Antenatal blood transfusion in South Africa: indications and practice in a high-HIV-prevalence setting

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BACKGROUND: Globally, data on antenatal blood transfusion practices are scarce. We sought to characterize the epidemiology of antenatal transfusion in South Africa.

STUDY DESIGN AND METHODS: A cross-sectional study was conducted of women who were transfused during pregnancy (>48 hr before anticipated delivery) at two hospitals in Durban and Soweto in 2014 to 2015. Medical record data on demographics, obstetric history, anemia, HIV status, and indications for blood transfusion were abstracted.

RESULTS: The records on a total of 560 transfused pregnant women were evaluated; mean age was 28 years, 98% were of black African ethnicity, and 28% were HIV positive. At time of transfusion, one-half were in the first trimester. Hemorrhage was noted in 76% of women, most of which was associated with abortion (67%) or ectopic pregnancy (27%). Most women were transfused with red blood cells (RBCs; median, 2 units); 14% of women were transfused with plasma and 2% with platelets. Median pre- and posttransfusion hemoglobin levels were 6.9 g/dL and 9.2 g/dL, respectively; the latter differed by hospital (8.7 g/dL vs. 9.5 g/dL; $p < 0.01$). Hemorrhage was associated with missing HIV status, lower gestational age, and transfusion of 3 or more RBC units (all $p < 0.01$). In contrast, diagnoses of anemia (Soweto only) were associated with HIV infection, later gestational age, and lower (<3 units) RBC dose (all $p < 0.01$).

CONCLUSION: Abortion and ectopic pregnancy with associated hemorrhage were the leading indications for antenatal transfusion and were concentrated in early gestation. By contrast, anemia was associated with HIV infection and transfusion in the third trimester.

Blood transfusion is critical to the management of obstetric complications. It is also an index of severity for morbidity outcomes given that both obstetric hemorrhage (OH) and antenatal anemia are major drivers of transfusion. OH, specifically, is a leading cause of maternal death, particularly in low-middle-income countries, where ready access to blood products is frequently lacking.[1–4]

ABBREVIATIONS: ART = antiretroviral therapy; CHB = Chris-Hani Baragwanath Hospital; KEH = King Edward VIII Hospital; OH = obstetric hemorrhage; REDS-III = Recipient Epidemiology and Donor Evaluation Study-III.

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Blood use offers insight into obstetric practices and outcomes, and can serve to identify deficiencies in care. Several studies have been conducted in South Africa to characterize peripartum blood use.[5–7] The findings suggest excess rates of transfusion, relative to those of several high-income countries, despite comparable rates of hemorrhage.[6] Reasons that have been postulated for these increased rates of transfusion include a high prevalence of antenatal anemia, rendering some patients unable to tolerate the physiological blood loss associated with delivery. High incidence of peripartum blood transfusion is not unique to South Africa; rather, it is a major challenge in sub-Saharan Africa, where there is already inability to meet regional transfusion demand.[3] Indeed, an estimated quarter of all maternal deaths in sub-Saharan Africa are attributed to lack of timely access to blood transfusion in times of emergency.[1]

While there is a growing literature on peripartum blood transfusion, data on blood transfusion in the antenatal period (i.e., during pregnancy but >48 hr before delivery) are virtually absent. One of the few studies that alluded to antenatal transfusion examined obstetric transfusion practices in Australia (n = 891,914 pregnancies) where the rate of obstetric blood transfusion had increased from 1.2% in 2001 to 1.6% in 2010; 91% of transfusions occurred during the birth admission rather than the antenatal period.[8] Given the paucity of data on antenatal transfusion, we sought to characterize its epidemiology in two large secondary-tertiary care, academic hospitals in South Africa, including description of the clinical (i.e., obstetric and comorbid) risk factors and transfusion practices. We describe and compare red blood cell (RBC) doses transfused per hospital, in relation to participants' hemoglobin levels. We estimate overall frequencies of OH and anemia and distributions of hemorrhage etiologies and transfusion indications, and then evaluate associations of these four outcomes with HIV status, gestational age, and transfusion dose.

MATERIALS AND METHODS

Study design and participants

We conducted a cross-sectional study of women who were transfused during pregnancy at two urban, publicly funded South African hospitals. During the study enrollment period from May 2014 through October 2015, all pregnant women who underwent an antenatal transfusion of RBCs, platelets, or plasma more than 48 hours before anticipated delivery were deemed eligible for inclusion. We prospectively identified eligible participants through daily review of ward admission logs in both the maternity and gynecological wards; this approach was complemented by direct communication with the blood bank and ward staff. We excluded minors (aged <18 years old) because South African law requires parental/guardian consent for participation in research. Following discharge, trained obstetric research nurses used a standardized form to abstract data, retrospectively, from the participant's medical record. We collected data on patient demographics, previous and current pregnancy history, HIV status and treatment, and indications for current hospitalization and blood transfusion.

The two hospitals, Chris-Hani Baragwanath Hospital (CHB) in Soweto (greater Johannesburg) and King Edward VIII Hospital (KEH) in Durban, provide both second-tier and tertiary obstetric services and serve predominantly urban, low-income, Black-African and Colored (denotes a specific mixed-race population group) populations. Both hospitals are broadly representative of the population and obstetric pathology in South Africa. Of note, South Africa has a high HIV prevalence, and HIV testing is performed routinely during prenatal care. We have previously reported on perinatal (i.e., within 48 hours of delivery) transfusions at these hospitals under the Recipient Epidemiology and Donor Evaluation Study-III (REDS-III).[5,6] South Africa is ranked by the World Bank as an upper-middle-income country. However, there is high income inequality mainly due to the high unemployment rate among black South Africans. As such, the study population should be considered as a population that more closely resembles that of low-middle- or low-income country (which is the case for most of sub-Saharan Africa).

This study received ethical approval from the committees representing the two participating hospitals (CHB and KEH) in addition to University of California San Francisco, the South African National Blood Service, and the REDS-III data-coordinating center (RTI International). We obtained written informed consent from all enrolled participants at CHB as required by the local Institutional Review Board of University of Witwatersrand; patients who were transferred or discharged before consent could be obtained were excluded. Data were collected under a waiver of consent at KEH.

Data collection

Machine-readable paper antenatal transfusion forms (available on request) allowed automated data entry. The electronic data were subsequently transferred to the data-coordinating center for cleaning, and analysis was performed at University of California San Francisco and its affiliated Vitalant Research Institute.

Outcomes of interest were OH, anemia, hemorrhage etiology, transfusion indications, and the number and type of units transfused. We used a convenience definition for OH, namely, whether it was recorded in the medical record, regardless of estimated blood loss. When multiple hemorrhage etiologies or transfusion indications were recorded per participant, clinician co-authors EMB and ELM adjudicated a single dominant indication. For the purposes of the study, anemia was based on reporting from clinical records and refers to medical (e.g., iron deficiency) rather than

acute anemia (e.g., in the setting of hemorrhage). Of note, sickle cell disease and malaria-related anemia are not endemic in South Africa. Abortion refers to termination of pregnancy; while this does not discriminate between spontaneous (i.e., miscarriage) and therapeutic abortion, the overwhelming majority were considered to be spontaneous in nature. The described units of RBCs refer to component RBC concentrates and not to whole blood transfusion. Ascertainment of clinical variables was based on documentation in the medical records and the judgment of the nurse who performed the data abstraction. Due to a problem with the abstraction of anemia data at KEH, data pertaining to anemia and anemia as a transfusion indication could only be analyzed at CHB. In many participants, anemia status and HIV status were not documented; for these variables we retained missing values in analyses by defining "missing" as a separate category.

Statistical analysis

Participant characteristics were summarized overall and by hospital using counts and percentages for categorical data and medians (interquartile ranges [IQRs]) or means (standard deviations [SDs]) for continuous variables. We compared transfusion practices between hospitals, including total units transfused and transfusion-related hemoglobin levels, using the Wilcoxon rank-sum tests. For each participant, the hemoglobin increment was calculated as the change in hemoglobin level (post- minus pretransfusion) divided by the number of RBC units transfused. Hemoglobin analyses were restricted to participants with nonmissing RBC units and pre- and posttransfusion hemoglobin values.

We report overall proportions of women with OH and with anemia and 95% confidence intervals (CIs) based on the Agresti-Coull method.[9] We used Pearson's chi-squared tests of independence to evaluate associations of these

TABLE 1. Overall and by hospital: demographic and clinical characteristics of study population

Characteristic	Overall (N = 560)	Soweto: CHB (N = 371)	Durban: KEH (N = 189)
Age, mean [(SD)	28.4 (5.8)	28.8 (6.0)	27.5 (5.4)
Race, n (%)			
Black	546 (98)	361 (97)	185 (98)
White	2 (0.4)	2 (0.5)	0 (0)
Colored	6 (1)	5 (1)	1 (0.5)
Asian	2 (0.4)	0 (0)	2 (1)
Missing	4 (0.7)	3 (0.8)	1 (0.5)
Gravidity, median (IQR)	3.0 (2.0-3.0)	3.0 (2.0-3.0)	2.0 (2.0-3.0)
Parity, median (IQR)	1.0 (1.0-2.0)	1.0 (1.0-2.0)	1.0 (1.0-2.0)
Length of stay, days, median (IQR)	3.0 (2.0-5.0)	3.0 (2.0-5.0)	4.0 (3.0-7.0)
Mother alive at discharge, n (%)			
Yes	513 (92)	334 (90)	179 (95)
No	2 (0.4)	0 (0)	2 (1)
Missing	45 (8)	37 (10)	8 (4)
Gestational age, median (IQR)	13.0 (8.0-20.0)	14.0 (8.0-19.5)	12.0 (8.0-21.0)
Gestational age (trimester), n (%)			
2-13 wk	283 (51)	180 (48)	103 (54)
14-25 wk	174 (31)	138 (37)	36 (19)
26-40 wk	79 (14)	45 (12)	34 (18)
Missing	24 (4)	8 (2)	16 (8)
Received prenatal care before admission (%), by gestational age, n (%)*			
Overall	116/560 (20.7)	71/371 (19.1)	45/189 (23.8)
2-13 weeks	9/283 (3)	8/180 (4)	1/103 (1)
14-25 weeks	38/174 (22)	23/138 (17)	15/36 (42)
26-40 weeks	69/79 (87)	40/45 (89)	29/34 (85)
Missing	0/24 (0)	0/8 (0)	0/16 (0)
Prenatal visits among those with care, median (IQR)	2.0 (1.0-4.0)	2.0 (1.0-3.0)	3.0 (2.0-5.0)
HIV status, n (%)			
HIV positive	158 (28)	118 (32)	40 (21)
HIV negative	163 (29)	124 (33)	39 (21)
Missing	239 (43)	129 (35)	110 (58)
ART use before pregnancy, n (%)†			
Yes	54 (10)	41 (11)	13 (7)
No	94 (17)	63 (17)	31 (16)
Missing	412 (74)	267 (72)	145 (77)

* Prenatal care status was unknown for 12 CHB and 2 KEH participants.
† Rates of ART use by HIV-positive participants were 33% at CHB and 30% at KEH.
ART = antiretroviral therapy; CHB = Chris-Hani Baragwanath Hospital; KEH = King Edward VIII Hospital; IQR = interquartile range; SD = standard deviation.

outcomes with clinical characteristics, including HIV status, gestational age (in trimesters), and RBC units (0-2 vs. ≥3). Descriptive statistics and statistical analyses were completed using computer software (R version 3.5.3).

RESULTS

The study enrolled 560 transfused women, with 371 at CHB in Soweto and 189 at KEH in Durban (Table 1). The mean age of participants was 28 (SD, 5.8) years, 98% were of black African ethnicity. At admission for transfusion, 78 (14%) were primigravidas; 51%, 31%, and 14% of subjects were in their first, second, and third trimesters, respectively, with a median gestational age of 13.0 weeks. Antenatal care was noted for 21%, increasing across trimesters. HIV status was missing in 239 (43%) women; 158 (28% of all women) were HIV positive. The availability of HIV status increased across trimesters (from 46% to 92%) and receipt of prenatal care (47% without vs. 97% with care). Of known HIV-positive women, 54 (28%) were on antiretroviral medication before pregnancy.

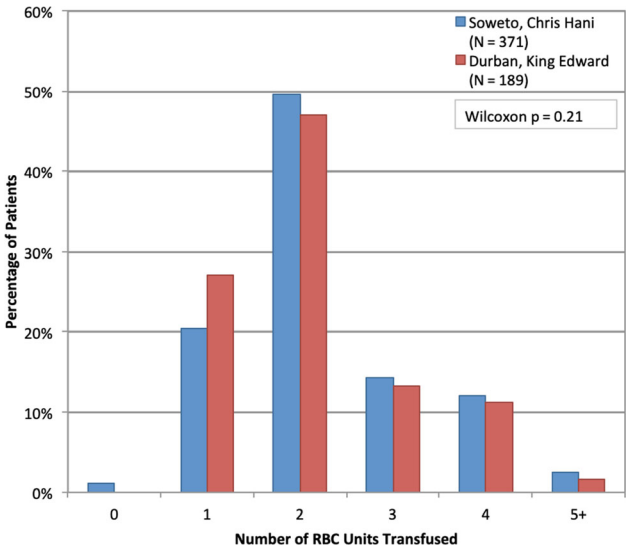

Fig. 1. Distributions of RBC units transfused, by hospital. Four women received no RBCs but received either plasma or platelets. [Color figure can be viewed at wileyonlinelibrary.com]

Transfusions included RBCs in all but four women (median, 2 units; Fig. 1); 14% of women were transfused with fresh-frozen plasma (median, 2 units) and 2% with platelets. Only 12 women (2.1%) received 5 or more RBC units, suggesting "massive transfusion," with no difference in median RBC units transfused between hospitals ($p = 0.21$). The unadjusted median (IQR) pre- and posttransfusion hemoglobin values were 6.9 (5.6-8.0) g/dL and 9.2 (8.0-9.9) g/dL, respectively; however, posttransfusion hemoglobin values were missing in a large percentage of cases, especially at CHB. The adjusted hemoglobin increment per RBC unit transfused was 0.90 (0.95) g/dL/unit (Table 1). Based on complete cases, pretransfusion hemoglobin levels did not differ between hospitals, but posttransfusion hemoglobin ($p = 0.006$) and hemoglobin increment per RBC ($p = 0.07$) was higher at CHB (Fig. 2).

OH was recorded in 354 (63%; 95% CI, 33%-41%) women overall (Table 2). Hemorrhage was associated with earlier gestational age, transfusion of 3 or more RBC units and with missing HIV status (all $p < 0.01$). Major etiologies related to OH included all types of abortion (68%) and ectopic pregnancy (27%); the number of recorded etiologies exceeded the number of women designated as having OH. Hemorrhage etiologies were associated with gestational

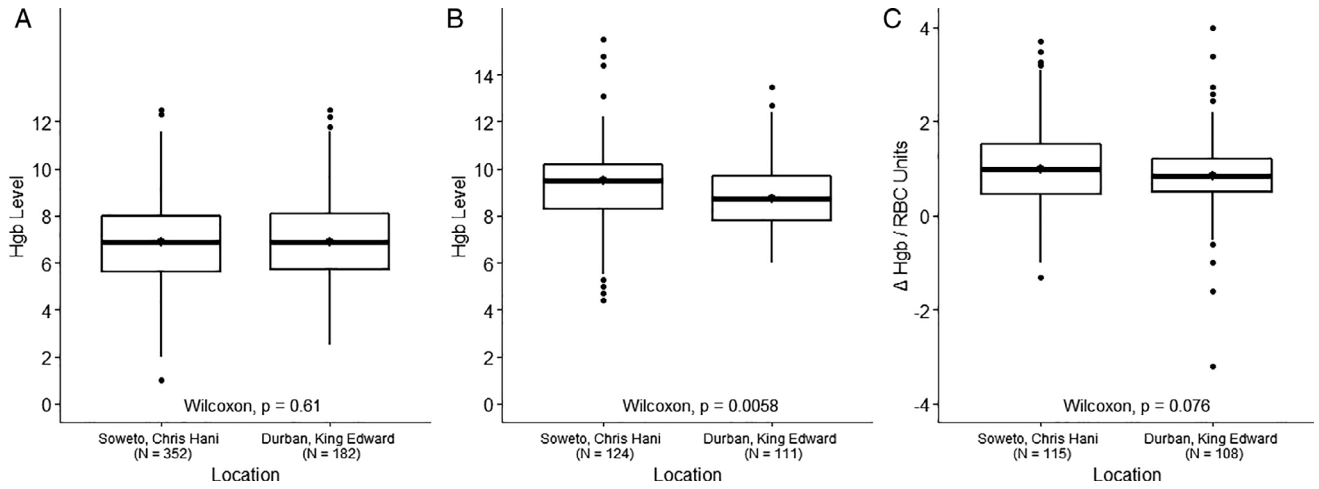

Fig. 2. Distributions (boxplots of median, IQR) of (A) pretransfusion hemoglobin (Hgb; g/dL); (B) posttransfusion hemoglobin; and (C) hemoglobin increment per RBC unit, by hospital. Data for posttransfusion hemoglobin and hemoglobin increment were missing in a large proportion of cases.

TABLE 2. Combined across two South African hospitals: number (percent) of obstetric hemorrhage and distribution of hemorrhage etiologies, by HIV status, gestational age, and transfusion dose

		HIV status				Gestational age (wk)*				RBC units transfused		
Outcome	All (N = 560)	HIV positive (N = 158)	HIV negative (N = 163)	Missing (N = 239)		2-13 (N = 283)	14-25 (N = 174)	26-40 (N = 79)		0-2 (N = 404)	3+ (N = 156)	
Obstetric Hemorrhage					p < 0.01				p < 0.01			p < 0.01
Yes	354 (63)	74 (47)	100 (61)	180 (75)		210 (74)	115 (66)	11 (14)		238 (59)	116 (74)	
No/Missing	206 (37)	84 (53)	63 (39)	59 (25)		73 (26)	59 (34)	68 (86)		166 (41)	40 (26)	
Hemorrhage Etiologies†					p < 0.01				p < 0.01			p < 0.01
• *Abortion related*												
Threatened	28 (7)	7 (8)	7 (6)	14 (7)		11 (4)	17 (12)	0 (0)		17 (6)	11 (8)	
Incomplete	237 (56)	49 (53)	71 (59)	117 (55)		123 (47)	102 (74)	1 (14)		157 (56)	80 (56)	
Complete	19 (4)	5 (5)	6 (5)	8 (4)		10 (4)	6 (4)	0 (0)		14 (5)	5 (3)	
Fetal death	4 (1)	2 (2)	1 (1)	1 (0)		0 (0)	4 (3)	0 (0)		3 (1)	1 (1)	
• *Ectopic pregnancy*	114 (27)	26 (28)	28 (23)	60 (28)		105 (40)	3 (2)	1 (14)		72 (26)	42 (29)	
• *Other*												
Placental abruption	5 (1)	1 (1)	3 (2)	1 (0)		0 (0)	3 (2)	2 (29)		3 (1)	2 (1)	
Placenta previa	4 (1)	0 (0)	2 (2)	2 (1)		0 (0)	1 (1)	3 (43)		4 (1)	0 (0)	
Surgical	14 (3)	3 (3)	3 (2)	8 (4)		13 (5)	1 (1)	0 (0)		12 (4)	2 (1)	

* Gestational age 24 trimester values missing.

† For some participants, multiple obstetric hemorrhage (OH) etiologies were provided. Percentages are based on all participants with column characteristic. Chi-squared tests were conducted among 425 participants with a listed etiology, and contrast all abortions versus ectopics versus other.

TABLE 3. At Chris-Hani Barawanath Hospital, Soweto: prevalence of anemia diagnosis and distribution of transfusion indications, by HIV status, gestational age, and transfusion dose

		HIV status				Gestational age (wk)*				RBC units transfused		
Outcome	All (N = 371)	HIV positive (N = 118)	HIV negative (N = 124)	Missing (N = 129)		2-13 (N = 180)	14-25 (N = 138)	26-40 (N = 45)		0-2 (N = 264)	3+ (N = 107)	
Anemia†					p < 0.01				p < 0.01			p < 0.01
Yes	92 (25)	45 (38)	32 (26)	15 (12)		24 (13)	28 (20)	39 (87)		75 (29)	17 (15)	
No	43 (12)	18 (15)	20 (16)	5 (4)		17 (9)	22 (16)	4 (9)		34 (13)	9 (8)	
Missing	236 (64)	55 (47)	72 (58)	109 (85)		139 (77)	88 (64)	2 (4)		151 (58)	85 (77)	
Transfusion Indication‡					p = 0.06				p < 0.01			p < 0.01
Hemorrhage	154 (42)	49 (425)	43 (35)	62 (48)		75 (42)	71 (51)	7 (16)		109 (42)	45 (41)	
Surgery/Anesthesia	54 (15)	14 (12)	19 (15)	21 (16)		44 (24)	6 (4)	1 (2)		31 (12)	23 (22)	
Anemia	29 (8)	16 (14)	7 (6)	6 (5)		5 (3)	7 (5)	17 (38)		28 (11)	1 (1)	
Other	43 (12)	11 (9)	19 (15)	13 (10)		19 (11)	22 (16)	2 (4)		31 (12)	12 (12)	
Missing	91 (25)	28 (24)	36 (29)	27 (21)		37 (21)	32 (23)	18 (40)		65 (24)	26 (25)	

* Eight trimester values missing.

† Chi-square p values contrast the three levels shown. Participants with missing HIV status are included in the analysis as a distinct category of HIV status.

‡ Chi-square p values contrast the five levels shown. Participants with missing HIV status are included in the analysis as a distinct category of HIV status.

age ($p < 0.01$) but not with HIV status or RBC dose. In the first trimester most OH was explained by incomplete abortion or ectopic pregnancy, in the second trimester by incomplete abortions, and in the third trimester by placental complications.

At CHB, anemia was reported in 25% (95% CI, 21%-29%) of 371 transfused women. Anemia status was not recorded in 64%, especially those with unknown HIV status, early in gestation, or receiving 3 or more RBC units (Table 3). Diagnosis of anemia was more common in HIV-positive participants (38% vs. <26%; $p < 0.01$), with no difference by antiretroviral therapy (ART) use among HIV-positive participants (39% vs. 38%). In addition, anemia occurrence increased across trimesters (from 13% to 87%; $p < 0.01$) and was higher among those transfused with fewer than 3 RBC units (29% vs. 15%; $p < 0.01$).

At CHB, a transfusion indication was noted for 75% of 371 participants. The most frequent indications for transfusion were hemorrhage (42%), surgery and anesthesia (15%), and anemia (8%). Mirroring its occurrence, anemia was a more common transfusion indication among HIV+ participants (14% vs. <6%), participants in the third trimester (38% vs. <6%) and those who received fewer than 3 RBC units (11% vs. 1%). Anemia as a transfusion indication was less common among the 4 HIV-positive patients on ART (10%) than among the 12 HIV-positive patients who were not on ART (16%); however, supporting evidence for this was limited. Hemorrhage and surgery dominated transfusion indications in the first trimester (66%) and accounted for most of the higher-volume transfusions. Hemorrhage alone dominated the second trimester (51%), and anemia dominated the third.

DISCUSSION

There is a paucity of data pertaining to antenatal transfusion. To our knowledge, this is one of the few studies that reports data on the epidemiology of antenatal transfusion practice. The findings indicate that one-half of antenatal transfusions in South African hospitals occurred in the first trimester, the overwhelming majority of which were confined to RBC use. Most transfusions were ascribed to hemorrhage, of which abortion (e.g., incomplete and threatened) and ectopic pregnancies accounted for the majority of cases, concentrated in early gestation. Anemia as an indication for transfusion increased with advancing gestational age and HIV infection. Transfusions appeared to be appropriate with regard to hemoglobin triggers and indications but higher posttransfusion hemoglobin at one hospital despite similar RBC transfusion doses suggested differences in transfusion practice between the two study hospitals.

Hemorrhage was reported in two-thirds of transfused women, most of which occurred early in pregnancy, with ectopic pregnancy and incomplete abortion leading both by underlying cause of bleeding as well as highest RBC use. Hemorrhagic complications including ectopic pregnancy and abortion may not be modifiable. Ectopic pregnancy, a life-threatening obstetric emergency, is common in South Africa. In one study in Transkei, South Africa, the incidence of ectopic pregnancy was 22 per 1000 live births and over one-third (37%) of cases presented with hemorrhagic shock.[10] Pelvic inflammatory disease is a leading risk factor for ectopic pregnancy, where repair of associated inflammatory damage is thought to impede normal passage of the conceptus to its implantation site in the uterus. Further, case fatality rates from ectopic pregnancy are 10-fold higher in developing African countries as compared to high-income countries, in large part due to a delayed or erroneous diagnosis.[11] A high proportion of ectopic pregnancies require blood transfusion. In a retrospective review of cases of ectopic pregnancy in a hospital in Western Tanzania, 33 of 88 (37.5%) cases required blood transfusion.[12] While not statistically significant, those in which diagnosis was ascertained by ultrasound versus peritoneal aspiration had lower mean numbers of units transfused and were less severely anemic. In another study in Cameroon, 25 of 144 (17%) cases of ectopic pregnancy required blood transfusion.[13]

Abortions accounted for two-thirds of transfusion indications during pregnancy. One study in neighboring Botswana evaluated blood use in 619 patients following abortion (neither we nor they could distinguish between induced and spontaneous abortions).[14] The investigators reported that the transfusion incidences of whole blood or RBC concentrates, plasma, and platelets were 9.5%, 1.3%, and 0.7%, respectively, concluding that blood use in that setting was low.

In our study, RBC transfusion for anemia was strongly associated with advanced gestational age. This supports findings from our prior studies of peripartum transfusion practice in South Africa,[5,6] which suggested that unaddressed antenatal anemia is a significant risk factor for later maternal transfusion. Anemia renders pregnant patients less likely to tolerate the physiological blood loss that accompanies delivery. It also is an established risk factor for poor infant outcomes, including cognitive impairment.[15] However, we posit that anemia's correlation with advancing gestational age in our study and others is, at least in part, attributable to its increasing measurement during gestation.[16–18] We found that anemia status was missing in 64% of CHB participants, especially those at early gestational ages. Nonetheless, our findings suggest opportunities for practice improvements. For example, one could envision studying an intervention to screen antenatal women more aggressively, with administration of hematinics (e.g., iron, folate) if so indicated.

Worldwide, 42% of pregnant women and 30% of women of childbearing age are anemic.[17] Complex social and medical factors have left the burden of anemia on low- and middle-income countries, with Africa suffering the highest prevalence.[17] While "physiological" anemia occurs in all pregnancies (i.e., given the disproportionate increase

in the plasma volume relative to the increase in RBC mass[19,20]), pathological anemia, most notably iron deficiency anemia, is also very common in pregnancy.[16–18] The underlying mechanisms are well established. In brief, these relate to an imbalance between demand (e.g., maintenance of the uteroplacental unit, fetal growth) and available RBC expansion. Demand for iron routinely exceeds any gain obtained through adaptive mechanisms (e.g., increased gastrointestinal absorption and amenorrhea) in pregnancy,[16] which increases from 0.8 mg/day in the first trimester to 7.5 mg/day in the third trimester.[18] In the absence of iron supplementation, dietary intake is often insufficient to prevent anemia.[20]

A previous study in one South African hospital found a significant difference in the prevalence of prenatal anemia in HIV-positive (71.3%) versus HIV-negative (28.7%) women.[21] Similarly, we found anemia to be more common in HIV-positive women (evaluated only at CHB), and overall we found that most women were ART-naïve at presentation. HIV status was frequently missing in our study, probably because over one-half of transfusions occurred in early pregnancy in association with high-acuity care (e.g., OH) before prenatal care and routine HIV testing could be initiated. In contrast, during the perinatal period, HIV status was missing in 2% of women transfused at the same hospitals.[5]

Our data suggest some variability in transfusion practices by hospital. The pretransfusion hemoglobin values were similar at CHB and KEH, suggesting that appropriate "transfusion triggers" and the number of blood products that were administered did not differ between hospitals. However, the posttransfusion hemoglobin and adjusted hemoglobin increment were higher at CHB, which could suggest liberal transfusion or overtransfusion at CHB, although confounding by transfusion indications or disease severity cannot be definitively excluded. Of note, this finding was shared by the parallel study that evaluated peripartum transfusion practices at the same hospitals.[5] While not unique to obstetrics, there has been significant investment in patient blood management programs over the past decade, mostly in high income countries. This followed recognition of comparable or even superior outcomes with restrictive transfusion thresholds,[22] across a range of clinical settings, including obstetrics.[23] While not as well formalized in low-middle-income countries, patient blood management strategies (including single-unit transfusions with reassessment and/or hemoglobin measurement in the stable nonbleeding patient rather than routine double-unit transfusions) are very relevant given pervasive challenges surrounding blood availability. Ironically, despite shortfall in provision of blood, inappropriate transfusion and overtransfusion is not uncommon,[24] and likely stems from relatively little education in transfusion medicine, coupled with a lack of standardization of transfusion practices as reflected by nonadherence to evidence-based guidelines.[25] Pertinent to the obstetric population, the Network for the Advancement of Patient Blood Management, Haemostasis and Thrombosis in collaboration with the International Federation of Gynaecology and Obstetrics and the European Board and College of Obstetrics and Gynaecology have published recommendations on prenatal iron therapy that could mitigate risk of transfusion.[26] These and other guidelines on patient blood management were developed during or after the index study.[27]

There were limitations to the study. First, data were abstracted from the clinical records and were thus often missing and subject to the judgment by the nurses who performed the abstraction. For example, posttransfusion hemoglobin values were often missing at CHB, and reporting of anemia (itself a limitation) was poorly abstracted at KEH, leading to exclusion of that variable from some analyses. As discussed above, most transfusions occurred early in gestation when prenatal care had not been initiated and under emergency circumstances that may have delayed routine tests. For the same reason, the association of HIV infection with anemia needs to be interpreted within the context of a large proportion with unknown HIV and anemia status. Second, we could not calculate the incidence of transfusion during pregnancy because it was difficult to establish an appropriate denominator of all pregnant women in a hospital system, and there would still be women who are unaware of their pregnancy status, particularly early in gestation. Third, our analysis was restricted to two obstetric services, limiting generalizability of the findings. Given their scope of practice (i.e., secondary- and/or tertiary-level care services), pathology in the selected hospitals may be different from smaller clinics, rural obstetric units, and emergency rooms, where other antenatal transfusions may occur. Furthermore, it is uncertain to what extent the findings are generalizable to other African and international settings. In addition, exclusion of minors (i.e., women <18 years old) may have limited the number of primigravid patients, thereby offering an incomplete characterization of antenatal anemia in this setting. Young women and/or primigravid women may well be at risk for antenatal bleeding.

Nonetheless, our study does offer rare insight into the epidemiology of antenatal transfusion practice, where data are sorely lacking. The findings suggest that hemorrhagic complications accompanying abortions and ectopic pregnancies in the first and second trimesters are the most common reasons for antenatal transfusion. However, anemia remains a frequent and potentially preventable indication in this South African setting, particularly during the third trimester. Finally, even when thresholds for transfusion are appropriate, variation in transfusion practice could reflect an area for improvement, through educational efforts and/or adherence to evidence-based transfusion guidelines.[28]

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CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

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