

ORIGINAL CLINICAL REPORT

OPEN

Vasopressor Use Among Adults With Sepsis in Uganda and Rwanda: A Multicenter Retrospective Cohort Study

OBJECTIVES: Africa has the highest global sepsis burden. Yet, sepsis treatment guidelines, including those for vasopressor use, incorporate data from high-income settings. We aimed to determine patterns of vasopressor use among adults admitted to hospital with sepsis in East Africa.

DESIGN: Retrospective cohort study.

SETTING: One hospital in Uganda and two hospitals in Rwanda.

PATIENTS: Adults admitted to hospital with sepsis, defined as suspected infection and greater than or equal to 2 quick Sequential Organ Failure Assessment criteria.

INTERVENTIONS: None.

MEASUREMENTS AND MAIN RESULTS: We performed an analysis of pooled data from two retrospective studies of adults with sepsis admitted to hospital in Rwanda or Uganda. Of 471 septic patients analyzed, 263 (57%) were female, the median (interquartile) age was 51 years (36–65), 121 (26%) were living with HIV, 113 (24%) received a vasopressor, and death occurred in 139 patients (30%). In the univariable logistic regression analysis, higher respiratory rate and Universal Vital Assessment (UVA) scores; lower blood pressure, oxygen saturation, and Glasgow Coma Scale score at the time of sepsis diagnosis; presence of abdominal infection; and receiving a greater volume of IV fluids predicted receipt of a vasopressor. In the multivariable analysis, higher UVA mortality risk scores (adjusted odds ratio 1.25; 95% CI, 1.14–1.27; $p < 0.001$) predicted vasopressor receipt. We replicated these findings in exploratory machine learning analyses.

CONCLUSIONS: In patients with sepsis in East Africa, UVA score and hospitalization in Uganda were predictive of vasopressor administration. Further research is required to address existing knowledge gaps in the role, timing, and indications for vasopressors in sepsis management in Africa.

Africa bears the world's highest sepsis burden with an estimated 16.7 million cases and 3.5 million sepsis-related deaths annually (1). Despite this burden, relatively few studies have evaluated sepsis management and outcomes in African settings (2, 3). International guidelines recommend vasopressors for the management of septic shock (2). However, the evidence supporting these recommendations is derived largely from studies conducted outside Africa, with limited representation of patients with HIV or tuberculosis, which are common in Africa and associated with increased sepsis mortality (4).

Evidence from randomized trials in high-income settings suggests that a fluid-restrictive strategy with earlier vasopressor initiation results in outcomes

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DOI: 10.1097/CCE.0000000000001481



KEY POINTS

Question: Among adults hospitalized with sepsis in East Africa, what are the patterns and predictors of vasopressor administration?

Findings: In this retrospective cohort study of 471 adults with sepsis in Uganda and Rwanda, higher illness severity predicted vasopressor administration. Patients who received vasopressors had higher heart and respiratory rates; lower blood pressure, oxygen saturation, and Glasgow Coma Scale scores; were more likely to have an abdominal infection and to be hospitalized in Rwanda; and received greater volumes of IV fluids.

Meaning: Among adults with sepsis in East Africa, greater illness severity and physiologic abnormalities were associated with vasopressor administration, while geographic differences suggest variation in treatment practices or resource availability. Early recognition of hemodynamic deterioration is critical in time-sensitive sepsis care, and prospective studies are needed to clarify the role and optimal timing of vasopressor use in African settings.

comparable to those of a more fluid-liberal approach with later vasopressor initiation (5, 6). In contrast, a trial in Zambia comparing a resuscitation bundle of IV fluids, dopamine, and blood transfusion with usual care among adults with sepsis and hypotension found higher mortality in the intervention group. Because the intervention was multifaceted, the increased mortality could not be conclusively attributed specifically to IV fluid or vasopressor administration (7).

Accordingly, the optimal management of septic shock in African settings, including the role of vasopressors, remains uncertain. We therefore aimed to characterize vasopressor use and identify clinical factors associated with vasopressor administration among adults with sepsis at three hospitals in Uganda and Rwanda.

MATERIALS AND METHODS

Design

In this secondary analysis, we pooled data from the entire parent population of two retrospective sepsis

cohorts, including 300 patients from Uganda and 171 patients from Rwanda (8, 9). We defined sepsis as suspected infection and greater than or equal to 2 quick sequential (sepsis-related) organ failure assessment criteria, including respiration rate of greater than or equal to 22 breaths per minute, systolic blood pressure less than or equal to 100 mm Hg, or a Glasgow Coma Scale (GCS) score less than 15 or documentation of altered mental status (10). Since lactate measurements were not routinely available to support a formal Sepsis-3 diagnosis of septic shock, we defined septic shock as hypotension with a mean arterial pressure (MAP) less than 65 mm Hg. Our study was not restricted to community-onset sepsis as we identified the first episode of sepsis that occurred during a patient's hospitalization. We conducted and reported this study in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

Participants

We obtained the Uganda data from a retrospective cohort study of the association between corticosteroid use and outcomes among adults admitted with sepsis at Mbarara Regional Referral Hospital (MRRH) located in southwestern Uganda between January 1, 2019 and December 31, 2023 (8). MRRH is an approximately 600-bed teaching hospital for the Mbarara University of Science and Technology Faculty of Medicine. As we investigated corticosteroid use for community-onset sepsis, which is typically managed outside the ICU, we excluded patients admitted to the ICU. We also excluded patients with COVID-19 for whom the benefit of corticosteroid use has been established (11).

We obtained the Rwanda data from a retrospective cohort study of adults admitted with sepsis to the University Teaching Hospital of Kigali (CHUK), a public academic tertiary referral hospital with approximately 565 beds, or the University Teaching Hospital of Butare (CHUB), a public academic referral hospital in the southern province of Rwanda with approximately 490 beds, between January 1, 2017 and December 31, 2017 (9). We collected similar data to those obtained in Uganda.

We defined the time of sepsis diagnosis as the time that a patient first met greater than or equal to 2 Quick Sequential (Sepsis-Related) Organ Failure Assessment (qSOFA) criteria (12). We defined vasopressor use as

any documented administration of a vasopressor that occurred at or after the onset of sepsis during the same hospitalization. The initial administration of a vasopressor did not necessarily occur at the same time as the onset of sepsis. Receipt of vasopressors among patients initially classified as not having hypotension at sepsis diagnosis reflected clinical deterioration after sepsis diagnosis rather than pre-hypotension vasopressor use or misclassification due to missing MAP or lactate data. We defined IV fluid volume received as the total volume of IV fluid administered during the hospital course.

Vasopressors were administered for hypotension at the discretion of the treating clinicians. None of the participating hospitals had dedicated institutional sepsis protocols or standardized criteria for vasopressor initiation during the study periods. Sepsis management instead followed international Surviving Sepsis Campaign guidelines (2). Norepinephrine and epinephrine were generally available throughout the study period in Rwanda and Uganda; however, dopamine was only available in Rwanda. Data on vasopressor dosing were not available. Supplemental oxygen was available through concentrators and oxygen cylinders at all sites, and mechanical ventilation was available in the ICU in Rwanda. The source of infection was documented in the medical record by the treating clinician.

Statistical Analysis

We did not perform a formal sample size calculation. Before imputation, we summarized categorical variables as numbers and percentages and compared them using the chi-square or Fisher exact tests. We reported continuous variables as medians with interquartile ranges (IQRs) and compared them using the Mann-Whitney *U* or Kruskal-Wallis tests. We report case fatality rates according to country and vasopressor use, but we did not perform adjusted analyses of the association between vasopressor use and mortality because of the high potential for residual confounding and bias inherent with such an observational comparison.

For predictive models, we performed multiple imputation using the R *mice* package, assuming data were missing at random. We generated five imputed datasets with 20 iterative cycles and set the random seed to 123 to ensure reproducibility. We did not apply imputation to all variables; instead, for each analysis

we imputed only the variables included in the corresponding model. We imputed routinely measured quantitative clinical variables using predictive mean matching, and we imputed binary variables using logistic regression. We performed imputation separately for the Uganda and Rwanda cohorts to account for site-level differences. We prespecified variables with more than 50% missing data for exclusion, but none met this threshold.

The primary outcome of interest was receipt of a vasopressor up to 28 days from admission. We determined predictors of receiving vasopressors with logistic regression. We adjusted multivariable models for covariates selected a priori including age, sex, and severity of illness using the Universal Vital Assessment (UVA) mortality risk score, IV fluid volume, and country (Uganda vs. Rwanda) (13, 14). For the predictive models, we calculated pairwise Pearson correlation coefficients among selected continuous clinical and laboratory variables to assess distributions and potential collinearity. We assessed associations among categorical predictors using Cramér *V*. We modeled vasopressor receipt as a separate outcome in the descriptive analyses.

In an exploratory analysis, we applied least absolute shrinkage and selection operator (LASSO) regression to identify predictors of vasopressor use under penalized variable selection. Predictors included demographic, physiologic, and laboratory features with natural splines incorporated for nonlinear relationships in temperature, MAP, oxygen saturation, and WBC concentration. We trained the model using five-fold cross-validation and evaluated them using the area under the receiver operating characteristic curve (AUC), area under the precision-recall curve (PR-AUC), precision, recall, and F1 score. We optimized thresholds within each fold based on F1 maximization. We reported performance metrics as mean $\pm$ SD across cross-validation folds, with bootstrap 95% CIs (500 iterations). We performed feature selection using LASSO at the minimum cross-validation error ($\lambda_{\min}$).

Statistical Software

We used SPSS (IBM SPSS Statistics; Version 29.0.2.0; Armonk, NY) or R (Version 4.3.1; R Foundation for Statistical Computing, Vienna, Austria) for analyses. R packages included *corrplot*, *glmnet* (Version 4.1-8), and *caret* and *pROC* for model training, hyperparameter

tuning, and performance evaluation. We defined statistical significance as p value of less than 0.05.

Ethical Considerations

The research ethics committee of Mbarara University of Science and Technology (MUST-2021-67: Improving Diagnostic Strategies for Post-Tuberculosis Lung Disease in Ugandan Primary Health Care Settings, amendment approved July 11, 2024), and the institutional review boards of the University of Rwanda (379/CMHS IRB/2018: Characterization of Sepsis in Tertiary Care Setting in Rwanda: Presentation, Diagnosis, Management, and Outcomes, approved December 11, 2018) and the University of Virginia (HSR Number 231639: Improving Diagnostic Strategies for Post-Tuberculosis Lung Disease in Ugandan Primary Health Care Settings, Reliance Agreement with MUST approved May 27, 2024) approved the study with waivers of consent. All procedures were followed in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975. Study staff abstracted clinical, physiologic, and laboratory data from paper medical records and entered them into a cloud-based Research Electronic Data Capture (REDCap, Vanderbilt University, Nashville, TN) database using password-protected accounts on secure servers accessible only to authorized personnel.

RESULTS

Baseline Characteristics and Case Fatality Rates

We included 471 total patients in our analysis: 300 who were admitted to MRRH, 95 who were admitted to CHUK, and 76 who were admitted to CHUB (**Table 1**). Of the 471 patients analyzed, 263 (57%) were female and the median (IQR) age was 51 years (36–65). Of the 467 patients with known HIV serostatus, 121 (26%) were living with HIV. The most common sites of infection were the abdomen (41%), lungs (37%), and urinary tract (15%). Nearly all patients received antibiotics (97%) and IV fluids (99%). Most patients, 445 of 471 (94%), were diagnosed with sepsis within three days of hospitalization (**Fig. 1**). Patient characteristics at the time of sepsis diagnosis were similar across groups stratified by time to sepsis diagnosis (**Table 2**).

In Uganda, all patients were admitted to the medical ward (**Table S1**, <https://links.lww.com/CCX/B682>). Of the 171 patients in Rwanda, patients were hospitalized in the following locations at the time of sepsis diagnosis: emergency ward (64, 37%), medicine ward (63, 37%), ICU (21, 12%), surgical ward (12, 7%), and obstetrics and gynecology ward (11, 6%) (**Table S1**, <https://links.lww.com/CCX/B682>).

Death by 28 days occurred in 139 (30%) of 471 patients. Of the 113 patients who received a vasopressor, 66 (58%) died in-hospital within 28 days of sepsis diagnosis compared with 73 (20%) of 358 patients who did not receive a vasopressor (**Table 1**). Death occurred in 49 Ugandan patients (16%) and 90 Rwandan patients (53%) (**Table S1**, <https://links.lww.com/CCX/B682>).

Predictors of Vasopressor Use

There were 113 patients (24%) who received a vasopressor during their hospitalization (**Fig. 2**). The median (IQR) time to vasopressor administration after sepsis diagnosis was 1 day (0–4) (**Fig. 1**). The proportion of patients living with HIV and each source of infection were similar between vasopressor recipients and non-recipients except for abdominal infection, which was present in 56 (50%) of vasopressor recipients compared with 133 (37%) of non-recipients (odds ratio [OR] 1.62; 95% CI, 1.06–2.48; $p = 0.03$) (**Table 1**). Of the 113 vasopressor recipients, 56 (50%) received norepinephrine, 50 (44%) received epinephrine, 23 (20%) received dopamine, and 18 (16%) received two vasopressors (**Fig. 2**; **Table S2**, <https://links.lww.com/CCX/B682>). Dopamine and combined vasopressors were only administered in Rwanda. Clinical characteristics according to vasopressors administered are found in **Table S3** (<https://links.lww.com/CCX/B682>).

Vasopressor recipients had higher heart and respiratory rates, and UVA scores, and lower blood pressure and GCS scores at the time of sepsis diagnosis (**Tables 1**; **Tables S4** and **S5**, <https://links.lww.com/CCX/B682>). Of the 140 patients with hypotension (MAP < 65 mm Hg) at sepsis diagnosis, 59 (42%) received a vasopressor compared with 53 (16%) of 326 patients who did not have hypotension at sepsis diagnosis (OR 3.75; 95% CI, 2.40–5.86; $p < 0.001$). Conversely, of the 112 vasopressor recipients with a recorded MAP at the time of sepsis diagnosis, 59 (53%)

TABLE 1.

Characteristics of Adults at Sepsis Diagnosis According to Vasopressor Use at Mbarara Regional Referral Hospital, Uganda, and at the University Teaching Hospitals of Butare and Kigali, Rwanda (2017–2023)

Demographic and Clinical Variables	Missing, <i>N</i> (%)	Total (<i>N</i> = 471)	Received Vasopressor (<i>N</i> = 113)	No Vasopressor (<i>N</i> = 358)	<i>p</i>
Age (yr)	4 (< 1)	51 (36–65)	52 (35–65)	51 (38–65)	0.26
Female	6 (1.2)	263/465 (56.6)	63/112 (56.3)	200/357 (56.0)	0.94
Temperature (°C)	45 (9.6)	37.4 (36.4–38.0)	37.1 (36.5–37.9)	37.5 (36.4–38.0)	0.17
Heart rate (beats/min)	1 (< 1)	124 (113–132)	126 (119–134)	123 (112–132)	0.03
Respiratory rate (brpm)	57 (12.1)	30 (26–36)	32 (27–39)	30 (25–35)	0.01
Systolic blood pressure (mm Hg)	1 (< 1)	92 (87–97)	89 (79–97)	92 (88–97)	0.001
Diastolic blood pressure (mm Hg)	5 (1.1)	58 (52–64)	54 (43–62)	59 (54–64)	< 0.001
Mean arterial pressure (mm Hg)	5 (1.1)	69 (64–74)	65 (56–73)	70 (65–75)	< 0.001
Oxygen saturation (%)	17 (3.6)	95 (90–98)	95 (90–98)	95 (91–97)	0.24
Glasgow Coma Scale score (<i>n</i>)	13 (2.8)	14 (13–15)	13 (11–15)	14 (13–15)	< 0.001
WBC (10 ³ /μL)	127 (27.0)	10.3 (6.2–13.2)	10.3 (5.4–13.8)	10.2 (6.4–12.5)	0.91
Hemoglobin	78 (16.6)	12.3 (10.5–12.8)	11.6 (9.8–12.6)	12.5 (11.2–13.0)	0.04
Platelets (10 ³ /μL)	130 (27.6)	171 (111–250)	167 (84–248)	175 (123–253)	0.09
UVA score (<i>n</i>)	0 (0)	6 (3–8)	6 (4–8.5)	6 (2–8)	0.04
UVA < 2, low risk	0 (0)	64/471 (13.6)	7/113 (6.2)	57/358 (15.9)	0.03
UVA 2–4, medium risk	0 (0)	123/471 (26.1)	32/113 (28.3)	91/358 (25.4)	
UVA > 4, high risk	0 (0)	284/471 (60.3)	74/113 (65.5)	210/358 (58.6)	
Pulmonary infection	1 (< 1)	174/470 (37.0)	38/112 (33.9)	136/358 (38.0)	0.49
Abdominal infection	2 (< 1)	191/469 (40.7)	56/113 (49.6)	135/356 (37.9)	0.03
Genitourinary infection	10 (2.1)	67/461 (14.5)	16/113 (14.2)	51/352 (14.8)	0.90
CNS infection	4 (< 1)	65/467 (13.9)	12/113 (10.6)	53/358 (15.0)	0.25
Tuberculosis	5 (1.1)	43/466 (9.2)	8/113 (7.1)	35/357 (9.8)	0.37
Malaria	83 (17.6)	38/388 (9.8)	5/81 (6.2)	33/311 (10.6)	0.22
Skin/soft-tissue infection	5 (1.1)	98/466 (21.0)	27/113 (23.9)	71/357 (19.9)	0.39
Hypotension (mean arterial pressure < 65)	5 (< 1)	140/466 (30.0)	59/112 (52.7)	81/354 (22.9)	< 0.001
Living with HIV	4 (< 1)	121/467 (25.9)	24/113 (21.2)	97/358 (27.1)	0.19
CD4 ⁺ T cells (μL)	101 (21.4)	178 (85–556)	110 (51–353)	264 (102–593)	0.04
Received antibiotics	4 (< 1)	454/467 (97.2)	108/113 (95.6)	346/358 (96.6)	0.22
Received IV fluids	57 (12.1)	410/414 (99.0)	95/96 (99.0)	315/324 (97.2)	0.93
Volume of IV fluids (L)	57 (12.1)	2 (1.5–2)	2 (1.5–2.4)	2 (1.5–2)	0.16
Received corticosteroids	1 (< 1)	84/470 (17.9)	24/113 (21.2)	60/357 (16.8)	0.19
Site of sepsis diagnosis	0 (0)				
Emergency ward	–	64/471 (13.6)	25/113 (22.1)	39/358 (10.9)	0.002

(Continued)

TABLE 1. (Continued)
Characteristics of Adults at Sepsis Diagnosis According to Vasopressor Use at Mbarara Regional Referral Hospital, Uganda, and at the University Teaching Hospitals of Butare and Kigali, Rwanda (2017–2023)

Demographic and Clinical Variables	Missing, N (%)	Total (N = 471)	Received Vasopressor (N = 113)	No Vasopressor (N = 358)	p
Medicine ward	–	363/471 (77.1)	61/113 (54.0)	302/358 (84.4)	< 0.001
ICU	–	21/471 (4.5)	13/113 (11.5)	8/358 (2.2)	< 0.001
Obstetrics and gynecology ward	–	11/471 (2.3)	9/113 (8.0)	2/358 (0.6)	< 0.001
Surgical ward	–	12/471 (2.5)	5/113 (4.4)	7/358 (2.0)	0.15
Death by 28 d	0 (0)	139 (30)	66 (58)	73 (20)	< 0.001

UVA = Universal Vital Assessment.
Values are presented as N (%) or median (interquartile range). Septic shock is defined as mean arterial pressure < 65 mm Hg at the time of sepsis diagnosis.
Note: Em dash (–) indicates data unavailable.

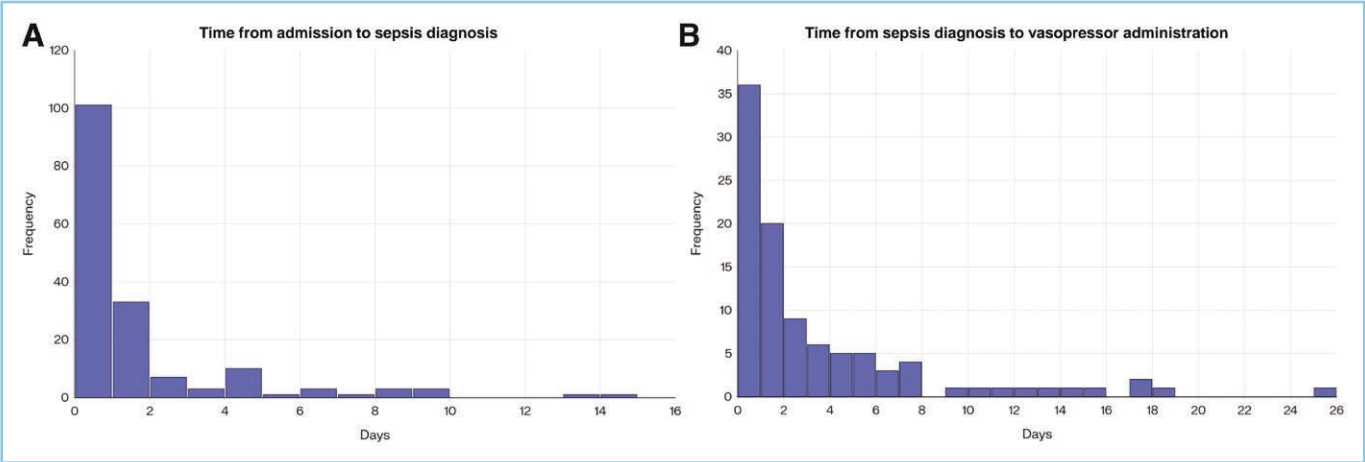


Figure 1. Histograms of (A) time from hospital admission to sepsis diagnosis and (B) time from sepsis diagnosis to vasopressor administration among adults with sepsis at Mbarara Regional Referral Hospital, Uganda, and at the University Teaching Hospitals of Butare and Kigali, Rwanda (2017–2023).

had hypotension (MAP < 65 mm Hg) compared with 81 (23%) of 354 patients who did not receive a vasopressor (OR 3.76; 95% CI, 2.40–5.88; $p < 0.001$).
In the univariable logistic regression analysis, predictors of receiving a vasopressor included higher respiratory rate and UVA scores; lower blood pressure, oxygen saturation, and GCS score at the time of sepsis diagnosis; presence of abdominal infection; and receiving a greater volume of IV fluids (Tables 3; Tables S6 and S7, <https://links.lww.com/CCX/B682>). In the multivariable analysis, higher UVA scores (adjusted OR [aOR] 1.25; 95% CI, 1.14–1.27; $p < 0.001$) predicted receiving a vasopressor, while hospitalization in Uganda (aOR 0.21; 95% CI, 0.11–0.40; $p < 0.001$) was

associated with lower odds of receiving a vasopressor (Tables 3; Tables S6 and S7, <https://links.lww.com/CCX/B682>).

Machine Learning Prediction

In the LASSO model for prediction of vasopressor use, discrimination was good, with an AUC of 0.78 ± 0.03 (95% CI, 0.76–0.80) at the minimum cross-validation error (lambda.min) (Table S8, <https://links.lww.com/CCX/B682>). Vasopressor recipients comprised a minority of the cohort (24%), so we also assessed metrics less sensitive to class imbalance: the PR-AUC was 0.58 ± 0.08 (95% CI, 0.53–0.65) and the F1 score was

0.48 ± 0.08 (95% CI, 0.42–0.54). A more parsimonious model using the 1-SE rule (λ 1 SE) yielded slightly lower discrimination (AUC 0.72 ± 0.04). The predictors identified by LASSO as most important for predicting vasopressor use were MAP, WBC concentration, oxygen saturation, temperature, platelet count, heart rate, age, GCS score, respiratory rate, and abdominal source of infection (**Fig. 3**), overlapping substantially with the physiologic derangements associated with vasopressor use in the logistic regression.

DISCUSSION

In this study of adults admitted with sepsis in Uganda and Rwanda, we found that almost a quarter of patients received a vasopressor during their hospitalization. For those receiving vasopressors, about half received a vasopressor within a day of sepsis diagnosis. As expected, vasopressor administration was associated with a high severity of illness as measured by UVA score at sepsis diagnosis. Despite greater initial severity of illness at the time of sepsis diagnosis, patients hospitalized in Uganda were less likely to receive a vasopressor and had decreased 28-day mortality compared with patients in Rwanda. Exploratory machine learning analyses replicated these findings with identification of similar predictors of vasopressor administration.

According to the Sepsis-3 operational definition, septic shock is defined as persistent hypotension requiring vasopressors to maintain MAP greater than 65 mm Hg and a serum lactate concentration greater than 2 mmol/L despite adequate volume resuscitation (12). This definition may be less applicable in Africa, where serum lactate testing is often unavailable and adequate fluid resuscitation is not well-defined. These limitations, together with differences in clinical staffing and patient monitoring across study sites, may contribute to variation in sepsis recognition and management, including vasopressor use (15). The timing of sepsis recognition may also influence subsequent management and outcomes. In our cohort, 6% of patients were diagnosed with sepsis greater than or equal to 3 days after admission, highlighting the need for prospective studies to identify factors associated with delayed recognition and their relationship with treatment timing and clinical outcomes. In addition, all patients in Uganda were admitted to medical wards, whereas some patients in Rwanda

were admitted to non-medical wards, potentially reflecting differences in illness severity, management, and outcomes. Nonetheless, illness severity and sepsis-associated mortality in our study were similar to those reported in prior African cohorts. In the Zambian trial of bundled resuscitation for septic shock that included dopamine, 28-day mortality was 54%, comparable to the 58% mortality among vasopressor recipients in our study (7). Similarly, in a prior study from MRRH, we reported 59% in-hospital mortality among patients with septic shock (16).

Predictors of vasopressor use in our study were broadly consistent with prior studies. Vasopressor recipients had lower blood pressure and oxygen saturation, higher heart and respiratory rates, lower GCS scores, and higher UVA scores, consistent with evidence that hypotension, tachycardia, tachypnea, altered mentation, impaired gas exchange, and greater organ dysfunction identify patients more likely to require vasopressor support (2, 12, 17, 18). However, only the UVA score remained an independent clinical predictor in the multivariable analysis, suggesting that overall illness severity may be more informative than individual physiologic abnormalities. The UVA score was derived and validated in large cohorts of hospitalized patients throughout Africa (13, 14). Higher UVA scores are also associated with clinical and immunologic subphenotypes of severe illness (19–21). Decreasing UVA scores over the first 6 hours of resuscitation from sepsis are associated with lower mortality (22).

Greater IV fluid administration was also associated with vasopressor use, consistent with evidence that prior fluid volume influences vasopressor initiation (23). This likely reflects persistent hypotension after initial fluid resuscitation, although differences in monitoring, clinical judgment, vasopressor availability, and local practice may also have contributed.

We found that vasopressor recipients were more likely to have sepsis from an intra-abdominal infection, consistent with evidence that abdominal sepsis has a greater propensity for hemodynamic instability and septic shock than several other infection sources. In the multicenter Sepsis Occurrence in Acutely ill Patients (SOAP) study (24), septic shock was more common at admission among patients with abdominal than respiratory sepsis (40.1% vs. 29.5%), and other cohorts have reported septic shock in approximately 47–57% of patients with intra-abdominal sepsis (24–26). This association may reflect source-specific

TABLE 2.

Characteristics According to Sepsis Diagnosis Time Among Adults at Mbarara Regional Referral Hospital, Uganda, and at the University Teaching Hospitals of Butare and Kigali, Rwanda (2017–2023)

Demographic and Clinical Variables	Missing, N (%)	Total, (N = 471)	Sepsis at Admission (N = 99)	Sepsis 24 hr After Admission (N = 8)	Sepsis 24–48 hr After Admission (N = 28)	Sepsis After 48 hr After Admission (N = 28)
Age (yr)	4 (< 1)	51.0 (36.0, 64.5)	43.0 (31.0, 60.5)	36.5 (26.8, 58.3)	38.0 (29.5, 55.3)	39.0 (25.5, 54.0)
Female	2 (< 1)	263 (56.6)	70 (70.7)	24 (75)	6 (75)	20 (71.4)
Temperature (°C)	45 (9.6)	37.4 (36.4, 38.0)	37.2 (36.5, 38.0)	36.7 (36.2, 37.8)	36.6 (36.4, 369)	37.1 (36.4, 37.92)
Heart rate (beats/min)	1 (< 1)	124.0 (113.0, 132.0)	111.5 (96.3, 124.0)	100.5 (81.0, 116.3)	98.5 (87.8, 111.0)	120.0 (105.8, 126.3)
Respiratory rate (brpm)	57 (12.1)	30.0 (26.0, 36.0)	24.0 (22.0, 28.0)	21.0 (20.0, 24.0)	22.0 (20.0, 22.0)	22.0 (20.0, 30.0)
Systolic blood pressure (mm Hg)	1 (< 1)	92.0 (87.0, 97.0)	97.0 (90.0, 120.0)	96.5 (90.8, 109.5)	95.0 (88.8, 105.3)	92.0 (86.5, 98.0)
Diastolic blood pressure (mm Hg)	5 (1.1)	58.0 (52.0, 64.0)	60.5 (52.8, 72.0)	60.0 (56.0, 65.0)	68.5 (61.0, 77.8)	57.0 (48.0, 63.5)
Mean arterial pressure (mm Hg)	5 (1.1)	69.3 (63.7, 74.3)	74.0 (65.2, 87.0)	72.0 (67.5, 80.3)	77.3 (69.3, 88.3)	68.0 (60.8, 74.0)
Oxygen saturation (%)	17 (3.6)	95.0 (90.0, 98.0)	95.0 (92.0, 98.0)	97.0 (93.3, 98.8)	96.0 (94.3, 98.0)	96.0 (94.0, 98.0)
Glasgow Coma Scale score (n)	13 (2.8)	14.0 (13.0, 15.0)	15.0 (11.0, 15.0)	15.0 (14.5, 15.0)	12.5 (9.8, 15.0)	15.0 (14.0, 15.0)
WBC (10 ³ /μL)	127 (27)	10.3 (6.2, 13.1)	7.9 (4.0, 13.6)	5.6 (3.9, 10.6)	7.5 (5.6, 11.5)	7.6 (5.6, 10.4)
Platelets (10 ³ /μL)	130 (27.6)	171.0 (111.0, 250.0)	177.0 (79.0, 305.3)	172.0 (102.0, 282.0)	157.5 (61.3, 239.8)	129.0 (30.0, 278.5)
UVA score (n)	0 (0)	6.0 (3.0, 8.0)	4.0 (1.0, 5.0)	2.0 (1.0, 4.0)	4.5 (1.8, 5.0)	2.0 (1.0, 4.0)
UVA < 2, low risk	0 (0)	64 (13.6)	27 (27.3)	9 (28.1)	2 (25)	9 (32.1)
UVA 2–4, medium-risk	0 (0)	123 (26.1)	42 (42.4)	17 (53.1)	2 (25)	13 (46.4)
UVA > 4, high risk	0 (0)	284 (60.3)	30 (30.3)	6 (18.8)	4 (50)	6 (21.4)
Pulmonary infection	1 (< 1)	174 (37)	36 (36.4)	14 (43.8)	2 (25)	10 (35.7)
Abdominal infection	2 (< 1)	191 (40.7)	41 (41.4)	10 (31.2)	6 (75)	13 (46.4)
Genitourinary infection	6 (1.3)	67 (14.4)	8 (8.1)	2 (6.2)	3 (37.5)	1 (3.6)
CNS	0 (0)	65 (13.8)	20 (20.2)	4 (12.5)	1 (12.5)	3 (10.7)

UVA = Universal Vital Assessment. Values are presented as N (%) or median (interquartile range).

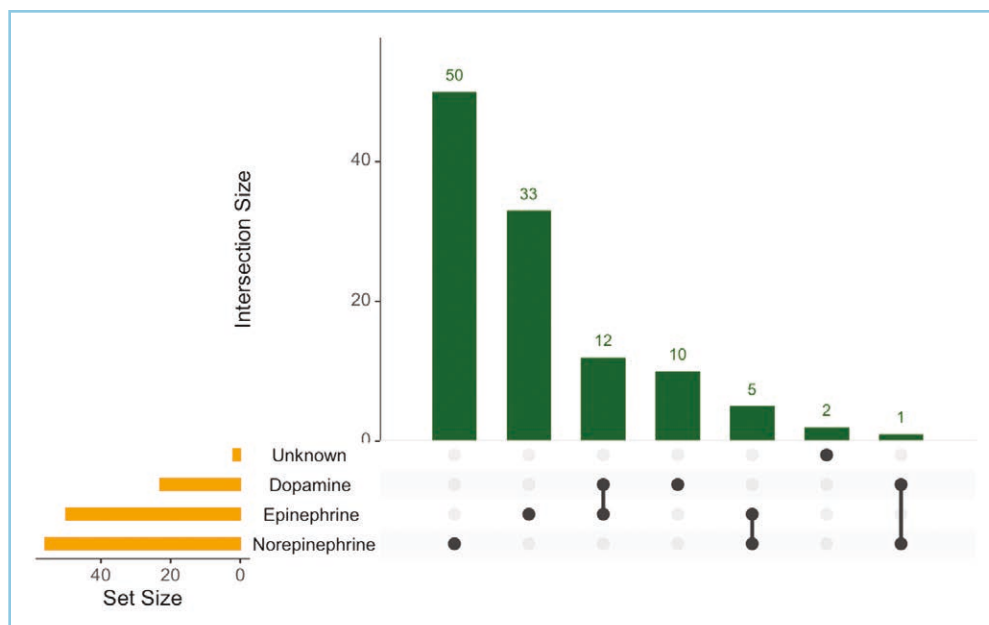


Figure 2. UpSet plot of vasopressors received by adults with sepsis at Mbarara Regional Referral Hospital, Uganda, and at the University Teaching Hospitals of Butare and Kigali, Rwanda (2017–2023).

differences in the host response. In the MARS cohort, abdominal sepsis was characterized by greater systemic inflammation, endothelial dysfunction, and coagulation activation than respiratory sepsis, providing a plausible biologic basis for more severe vasodilatory shock and vasopressor requirement (27). These findings are consistent with our observation that infection source may be associated with vasopressor requirements and emphasize the importance of early recognition of hemodynamic deterioration, timely source control, and appropriate antimicrobial therapy in patients with intra-abdominal sepsis.

Our LASSO model showed good discrimination for vasopressor use (AUC 0.78) and identified predictors similar to those from logistic regression and prior machine learning studies. Previous models using physiologic and laboratory data or longitudinal vital signs have achieved AUCs of approximately 0.75–0.83 and have consistently identified declining blood pressure, tachycardia, and tachypnea as important predictors of vasopressor initiation (28–30). More complex models incorporating SOFA scores and lactate have reported higher discrimination (2), although reliance on laboratory and monitoring data may limit their applicability in resource-limited settings. Hospitalization in Uganda was independently associated with lower odds of vasopressor use, which may reflect differences across sites

in clinical practice, resource availability, patient populations, or other unmeasured factors. These findings suggest that the performance and determinants of vasopressor prediction may vary across health systems and support the need for external validation in diverse settings.

Consistent with international guidelines, norepinephrine and epinephrine were the most frequently used vasopressors in our study (2, 31). A randomized trial in patients with shock that compared outcomes between norepinephrine with epinephrine showed

no difference in 90-day mortality and vasopressor-free days (32). However, use of norepinephrine in patients with hypotension leads to lower mortality and lower risk of arrhythmias compared with dopamine (33). A recent systematic review that found that peripheral administration of vasopressors can be done safely was supported by recent studies from Rwanda and Uganda in which extravasation occurred rarely (34, 35). Given these collective findings, for patients with non-fluid-responsive septic shock in Africa, we concur with international guidelines that favor norepinephrine or epinephrine as the first administered vasopressor (2, 31). In addition, in the absence of vasopressin, it remains unclear whether, when, or which second vasopressor should be added (2, 36).

Our study had limitations. First, the retrospective design introduced inherent biases and incomplete data capture. Second, inclusion of patients from regional and tertiary referral hospitals in Uganda and Rwanda may limit generalizability to other African settings. Third, differences across sites in sepsis management, diagnostic capacity (including lactate testing), ICU availability, monitoring infrastructure, and data collection periods may have contributed to heterogeneity in vasopressor use and outcomes. Furthermore, Rwanda data were collected in 2017, whereas Uganda data were collected from 2019 to 2023, potentially introducing temporal and systemic

TABLE 3.

Logistic Regression Predictors of Receiving a Vasopressor Among Adults With Sepsis at Mbarara Regional Referral Hospital, Uganda, and at the University Teaching Hospitals of Butare and Kigali, Rwanda (2017–2023)

Demographic and Clinical Variables	OR	95% CI	<i>p</i>	Adjusted OR	95% CI	<i>p</i>
Age (yr)	0.99	0.98–1.00	0.20	1.00	0.99–1.01	0.91
Female	0.98	0.64–1.51	0.94	0.79	0.49–1.27	0.33
UVA score (<i>n</i>)	1.07	1.00–1.15	0.04	1.25	1.14–1.27	< 0.001
UVA > 4, high risk	1.35	0.87–2.10	0.19			
Temperature (°C)	0.86	0.70–1.06	0.16			
Heart rate (beats/min)	1.01	1.00–1.02	0.11			
Respiratory rate (brpm)	1.05	1.01–1.09	0.005			
Systolic blood pressure (mm Hg)	0.99	0.98–1.00	0.09			
Diastolic blood pressure (mm Hg)	0.97	0.95–0.99	0.001			
Mean arterial pressure (mm Hg)	0.97	0.95–0.99	0.004			
Oxygen saturation (%)	0.95	0.91–0.99	0.006			
Glasgow Coma Scale score (<i>n</i>)	0.78	0.71–0.85	< 0.001			
WBC (10 ³ /μL)	1.00	0.96–1.05	0.90			
Platelets (10 ³ /μL)	1.00	1.00–1.00	0.06			
Pulmonary infection	0.85	0.55–1.33	0.49			
Abdominal infection	1.62	1.06–2.48	0.03			
Genitourinary infection	0.96	0.52–1.76	0.90			
CNS infection	0.68	0.35–1.31	0.25			
Tuberculosis	0.69	0.31–1.54	0.37			
Malaria	0.55	0.21–1.45	0.22			
Skin/soft-tissue infection	1.25	0.75–2.07	0.39			
Hypotension (mean arterial pressure < 65)	3.76	2.40–5.88	< 0.001			
Living with HIV	0.71	0.43–1.19	0.19			
Received antibiotics	0.50	0.16–1.56	0.23			
Received IV fluids	0.91	0.09–8.80	0.93			
Volume of IV fluids (L)	1.32	1.09–1.61	0.006	1.21	0.95–1.53	0.14
Received corticosteroids	1.35	0.79–2.27	0.28			
Uganda	0.45	0.29–0.68	< 0.001	0.21	0.11–0.40	< 0.001

OR = odds ratio, UVA = Universal Vital Assessment.

Septic shock is defined as mean arterial pressure < 65 mm Hg at the time of sepsis diagnosis. ORs for categorical variables are reported relative to the indicated reference category. For continuous variables, ORs represent the change in odds associated with a one-unit increase in the predictor.

biases. Finally, because all ICU patients were in Rwanda and represented a small proportion of the cohort, adjustment for country may not have fully accounted for differences in level of care. These limitations emphasize the need for prospective, multicenter studies across diverse healthcare settings to better define vasopressor use in sepsis management in Africa.

CONCLUSIONS

Our study highlights the role of vasopressors in the management of sepsis in Uganda and Rwanda, where healthcare resources are often limited. Our findings are hypothesis-generating and suggest a need for context-specific prospective studies to evaluate vasopressor

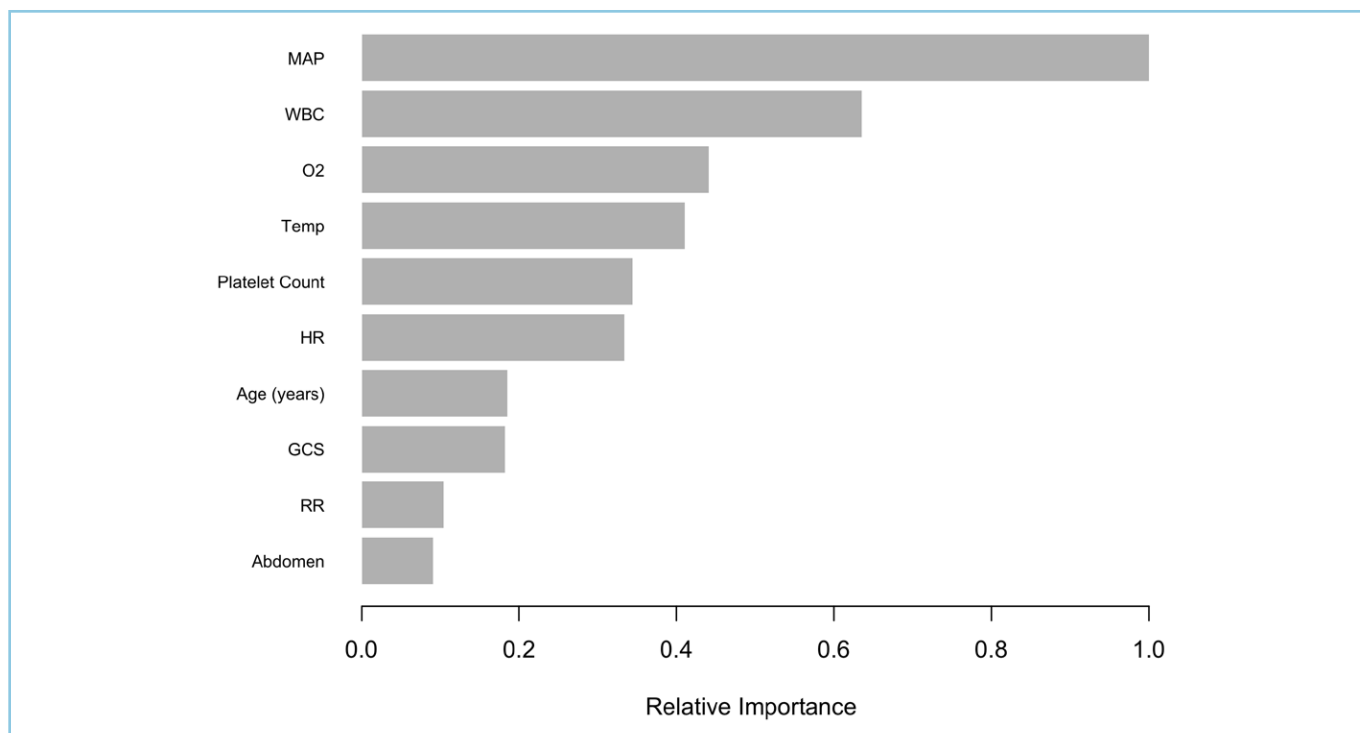


Figure 3. Variable importance plot from the least absolute shrinkage and selection operator model demonstrating the relative contribution of predictors associated with receipt of a vasopressor among adults with sepsis at Mbarara Regional Referral Hospital, Uganda, and at the University Teaching Hospitals of Butare and Kigali, Rwanda (2017–2023). GCS = Glasgow Coma Scale, HR = hazard ratio, MAP = mean arterial pressure, RR = respiratory rate.

initiation strategies, including timing relative to fluid resuscitation, in patients with sepsis in Africa. To ultimately enhance survival from sepsis in Africa, further studies across diverse settings are needed to determine the role of adjunctive therapies, refine treatment protocols, and delineate the optimal use of vasopressors.

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The authors have disclosed that they do not have any potential conflicts of interest.

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