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# Antenatal Care Visit Attendance Frequency and Birth Outcomes in Rural Uganda: A Prospective Cohort Study

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## Abstract

**Objectives** Antenatal care (ANC) is designed to improve pregnancy outcomes by providing screening and treatment for preventable and treatable diseases. However, data are lacking on whether ANC affects stillbirth risk. We hypothesized stillbirth risk in Uganda is lower in women attending the recommended ≥ 4 ANC visits compared to those attending ≤ 3.

**Methods** We performed a secondary analysis of subset of 1,785 women enrolled in a prospective cohort of postpartum infection who presented to a regional referral hospital for delivery. Our primary outcome was documented stillbirth; a secondary composite poor birth outcome included stillbirth, early neonatal death, low birth weight (< 2500 g), and 5-min APGAR score < 7. We performed multivariable logistic regression analyses to identify independent correlates of stillbirth and poor birth outcome.

**Results** Of 1,785 participants, 58 (3%) pregnancies resulted in stillbirth and 198 (11%) had a poor birth outcome. Of 1,236 women attending ≥ 4 ANC visits, 31 (2.5%) had a stillbirth, compared to 27/510 (5.2%) attending ≤ 3. In multivariable analyses controlling for age, parity, distance traveled, referral status to hospital, malaria prophylaxis, and syphilis infection; attending ≥ 4 ANC visits was associated with significantly reduced odds of stillbirth (aOR 0.5, 95% CI 0.3–0.9, $P = 0.02$) and poor birth outcome (aOR 0.66, 95% CI 0.4–0.96, $P = 0.03$). Malaria prophylaxis was also independently associated with reduced odds of stillbirth (aOR 0.05, 95% CI 0.2–1.0, $P = 0.04$).

**Conclusions** Attending ≥ 4 ANC visits was associated with reduced odds of stillbirth and poor birth outcomes in this Ugandan cohort, which may be related to more comprehensive infection screening, treatment, and prevention services.

**Keywords** Stillbirth · Uganda · Antenatal care · Resource-limited setting · Neonatal death

## Significance Statement

### What is Already Known on This Subject?

Antenatal care (ANC) is designed to improve pregnancy outcomes by providing screening and treatment for diseases affecting maternal and fetal outcomes. However, data are lacking on whether ANC affects stillbirth risk.

### What This Study Adds

In Uganda, we found that attending the recommended number of antenatal care visits is protective against stillbirth. Additional stillbirth risk factors include distance from hospital, being referred to hospital, a diagnosis of hypertension, and not receiving malaria prophylaxis during pregnancy.

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## Introduction

Stillbirths are as common as neonatal deaths, with 2.6 million worldwide each year (Cousens et al. 2011; You et al. 2015) but are understudied compared to other poor birth outcomes (Lawn et al. 2011). Additionally, stillbirths disproportionately occur in resource-limited settings (RLS). However, research on the topic has been performed mostly in high resource settings, with one review estimating 3% of stillbirth research is performed in RLS (Cousens et al. 2011; Froen et al. 2009), despite nearly 90% of stillbirths occurring in RLS (Lawn et al. 2011). Risk factors for stillbirth in RLS likely differ from those in developed countries, with a higher proportion due to infectious etiologies and prolonged labor (Causes of Death Among Stillbirths 2011; Lawn et al. 2011; WHO 2007).

Though infections are thought to contribute substantially to stillbirth risk in RLS, 15% to > 70% of stillbirths are unexplained (McClure et al. 2015), in part because placental pathology and fetal autopsy are difficult and costly to obtain (Page et al. 2017). Additionally, to the best of our knowledge there are no published prospective cohort studies about confirmed stillbirths in a RLS hospital setting. Case–control studies published from Ghana (Yatich et al. 2010), Mozambique (Geelhoed et al. 2015), and Ethiopia (Berhie and Gebresilassie 2016) identify malaria and referral to tertiary care during childbirth as important risk factors for stillbirth. However, differences in infectious disease burden (e.g. malaria and other parasites, HIV) between settings and unique cultural situations (religious preferences, family size, employment availability) necessitate additional research in other RLS. To date, one retrospective cohort study has been published on stillbirth risk factors in Uganda, finding that multiple gestation and adverse outcomes in a prior pregnancy were associated with stillbirth (Kiguli et al. 2015; Kujala et al. 2017).

ANC programs are designed to diagnose, prevent, and treat common causes of stillbirth. In 2002, the World Health Organization (WHO) recommended four antenatal care visits with a midwife who administers vaccinations, screens for hypertension, determines maternal hemoglobin and Rh status, performs syphilis testing (when available), and prescribes malaria prophylaxis, nutritional supplements and de-worming medicines (WHO 2002). Starting in 2016, WHO increased the recommended number of visits to eight in an attempt to reduce perinatal deaths and improve maternal satisfaction (WHO 2016). Women sometimes attend fewer than the recommended number of visits due to human resource limitations at ANC clinics and challenges women face accessing care. Attending three or fewer ANC visits is a risk factor for early neonatal death in Bangladesh (Dey et al. 2019) and poor birth outcomes in Ghana (Yatich et al. 2010), however, data are lacking on the association between ANC attendance and stillbirth risk. To address this gap in knowledge, we conducted a secondary analysis of data collected in 2015 as part of a large prospective cohort study of postpartum infection in Mbarara, Uganda. Our objective was to determine the association between stillbirth and ANC. We hypothesized that risk of stillbirth was significantly lower in women attending at least four ANC visits compared to those attending three or fewer. Additionally, we hypothesized that risk of other poor birth outcomes would be less for women attending the recommended number of ANC visits.

## Methods

### Study Site, Participant Recruitment, and Ethics

This secondary analysis was performed on data collected from a cohort of participants recruited from the maternity ward at Mbarara Regional Referral Hospital (MRRH) in Mbarara, Uganda between March and October 2015 to determine postpartum infection incidence and associated risk factors (Ngonzi et al. 2018). MRRH serves a primarily rural catchment area with a population of nine million people and reports approximately 11,000 deliveries per year. All women who presented to MRRH for delivery or within the first six weeks postpartum were screened for enrollment into the original study and were eligible if they spoke English or Runyankole (the local language) well enough to provide written informed consent, and were reachable by phone after discharge for follow-up. The study was conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments and was approved by the institutional ethics review boards at Mbarara University of Science and Technology (08/10-14), Partners Healthcare (2014P002725/MGH), and the Uganda National Council of Science and Technology (HS/1729). All persons gave their informed consent prior to their inclusion in the study.

### Sample Size and Data Collection

To achieve the initial study objective of determining postpartum infection incidence and associated risk factors, 4231 women were prospectively enrolled. All febrile and hypothermic women ($n = 205$) and a random subset of normothermic participants ($n = 1708$) from the original cohort were chosen for additional data collection using a random number generator. A structured face-to-face interview in English or Runyankole was conducted with each participant to gather information on sociodemographics, prior medical and obstetric history, and antenatal care. Chart review

was performed to record maternal and neonatal hospital diagnoses, treatments, and outcomes. Number of ANC visits attended was obtained from the pariticipant's ANC card when available, and otherwise through participant report. This analysis includes the 1785/1913 (89%) participants in the cohort with interview or chart review data. Data from all 1785 participants were included in the final analysis, even if they were missing data on specific variables. Post-hoc power calculation of the sample size demonstrated 80% power to detect a doubling risk of stillbirth from 3 to 6%, comparing those attending four or more ANC visits to those attending three or fewer. Gestational age was defined by participant report of last normal menstrual period, or chart documentation of last normal menstrual period if participant report was missing. Data were entered into a Research Electronic Capture (REDCap) database (Harris et al. 2009).

## Data Analysis

Our primary exposure variable was the number of ANC visits attended, dichotomized as four or more visits versus three or fewer visits. This exposure variable has been utilized in previous studies of pregnancy outcomes (Asundep et al. 2014; Dey et al. 2019), and attending four or more ANC visits is defined as adequate antenatal care, according to WHO guidelines followed in Uganda during study enrolment (WHO 2002). Our primary outcome variable was chart-documented stillbirth, defined as a pregnancy in which one or more babies was born dead at a gestational age of $\geq 28$ weeks, the defined age of viability in Uganda. Our secondary outcome variable was a composite poor birth outcome, including stillbirth, early neonatal death within two weeks of hospital discharge, low birth weight ($<2500$ g), and 5-min APGAR score $<7$.

Demographic characteristics and outcomes were compared by dichotomized ANC attendance using student's t-test or Wilcoxon Rank Sum for continuous variables and Chi-squared analysis for categorical variables, with $P$-values $<0.05$ considered statistically significant. Separate multivariable logistic regression models were created to determine the independent association between dichotomized ANC attendance and the primary stillbirth outcome and secondary composite poor birth outcome. The stillbirth model included variables considered potential confounders from prior studies on stillbirth performed by Yatich in Ghana (Yatich et al. 2010), Geelhoed in Mozambique (Geelhoed et al. 2015), and Berhie in Ethiopia (Berhie and Gebresilassie 2016), including age, parity, distance from domicile to hospital, referral to hospital for care, and syphilis infection during pregnancy. Additional variables included in the poor birth outcome model were receipt of malaria prophylaxis during pregnancy (or taking trimethoprim/sulfamethoxazole prophylaxis, if living with HIV), preeclampsia chart diagnosis, number of hours in labor, delivery mode, and HIV serostatus. All variables with $P$-values $<0.05$ in the final model were considered significant predictors of stillbirth. All deliveries were included in the primary analyses. We graphically depicted the proportion of stillbirths and poor birth outcomes for each increasing ANC visit from 1–4, and fit unadjusted models of ANC as a continuous variable on stillbirth and poor birth outcomes to assess change in these outcomes with each increase in number of ANC visits. Sensitivity analyses restricted to women delivering at $\geq 39$ weeks' gestation were also performed for both outcomes, to account for the possibility that women giving birth at $<39$ weeks' gestation might have delivered prior to their fourth ANC visit. All analyses were performed using Stata software (Version 12.0, StataCorp, College Station, TX).

## Results

Over 99% of eligible women who presented to MRRH during the study timeframe were enrolled (4231). Interview and chart review data were missing from less than 10% of participants for any variable. Of the 1785 participants who underwent interview and chart review, 58 (3%) pregnancies resulted in stillbirth and 198 (11%) had a poor birth outcome, as defined by our criteria. Overall, 1236 (71%) of participants attended at least four ANC visits and 510 (29%) attended less than four ANC visits (Table 1). Stillbirth risk was 5.3% among women attending three or fewer ANC visits, and 2.5% among women attending four or more ANC visits ($P=0.003$, Table 1), and poor birth outcome was observed in 16% of women attending three or fewer ANC visits, and 10% among women attending four or more ANC visits ($P<0.0001$ Table 1). A lower proportion of women attending four or more ANC visits delivered preterm (104, 9%) than women attending three or less ANC visits (80, 17%, $P<0.001$, Table 1). In unadjusted models, we identified a significant trend for the relationship between ANC visits and both outcomes such that an increase in number of ANC visits was associated with a decreased odds of stillbirth (OR 0.63, 95% confidence interval [CI] 0.5–0.9, $P=0.007$) and decreased odds of poor birth outcome (OR 0.69, 95% CI 0.6–0.8, $P<0.001$, Fig. 1).

Of 58 women who had a stillbirth, 93% were singleton pregnancies and four (7%) were twin pregnancies with at least one stillborn twin (Table 2). Of women without a stillbirth, 97% birthed live singletons, 3% birthed live twins, and 0.06% birthed live triplets. Significantly fewer women who had a stillbirth (86%) were married compared to those with all-live births (93%, $P=0.04$, Table 1). Over one-third of stillbirths (34%) were delivered preterm (28–36 weeks), while only 11% of live births were preterm ($P<0.0001$). Women who had a stillbirth were less likely to

**Table 1** Demographic, antenatal and intrapartum characteristics of a cohort of women presenting to a Ugandan regional referral hospital for delivery, comparing those who attended four or more antenatal care visits to those attending three or fewer visits

| Characteristic | ≤ 3 ANC[a] Visits (n = 510) | ≥ 4 ANC visits (n = 1236) | *P*-value* |
|---|---|---|---|
| Demographics | | | |
| Age category | | | 0.6 |
| ≤ 19 | 69 (14) | 167 (14) | |
| 20–34 | 395 (77) | 974 (89) | |
| > 34 | 46 (9) | 95 (79) | |
| Married | 462 (90) | 1179 (94) | < 0.001 |
| Monthly income[b] (median USD[c], IQR[d]) | $35 (17, 104) | $54 (28, 104) | 0.008 |
| Employment outside the home | 164 (32) | 520 (42) | < 0.001 |
| Obstetric | | | |
| Singleton pregnancy | 499 (97%) | 1199 (96%) | 0.2 |
| Gestational age | | | < 0.001 |
| Non-viable: < 28 weeks | 3 (0.6) | 1 (0.08) | |
| Preterm: ≥ 28 to < 37 weeks | 80 (17) | 104 (9) | |
| Term: ≥ 37 to 42 weeks | 337 (72) | 960 (81) | |
| Postdates: > 42 weeks | 51 (11) | 114 (10) | |
| Parity prior to delivery | | | 0.001 |
| 0 (primiparous) | 199 (39) | 584 (47) | |
| 1–3 (multiparous) | 257 (50) | 573 (46) | |
| ≥ 4 (grand multiparous) | 59 (11) | 92 (7) | |
| Antenatal diagnoses and treatments | | | |
| HIV-infected | 59 (12) | 154 (12) | 0.6 |
| Participant-reported diagnoses during this pregnancy | | | |
| Sexually transmitted infection | 10 (2) | 47 (4) | 0.05 |
| Syphilis | 7 (1) | 30 (2) | 0.2 |
| Urinary tract infection | 10 (4) | 30 (2) | 0.6 |
| Malaria | 46 (9) | 129 (10) | 0.4 |
| Hypertension | 3 (0.3) | 6 (0.5) | 0.6 |
| Vaginal bleeding | 1 (0.2) | 6 (0.5) | 0.3 |
| Participant-reported treatments during this pregnancy | | | |
| Folic acid supplementation | 463 (90) | 1142 (91) | 0.2 |
| Iron supplementation | 454 (88) | 1165 (93) | < 0.001 |
| Malaria prophylaxis with IPTp[e] or TMP/SMX[f] | 453 (88) | 1168 (94) | < 0.001 |
| Deworming medications | 453 (88) | 1157 (93) | 0.002 |
| Intrapartum factors and outcomes | | | |
| Hours in labor (median hours, IQR) | 12 (8, 20) | 12 (8, 19) | 0.6 |
| Cesarean delivery | 238 (48) | 627 (51) | 0.2 |
| Referred to MRRH[g] for care | 72 (14) | 154 (12) | 0.3 |
| Distance from MRRH (median km[h], IQR) | 12 (4, 35) | 17 (4, 37) | 0.4 |
| Diagnoses during labor | | | |
| Fetal distress | 29 (6) | 70 (6) | 1.0 |
| Cord prolapse | 3 (0.6) | 4 (0.3) | 0.3 |
| Chorioamnionitis | 3 (0.6) | 0 (0) | 0.03 |
| Pre-eclampsia | 7 (1) | 17 (1) | 1.0 |
| Stillbirth | 27 (5) | 31 (3) | 0.003 |
| Poor birth outcome | 78 (16) | 118 (10) | < 0.001 |

[a]ANC: antenatal care; [b]reported by participant in Ugandan Shillings, converted to [c]USD (United States Dollar) using exchange rate for study start date (March 1, 2015: 1 USD = 2890 Ugandan Shillings); [d]IQR: interquartile range; malaria prophylaxis by [e]IPTp (intermittent preventative treatment in pregnancy) with either sulfadoxine-pyrimethamine or dihydroartemisinin-piperaquine, or by routine prophylactic trimethoprim/sulfamethoxazole in participants living with HIV; [f]TMP/SMX: trimethoprim/sulfamethoxazole; [g]MRRH: Mbarara Regional Referral Hospital; [h]km: kilometers. Results listed as "n (%)" unless otherwise noted. Tests of association between cohort characteristics and the presence or absence of stillbirth were performed using chi-squared, Wilcoxon rank sum, and t tests

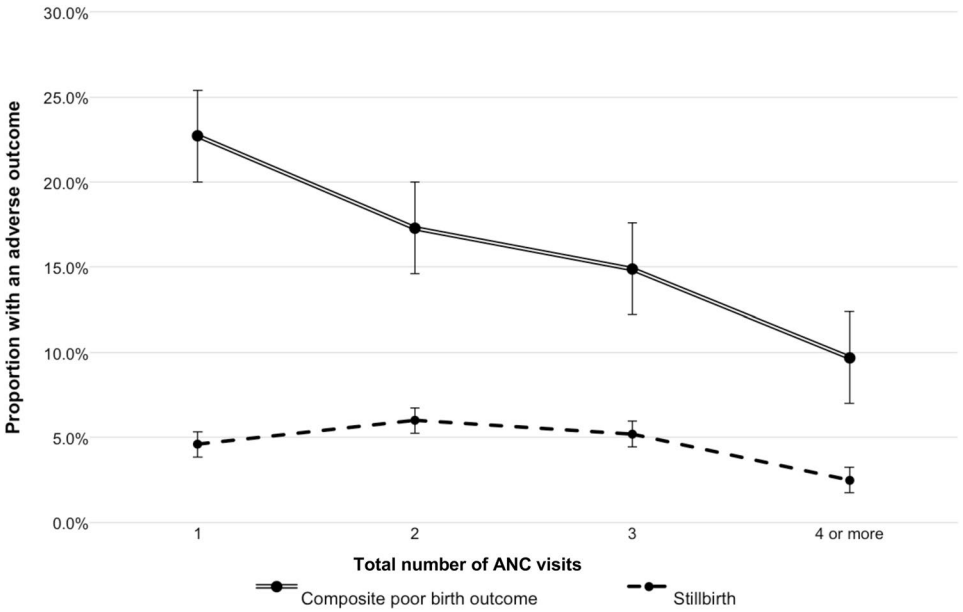


**Fig. 1** Relationship between total number of antenatal care (ANC) visits and adverse birth outcomes. Error bars represent standard error. Participants with zero ANC visits were excluded from this graph due to small sample size, with only 7 in the composite poor birth outcome group and 0 in the stillbirth group

be primiparous (36% vs. 44%, $P=0.04$) and more likely to be grand multiparous (19% vs. 9%, $P=0.04$, Table 2) than women without stillbirth. Monthly income and employment outside the home were similar in both groups (Table 1). Hypertension was more common in women who had stillbirths (4% vs. 0.4%, $P=0.03$, Table 2), but there were no other significant differences in past medical or obstetric history between women who had a stillbirth and women who did not, including HIV prevalence (11% vs. 12%, $P=0.68$, Table 2).

All women reported receiving similar levels of recommended medical prophylaxis and treatment given at ANC visits, including folic acid and iron supplementation, and deworming medications (Fig. 2), though women who had a stillbirth were more likely to report not receiving malaria prophylaxis (83% vs. 91%, $P=0.03$, Table 2, Fig. 2). Women with stillbirths self-reported lower rates of testing for HIV (93% vs. 98%, $P=0.03$), and malaria (45% vs. 58%, $P=0.049$) during pregnancy. Labor duration (median: 12 h in both groups, $P=0.21$) and Cesarean delivery rates (61% vs. 50%, $P=0.12$, Table 1) did not differ significantly between groups. However, women who had a stillbirth were more likely to have been referred to MRRH from another facility for care (30% vs. 13%, $P<0.0001$), live further from MRRH (median 28 km vs. 12 km, $P=0.008$), and have a chart diagnosis of fetal distress (16% vs. 5%, $P=0.001$, Table 2).

In multivariable logistic regression analysis, attending four or more ANC visits was associated with significantly reduced odds of stillbirth (adjusted odds ratio [aOR] 0.5, 95% CI 0.3–0.9, $P=0.02$), as was receipt of malaria prophylaxis during pregnancy (aOR 0.5, 95% CI 0.2–1.0, $P=0.04$, Table 3). Referral to MRRH was associated with increased odds of stillbirth (aOR = 2.3, 95% CI 1.2–4.4, $P=0.01$), but report of syphilis infection was not. The association between ANC attendance and stillbirth was unchanged in a sensitivity analysis restricted to 1350 women who delivered at ≥ 39 weeks' gestation (aOR = 0.45, 95% CI 0.20–0.97, $P=0.04$), and odds ratios were similar for all other variables.

Attending four or more ANC visits was also significantly associated with reduced odds of the composite poor birth outcome (aOR 0.66, 95% CI 0.5–0.9, $P=0.02$), and referral to MRRH from another facility for care was associated with increased odds of poor birth outcome (aOR = 1.7, 95% CI 1.0–2.8, $P=0.046$, Table 3). The association between ANC attendance and poor birth outcome was similar in a sensitivity analysis restricted to women delivering at ≥ 39 weeks' gestation, though the association between ANC attendance and poor birth outcome was no longer statistically significant (aOR = 0.7, 95% CI 0.4–1.1, $P=0.09$).

## Discussion

### Main Findings

In this cohort of pregnant women living in rural Uganda and presenting to a tertiary care hospital for delivery, attending at least four ANC visits was associated with significantly reduced odds of stillbirth. This association remained significant both when controlling for measured potential confounders, and restricting the analysis to women delivering ≥ 39 weeks' gestation, and is consistent with findings from other resource-poor settings that number of ANC visits is an important stillbirth predictor (Anu et al. 2019; Obadi et al. 2018; Rosario et al. 2019). Additionally, attending at

**Table 2** Demographic, antenatal and intrapartum characteristics of a cohort of women presenting to a Ugandan regional referral hospital for delivery, comparing those who had a stillbirth to those who delivered one or more live neonates

| Characteristic | Stillbirth n = 58 | No stillbirth n = 1727 | *P*-value* |
|---|---|---|---|
| Demographic and obstetric | | | |
| Age category | | | 0.4 |
| ≤ 19 | 9 (16) | 227 (13) | |
| 20–34 | 41 (72) | 1329 (79) | |
| > 34 | 7 (12) | 134 (8) | |
| Married | 50 (86) | 1592 (93) | 0.04 |
| Singleton pregnancy | 54 (93) | 1652 (97) | 0.2 |
| Parity prior to delivery | | | 0.04 |
| 0 (primiparous) | 21 (36) | 763 (44) | |
| 1–3 (multiparous) | 26 (45) | 805 (47) | |
| ≥ 4 (grand multiparous) | 11 (19) | 159 (9) | |
| Prior cesarean delivery | 4 (7) | 352 (23) | 0.002 |
| Antenatal care, diagnoses and treatments | | | |
| Attended ≥ 4 ANC[d] visits during this pregnancy | 31 (53) | 1218 (71) | 0.003 |
| HIV-infected | 6 (11) | 212 (12) | 0.7 |
| Participant-reported diagnoses during this pregnancy | | | |
| Sexually transmitted infection | 2 (3) | 55 (3) | 0.7 |
| Syphilis | 2 (3) | 35 (2) | 0.4 |
| Urinary tract infection | 1 (2) | 49 (3) | 1.0 |
| Malaria | 7 (12) | 168 (10) | 0.6 |
| Hypertension | 2 (4) | 6 (0.4) | 0.03 |
| Vaginal bleeding | 0 (0) | 7 (0.4) | 1.0 |
| Participant-reported treatments during this pregnancy | | | |
| Folic acid supplementation | 53 (91) | 1553 (91) | 1.0 |
| Iron supplementation | 51 (88) | 1569 (92) | 0.3 |
| Malaria prophylaxis with IPTp[e] or TMP/SMX[f] | 48 (83) | 1575 (91) | 0.03 |
| Deworming medications | 51 (88) | 1559 (91) | 0.4 |
| Intrapartum factors and outcomes | | | |
| Hours in labor (median hours, IQR) | 12 (10, 24) | 12 (8,19) | 0.2 |
| Cesarean delivery | 34 (61) | 841 (50) | 0.1 |
| Referred to MRRH[g] for care | 17 (30) | 214 (13) | < 0.001 |
| Distance from MRRH (median km[h], IQR) | 28 (5, 57) | 12 (4, 34) | 0.008 |
| Diagnoses during labor | | | |
| Fetal distress | 9 (16) | 91 (5) | 0.001 |
| Cord prolapse | 1 (2) | 6 (0.4) | 0.2 |
| Chorioamnionitis | 0 (0) | 3 (0.2) | 0.9 |
| Pre-eclampsia | 3 (5) | 23 (1) | 0.05 |

[a]Reported by participant in Ugandan Shillings, converted to [b]USD (United States Dollar) using exchange rate for study start date (March 1, 2015: 1 USD = 2890 Ugandan Shillings); [c]IQR: interquartile range. [d]ANC: antenatal care; malaria prophylaxis by [e]IPTp (intermittent preventative treatment in pregnancy) with either sulfadoxine-pyrimethamine or dihydroartemisinin-piperaquine, or by routine prophylactic trimethoprim/sulfamethoxazole in participants living with HIV; [f]TMP/SMX: trimethoprim/sulfamethoxazole; [g]MRRH: Mbarara Regional Referral Hospital; [h]km: kilometers. Results listed as "n (%)" unless otherwise noted. Tests of association between cohort characteristics and the presence or absence of stillbirth were performed using chi-squared, Wilcoxon rank sum, and t tests

least four ANC visits was associated with reduced odds of a composite poor birth outcome, including early neonatal death, low birth weight (< 2500 g), 5-min APGAR score < 7, and stillbirth. To our knowledge, this is one of the first studies documenting an association between ANC attendance and stillbirth risk in a resource-limited setting.

Antenatal risk factors associated with stillbirth included maternal report of hypertension and not receiving malaria prophylaxis during pregnancy. These findings support data from developed countries that maternal hypertension is associated with stillbirth (Causes of Death Among Stillbirths 2011). A Zambian study reported that receiving two

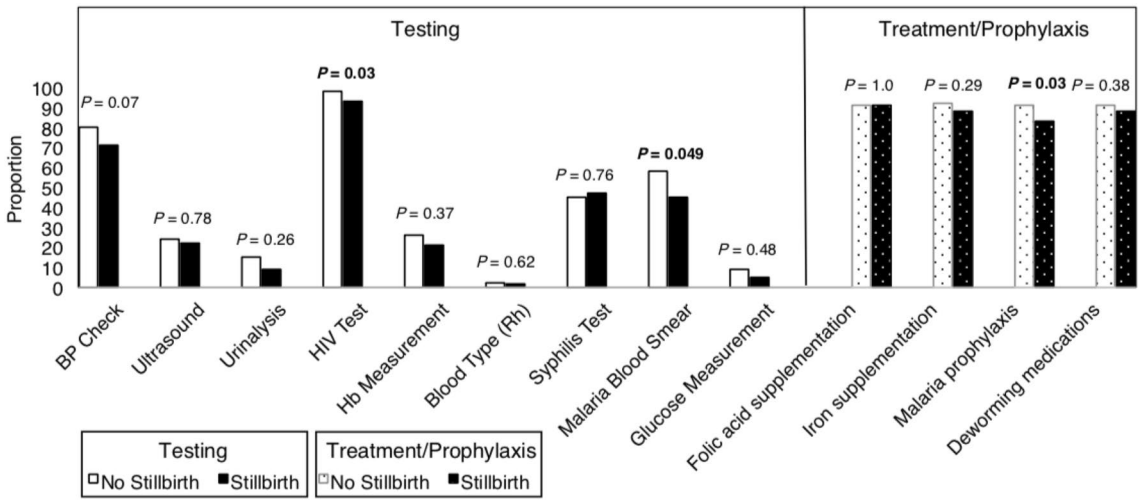


**Fig. 2** Antenatal care components received according to patient report, comparing stillbirth to no stillbirth. *Ultrasound* Fetal ultrasound, *BP* blood pressure, *HIV* human immunodeficiency virus, *Hb* hemoglobin

**Table 3** Univariable and multivariable logistic regression models of factors associated with stillbirth and poor birth outcomes, including early neonatal death within 2 weeks of hospital discharge, low birth weight (< 2500 g), 5-min APGAR score < 7, and stillbirth

| Characteristic | Unadjusted | | Adjusted | |
|---|---|---|---|---|
| | OR[a] (95% CI[c]) | *P*-value* | aOR[b] (95% CI) | *P*-value* |
| Stillbirth | | | | |
| Attended antenatal clinic ≥ 4 times | 0.5 (0.3–0.8) | 0.004 | 0.5 (0.3–0.9) | 0.02 |
| Malaria prophylaxis during pregnancy | 0.5 (0.2–0.9) | 0.03 | 0.5 (0.2–1.0) | 0.04 |
| Referred to MRRH[e] for care | 3.0 (1.6–5.3) | < 0.001 | 2.3 (1.2–4.4) | 0.01 |
| Distance from domicile to MRRH[e] (in km[f]) | 1.0 (1.0–1.0) | 0.02 | 1.0 (1.0–1.0) | 0.08 |
| Parity | 1.2 (1.1–1.4) | 0.005 | 1.2 (1.0–1.5) | 0.09 |
| Age | 1.0 (0.99–1.1) | 0.17 | 0.99 (0.9–1.1) | 0.72 |
| Reported syphilis during pregnancy | 1.7 (0.4–7.3) | 0.47 | 0.9 (0.1–6.8) | 0.92 |
| Poor birth outcome | | | | |
| Attended antenatal clinic ≥ 4 times | 0.6 (0.4–0.8) | < 0.001 | 0.6 (0.5–0.9) | 0.02 |
| Referred to MRRH[e] for care | 2.1 (1.4–3.0) | < 0.001 | 1.7 (1.0–2.8) | 0.046 |
| Age | 0.99 (0.96–1.0) | 0.3 | 0.96 (0.9–1.0) | 0.07 |
| Parity | 1.1 (0.98–1.2) | 0.1 | 1.1 (0.96–1.3) | 0.2 |
| Distance from domicile to MRRH[e] (in km[f]) | 1.0 (0.99–1.0) | 0.1 | 1.0 (0.99–1.0) | 0.5 |
| Syphilis during pregnancy | 1.9 (0.8–4.4) | 0.1 | 2.3 (0.8–6.2) | 0.1 |
| Pre-eclampsia | 4.5 (2.0–10.4) | < 0.001 | 2.2 (0.6–8.4) | 0.2 |
| Hours in labor | 0.99 (0.99–1.0) | 0.8 | 0.99 (0.98–1.0) | 0.4 |
| Cesarean delivery | 1.1 (0.9–1.5) | 0.4 | 1.0 (0.7–1.5) | 0.9 |
| HIV-infected | 0.8 (0.5–1.4) | 0.5 | 1.0 (0.6–1.8) | 0.9 |

[a]OR: odds ratio; [b]aOR: adjusted odds ratio; [c]CI: confidence interval; [d]ANC: antenatal care; [e]MRRH: Mbarara Regional Referral Hospital; [f]km: kilometers. Tests of association between cohort characteristics and the presence or absence of stillbirth were performed using univariable and multivariable logistic regression analysis

or more doses of malaria prophylaxis during pregnancy was associated with a 45% reduction in adverse birth outcomes (Chico et al. 2017). Furthermore, only 83% of women with stillbirths received malaria prophylaxis, compared to 91% of those who did not have a stillbirth ($P = 0.03$), supporting WHO malaria prophylaxis guidelines and suggesting that malaria prophylaxis may specifically protect against stillbirth by decreasing malaria incidence, severity, and low birth weight (WHO 2014).

Intrapartum risk factors associated with stillbirth included fetal distress and referral to MRRH from another facility for care, similar to findings reported in a Mozambican stillbirth study (Geelhoed et al. 2015). Women with stillbirth also lived further from MRRH. Though women with high-risk pregnancies traveling far from home to reach a referral hospital could be expected to have high morbidity, there are additional implications for clinical practice. Based on the association we report between referral to MRRH and poor birth outcomes, we advocate for additional training for community health care providers in rapid patient triage and referral to minimize further delays in care that could lead to poor outcomes. Such training could equip community providers with tools to identify women at high risk for stillbirth and refer them to advanced care centers for care before stillbirth is imminent. Our findings also suggest that pregnant women referred to a regional referral hospital for delivery should be considered high-risk for adverse outcomes and monitored closely. As resources allow, monitoring women *en route* to MRRH and immediately upon arrival should be prioritized. Additionally, though ambulances would be the ideal transport modality for women with obstetric emergencies, they are often difficult to access in Uganda, and most women are transported by private vehicles or motorcycles. Improved availability of ambulance services would also likely improve birth outcomes of those needing referral to MRRH.

We note the high cesarean delivery rate in this cohort (51%), both for participants with (61%) and without (50%) stillbirth ($P = 0.1$). It is possible that referrals from facilities without access to cesarean delivery contribute to these high rates. However, these rates call for further investigation, particularly as they may point to important and addressable gaps in the quality of care received by women either at this institution or in referring institutions. For example, at least 30% of cesareans performed in women delivering stillbirths had a fetal indication for the procedure (e.g. cord presentation or fetal distress), indicating either a failure to adequately diagnose fetal demise prior to delivery, or delays in achieving a cesarean birth in a timely fashion to prevent demise.

## Strengths and Limitations

Strengths of our study are the large cohort size with 99% of all eligible women presenting to MRRH during the study period enrolled, the prospective assessment of birth outcomes, and < 10% missing data for key variables. Stillbirth report was cross-referenced with APGAR scores of zero at one and five minutes to separate stillbirths from early neonatal deaths. However, it is possible that despite this cross-validation, some early neonatal deaths may have been misdiagnosed as stillbirths. The generalizability of our results is limited by the secondary nature of this analysis, regional referral hospital setting, a population enriched with fever or hypothermia, and incomplete measurement of social determinants of health. Another limitation is that prior delivery mode and ANC risk factor data was collected by retrospective self-report, which may have resulted in inaccurate reporting or recall bias, especially among women with adverse pregnancy outcomes. Lastly, chart documentation of participants' diagnoses and treatment was often incomplete or uncharted, limiting our ability to draw inferences about hospital diagnoses or treatments.

## Interpretation

These results address gaps in knowledge about stillbirth risk factors both in Uganda, and in RLS in general; and support previous recommendations that women should attend at least four ANC visits. It is important to acknowledge that social determinants of health likely impact both ANC attendance and stillbirth. Important social determinants measured in this study including marital status, income, and employment were significant predictors of ANC attendance. A woman's ANC attendance may be a proxy for equally important social factors. Further research on social determinants of ANC attendance and stillbirth risk is warranted in resource-limited settings. New WHO recommendations released in 2016 recommend eight ANC visits during pregnancy, which may be challenging for many RLS to implement due to limitations in human resources, space, and supplies. The effect of attending more than four ANC visits should be studied in RLS to determine the optimal number of contact points during pregnancy, and how to capture and retain women in ANC during pregnancy. Though our study did not find differences in receipt of ANC-recommended prophylactic medications and supplements between women with and without stillbirths, these treatments have been individually established to be effective at reducing pregnancy-related morbidity and improving outcomes in other studies (WHO 2016). Additional studies would be helpful to determine the specific elements of ANC leading to decreased risk of stillbirth and poor birth outcome. In our study, women who had a stillbirth self-reported higher rates of malaria and HIV testing during pregnancy. However, these findings, and other self-reported data may be influenced by recall bias, particularly after a devastating event such as stillbirth.

Among women living in Uganda and presenting for delivery at a referral hospital, attending four or more ANC visits appears to protect against stillbirth and poor birth outcomes. Future research studies should address which ANC components are most protective, and the optimal number of ANC visits in RLS. Studies should also aim to determine the overall rates of stillbirth in Uganda, and prevalence of risk factors associated with stillbirth, including hypertension, referral and access to tertiary care hospitals, and malaria prophylaxis receipt. In the absence of further

studies, pregnant women should be encouraged to attend at least four antenatal care visits, to improve birth outcomes.

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## Compliance with Ethical Standards

**Conflict of interest** The authors declare that they have no conflict interests.

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