HHS Public Access

Author manuscript

Int J Gynaecol Obstet. Author manuscript; available in PMC 2018 June 01.

Published in final edited form as:

Int J Gynaecol Obstet. 2017 June ; 137(3): 282–289. doi:10.1002/ijgo.12136.

Maternal and neonatal outcomes among women with HIV infection and their infants in Malawi

Michelle S. Chevalier[1,*], **Caroline C. King**[2], **Sascha Ellington**[2], **Jeffrey Wiener**[2], **Dumbani Kayira**[3], **Charles S. Chasela**[4], **Denise J. Jamieson**[2], and **Athena P. Kourtis**[2]

[1]Division of Global HIV and Tuberculosis, Center for Global Health, Centers for Disease Control and Prevention, Atlanta, GA, USA

[2]Division of Reproductive Health, National Center for Chronic Disease Prevention and Health Promotion, Centers for Disease Control and Prevention, Atlanta, GA, USA

[3]University of North Carolina Project Malawi, Lilongwe, Malawi

[4]Epidemiology and Strategic Information, Human Sciences Research Council, Pretoria, South Africa

Abstract

Objective—To describe maternal and neonatal morbidity and mortality among women with HIV infection and their infants.

Methods—A secondary analysis was undertaken of data obtained in the BAN Study, a trial of postnatal antiretrovirals among pregnant women with HIV infection enrolled in 2004–2010. Mothers and infants had 13 scheduled visits through 48 weeks of follow-up. Serious maternal morbidity and mortality were examined at delivery (n=2791), from delivery to 6 weeks later (n=2369) and from 7 to 48 weeks (n=1980). Neonatal morbidity and mortality were examined (n=2685).

Results—Of 2791 deliveries, 169 (6.1%) were by cesarean (153 emergency). Compared with women with vaginal delivery, those with cesarean delivery had lower prenatal HIV viral loads (*P*=0.016) and increased odds of pre-eclampsia/eclampsia (odds ratio [OR] 10.8, 95% CI 4.4–26.8). Women with cesarean delivery also had increased odds of serious infection with 14 days of delivery (OR 3.0, 95% CI 1.3–7.4) and severe anemia (grade 3 or 4) by 6 weeks (OR 6.7, 95% CI 2.3–19.1). Infants born by cesarean had increased odds of a low 5-minute Apgar score (OR 8.1, 95% CI 3.5–18.6) and admission to an intensive care unit (OR 5.4, 95% CI 3.7–7.8).

Conclusion—Odds of serious maternal and neonatal morbidity were higher after cesarean than vaginal delivery, despite lower maternal viral loads.

[*]Correspondence: Michelle S. Chevalier, 1600 Clifton Rd NE, MS E04, Atlanta, GA 30333, USA. mchevalier@cdc.gov.

Author contributions

All authors contributed significantly to the study design. DK and CSC collected data. MSC and CCK analyzed data. MSC, CCK, and APL drafted the manuscript. All authors were involved in interpretation of the data, revised the manuscript critically for important intellectual content, and provided final approval for the manuscript.

Conflict of interest

The authors have no conflicts of interest.

Keywords

Cesarean delivery; HIV; Malawi; Maternal morbidity; Mortality; Neonatal morbidity

1 INTRODUCTION

Approximately 18 million women are living with HIV type 1 infection worldwide.[1] Globally, HIV infection and maternal mortality remain the two leading causes of death for women aged 15–49 years.[2] Pregnant women with HIV infection have an estimated maternal mortality almost eight times higher than that of uninfected women,[3] and in areas with high prevalence, HIV infection is estimated to account for 12%–50% of maternal deaths.[4]

Pregnancy-related morbidity is also increased in women with HIV infection: their risk of major puerperal sepsis is two times higher than that of uninfected women, and their risk of preterm labor and delivery is increased by 30%, even after adjusting for comorbidities, socioeconomic factors, and treatment with antiretroviral (ARV) therapy.[5] Increased risks of postpartum and neonatal morbidity have also been suggested with both elective and emergency cesarean delivery compared with vaginal delivery.[6,7] Most of this evidence derives from resource-rich settings, and maternal morbidity and mortality among women with HIV infection in resource-limited settings was recently identified as a priority for researchers and stakeholders to assess and develop appropriate public health interventions.[8]

To better describe maternal and neonatal outcomes among women with HIV infection and their infants in a resource-limited setting, a secondary analysis was undertaken of the Breastfeeding, Antiretrovirals, and Nutrition (BAN) Study, a clinical trial among 2369 mother–infant pairs.[9] The aims of the present secondary analysis were to describe serious maternal and neonatal morbidity and mortality among women with HIV infection and their infants, overall and by delivery type, and to determine risk factors for postpartum maternal complications or mortality.

2 MATERIALS AND METHODS

Full details of the BAN Study—a randomized clinical trial of postnatal ARVs for prevention of HIV transmission during breastfeeding—have been reported previously.[9] Briefly, between April 2004 and January 2010, 3572 pregnant women with HIV infection referred to the BAN study clinic at Bwaila Hospital in Lilongwe, Malawi, were screened for enrollment in the BAN Study (Figure 1). Overall, 3109 met the prenatal eligibility criteria: aged 14 years or older, pregnancy of 30 weeks or less, CD4+ T-cell count of at least 250 cells per μL (≥200 cells per μL before July 24, 2006; change in accordance with Malawi Ministry of Health guidelines for HIV treatment), hemoglobin of 70 g/L or higher, an alanine aminotransferase concentration of no more than 2.5 times the upper limit of the normal range, no presence of other active serious infection, and no previous use of any ARV agents. Women who met these criteria were enrolled and followed up prospectively for up to four prenatal study visits, at which they received iron and folate supplements, screening for anemia and syphilis, malaria prophylaxis, mosquito nets, and tetanus toxoid vaccination. Co-trimoxazole

prophylaxis was initiated for eligible women (CD4+ <500 cells per μL) and all infants in June 2006, in accordance with WHO guidelines.[10]

The women were asked to deliver at Bwaila Hospital. However, women who delivered elsewhere (21.7%) were eligible for randomization to the BAN interventions if the mother and neonate arrived at the hospital within 36 hours of delivery. The BAN Study captured 2791 (89.8%) of the 3109 women's deliveries, and the current secondary analysis presents the labor and delivery characteristics of these women and their neonates. On delivery, 2382 women met the postnatal eligibility criteria for randomization to the BAN Study interventions. These criteria included neonatal birth weight of 2000 g or more, the mother's acceptance of a 7-day maternal and neonatal perinatal ARV regimen, enrollment within 36 hours of delivery, and the exclusion of any serious maternal or infant medical conditions that would preclude participation in the study. Postpartum complications beyond the delivery visit are presented among this group of mothers and their infants.

At delivery, all 2791 mothers and neonates received single-dose nevirapine (Viramune, Boehringer Ingelheim Pharmaceuticals, Ridgefield, CT, USA), followed by 1 week of twice daily zidovudine and lamivudine (Combivir [GlaxoSmithKline and Shire Pharmaceuticals Group, Basingstoke, UK] for mothers, and Retrovir [GlaxoSmithKline, Zebulon, NC, USA] and Epivir (GlaxoSmithKline and Shire Pharmaceuticals Group, Basingstoke, UK) for infants). Within a week of delivery, 2369 mother–infant pairs underwent randomization using a factorial design to a two-group maternal nutritional intervention and a three-group ARV intervention consisting of a maternal triple-drug ARV regimen (n=879), infant nevirapine (n=852), or neither (n=668) during breastfeeding. Mothers were counseled to exclusively breastfeed for 24 weeks, then wean over 4 weeks to complete breastfeeding by 28 weeks after delivery.

The 2369 mother–infant pairs were followed up at 1, 2, 4, 6, 8, 12, 18, 21, 24, 32, 36, 42, and 48 weeks after delivery. At each visit, anthropometrics, vital signs, and medical history were collected and a complete physical examination was performed on the mother and infant. All infants received routine vaccinations which included Bacillus Calmette–Guérin, polio, diphtheria, pertussis, tetanus, *Haemophilus influenza*, hepatitis B, and measles. Infants who tested positive for HIV infection were referred to care, and these mother–infant pairs were no longer followed up. Participants were counseled to return to the study site for care between visits if either the mother or child became ill. If a condition identified at a follow-up or interim visit met the criteria for an adverse event or a serious adverse event, it was documented on the appropriate study form.

The BAN Study protocol was approved by the Malawi National Health Science Research Committee and institutional review boards at the University of North Carolina at Chapel Hill and the US Centers for Disease Control and Prevention. All women provided written informed consent.

For the present analysis, serious maternal morbidity and mortality were examined at delivery (n=2791), from delivery to 6 weeks later (n=2369), and from 7 to 48 weeks (n=1980). Neonatal morbidity was examined for all singletons and first-born infants in multiple

deliveries who had an initial infant evaluation form completed (n=2685). In addition to that infant form, maternal and neonatal morbidity outcomes were derived from delivery history questionnaires and records of laboratory adverse events and serious adverse events. Adverse events were graded using normative value cutoffs from toxicity tables for adults or infants from the National Institute of Health, Division of AIDS.[11] Serious adverse events were defined as any fatal or life-threatening event requiring hospitalization or prolongation of hospital stay, or which resulted in persistent or significant disability. Maternal mortality was defined as any death that occurred from delivery to 48 weeks. Neonatal death was defined as death by 28 days of life, and was assessed among singletons and first-born infants.

Maternal morbidity is defined as any health condition attributed to and/or aggravated by pregnancy and childbirth that has a negative impact on the woman's well-being.[12] For the present analysis, maternal morbidities were presented separately for delivery (pre-eclampsia/eclampsia, hemorrhage, blood transfusion, intrapartum fever, puerperal sepsis/endometritis, stillbirth, and prolonged hospital stay) and postpartum (infection, grade 1–4 anemia) complications. Delivery complications were analyzed for all mothers who delivered during the study (n=2791). A "prolonged hospital stay" was defined as admission to the postpartum ward for more than 48 hours after vaginal delivery and more than 7 days after cesarean delivery. Stillbirth was defined as fetal loss at 20 weeks' gestation or more. The category "obstetric complications" included pre-eclampsia/eclampsia documented at delivery, maternal hemorrhage, blood transfusion, stillbirth, prolonged hospitalization stay, and infection up to 14 days after delivery. Postpartum complications were only assessed for women who underwent randomization (n=2369). "Infection" includes all instances of puerperal sepsis/endometritis, serious febrile illness/sepsis, malaria, intrapartum fever, pneumonia, meningitis, tuberculosis, pelvic inflammatory disease, and syphilis at delivery or from delivery to 2 weeks if a serious adverse event. Neonatal morbidity was defined as a low Apgar score, admission to the intensive care unit, low birth weight, macrosomia, or neonatal sepsis.

The data were stratified by mode of delivery: vaginal delivery, which includes natural spontaneous vaginal deliveries and vacuum deliveries; and cesarean delivery, which includes elective and emergency cesareans. Maternal and infant baseline characteristics were compared by mode of delivery using the Wilcoxon rank-sum test for continuous variables and X^2 test for categorical variables. Potential predictors for maternal outcomes were evaluated with a manual backwards logistic regression ($P<0.1$ to stay); associations with neonatal outcomes have been reported previously.[13] The outcomes assessed were prolonged hospital stay, infection up to 14 days after delivery, anemia up to 6 weeks after delivery, and mortality up to 48 weeks after delivery. Potential predictors included mode of delivery, maternal age (>29 years), body mass index (<20, calculated as weight in kilograms divided by the square of height in meters), CD4+ T-cell count (<500 cells per μL), log HIV viral load, prenatal anemia (hemoglobin <110 g/L), and hemorrhage. All analyses were adjusted for the maternal ARV and nutritional study group. Data were analyzed using SAS 9.3 (SAS Institute, Cary, NC, USA). $P<0.05$ was considered significant.

3 RESULTS

Of the 2791 deliveries, 2622 (93.9%) were vaginal (2582 natural spontaneous, 40 vacuum) and 169 (6.1%) by cesarean (16 elective, 153 emergency). The location of delivery was a health facility for 2387 (85.5%) women, home for 237 (8.5%), and “other” for 159 (5.7%). Table 1 shows maternal characteristics. The median age at delivery was 25 years; 1841 (66.0%) had only primary education, and 2426 (86.9%) had one or more previous pregnancies. Women who delivered by cesarean had a significantly lower median prenatal HIV viral load than did women who delivered vaginally (P=0.016). Women who delivered by cesarean were also more likely to have higher than primary education and be primigravidas compared with those who delivered vaginally (Table 1).

Obstetric complications within 2 weeks of delivery were reported for 243 (8.7%) mothers. A prolonged hospital stay and infection were the most frequent within the first 2 weeks (Table 2). Compared with vaginal delivery, cesarean delivery was associated with 8-times higher overall odds of complications; odds of individual complications such as pre-eclampsia/eclampsia at delivery, stillbirth, prolonged hospitalization, and infection by 2 weeks were also increased with cesarean (Table 2).

Within 6 weeks of delivery, 834 (35.3%) of 2365 mothers had documented anemia of grade 1–2 and 18 (0.8%) had anemia of grade 3–4. Women with cesarean delivery had significantly higher odds of anemia of both grade 1–2 and grade 3–4 than did women who had a vaginal delivery (Table 2).

After adjustment for the maternal ARV and nutritional intervention group and other factors, cesarean delivery remained significantly associated with prolonged hospital stay (adjusted odds ratio [aOR] 16.2, 95% confidence interval [CI] 10.0–26.5), infection within 2 weeks of delivery (aOR 3.3, 95% CI 1.4–8.1), and anemia within 6 weeks (aOR 5.6, 95% CI 3.8–8.5). In addition to cesarean delivery, other significant predictors of prolonged hospital stay in multivariable analysis were hemorrhage (aOR 57.1, 95% CI 23.7–137.9) and maternal age older than 29 years (aOR 1.7, 95% CI 1.1–2.7). Additional predictors of infection within 2 weeks of delivery included prenatal anemia (aOR 2.5, 95% CI 1.3–5.0) and postpartum hemorrhage (aOR 9.0, 95% CI 2.5–32.2). Predictors of anemia in addition to cesarean delivery were prenatal anemia (aOR 5.2, 95% CI 4.2–6.3) and hemorrhage (aOR 13.1, 95% CI 4.3–40.0).

There were no maternal deaths in the first 42 days after delivery, but 9 (0.5%) of the 1980 women followed up through 48 weeks died: three due to complications of tuberculosis, two due to renal failure, and one each due to hepatic necrosis, pneumonia, perforated viscus, and unknown cause. Cesarean delivery was not associated with maternal mortality (Table 2), but women with postpartum anemia (≤48 weeks; hemoglobin <110 g/L) had four-times higher odds of mortality than did mothers without anemia (aOR 4.8, 95% CI 1.2–19.4).

Stillbirth was recorded for 45 (1.7%) of 2649 infants. Low birth weight (>2000 g and ≤2500 g) was recorded for 283 (10.6%) of 2670 neonates, and 239 (8.9%) of 2679 were admitted to an intensive care unit. Cesarean delivery was associated with increased odds of low Apgar

scores at 5 minutes and admission to an intensive care unit compared with vaginal delivery (Table 3).

There were 12 (0.4%) neonatal deaths, which occurred in the first 22 days of life: six from neonatal sepsis, three from pneumonia, one from sudden infant death of unknown etiology, one from complications of diabetes insipidus, and one from an acute illness of unknown etiology. There was no significant association between mode of delivery and neonatal death (Table 3). The neonatal mortality rate was 4.5 neonatal deaths per 1000 live births. Including stillbirths with neonatal deaths, the combined mortality rate was 20.6 per 1000 births.

4 DISCUSSION

In the present study, 9% of mothers had one or more complication within 2 weeks of delivery, with the odds of any complication significantly increased with cesarean delivery. Cesarean delivery was also associated with blood loss and increased odds of pre-eclampsia/eclampsia at delivery, stillbirth, prolonged hospital stay, infection within the first 14 days, and anemia within 6 weeks of delivery. Neonates born by cesarean also had higher odds of complications than did those delivered vaginally, including a low 5-minute Apgar score and admission to an intensive care unit. These results highlight potential areas for improved outcomes and CD practices.

Cesareans have previously been associated with increased postpartum morbidity among women with and without HIV infection in resource-rich and resource-limited settings.[6,7,14] The risk of complications is highest for emergency cesarean delivery, and intermediate for elective cesarean.[6] In Malawi, cesarean delivery is rare (4.6%) and mostly performed as an emergency without preoperative preparation,[15] so it is not surprising that 91% of cesareans in the BAN Study were emergency procedures and had a higher complication rate than vaginal deliveries.

More than one-third of BAN mothers were anemic within 6 weeks of delivery, and the strongest predictors for postpartum anemia were prenatal anemia, cesarean delivery, and obstetric hemorrhage. Prenatal and postpartum anemia were associated with maternal infection within 2 weeks of delivery and maternal mortality by 48 weeks, respectively. In a matched-pairs analysis of Swiss women with and without HIV infection undergoing elective cesarean delivery,[16] postoperative anemia occurred in 49% of women with HIV infection and 9% of uninfected women. In the European Collaborative Study,[17] mild anemia was the most prevalent complication among women with and without HIV infection after cesarean delivery, but it was more frequent among women with HIV infection. In Malawi, the prevalences of anemia and severe anemia (grade 3–4) during pregnancy range from 39% to 72% and 3.6% to 4.0%, respectively.[18] The estimated relative risks of mortality associated with moderate and severe anemia for women in low-income countries have been reported as 1.35 and 3.51, respectively.[18] The women in the BAN Study received iron and folate supplements and underwent screening for anemia, which could explain the lower anemia prevalence in this HIV cohort compared with the other estimates from Malawi. These data suggest that prenatal surveillance and improved nutritional supplementation with iron-rich

foods and/or vitamin supplements might reduce anemia-related morbidity and mortality in resource-limited settings.

Low maternal CD4+ count and high HIV-1 viral load have been associated with maternal and infant mortality in previous studies.[19,20] However, we did not find such significant associations when evaluating severe (CD4 <200 cells per μL) or moderate (CD4+ 200–500 cells per μL) levels of immunosuppression. The women who enrolled in the BAN Study had CD4 counts of more than 200 cells per μL, and most had viral loads of less than 50 000 copies per mL; thus, analyses of the effect of advanced HIV disease were limited.

Maternal and neonatal deaths were rare. Worldwide, 75% of maternal deaths are due to hemorrhage, infection, severe pre-eclampsia/eclampsia, complications of delivery, and unsafe abortion; the remaining deaths are due to indirect causes such as malaria, HIV/AIDS, anemia, and tuberculosis.[21] In Malawi, hemorrhage, infection, and hypertensive disorders of pregnancy are the three leading causes of maternal death;[22] the maternal mortality ratio is estimated as 680 deaths per 100 000 live births.[23] In the present study, maternal mortality was zero during the immediate postpartum period (up to 6 weeks after delivery), and 0.5% by 48 weeks. All maternal deaths were due to indirect causes, mainly complications of HIV. The Malawi Demographic and Health Survey[24] reported a neonatal mortality rate of 27 deaths per 1000 live births; in the present study, the rate was estimated as 4.5 per 1000 live births. The reduced maternal and neonatal mortality in BAN—despite including a population of women with HIV infection and their infants—could be attributed to enhanced prenatal and postpartum medical monitoring and clinical care. The frequent medical follow-up and provision of vaccines, prophylactic drugs, and nutritional supplements for all participants exceeds the standard of care for Malawi, highlighting achievable goals for this resource-limited setting.

Strengths of the present secondary analysis are the large sample size and well-documented medical follow-up of BAN participants. Health facility deliveries were more frequent in the BAN Study (86%) compared with the country overall (73%),[25] which could affect comparisons.[14] Limitations include the rarity of elective cesarean delivery, which prohibited statistical comparisons by type of cesarean, and the lack of a comparison group of women without HIV infection. Other limitations were that only serious clinical events (those necessitating or prolonging hospitalization) were included. Additionally, as with all large, longitudinal studies, there were missing data. For four factors assessed (baseline viral load, body mass index, estimated blood loss, and Apgar score at 5 minutes), the proportion of missing data differed significantly between vaginal and cesarean deliveries; missing data could have affected the results.

The present study provides frequencies and predictors of maternal and neonatal morbidities by delivery type among women with HIV infection before the introduction of prenatal ARV therapy in Malawi. As option B+ rolls out in the country and women with HIV infection are given ARV therapy before delivery,[26] these data can provide a comparison for tracking the effectiveness of prenatal ARV therapy on maternal and neonatal outcomes among women with HIV infection in similar settings.

Acknowledgments

We are grateful to the BAN Study team at University of North Carolina at Chapel Hill (Chapel Hill, NC, USA), Centers for Disease Control and Prevention (Atlanta, GA, USA), and UNC Project (Lilongwe, Malawi), including Linda Adair, Yusuf Ahmed, Mounir Ait-Khaled, Sandra Albrecht, Shrikant Bangdiwala, Ronald Bayer, Margaret Bentley, Brian Bramson, Emily Bobrow, Nicola Boyle, Sal Butera, Charity Chavula, Joseph Chimerang'ambe, Maggie Chigwenembe, Maria Chikasema, Norah Chikhungu, David Chilongozi, Grace Chiudzu, Lenesi Chome, Anne Cole, Amanda Corbett, Amy Corneli, Anna Dow, Ann Duerr, Henry Eliya, Joseph Eron, Sherry Farr, Yvonne Owens Ferguson, Susan Fiscus, Valerie Flax, Ali Fokar, Shannon Galvin, Laura Guay, Chad Heilig, Irving Hoffman, Elizabeth Hooten, Mina Hosseinipour, Michael Hudgens, Stacy Hurst, Lisa Hyde, David Jones, Elizabeth Jordan-Bell, Zebrone Kacheche, Esmie Kamanga, Gift Kamanga, Coxcilly Kampani, Portia Kamthunzi, Deborah Kamwendo, Cecilia Kanyama, Angela Kashuba, Damson Kathyola, Peter Kazembe, Rodney Knight, Robert Krysiak, Jacob Kumwenda, Hana Lee, Edde Loeliger, Dustin Long, Misheck Luhanga, Victor Madhlopa, Maganizo Majawa, Alice Maida, Cheryl Marcus, Francis Martinson, Navdeep Thoofer, Chrissie Matiki (deceased), Douglas Mayers, Isabel Mayuni, Marita McDonough, Joyce Meme, Ceppie Merry, Khama Mita, Chimwemwe Mkomawanthu, Gertrude Mndala, Ibrahim Mndala, Agnes Moses, Albans Msika, Wezi Msungama, Beatrice Mtimuni, Jane Muita, Noel Mumba, Bonface Musis, Charles Mwansambo, Gerald Mwapasa, Jacqueline Nkhoma, Megan Parker, Richard Pendame, Ellen Piwoz, Byron Raines, Zane Ramdas, John Rublein, Mairin Ryan, Ian Sanne, Christopher Sellers, Diane Shugars, Dorothy Sichali, Wendy Snowden, Alice Soko, Allison Spensley, Jean-Marc Steens, Gerald Tegha, Martin Tembo, Roshan Thomas, Hsiao-Chuan Tien, Beth Tohill, Charles van der Horst, Esther Waalberg, Elizabeth Widen, Cathy Wilfert, Patricia Wiyo, Innocent Zgambo, and Chifundo Zimba. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention. The Breastfeeding, Antiretrovirals, and Nutrition Study was supported by grants from the Prevention Research Centers Special Interest Project of the Centers for Disease Control and Prevention (SIP 13-01 U48-CCU409660-09, SIP 26-04 U48-DP000059-01, and SIP 22-09 U48-DP001944-01), Bill & Melinda Gates Foundation (OPP53107), the National Institute of Allergy and Infectious Diseases, the University of North Carolina Center for AIDS Research (P30-AI50410), the Carolina Population Center (R24 HD050924), the National Institutes for Health Fogarty AIDS International Training and Research Program (DHHS/NIH/FIC 2-D43 TW001039), and Fogarty FICRS (R24TW007988; the American Recovery and Reinvestment Act). The ARVs used in the BAN Study were donated by Abbott Laboratories, GlaxoSmithKline, Boehringer Ingelheim, Roche Pharmaceuticals, and Bristol-Myers Squibb. The Call to Action PMTCT program, from which BAN mothers were recruited, was supported by the Elizabeth Glaser Pediatric AIDS Foundation, the United Nations Children's Fund, the World Food Program, the Malawi Ministry of Health and Population, Johnson and Johnson, and the US Agency for International Development.

References

1. The Joint United Nations Programme on HIV/AIDS (UNAIDS). Report on the Global HIV/AIDS Epidemic. 2013. Available from: http://www.unaids.org/sites/default/files/en/media/unaids/contentassets/documents/epidemiology/2013/gr2013/UNAIDS_Global_Report_2013_en.pdf. Accessed December 21, 2016
2. World Health Organization. Women's Health: Fact sheet N°334. Updated Sept. 2013. Available from: http://www.who.int/mediacentre/factsheets/fs334/en/. Accessed December 21, 2016
3. Calvert C, Ronsmans C. The contribution of HIV to pregnancy-related mortality: a systematic review and meta-analysis. AIDS. 2013; 27(10):1631–9. [PubMed: 23435296]
4. Zaba B, Calvert C, Marston M, Isingo R, Nakiyingi-Miiro J, Lutalo T, et al. Effect of HIV infection on pregnancy-related mortality in sub-Saharan Africa: secondary analyses of pooled community-based data from the network for Analysing Longitudinal Population-based HIV/AIDS data on Africa (ALPHA). Lancet. 2013; 381(9879):1763–71. [PubMed: 23683643]
5. Bansil P, Jamieson DJ, Posner SF, Kourtis AP. Hospitalizations of pregnant HIV-infected women in the United States in the era of highly active antiretroviral therapy (HAART). J Womens Health. 2007; 16(2):159–62.
6. Marcollet A, Goffinet F, Firtion G, Pannier E, Le Bret T, Brival ML, et al. Differences in postpartum morbidity in women who are infected with the human immunodeficiency virus after elective cesarean delivery, emergency cesarean delivery, or vaginal delivery. Am J Obstet Gynecol. 2002; 186(4):784–9. [PubMed: 11967508]
7. Read JS, Tuomala R, Kpamegan E, Zorrilla C, Landesman S, Brown G, et al. Mode of delivery and postpartum morbidity among HIV-infected women: the women and infants transmission study. J Acquir Immune Defic Syndr. 2001; 26(3):236–45. [PubMed: 11242196]

8. Kendall T, Danel I, Cooper D, Dilmitis S, Kaida A, Kourtis AP, et al. Eliminating preventable HIV-related maternal mortality in sub-Saharan Africa: what do we need to know? J Acquir Immune Defic Syndr. 2014; 67(Supp 4):S250–8. [PubMed: 25436825]

9. Chasela CS, Hudgens MG, Jamieson DJ, Kayira D, Hosseinipour MC, Kourtis AP, et al. Maternal or Infant Antiretroviral Drugs to Reduce HIV-1 Transmission. N Engl J Med. 2010; 362(24):2271–81. [PubMed: 20554982]

10. World Health Organization. Guidelines on co-trimoxazole prophylaxis for HIV-related infections among children, adolescents and adults in resource-limited settings. World Health Organization; Geneva, Switzerland: 2006.

11. Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events. 2004. Available from: http://www.niaid.nih.gov/LabsAndResources/resources/DAIDSClinRsrch/Documents/daidsaegradingtable.pdf. Accessed December 21, 2016

12. Firoz T, Chou C, von Dadelszen P, Agrawal P, Vanderkruik R, Tunçalp O, et al. Measuring maternal health: focus on maternal morbidity. Bulletin of the World Health Organization. 2013; 91:794–796. [PubMed: 24115804]

13. Kourtis AP, Wiener J, Kayira D, Chasela C, Ellington SR, Hyde L, et al. Health outcomes of HIV-exposed uninfected African infants. AIDS. 2013; 27(5):749–59. [PubMed: 23719347]

14. Duarte G, Read JS, Gonin R, Freimanis L, Ivalo S, Melo VH, et al. Mode of delivery and postpartum morbidity in Latin American and Caribbean countries among women who are infected with human immunodeficiency virus-1: the NICHD International Site Development Initiative (NISDI) Perinatal Study. Am J Obstet Gynecol. 2006; 195(1):215–29. [PubMed: 16677591]

15. World Health Organization. Country Profiles on Maternal and Perinatal Health. Malawi: 2015. Available from: http://www.who.int/maternal_child_adolescent/epidemiology/profiles/maternal/mwi.pdf. Accessed Dec 19, 2016

16. Lapaire O, Irion O, Koch-Holch A, Holzgreve W, Rudin C, Hoesli I. Increased peri- and post-elective cesarean section morbidity in women infected with human immunodeficiency virus-1: a case-controlled multicenter study. Arch Gynecol Obstet. 2006; 274(3):165–9. [PubMed: 16715290]

17. European Mode of Delivery Collaboration. Elective caesarean-section versus vaginal delivery in prevention of vertical HIV-1 transmission: a randomised clinical trial. Lancet. 1999; 353(9158): 1035–9. [PubMed: 10199349]

18. Munasinghe S, van den Broek N. Anemia in Pregnancy in Malawi-A Review. Malawi Med J. 2006; 18(4):160–74. [PubMed: 27529009]

19. Chilongozi D, Wang L, Brown L, Taha T, Valentine M, Emel L, et al. Morbidity and mortality among a cohort of human immunodeficiency virus type 1-infected and uninfected pregnant women and their infants from Malawi, Zambia, and Tanzania. Pediatr Infect Dis J. 2008; 27(9):808–14. [PubMed: 18679152]

20. Giuliano M, Andreotti M, Liotta G, Jere H, Sagno JB, Maulidi M, et al. Maternal antiretroviral therapy for the prevention of mother-to-child transmission of HIV in Malawi: maternal and infant outcomes two years after delivery. PLoS One. 2013; 8(7):e68950. [PubMed: 23894379]

21. World Health Organization. Maternal Mortality. 2015. Available from: http://www.who.int/mediacentre/factsheets/fs348/en/. Accessed December 21, 2016

22. Colbourn T, Lewycka S, Nambiar B, Anwar I, Phoya A, Mhango C. Maternal mortality in Malawi, 1977–2012. BMJ Open. 2013; 3(12):e004150.

23. United NationsChildren's Emergency Fund (UNICEF). Statistics; Malawi: 2013. Available from: http://www.unicef.org/infobycountry/malawi_statistics.html. Accessed December 21, 2016

24. Malawi National Statistical Office. Malawi Demographic and Health Survey 2015–2016. Available from: http://dhsprogram.com/pubs/pdf/PR73/PR73.pdf. Accessed Dec 19, 2016

25. National Statistical Office, ICF Macro. Malawi Demographic and Health Survey 2010. http://dhsprogram.com/pubs/pdf/FR247/FR247.pdf. Published September 2011. Accessed February 24, 2017

26. van Lettow M, Bedell R, Mayuni I, Mateyu G, Landes M, Chan AK, et al. Towards elimination of mother-to-child transmission of HIV: performance of different models of care for initiating

lifelong antiretroviral therapy for pregnant women in Malawi (Option B+). J Int AIDS Soc. 2014; 17(1):18994. [PubMed: 25079437]

Synopsis

Odds of serious maternal and neonatal morbidity were higher after cesarean than vaginal delivery, despite lower maternal viral loads.

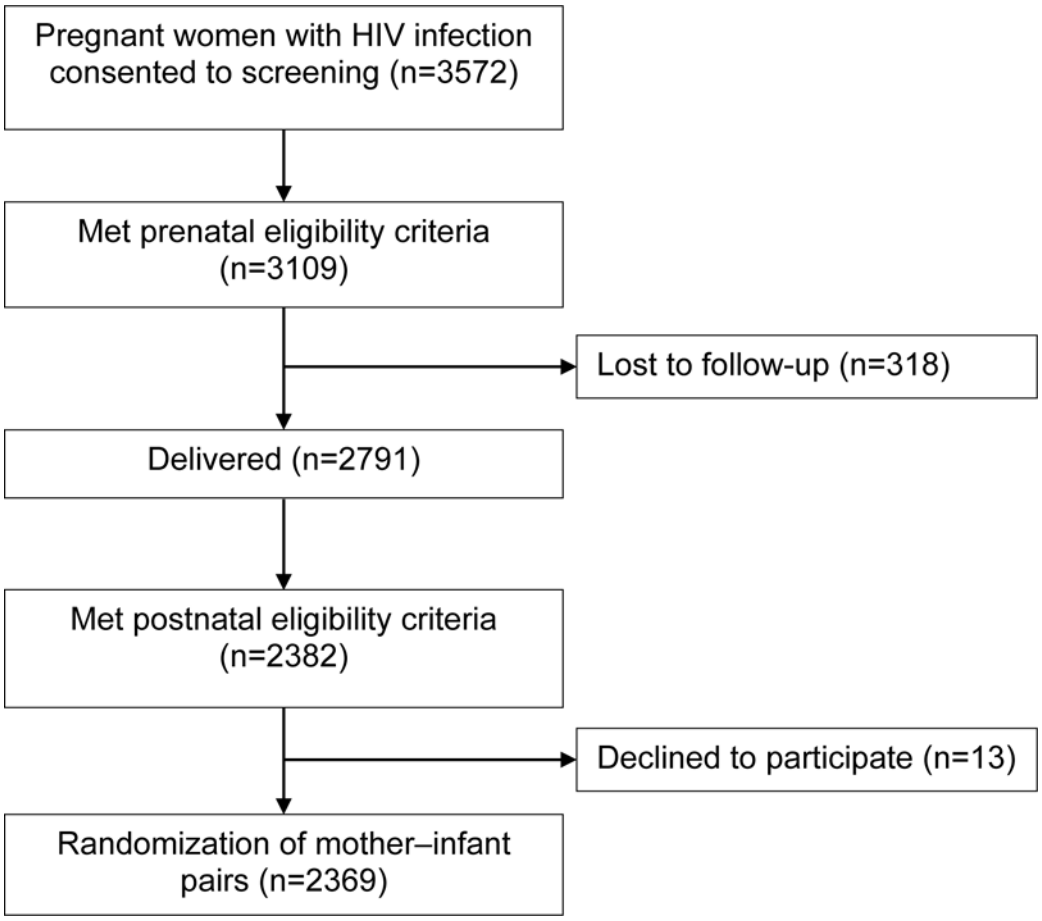

Figure 1.
Enrollment of mother–infant pairs.

Int J Gynaecol Obstet. Author manuscript; available in PMC 2018 June 01.

Table 1

Maternal characteristics by delivery type.[a]

Characteristic	All mothers (n=2791)	Delivery method			
		Vaginal delivery (n=2622)	Cesarean delivery (n=169)	*P* value[b]	Odds ratio (95% confidence interval)[c]
Demographics					
Age, y[d]	25.4 (22.1–29.2)	25.4 (22.2–29.2)	25.2 (21.3–29.2)	0.489	–
Married[e]	2584 (93.1)	2429 (93.1)	155 (91.7)	–	0.8 (0.5–1.4)
No electricity at home[f]	1039 (81.5)	973 (81.6)	66 (80.5)	–	0.9 (0.5–1.6)
Education[g]				–	1.5 (1.1–2.1)
Primary school (0–9 y)	1841 (66.4)	1744 (66.9)	97 (57.4)		
Secondary/college (10–13+ y)	933 (33.6)	861 (33.1)	72 (42.6)		
Gravidity[h]				–	2.1 (1.4–3.1)
1st pregnancy	354 (12.7)	316 (12.1)	38 (22.5)		
≥2 pregnancies	2426 (87.3)	2295 (87.9)	131 (77.5)		
Health indices					
CD4+ T-cell count, per μL[i]	438 (328–580)	438 (328–580)	429 (336–560)	0.671	–
HIV viral load, copies per mL[j,k]	17 481 (4889–55 455)	17 663 (5112–55 833)	11 036 (3004–39 445)	0.016	–
Hemoglobin, g/L[l]	108 (100–117)	108 (100–117)	109 (101–116)	0.953	–
Body mass index[m]	23.1 (21.5–25.2)	23.1 (21.5–25.2)	23.3 (22.0–25.5)	0.113	–
<20	174 (8.2)	167 (8.3)	7 (6.0)	–	0.7 (0.3–1.6)
Albumin, g/L[n]	28 (26–30)	28 (26–30)	29 (26–31)	0.032	–

[a]Values are given as median (interquartile range) or number (percentage), unless indicated otherwise.

[b]Wilcoxon rank-sum or X^2 test.

[c]Compare baseline maternal characteristics by delivery type (vaginal delivery as the referent group).

[d]Data missing for 36 (35 vaginal delivery, 1 cesarean delivery).

[e]Data missing for 14 (all vaginal delivery).

[f] Data missing for 1516 (1429 vaginal delivery, 87 cesarean delivery).

[g] Data missing for 17 (all vaginal delivery).

[h] Data missing for 11 (all vaginal delivery).

[i] Data missing for 10 (9 vaginal delivery, 1 cesarean delivery).

[j] Data missing for 435 (398 vaginal delivery, 37 cesarean delivery).

[k] The proportion of missing data differed significantly by delivery method for HIV viral load and body mass index, with a lower proportion of women who delivered vaginally than delivering by cesarean missing these data.

[l] Data missing for 7 (6 vaginal delivery, 1 cesarean delivery).

[m] Calculated as weight in kilograms divided by the square of height in meters. Data missing for 665 (612 vaginal delivery, 53 cesarean delivery).

[n] Data missing for 55 (50 vaginal delivery, 5 cesarean delivery).

Table 2

Labor characteristics and maternal morbidity and mortality, by delivery type.[a]

Characteristic/complication	All mothers	Delivery method		
		Vaginal delivery	Cesarean delivery	Odds ratio (95% confidence interval)[b]
Labor and delivery characteristics				
Pre-eclampsia/eclampsia	20/2791 (0.7)	12/2622 (0.5)	8/169 (4.7)	10.8 (4.4–26.8)
Estimated blood loss, mL[c]	100 (100–200)	100 (100–150)	500 (300–800)	_[d]
Hemorrhage	32/2791 (1.1)	32/2622 (1.2)	0/169	0.2 (0.0–3.9)
Blood transfusion	11/2791 (0.4)	9/2622 (0.3)	2/169 (1.2)	3.5 (0.8–16.2)
Intrapartum fever	5/2791 (0.2)	4/2622 (0.2)	1/169 (0.6)	3.9 (0.4–35.1)
Puerperal sepsis/endometritis	22/2791 (0.8)	21/2622 (0.8)	1/169 (0.6)	0.7 (0.1–5.5)
Stillbirths	45/2649 (1.7)	39/2488 (1.6)	6/161 (3.7)	2.4 (1.0–5.8)
Prolonged hospital stay[e]	151/2778 (5.4)	105/2609 (4.0)	46/169 (27.2)	8.9 (6.0–13.2)
Postpartum complications				
Infection ≤14 d after delivery[f]	42/2369 (1.8)	36/2238 (1.6)	6/131 (4.6)	3.0 (1.3–7.4)
Anemia ≤6 wk after delivery				
Grade 1 and 2[g]	834/2365 (35.3)	745/2234 (33.3)	89/131 (67.9)	4.3 (2.9–6.2)
Grade 3 and 4[h]	18/2365 (0.8)	13/2234 (0.6)	5/131 (3.8)	6.7 (2.3–19.1)
All obstetric complications[i]	243/2791 (8.7)	182/2622 (6.9)	61/169 (36.1)	8.0 (5.3–12.0)
Mortality				
0–6 wk after delivery	0/2369	–	–	–
7–48 wk after delivery	9/1980 (0.5)	8/1871 (0.4)	1/109 (0.9)	2.1 (0.3–17.3)

[a] Values are given as number/total number (percentage) unless indicated otherwise.

[b] Compare outcomes for cesarean and vaginal deliveries (referent group). For postpartum complications beyond delivery, they were adjusted for the antiretroviral and nutritional intervention group.

[c] Values are given as median (interquartile range). Data missing for 757 (731 vaginal delivery, 26 cesarean delivery). The proportion of missing data differed significantly by delivery method, with a lower proportion of cesarean deliveries missing this information ($P<0.001$).

[d] $P<0.001$ (Wilcoxon rank-sum test).

[e] >48 h after natural spontaneous vaginal delivery; >7 d after cesarean delivery.

[f] Puerperal sepsis/endometritis, serious febrile illness/sepsis, intrapartum fever, malaria, pneumonia, meningitis, tuberculosis, pelvic inflammatory disease, and syphilis.

[g] Hemoglobin 70–110 g/L.

[h] Hemoglobin <70–110 g/L.

[i] Hemorrhage, pre-eclampsia/eclampsia, prolonged hospital stay, blood transfusion, stillbirth, and infection from delivery until 2 weeks after delivery. Women with multiple complications were only counted once.

Table 3

Neonatal complications by delivery type.[a]

Complication	All mothers (n=2685)	Delivery method		
		Vaginal delivery (n=2531)	Cesarean delivery (n=154)	Odds ratio (95% confidence interval)[b]
5-min Apgar score <7[c]	25 (1.1)	16 (0.8)	9 (5.9)	8.1 (3.5–18.6)
Admission to an intensive care unit[d]	239 (8.9)	192 (7.6)	47 (30.7)	5.4 (3.7–7.8)
Low birth weight[e,f]	283 (10.6)	261 (10.4)	22 (14.5)	1.5 (0.9–2.3)
Macrosomia[e,g]	35 (1.3)	32 (1.3)	3 (2.0)	1.6 (0.5–5.2)
Neonatal sepsis	106 (3.9)	100 (4.0)	6 (3.9)	1.0 (0.4–2.3)
Neonatal mortality	12 (0.4)	10 (0.4)	2 (1.3)	3.3 (0.7–15.3)

[a] Values are given as number (percentage) unless indicated otherwise.

[b] Odds ratios from logistic regression compare cesarean with vaginal deliveries (referent group).

[c] Data missing for 464 (462 vaginal delivery, 2 cesarean delivery). The proportion of missing data differed significantly by delivery method, with a lower proportion of cesarean deliveries missing this information.

[d] Data missing for 6 (5 vaginal delivery, 1 cesarean delivery).

[e] Data missing for 15 (13 vaginal delivery, 2 cesarean delivery).

[f] >2000g and ≤2500 g.

[g] >4000 g.