Obstetric admissions and outcomes in an intensive care unit in Malawi

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ABSTRACT
Background: Despite international commitment to Millennium Development Goal 5, maternal mortality remains high in low- and middle-income countries (LMICs) of sub-Saharan Africa. This is in part due to infrastructure gaps, including availability of intensive care units (ICUs). We sought to use obstetric ICU utilization as a marker of severe maternal morbidity and provide an initial characterization of its relationship with in-hospital mortality.
Methods: A prospective observational cohort study of all obstetric subjects admitted to the ICU of Kamuzu Central Hospital in Malawi from September 2016 to March 2018. We reviewed charts at the time of ICU admission to assess the indication for admission, clinical characteristics and laboratory values. Subjects were followed until death or discharge. The primary outcome was in-hospital mortality.
Results: One-hundred-and-five obstetric patients were admitted to the study ICU (23% of all admissions). The median age was 26 years. The majority (79%) had undergone recent surgery; 40 (52%) an abdominal postnatal or cesarean hysterectomy and 31 (40%) a cesarean delivery without hysterectomy. Ninety-five percent required mechanical ventilation and 48% required vasopressors. Overall in-hospital mortality was 49%.
Conclusions: The proportion of obstetric subjects admitted to the ICU in Malawi is nearly 1 in 4, which exceeds that found in high-income countries by orders of magnitude. Intensive care unit admission was associated with high mortality in this population. Investments in improving infrastructure and care gaps may include addressing available ICU bed and blood-banking needs, and increasing the number of providers trained in managing critical illness among obstetric patients.

Keywords: Critical care; Global health; Quality improvement

Introduction

Maternal morbidity and mortality remain significantly high in sub-Saharan Africa despite international commitment to Millennium Development Goal 5.[1] In this region, a woman's lifetime risk of maternal mortality is 1 in 38, compared to 1 in 2000 in North America and 1 in 5100 in Europe.[2] Admission to an intensive care unit (ICU) has recently been identified as a marker of severe maternal morbidity by the American College of Obstetrics and Gynecology.[3] Indication for ICU admission in the puerperium may be elective, such as a planned admission for maternal congenital heart disease, or emergency, such as an admission for postpartum hemorrhage or acute respiratory failure.

Intensive care unit admission remains rare for obstetric subjects in high-income countries, accounting for less than 1% of ICU admissions.[4,5] In sub-Saharan Africa, however, where more than half of all maternal deaths worldwide occur, obstetric patients account for a larger proportion, but poorly quantified number, of ICU admissions.[6–8] The provision of quality intensive care has the potential to decrease maternal mortality in this region, but the literature to date is largely retrospective and lacking in clinical detail which limits the ability to derive conclusions about where investments should be made. The purpose of this study was to prospectively determine the proportion of obstetric admissions to an ICU at a central referral hospital in Malawi and to

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describe the ICU course and outcomes for this high-risk population.

Malawi is a country in southern Africa with a population of 18 million people, a life expectancy of 63.8 years, and a Human Development Index (HDI) rank of 170 out of 187 countries.[9] It is the sixth poorest country in sub-Saharan Africa.[10] In Malawi, the crude birth rate is estimated to be 32.2 births per 1000 population[11], with skilled birth attendant coverage of 89.8%.[12] Intensive care unit bed availability is approximately 1 per million population and these beds are located at the central hospital level.[6,7,13]

Kamuzu Central Hospital (KCH) is a central referral hospital in the Central Region of Malawi with a catchment area of approximately 5 million. The ICU at KCH is a five-bed unit which offers a one-to-one nurse-to-patient ratio, continuous non-invasive vital sign monitoring, mechanical ventilation with a titratable fraction of inhaled oxygen and intravenous medication infusions. Hemodialysis is available within the hospital if patients can be transferred to the nearby unit where it is provided. Clinical care in the ICU is directed by clinical officers in Anesthesiology.[14] No staff members have consultant-level expertise in intensive care medicine. The study hospital also has four high-dependency units (HDUs) which serve as both 'step-up' and 'step-down' units for patients with critical illness.[15] These units are classified by the four major services of KCH: Surgery, Obstetrics and Gynecology, Medicine and Pediatrics. Clinical care in these units includes a higher nurse-to-patient ratio and more frequent vital sign monitoring than available on the general wards but mechanical ventilation and titratable oxygen are not available.

Methods

This was a prospective, observational cohort study of obstetric patients admitted to the ICU of KCH from September 2016 to March 2018. The study was approved by the National Health Sciences Research Council of Malawi and the Institutional Review Boards of Columbia University and the University of North Carolina; the requirement for written informed consent was waived by all. The primary outcome was in-hospital mortality.

Data were collected prospectively by clerks specifically trained for this study. The clerks reviewed the medical charts at the time of ICU admission and followed subjects through the hospital course to death or discharge. Data collected included date of hospital admission, location before ICU admission, vital signs and laboratory measurements (e.g. serum hemoglobin, electrolytes) on admission to ICU, human immunodeficiency virus (HIV) serostatus, malaria point-of-care testing, treatments used during ICU stay (e.g. mechanical ventilation), clinical characteristics during the ICU course (e.g. development of fever or oliguria), the hospital location to which subjects were discharged, the length of stay in ICU and hospital discharge date. Vital signs were initially collected as continuous values, but for the purposes of logistic regression modeling were converted into clinically relevant categories based on normal values in pregnancy. Missing values were fewer than 5% for all clinical variables, except for the oxygen saturation at ICU admission (8%), malaria status (23%) and laboratory measurements, for which the proportion of missing values ranged from 11–23% (Appendix). The proportion of missing values decreased over time as the study protocols were accepted and implemented at the study site; these data were not considered missing at random and were not imputed in the analyses. All records were initially kept on paper in a de-identified manner and then maintained in a de-identified and secure electronic database.

We evaluated all admissions to the ICU and first determined the proportion of subjects admitted to the ICU with obstetric illness (e.g. postpartum hemorrhage, eclampsia) based on the primary admitting service and the primary admission diagnosis. Re-admissions and those missing outcome data were excluded. We described the obstetric cohort, including the demographics, the vital signs and laboratory values at ICU admission, specific clinical signs during the ICU course including the development of fever (temperature >38.4C) or oliguria (urine output <0.5 mL/kg/h for at least six hours). We described the therapies provided during the ICU course, including the provision and length of mechanical ventilation, blood transfusions (e.g. any and all blood products inclusive of whole blood and component products) and the use of hemodialysis. We looked for differences in clinical characteristics between those who survived to hospital discharge and those who did not, using chi-square tests for categorical variables and the student's t-test or analysis of variance for continuous variables, as appropriate. We performed univariate analyses to determine the unadjusted odds ratios (OR) and 95% confidence intervals (CI) of independent variables with in-hospital mortality, followed by a multivariable analysis of those variables which reached statistical significance with $P < 0.20$. To avoid overfitting a model given our sample size, variable selection for the multivariable analysis was limited to five predictors. Statistical significance was otherwise defined as $P < 0.05$ for all analyses. All statistical analyses were conducted using StataSE/14.2 (StataCorps, College Station, TX).

Results

During the study period there were 456 admissions to the study ICU and 105 (23%) were obstetric subjects, compared to 194 (44%) admitted from the General Sur-

gery service and 141 (32%) admitted from the Medicine and Pediatric services. Seven subjects were missing outcome data and were excluded from subsequent analysis for a total cohort of 98 obstetric subjects. The median age was 26 years, with an interquartile range (IQR) of 20–33 years and an overall range of 17–45 years. The majority of subjects (79%) had undergone a surgical procedure within the index hospitalization and among these, 40 (52%) had received an abdominal postnatal or cesarean hysterectomy, while 31 (40%) had undergone a cesarean delivery without hysterectomy.

Obstetric subjects were admitted to the ICU from the Operating Theater (44%), the High-Dependency Unit (44%), the Obstetrics Ward (6%) and as direct ICU transfers from outside hospitals (6%). Indications for admission were varied and included common critical illnesses such as shock states (40%), respiratory failure (22%) and hypertensive disorders (11%), as well as assault (1%), abortion complications (1%) and anesthetic complications (4%) (Table 1). Almost half (46%) of subjects were admitted with anemia (plasma hemoglobin <9.0 g/dL) and 9% were admitted with more severe anemia (plasma hemoglobin <5.0 g/dL). The median serum creatinine value for all subjects at ICU admission was 1.1 mg/dL (IQR 0.7–2.2). A total of nine subjects (10%) were HIV positive at ICU admission and two of these cases were new HIV diagnoses.

During the ICU course, 92 (95%) subjects had mechanical ventilation for a median of two days (IQR 1–4, range 1–28 days) and four (4%) received a tracheostomy. Four subjects (4%) received hemodialysis. Blood products were ordered for 62 (63%) subjects and 39 (63%) ultimately received a transfusion. Oliguria was observed for at least six hours in 57 (84%) subjects. Vasopressor therapy was provided to 48% of all subjects. The median length of stay in ICU was two days (IQR 1–5 days). Intensive care unit mortality was 41% and overall in-hospital mortality was 49%.

Table 1 Primary Indication for Intensive Care Unit (ICU) Admission Among Obstetric Subjects Admitted to the Study ICU. From September 2016 through March 2018

Reason for Admission	Number of patients (% of total cohort)
Shock states	39 (40)
Hemorrhagic	26
Septic	10
Cardiogenic	1
Other	2
Respiratory failure	21 (22)
Hypertensive Diseases of Pregnancy	11 (11)
Cardiac arrest	5 (5)
Peritonitis or Necrotic uterus[a]	5 (5)
Malaria	4 (4)
Anesthetic complications	4 (4)
Postoperative monitoring	3 (3)
Ruptured uterus	2 (2)
Unknown	2 (2)
Assault	1 (1)
Complications of abortion	1 (1)

[a]Necrotic uterus is a term used in Malawi to refer to a deep infection localized to the layers of the uterus and not extending to the peritoneum, usually seen postoperatively after a procedure such as a cesarean section.

Using univariate analysis, the following variables were associated with in-hospital mortality: increasing age (unadjusted OR for each year (95% CI) 0.94 (0.89 to 0.99), P=0.040), creatinine (mg/dL) at ICU admission (unadjusted OR for each point 1.53 (95% CI 1.03 to 2.28), P=0.035), and fever at any point during the ICU stay (OR 3.12 (1.34 to 7.26), P=0.008) (Supplementary Table 1). The adjusted analysis included age, tachypnea (respiratory rate >22 breaths per minute at ICU admission), hemoglobin <5.0 g/dL at ICU admission, creatinine, and fever during the ICU course. No predictor reached statistical significance (Supplementary Table 2).

Discussion

This study demonstrates that obstetric subjects account for a substantial proportion (23%) of ICU admissions at this central referral hospital in Malawi, which is consistent with reports from other LMICs.[16–19] This highlights the fact that investments in improving obstetric critical care have the potential to decrease maternal mortality in LMICs. However, overall in-hospital mortality was high (49%) despite the provision of a relatively sophisticated level of care in this low-resourced, low-income environment. This underscores the fact that investments should focus on earlier identification of these subjects to improve the potential for better outcomes. Any and all investments will have to be couched in the context of the whole healthcare system with Ministry of Health oversight. Quality improvement investments need not be costly: a first step could be training in obstetrics for ICU specialists and/or training in critical care medicine for obstetric specialists in these regions, to improve the ability to understand, identify and treat peripartum illness.

Obstetric ICU subjects in this study were generally young and admitted to the ICU after surgery. Although these associations have been described in previous retrospective studies of ICU subjects in low-resource countries of sub-Saharan Africa,[20–22] the strengths of this study include its prospective design and the level of clinical detail collected. These data serve as a useful starting point for discussions of obstetric critical care and maternal mortality in this region.

Global health research is demonstrating that quality primary or antenatal care will not be sufficient to address global maternal health improvement goals.

Access to quality hospital care is essential to better maternal outcomes. In Tanzania, for example, direct maternal mortality was found to be lower when women had access to a hospital rather than a lower level clinical facility.[23] Hospital admission in advance of the due date (e.g. maternal waiting homes) is re-emerging as a potential intervention to anticipate and address peripartum complications.[24] Nevertheless, hospital care is not in and of itself sufficient; this study demonstrates that in the areas of the world with the least resources, obstetric critical care is in demand. Intensive care services include at a minimum, a high nurse-to-patient ratio, supplemental oxygen therapy and frequent or continuous vital sign monitoring. In the World Health Organization (WHO) publication 'Monitoring Emergency Obstetric Care: A Handbook', emergency obstetric care also includes eight signal functions (Table 2).[25] The WHO currently recommends that any facility providing surgery or cesarean deliveries should also provide intensive care[26] but most hospitals in LMICs lack these services. This problem is particularly dire in sub-Saharan Africa, where reported ICU bed availability is 1 per million population[13] compared to 200 per million in the United States and 58 per million in Sweden.[27]

Integrating quality intensive care services into obstetric care at the central referral hospital level in LMIC will likely require multilevel investment, as it has in other medical advances in global health.[28] In general, this will include (1) collaboration between obstetricians, maternal-fetal medicine specialists, intensivists and non-physician providers (who frequently account for the majority of healthcare providers in LMICs) to develop clinical protocols for the early identification and treatment of obstetric critical illness states, as well as transfer protocols between district hospitals and central referral hospitals; (2) collaboration with public health administrators to expand critical care services within central referral hospitals; and (3) investment in critical care infrastructure (e.g. oxygen supply chains, mechanical ventilation, blood banking).

Although maternal mortality in sub-Saharan Africa occurs across all stages of the pregnancy, postpartum deaths represent over half of all deaths across all regions of Africa.[29] A recent systematic analysis by the WHO revealed that the leading cause of maternal death worldwide was hemorrhage (27.1%, 95% CI 19.9 to 36.2%) and the majority of these are postpartum hemorrhage.[30] Post-partum complications frequently require surgical intervention or critical care services, both of which require hospital admission. Our study is consistent with these findings, with most subjects admitted after either a cesarean section or a postnatal abdominal hysterectomy. However, our data also demonstrate a deficiency in the peri-operative care of obstetric subjects at this central referral hospital. The gap between the recommendation for blood transfusion (n=62) and the administration of blood products (n=39) is notable. Blood transfusion is a potentially life-saving intervention for subjects in hemorrhagic shock and although blood bank services in LMICs face many challenges,[31] this may be another important target for quality improvement research.

There are also several data points that indicate a potentially high prevalence of acute kidney injury in this population: oliguria was common (84%) and the creatinine values measured at ICU admission were at the high end of the normal reference range for women, pregnant or otherwise (median 1.1 mg/dL, IQR 0.7–2.2).[32] All patients who required hemodialysis ultimately died. Elevated creatinine is a delayed marker of acute kidney injury and since this was measured at ICU admission in this study, it indicates that any acute kidney injury which occurred likely preceded ICU admission. Future research may focus on improving peri-operative care to reduce the contribution of acute kidney injury to ICU admission and to obstetric mortality.

This study has several limitations. First, it is a single institution study. The provision of critical care in sub-Saharan African countries is very limited and generally only available at central referral hospitals. Future studies may try to aggregate data from several referral hospitals to increase generalizability. In the same vein, given that our sample size is small, these data are not meant to make broad generalizations about public health based on all the clinical data presented, but rather to call attention to, and to provide pilot data for, future investigations. Second, because of limited diagnostic technology and documentation, it is possible that a proportion of patients were admitted for gynecological disease rather than pure obstetric pathologies. However, given our experience at this study site we do not think that this is the case for most patients. Finally, because

Table 2 Basic and comprehensive emergency obstetrical care signal functions[25]

Basic emergency obstetric care	Comprehensive emergency obstetric care
Administer parenteral antibiotics	All six basic signal functions as well as:
Administer uterotonic medications	Perform blood transfusion
Administer parental anticonvulsants for pre-eclampsia and eclampsia	Perform surgery (e.g. cesarean section)
Perform manual removal of placenta	
Perform removal of retained products (e.g. manual vacuum aspiration)	
Perform assisted vaginal delivery (e.g. forceps)	

Appendix 1 Proportion of Missing Responses in Clinical Variables of Interest (n = 98)

Variable	Missing, n (%)
Sex	0 (0)
Age	0 (0)
Location before ICU admission	0 (0)
Vital Signs	
Heart rate, beats per minute	2 (2)
Mean arterial pressure, mmHg	2 (2)
Temperature, °Celsius	3 (3)
Respiratory rate, breaths per minute	4 (4)
Oxygen saturation, percentage	7 (8)
Postoperative status	
Suspected infection at ICU admission, n (%)	
Laboratory values	
Hemoglobin (g/dL)	10 (11)
White blood cell count ((cells x10^9/L)	10 (11)
Platelet count ((cells $\times 10^9$/L)	10 (11)
Creatinine (μmol/L)	21 (23)
HIV status	12 (13)
Malaria status	21 (23)
Provision of mechanical ventilation, n (%)	1 (1)
Oliguria (urine output <0.5 mL/kg/h for >6 h during ICU stay)	3 (3)
Length of stay (days)	1 (1)
ICU mortality, n (%)	0 (0)
Hospital mortality, n (%)	0 (0)

ICU: Intensive Care Unit. HIV: human immunodeficiency virus.

of limited ICU bed availability, some proportion of critically ill obstetric subjects are likely to be treated in other hospital areas such as the HDUs and/or the wards. This is not uncommon at central hospitals in the region and given the severely limited supply of ICU beds in Malawi a reality of clinical care in resource-limited settings. Future studies may take this into account and register patients from these areas. Finally, due to limitations in funding and staffing, we were unable to rigorously assess the etiology and outcomes of certain diagnostic groups.

In conclusion, obstetric utilization of ICU resources in Malawi is high compared to high-income and well-resourced settings and is associated with high in-hospital mortality. Collaborative investments in quality intensive care, including education, early triage services and blood banking is an important first step to improving maternal mortality. These efforts should be made in concert with local stakeholders to maximize their impact. In parallel, given that one in four subjects may be recently or currently pregnant, ICU providers need to assure that they are well-versed in both the physiology of peri- and postpartum subjects and their underlying disease etiology.

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Appendix B. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijoa.2019.03.004.