7                   | 100% (92-100)        | 14.4% (10.8-23.3)    | 5.5% (2.6-6.8)                     | 100% (87-100)                      | 15.6 (45)        |
| SI ≥ 0.9                   | 100% (92-100)        | 45.9% (34.1-54.1)    | 5.0% (3.2-6.7)                     | 100% (89-100)                      |                  |

Table 5: The 95%, 98% and 99% specificities of shock index according to the adverse maternal outcome

| Outcomes                  | 95% specificity (95% CI) | 98% specificity (95% CI) | 99% specificity (95% CI) | Prevalence % (n) |
|----------------------------|--------------------------|--------------------------|--------------------------|------------------|
| ICU admission              | 1.55 (1.4-1.83)          | 1.72 (1.55-2.2)          | 1.86 (1.63-2.12)         | 26.3 (76)        |
| Blood transfusion ≥5 units | 1.53 (1.37-1.80)         | 1.67 (1.51-2.10)         | 1.78 (1.60-2.05)         | 33.9 (88)        |
| Hemoglobin <7 g/dL         | 1.57 (1.39-1.86)         | 1.75 (1.66-2.2)          | 1.82 (1.61-2.07)         | 42.2 (122)       |
| End-organ failure          | 1.59 (1.42-1.89)         | 1.89 (1.57-2.10)         | 1.93 (1.67-2.25)         | 11.8 (34)        |
| Invasive surgical intervention | 1.56 (1.35-1.84)         | 1.77 (1.58-2.15)         | 1.89 (1.65-2.18)         | 23.9 (69)        |
| Death                     | 1.60 (1.37-1.88)         | 1.90 (1.71-2.19)         | 2.00 (1.74-2.28)         | 15.6 (45)        |
treatment decisions and reduce adverse events, through timely resuscitation and referral.

In nonobstetric populations, several studies have suggested normal SI as 0.5–0.7, and SI ≥ 0.9 has been associated with increased mortality and morbidity in some studies.\[17-19\] The hemodynamic changes in pregnancy and postpartum may delay the recognition of hypovolemia. Thresholds must be derived from obstetric populations and be validated for PPH. Few obstetric studies have defined normal SI as 0.7–0.9.\[19\] This threshold was consistent with the findings of this study.

The performance of the upper limits of SI ≥ 0.7 and SI ≥ 0.9 were tested during the analysis of the result of this study. For all the maternal adverse outcomes evaluated, SI ≥ 0.9 was a superior predictor and thus may be a valuable threshold in a low resource setting, where mortality is highest and often related to delays in complication recognition, transportation, and poor quality of care at the health facility. A threshold of SI ≥ 0.9 is proposed by the authors to be the trigger point to alert community healthcare providers of the need for urgent transfer to a higher-level facility and for the institution of interventional measures for women who developed PPH in the tertiary facility.

The analysis of centile specificity showed two potential SI thresholds indicating a high risk of adverse events: SI ≥ 1.5 and SI ≥ 1.7. SI ≥ 1.7 was the superior predictor for all adverse maternal outcomes apart from a massive blood transfusion. This second threshold of SI ≥ 1.7 is proposed by the authors to serve as a trigger for identification of the most seriously ill patients even in tertiary healthcare centers.

The limitation of this study is that it is a retrospective and a single-center study. The authors recommend a prospective multicenter study in low-resource settings to further test the validity of these SI threshold found in this study.

**Conclusion**

Shock index is a superior predictor of adverse maternal outcomes in women with primary postpartum hemorrhage when compared with other vital signs parameters. From findings of this study, the authors propose thresholds of SI ≥ 0.9 as an alert trigger for referral to a tertiary care facility and SI ≥ 1.7 as a trigger point for identifying critically ill women that need urgent intervention, with the aim of promptly identifying and managing obstetric shock to reduce maternal morbidity and mortality associated with PPH in developing countries.

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**Conflicts of interest**

There are no conflicts of interest.

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