OPEN ACCESS
©NIJPP
Publications 2024
ONLINE ISSN:2992-5479
PRINT ISSN:2992-605X

NEWPORT INTERNATIONAL JOURNAL OF PUBLIC HEALTH AND PHARMACY (NIJPP)

Volume 5 Issue 2 2024

https://doi.org/10.59298/NIJPP/2024/523942135

Incidence and Determinants of Adverse Neonatal Outcomes among HIV-Positive Pregnant Women: A Prospective Cohort Study at Regional Referral Hospitals in Uganda

[1]Bataringaya Geoffrey Tabu, [1]Fernando Perez Ramirez, [1]Ddamulira Adam, [2]Eilu Emmanuel and [3]Ugwu Okechukwu Paul-Chima

[1]Department of Obstetrics and Gynecology Kampala International University Uganda.
[2]Department of Microbiology Kampala International University Uganda
[3]Department of Publication and Extension, Kampala International University Uganda

ABSTRACT

HIV infection remains a significant global health challenge, affecting over 37.9 million people worldwide. Despite widespread access to antiretroviral therapy (ART), adverse neonatal outcomes are prevalent among pregnant women living with HIV. This prospective cohort study aimed to determine the incidence and factors associated with early adverse neonatal outcomes among HIV-positive mothers at Mubende and Fort Portal Regional Referral Hospitals (MRRH and FRRH), compared to HIV-negative mothers. The study excluded mothers with known risks for adverse neonatal outcomes. Neonates were monitored from birth to discharge within 7 days for adverse outcomes. Among 203 participants, 135 were HIV-negative and 68 were HIV-positive. Adverse neonatal outcomes were more frequent in the HIV-positive group (39.7% vs. 28.1%), although the difference was not statistically significant (P=0.096). Prematurity (20.6% vs. 8.1%, P=0.031) and low birth weight (25.0% vs. 12.6%, P=0.047) were significantly higher among HIV-positive mothers. Multivariate analysis identified detectable viral load as a significant risk factor for early neonatal adverse outcomes (aRR=4.036, CI=1.428-11.406, P=0.008). These findings underscore the importance of close monitoring and viral load suppression in HIV-positive mothers. Further research is needed to understand the causes of detectable viral loads in mothers on ART and to capture neonatal adverse outcomes beyond 7 days post-delivery.

Keywords: HIV, Adverse neonatal outcomes, Antiretroviral therapy (ART), Viral load, Prematurity, Low birth weight, Public health and Maternal health

INTRODUCTION

HIV was believed to have its origin in chimpanzees in West Africa in the 1930s and was spread to people through blood transfusions during hunting [1]. Then over several years, the virus spread throughout Africa and other regions of the world [2]. It wasn't until the early 1980s that HIV and AIDS became widely known when unusual types of pneumonia, cancer, and other illnesses were being reported. In 1982, after Canada reported its first case of AIDS, the illness was given the name Acquired Immune Deficiency Syndrome (AIDS) and in 1987 the first anti-retroviral drug was approved [3]. HIV was first suspected to be transmitted from mother to child through breastfeeding in 1986 [4]. Then in 1990, the first HIV epidemic among pregnant women was reported and in 1994, zidovudine was the first available antiretroviral agent for reducing mother-to-child HIV transmission [5]. Since then, numerous methods based on various ART regimen have been employed to restrict maternal infantile transmission, with the most recent one using option B+, which is currently recommend by WHO [6-8].

Aims of the study

To determine the incidence and factors associated with early adverse neonatal outcomes among mothers living with HIV compared with HIV-negative mothers at Mubende and Fortportal Regional Referral Hospitals.

Specific objectives

1. To compare the incidence of early adverse neonatal outcomes among newborns of mothers living with HIV and HIV-negative mothers at Mubende and Fortportal Regional Referral Hospitals.
2. To determine the association between HIV status and common early adverse neonatal outcomes among mothers at Mubende and Fortportal Regional Referral Hospitals.
3. To assess the factors associated with early adverse neonatal outcomes among newborns to mothers living with HIV at Mubende and Fortportal Regional Referral Hospitals.

Research questions

1. What is the difference in the incidence of early adverse neonatal outcomes among newborns of mothers living with HIV and newborns of HIV-negative mothers at Mubende and Fortportal Regional Referral Hospitals?
2. What is the association between HIV status and common early adverse neonatal outcomes among mothers at Mubende and Fortportal Regional Referral Hospitals?
3. What are the factors associated with early adverse neonatal outcomes among newborns to mothers living with HIV/AIDS at Mubende and Fortportal Regional Referral Hospitals?

METHODOLOGY

Study design

This was a prospective cohort study that was carried out at Mubende and Fortportal regional referral hospitals in Uganda.

Study setting

The study was carried out in the Obstetrics and Gynecology department of Mubende and Fortportal Regional Referral Hospitals particularly in the maternity and the postnatal wards of Mubende and Fortportal Regional Referral Hospitals. Mubende Regional Referral Hospital has a bed capacity of 175 beds and provides a range of medical services, including obstetrics and gynecology, with 4 specialists, a resident doctor, 5 intern doctors, and 13 midwives. The hospital's obstetrics and gynecology department has 40 beds, and the hospital provides free antenatal care services to all pregnant women, with a range of 20-30 antenatal visits per day. Fortportal Regional Referral Hospital has a maternity ward which has a bed capacity of 40. Both hospitals have NICU which provides level II neonatal care services (specialist care) to both in-born and out-born babies, and also admits critically ill neonates who required advanced respiratory and cardiovascular support. The units are manned by pediatricians, pediatric residents, medical officers, and nurses.

Target population

All pregnant women living with HIV and those of HIV negative status who delivered at Mubende and Fortportal Regional Referral Hospitals during the study period.

Eligible patient

All mothers that delivered at Mubende and Fortportal Regional Referral Hospitals maternity during the study period.

Study participants

All eligible patients who consented to participate in the study.

Eligibility criteria

Inclusion Criteria

All mothers aged between 18-45 years who delivered at Mubende and Fortportal Regional Referral Hospitals maternity at or above 28 weeks of gestation during the study period that consented to participate in the study.

Exclusion Criteria

- Mothers who had multifetal gestation/delivery.
- Mothers who had a history of Hypertensive disorders in Pregnancy in current delivery.
- Mothers who had history of diabetes in pregnancy
- Mothers who suffered Antepartum Hemorrhage in current pregnancy.
- Mothers who delivered on the way to the Hospital

Sample size determination

Sample size formula for the method described in Kelsey was used:

$$n_1 = \frac{[\left(Z_{\frac{\alpha}{2}}\sqrt{(r+1)pq}\right) + Z_{1-\beta}\sqrt{rp_1q_1 + p_2q_2}\,]^2}{r(p_1 - p_2)^2}$$

$$n_2 = rn_1$$

And where

n_1= number of exposed
n_2=number of unexposed
$Z_{\frac{\alpha}{2}}$: Standard normal deviate for two-tailed test based on alpha level (relates to the confidence Interval level)
$Z_{1-\beta}$: Standard normal deviate for one-tailed test based on beta level (relates to the power level)
r = ratio of unexposed to exposed.
p_1 = proportion of exposed with disease and $q_1 = 1 - p_1$.
p_2 = proportion of unexposed with disease and $q_2 = 1 - p_2$.
n_1 = 68.
n_2 =135.
n = 203. The sample size required in this study was 203.

Participants flow chart

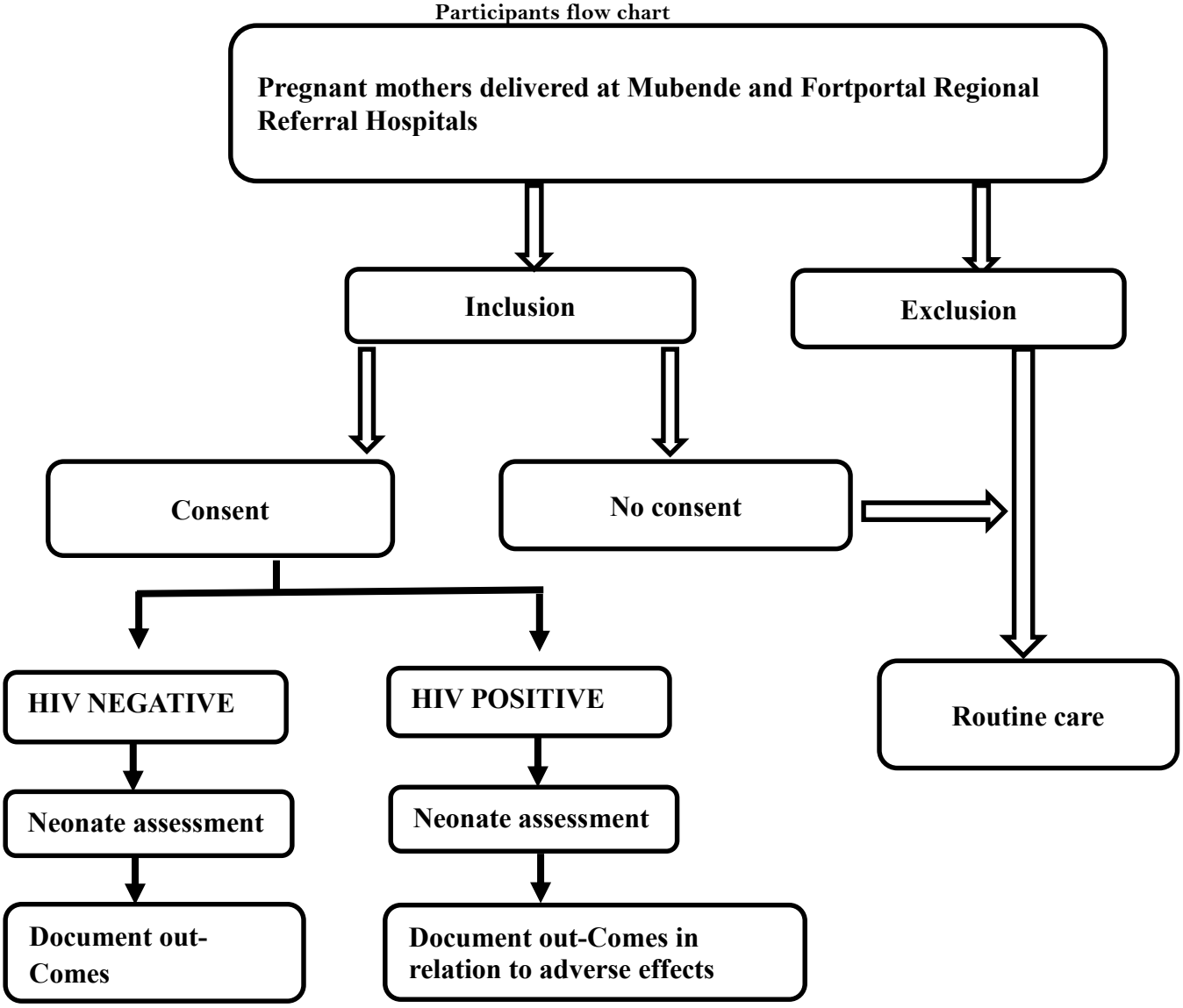

Figure 1: Data collection instruments

A checklist was used to collect data from the patients who had consented. Information related to mothers and neonates such as sociodemographic factors and medical factors was documented. The findings on clinical assessment were also documented. The questionnaire was translated to Luganda and Rutoro for the participants who could not understand English.

Sampling technique

Participants were recruited from both mothers living with HIV and HIV negative mothers who fulfilled the inclusion criteria. For every 2 HIV negative mothers recruited, 1 HIV positive mother was recruited until the required sample size was achieved.

Study procedure

History taking, Physical examination and data collection

Every mother that delivered at Mubende and Fortportal Regional Referral Hospitals maternity was informed about the study and written consent was obtained. Then an interview was conducted with the mothers and details about sociodemographic characteristics which were focused on the age, residence, level of education, number of children, marital status, occupation and the tribe documented. The medical factors such as the HIV status, current ART regimen of the mothers and updated viral load were documented as well. This information was obtained from the ANC records as well as patient's files in postnatal and HIV clinic records with their consent. On clinical assessment the different adverse neonatal outcomes assessed included stillbirth, low birth weight, preterm birth, and Apgar score at fifth minute. Stillbirth was defined using Apgar score to a newborn above 28 gestational week who scored a total 0 in the first and at the fifth minutes. Preterm birth was assessed using Ballard score to estimate the gestational age (the new Ballard score neuromuscular maturity rating sign score,1991). A preterm birth was considered to be any delivery with an equivalent score of 30 or less according to the Ballard score assessment. Low birth weight was assessed by measuring the neonate using the neonate weighing scale and was considered low birth weight if the neonate weighed < 2500 g (LBW). During Physical examination, any congenital abnormality was identified as well as the need for NICU care.

Validity of data collection instrument

A pilot study was carried out to pre-test the questionnaire and confirm its effectiveness using a Content Validity Index. The questionnaire was distributed to two gynecologists in Mubende and Fortportal Regional Referral Hospitals, and content validation was done. The domain and items were reviewed again and graded by the gynecologists. The score for content validity was determined. A content validity index of at least 0.80 was regarded as satisfactory, according to [9-10] who carried out a related study that was used in this technique.

Reliability of data collection

The data was gathered using a pretested questionnaire and the alpha value of Cronbach's Coefficient was more than 0.8, it was assumed that the questionnaire questions were reliable and consistent [11]. Additionally pretested baby weighing scales were used to guarantee accuracy.

Data analysis plan

Data from questionnaires was entered in Microsoft Excel 2010, and thereafter exported to SPSS 26 series for Windows for analysis. Frequencies and corresponding percentages were used to determine the baseline characteristics. Cross tabulation with a chi square test were used to compare the baseline characteristics between the HIV positive mothers and negative mothers.

Objective 1: The incidence of early adverse neonatal outcomes among mothers living with HIV and HIV negative mothers who delivered at Mubende and Fortportal Regional Referral Hospitals in the Obstetrics and gynecology department were computed as a percentage of neonates who presented with early adverse neonatal outcomes over all neonates born to mothers living with HIV and HIV negative mothers. The significance in difference in occurrence of adverse neonatal outcomes between mothers living with HIV and HIV negative mothers was determined using Chi-square test, regarding $p<0.05$ as statistically significant. A clustered bar graph was used to present this data.

Objective 2: The comparison of the different forms of adverse neonatal outcomes among mothers living with HIV and HIV negative mothers were summarized as percentages, frequencies, presented in a table**.** And the significance in difference in forms of different adverse neonatal outcomes among mothers living with HIV and HIV negative mothers were determined using Chi-square test, regarding $p<0.05$ as statistically significant.

Objective 3: Factors associated with early adverse neonatal outcomes were analyzed by both bivariate and multivariate Poisson analysis. To prevent excluding significant factors from the multivariate analysis, biologically plausible variables and those with p values ≤ 0.2 at bivariate level were analysed at the multivariate level. Variables were considered significant in the final multivariate model if p value was ≤ 0.05. The measure of association was reported as risk ratios (RRs) with corresponding 95% CI and p-values. All statistical analyses were carried out in SPSS 26 series for Windows.

Ethical considerations

Informed consent

Respect for participants' informed permission and voluntary recruitment was followed. Before being asked to sign an informed consent form, participants got a detailed explanation of the study in both English and, where necessary, their local language.

Privacy and confidentiality

Participants were identified by number codes. For reasons of privacy, the information provided by respondents was kept private throughout the research. There was careful adherence to the respondents' rights and fair treatment, minimizing any injury and inconvenience to them. Without their permission, participants' information was not disclosed to the public.

Selection of participants

To guarantee that everyone had an equal chance of being chosen for the study, participants were chosen using a consecutive sampling approach. Eligibility requirements were strictly followed.

Approval procedure

The faculty, postgraduate directorate, the research ethics committee of Bishop Stuart University (BSU-REC-2023-118), and the department of obstetrics and gynecology of Mubende and Fortportal Regional Referral Hospitals all provided their approval before the study was carried out. The hospital management of Mubende and Fortportal Regional Referral Hospitals received a copy of the approval letter. Before conducting the study, permission was obtained from the management of Mubende and Fortportal Regional Referral Hospitals. The study was submitted for registration to the National Council for Science and Technology of Uganda.

RESULTS

Study profile

During the study period, 203 mothers consented to participate in the study. Sixty eight of the mothers were HIV positive while 135 were HIV negative. All the 203 mothers were followed up to assess for adverse neonatal outcomes. None of the mothers was lost to follow up.

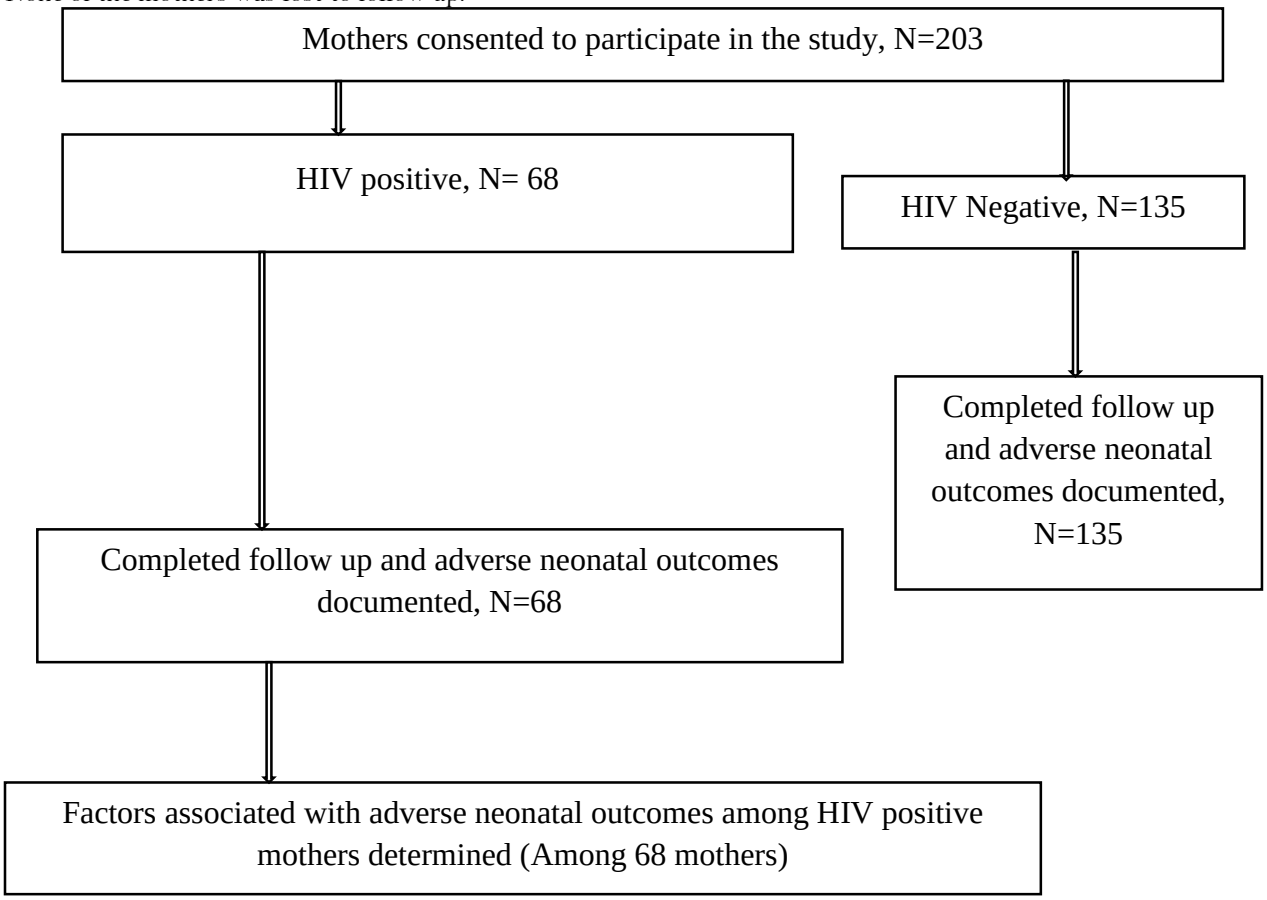

Figure 2: Study profile and overview of the results

Baseline characteristics of the study participants

In this study that enrolled 203 participants including 135 HIV negative and 68 HIV positive, majority of the study participants were in the age group of 20-34 years 147(72.4%). Majority of the study participants were married 131(64.5%) and had atleast 4 antenatal care visits 156(76.8%). All HIV positive mothers were on ART and were taking the same regimen (Tenofovir, Lamivudine and Dolutegravir). There was no statistically significant difference

between the HIV positive and HIV negative participants in terms of the baseline characteristics since all the p values were greater than 0.05 as shown in table 1 below.

Table 1: Baseline characteristics of study participants

Characteristic	Overall N=203 n(% of 203)	HIV negative N=135 n(% of 135)	HIV positive N=68 n(% of 68)	Chi square p value
Age				0.109
20 – 34	147(72.4)	94(69.6)	53(77.9)	
<20	36(17.7)	30(22.2)	6(8.8)	
35+	20(9.9)	11(8.1)	9(13.2)	
Education level				0.064
Non formal	31(15.3)	14(10.4)	17(25.0)	
Primary	99(48.8)	61(45.2)	38(55.9)	
Secondary	65(32.0)	54(40.0)	11(16.2)	
Tertiary	8(3.9)	6(4.4)	2(2.9)	
Religion				0.260
Christian	180(88.7)	118(87.4)	62(91.2)	
Muslim	9(4.4)	4(3.0)	5(7.4)	
Other	14(6.9)	13(9.6)	1(1.5)	
Marital status				0.803
Married/cohabiting	131(64.5)	86(63.7)	45(66.2)	
Divorced/separated	34(16.7)	25(18.5)	9(13.2)	
Single	38(18.7)	24(17.8)	14(20.6)	
Children number				0.118
<5	171(84.2)	119(88.1)	52(76.5)	
5+	32(15.8)	16(11.9)	16(23.5)	
Employment status				0.059
Employed	77(37.9)	59(43.7)	18(26.5)	
Unemployed	126(62.1)	76(56.3)	50(73.5)	
ANC visits				0.644
<4	47(23.2)	34(25.2)	13(19.1)	
4+	156(76.8)	101(74.8)	55(80.9)	

HIV=Human immune deficiency virus, ANC=Antenatal care.

Incidence of early adverse neonatal outcomes among newborns of mothers living with HIV and HIV negative mothers at Mubende and Fortportal Regional Referral Hospitals.

In this study, where 65 of the 203 (32.0%) study participants had adverse neonatal outcomes (Incidence: 320 adverse outcomes per 1,000 deliveries overall), 27 of the 68 (39.7%) HIV positive mothers had adverse neonatal outcomes (Incidence: 397 adverse outcomes per 1,000 deliveries among HIV positive mothers) while only 38 of the 135 (28.1%) HIV negative mothers had the adverse outcomes (Incidence: 281 adverse outcomes per 1,000 deliveries among HIV negative mothers). Though the adverse outcomes were more in the HIV positive mothers (39.7% versus 28.1%), the difference was not statistically significant since the chi square p value was 0.096.

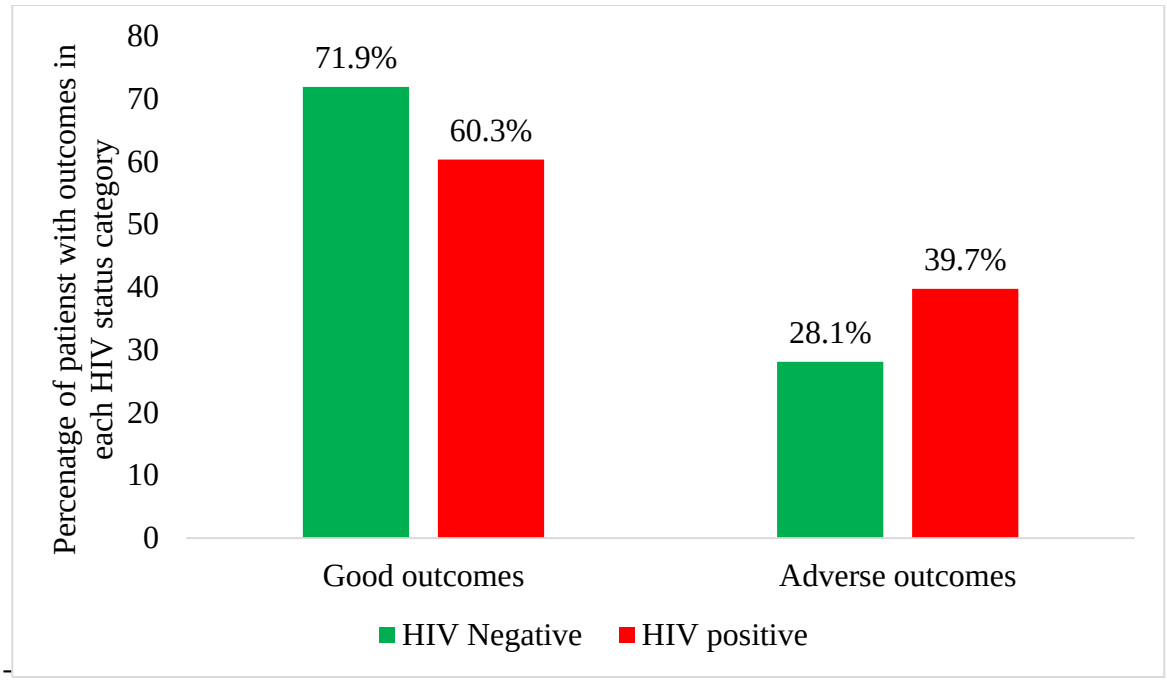

Figure 3: Comparison of the outcomes between the HIV positive and HIV negative mothers

Relation between the common forms of early adverse neonatal outcomes among mothers living with HIV and HIV negative mothers at Mubende and Fortportal Regional Referral Hospitals.

In this study, the commonest adverse outcome was low birth weight seen among 34(16.7%) of the study participants, followed by preterm birth 27(13.3%), asphyxia 25(12.3%) and lastly still birth 16(7.9%) with 36(17.7%) of the neonates with adverse outcomes admitted to NICU. Though all neonatal adverse outcome categories were more in the HIV positive group, only prematurity (20.6% versus 8.1%, P=0.031) and low birth weight (25.0% versus 12.6%, P=0.047) had a statistically significant difference. Among HIV positive mothers, the risk for preterm birth was increased by 2.454 times while the risk for low birth weight was increased by 2.038 times

The detailed results of the different adverse outcomes are shown in table 2 below.

Table 2: Relation between common forms of early adverse neonatal outcomes and among mothers living with HIV and HIV negative mothers at Mubende and Fortportal Regional Referral Hospitals.

Outcome	Overall N=203 n(% of 203)	HIV negative N=135 n(% of 135)	HIV positive N=68 n(% of 68)	RR(95% CI)	P value
Adverse outcomes					0.096
None	138(68.0)	97(71.9)	41(60.3)		
One or more	65(32.0)	38(28.1)	27(39.7)	1.411(0.947-2.100)	
Still birth					0.974
No	187(92.1)	126(93.3)	61(89.7)		
Yes	16(7.9)	9(6.7)	7(10.3)	1.037(0.954-1.127)	
Still birth type					0.522
Fresh	3(1.5)	1(11.1)	2(28.6)	1.191(0.804-1.763)	
Macerated	13(6.4)	8(88.9)	5(71.4)		
Preterm birth					**0.031**
No	176(86.7)	124(91.9)	54(79.4)		
Yes	27(13.3)	**11(8.1)**	**14(20.6)**	2.454(1.066-5.647)	
LBW					**0.047**
No	169(83.3)	118(87.4)	51(75.0)		
Yes	34(16.7)	**17(12.6)**	**17(25.0)**	2.038(1.006-4.132)	
Asphyxia					0.272
No	178(87.7)	121(89.6)	57(83.8)		
Yes	25(12.3)	14(10.4)	11(16.2)	1.060(0.957-1.173)	
NICU Admission					0.140
No	167(82.3)	114(84.4)	53(77.9)		
Yes	36(17.7)	21(15.6)	15(22.1)	1.067(0.950-1.198)	

HIV=Human immune deficiency virus, NICU=Neonatal intensive care unit.

Factors associated with early adverse neonatal outcomes among newborns to mothers living with HIV at Mubende and Fortportal Regional Referral Hospitals.

At bivariate level of analysis, the variables that had a p value less than 0.2 and therefore qualified for multivariate analysis were: age ≥35 years (advanced maternal age, P=0.038), being unemployed (P=0.114), attending antenatal care for less than 4 times (P=0.198) and having a detectable viral load (P=0.016).

Table 3: Bivariate analysis of factors associated with early adverse neonatal outcomes among newborns to mothers living with HIV at Mubende and Fortportal Regional Referral Hospitals.

Characteristic	Good outcomes, N=41 n(% of 68)	Adverse outcomes, N= 27 n(% of 68)	Bivariate analysis		
			cRR	95% CI	P value
Age					
20 - 34	34(50.0)	19(27.9)	1		
<20	4(5.9)	2(2.9)	0.895	0.150-5.347	0.903
35+	3(4.4)	6(8.8)	1.860	1.035-3.341	**0.038**
Education level					
Non formal	9(13.2)	8(11.8)	0.889	0.047-16.661	0.937
Primary	24(35.3)	14(20.6)	0.583	0.034-10.075	0.711
Secondary	7(10.3)	4(5.9)	0.571	0.028-11.849	0.718
Tertiary	1(1.5)	1(1.5)	1		
Religion					
Christian	37(54.4)	25(36.8)	1		
Muslim	3(4.4)	2(2.9)	0.987	0.154-6.337	0.989
Other	1(1.5)	0(0.0)	N/A		
Marital status					
Married/cohabiting	26(38.2)	19(27.9)	1		
Divorced/separated	6(8.8)	3(4.4)	0.684	0.152-3.088	0.622
Single	9(13.2)	5(7.4)	0.760	0.219-2.635	0.666
Children number					
<5	33(48.5)	19(27.9)	1		
5+	8(11.8)	8(11.8)	1.737	0.561-5.382	0.339
Employment status					
Employed	8(11.8)	10(14.7)	1		
Unemployed	33(48.5)	17(25.0)	2.426	0.809-7.279	**0.114**
ANC visits					
<4	7(10.3)	6(8.8)	1.388	0.410-4.694	**0.198**
4+	34(50.0)	21(30.9)	1		
Viral load					
Undetectable(<1000copies/mL)	19(27.9)	3(4.4)	1		
Detectable(>1000copies/mL)	22(32.4)	24(35.3)	3.826	1.290-11.350	**0.016**
ART initiation					
Before conceiving	32(47.1)	21(30.9)	1		
After Conceiving	9(13.2)	6(8.8)	1.016	0.315-3.275	0.979

cRR= crude risk ratio, Ref= Reference category, CI= Confidence interval,

At multivariate level of analysis, only the presence of a detectable viral load increased the risk of early neonatal adverse outcomes (aRR=4.036, CI=1.428-11.406, P=0.008). A Mother that had a detectable viral load was 4.036 times more likely to have early adverse neonatal outcomes. The rest of findings at multivariate level of analysis are shown in table 4 below.

Table 4: Multivariate analysis of factors associated with early adverse neonatal outcomes among newborns to mothers living with HIV at Mubende and Fortportal Regional Referral Hospitals.

Characteristic	Bivariate analysis			Multivariate analysis		
	cRR	95% CI	P value	aRR	95% CI	P value
Age						
20 - 34	1					
<20	0.895	0.150-5.347	0.903	1.043	0.356-3.057	0.939
35+	1.860	1.035-3.341	0.038	1.600	0.864-2.962	0.135
Employment status						
Employed	1					
Unemployed	2.426	0.809-7.279	0.114	1.609	0.940-2.756	0.083
ANC visits						
<4	1					
4+	0.721	0.213-2.437	0.198	1.086	0.552-2.135	0.811
Viral load						
Un detectable	1					
Detectable	**3.826**	**1.290-11.350**	**0.016**	**4.036**	**1.428-11.406**	**0.008**

aRR= Adjusted risk ratio, Ref= Reference category, CI= Confidence interval,

DISCUSSION, CONCLUSION AND RECOMMENDATIONS

This study was aimed at determining the incidence and factors associated with early adverse neonatal outcomes among mothers living with HIV at Mubende and Fortportal Regional Referral Hospitals. We enrolled 203 participants including 135 HIV negative and 68 HIV positive, majority of whom were in the age group of 20-34 years 147(72.2%) years. All HIV positive mothers were on ART and were taking the same regimen (Tenofovir, Lamivudine and dolutegravir). The fact that all HIV positive mothers were on ART is an indicator of the progress in privation of mother to child transmission. We noted that there was no statistically significant difference between the HIV positive and HIV negative participants in terms of age, marital status, antenatal care attendance, employment status and number of children. Given that the mothers with a high risk for adverse neonatal outcomes were excluded from the study, the fact that there was no significant difference between the HIV positive and HIV negative participants in the baseline characteristics is an indicator that any differences noted in the neonatal outcomes could be attribute to the HIV related factors.

Incidence of early adverse neonatal outcomes among newborns of mothers living with HIV and HIV negative mothers at Mubende and Fortportal Regional Referral Hospitals

The first objective of this study was to determine the incidence of early adverse neonatal outcomes among new-borns of mothers living with HIV and HIV negative mothers at Mubende and Fortportal Regional Referral Hospitals. We noted that 27 of the 68 (39.7%) HIV positive mothers had adverse neonatal outcomes while only 38 of the 135 (28.1%) HIV negative mothers had the adverse outcomes. Though the adverse outcomes were more in the HIV positive mothers (39.7% versus 28.1%), the difference was not statistically significant since the chi square p value was 0.096. Our findings were in agreement with studies by [12,13] adverse neonatal outcomes were high regardless of the HIV status of the mothers, Shava et al (2019) in Botswana who reported no significant difference in adverse outcomes among HIV positive and HIV negative mothers , and [14] in Uganda who also reported no significant difference in occurrence of adverse birth outcomes between mothers living with HIV and those found to be HIV negative. Contrary to our findings, other studies reported a significant difference in adverse outcomes between HIV positive and HIV negative mothers. For example, [15] reported a high incidence of adverse neonatal outcomes among mothers living with HIV compared to the non-infected mothers in China. Similar results were reported among children born to mothers living with HIV by [16-17] in Mozambique. Though it's true that the early neonatal adverse outcomes in this study were more in the HIV positive mothers, a statistically significant difference could not be demonstrated. The reason for not having a significant difference between the neonatal outcomes between the HIV positive and HIV negative mothers could be because all the mothers in our study were taking ART, which ART has been reported by a number of studies to reduce the risk of adverse neonatal outcomes among HIV positive mothers. According to a study conducted in [18-19], among pregnant women living with HIV on ART and the untreated women living with HIV, there was a higher probability of a neonate being born with low birth weight, a stillbirth, or a small for gestational age among the untreated mothers living with HIV than it was found among those on ART. [20-24], observed similar findings in South Africa, where there were decreasing tendencies for preterm birth, low birth weight, and stillbirths among mothers receiving ART treatment compared to those who were not. Also the fact that we only captured the adverse outcomes occurring in the first 7 days of life could have resulted in not having a significant difference.

Common forms and the relationship of early adverse neonatal outcomes among mothers living with HIV and HIV negative mothers at Mubende and Fortportal Regional Referral Hospitals

The second objective of this study was to describe the common forms of early adverse neonatal outcomes among mothers living with HIV and HIV negative mothers at Mubende and Fortportal Regional Referral Hospitals. We noted that the commonest adverse outcome was low birth weight seen among 34(16.7%) of the study participants, followed by preterm birth 27(13.3%). Though all neonatal adverse outcome categories were more in the HIV positive group, only prematurity (20.6% versus 8.1%, P=0.031) and low birth weight (25.0% versus 12.6%, P=0.047) had a statistically significant difference. These findings were comparable to the findings in Lesotho where low birth weight was the most prevalent adverse neonatal outcome among mothers living with HIV [25-27]. Similarly a study conducted in China by [28-29] revealed that among Chinese mothers living with HIV, there was a high prevalence of low birth weight and preterm birth. The significant difference in low birth weight and prematurity between HIV positive and HIV negative mothers is possibly because of the altered immunological responses in HIV positive mothers as well as placenta development disorders reported to occur [30]. In addition, maternal weight loss due to reduced nutritional intake associated with appetite loss, oral ulcers, mal-absorption, and altered metabolism is prevalent among women living with HIV/AIDS, and these factors could cause them to give birth to infants with low birth weight.

Factors associated with early adverse neonatal outcomes among newborns to mothers living with HIV at Mubende and Fortportal Regional Referral Hospitals.

The third objective of this study was to assess the factors associated with early adverse neonatal outcomes among newborns to mothers living with HIV at Mubende and Fortportal Regional Referral Hospitals. Our study revealed that the presence of a detectable viral load increased the risk of neonatal adverse outcomes (aRR=4.036, CI=1.428-11.406, P=0.008). A Mother that had a detectable viral load was 4.036 times more likely to have early adverse neonatal outcomes. Presence of a detectable viral load is an indicator of inadequate suppression of the virus. The increased risk of adverse outcomes among mothers with a detectable viral load means that mothers in whom the virus is not properly supressed are at higher risk of having adverse ne who reported that Low birth weight was associated with low CD4 count, another indicator of inadequate suppression of the virus. Other studies reported that the risk of unfavourable neonatal outcomes varied between antiretroviral medications. When assessing the advantages and risks of antiretroviral therapy for perinatal HIV prevention in low-income countries, [30-34] found that tenofovir-based ART was linked to greater rates of preterm birth before 34 weeks (6.0% vs. 2.6%), as well as early infant mortality. The effect of ART regimes could not be assessed because all HIV positive mothers enrolled in this study were on the same ART regimen. Some studies reported that mothers on ART were more likely to experience negative newborn outcomes such as stillbirth, preterm delivery and low birth weight [35-38]. For example in Malawi, reported that perinatal mortality was significantly associated with ARV exposure. We could not compare mothers on ART to those not on ART in this study because all the mothers enrolled were already enrolled on ART. Though we compared the timing of ART (Initiation before pregnancy versus initiation after conception), we did not find any significant association.

Strength of the study

This was a prospective cohort done in two centres which increased the internal validity and generalizability of the findings.

Study limitation

All HIV positive mothers in this study were on ART and taking the same regimen (Tenofovir, Lamivudine and dolutegravir) making it impossible to study the effect of ART on adverse neonatal outcomes. The follow up stopped at 7 days, therefore the adverse outcomes occurring after 7 days could not be captured.

CONCLUSION

The incidence of adverse neonatal outcomes was higher in HIV positive mothers, but the difference was not statistically significant. All neonatal adverse outcomes categories were more in the HIV positive mothers with a statistically significant difference noted in prematurity and low birth weight. Having a detectable viral load, significantly increased the risk of having adverse neonatal outcomes.

RECOMMENDATIONS

All HIV positive mothers should be closely monitored to ensure that the viral load is undetectable. Another study should be done to assess the reasons for having detectable viral loads among mothers taking ART. The areas to be assessed should include adherence. Another large prospective study with a longer follow up should be done in order to capture even the neonatal adverse outcomes occurring after 7 days.

REFERENCES

1. Bensimon, G, Lacomblez, L. (1994). *The New England Journal of Medicine Downloaded from nejm.org at KIZ - ABT LITERATURVERWALTUNG on November 21, 2014. For personal use only. No other uses without permission. Copyright © 1994 Massachusetts Medical Society. All rights reserved.*
2. Adachi, K., Nielsen-saines, K., & Klausner, J. D. (2016). *Chlamydia trachomatis Infection in Pregnancy : The Global Challenge of Preventing Adverse Pregnancy and Infant Outcomes in Sub-Saharan Africa and Asia. 2016.*
3. Adesina, O. A., Michael, O. S., Ogunbosi, B. O., Akinyemi, J. O., & Modupe, A. (2015). *AND PRETERM DELIVERY AMONG HIV-INFECTED PREGNANT WOMEN AT THE. 32*(April).
4. Bhutta, Z. A., Darmstadt, G. L., & Lawn, J. E. (2010). Stillbirths – the Global Picture and Evidence-based solutions. *BioMedCentral.*
5. Centers for Disease Control and Prevention. (1981). Kaposi's sarcoma and Pneumocystis pneumonia among homosexual men — New York City and California. *MMWR. Morbidity and Mortality Weekly Report*, *30*(25), 305–308.
6. Ezechi, O. C., Gab-Okafor, C. V., Oladele, D. A., Kalejaiye, O. O., Oke, B. O., Ohwodo, H. O., Adu, R. A., Ekama, S. O., Musa, Z., Onwujekwe, D. I., David, A. N., & Ujah, I. A. (2013). Pregnancy, obstetric and neonatal outcomes in HIV positive Nigerian women. *African Journal of Reproductive Health*, *17*(3), 160–168. https://doi.org/10.1016/s0020-7292(12)60669-9
7. Brogly, S. B., Abzug, M. J., Watts, D. H., Cunningham, C. K., Williams, P. L., Oleske, J., Conway, D., Sperling, R. S., Spiegel, H., & Van Dyke, R. B. (2010). Birth defects among children born to human immunodeficiency virus-infected women: Pediatric AIDS clinical trials protocols 219 and 219C. *Pediatric Infectious Disease Journal*, *29*(8), 721–727. https://doi.org/10.1097/INF.0b013e3181e74a2f
8. Burnett, E., Loucks, T. L., & Lindsay, M. (2015). Perinatal outcomes in HIV positive pregnant women with concomitant sexually transmitted infections. *Infectious Diseases in Obstetrics and Gynecology*, *2015*. https://doi.org/10.1155/2015/508482
9. Fowler, M. G., Qin, M., Fiscus, S. A., Currier, J. S., Flynn, P. M., Chipato, T., McIntyre, J., Gnanashanmugam, D., Siberry, G. K., Coletti, A. S., Taha, T. E., Klingman, K. L., Martinson, F. E., Owor, M., Violari, A., Moodley, D., Theron, G. B., Bhosale, R., Bobat, R., … Mofenson, L. M. (2016). Benefits and Risks of Antiretroviral Therapy for Perinatal HIV Prevention. *New England Journal of Medicine*, *375*(18), 1726–1737. https://doi.org/10.1056/nejmoa1511691
10. Favarato, G., Townsend, C. L., Peters, H., Sconza, R., Bailey, H., Cortina-Borja, M., Tookey, P., & Thorne, C. (2019). Stillbirth in Women Living with HIV Delivering in the United Kingdom and Ireland: 2007-2015. *Journal of Acquired Immune Deficiency Syndromes*, *82*(1), 9–16. https://doi.org/10.1097/QAI.0000000000002087
11. Committee, C. and T. S. A. (CTSA) C. C. E. K. F. (2011). Principles of Community Engagement. *NIH Publication No. 11-7782*, http://www.cdc.gov/ phppo/pce/.
12. Delicio, A. M., Lajos, G. J., Amaral, E., Cavichiolli, F., Polydoro, M., & Milanez, H. (2018). Adverse effects in children exposed to maternal HIV and antiretroviral therapy during pregnancy in Brazil: A cohort study. *Reproductive Health*, *15*(1), 1–16. https://doi.org/10.1186/s12978-018-0513-8
13. Ejigu, Y., Magnus, J. H., Sundby, J., & Magnus, M. C. (2019). Pregnancy outcome among HIV-infected women on different antiretroviral therapies in Ethiopia: A cohort study. *BMJ Open*, *9*(8). https://doi.org/10.1136/bmjopen-2018-027344
14. Ezechi, O., Gab-Okafor, C., Oladele, D., Kalejaiye, O., Oke, B., & Ohwodo, H. (2013). Pregnancy, obstetric and neonatal outcomes in HIV positive Nigerian women. *African Journal of Reproductive Health*, *17*(3).
15. Favarto, G. (2017). Stillbirth in HIV-infected women delivering in UK/Ireland between 2001 and 2015. *Ucl*, *20*(5), 75.
16. Fentie, E. A., Yeshita, H. Y., & Bokie, M. M. (2022). Low birth weight and associated factors among HIV positive and negative mothers delivered in northwest Amhara region referral hospitals, Ethiopia,2020 a comparative crossectional study. *PLOS ONE*, *17*(2), e0263812. https://doi.org/10.1371/journal.pone.0263812
17. González, R., Rupérez, M., Sevene, E., Vala, A., Maculuve, S., Bulo, H., Nhacolo, A., Mayor, A., Aponte, J. J., Macete, E., & Menendez, C. (2017). Effects of HIV infection on maternal and neonatal health in southern Mozambique: A prospective cohort study after a decade of antiretroviral drugs roll out. *PLoS ONE*, *12*(6). https://doi.org/10.1371/journal.pone.017813
18. Gwelo, A. S., & Mbishi, J. V. (2019a). Determinants of adverse neonatal outcomes among postnatal women in Dar es Salaam-Tanzania. *African Health Sciences*, *19*(2), 1924–1929. https://doi.org/10.4314/ahs.v19i2.15
19. Jackson-Gibson, M., Zash, R., Mussa, A., Caniglia, E. C., Diseko, M., Mayondi, G., Mabuta, J., Morroni, C.,

Mmalane, M., Lockman, S., Makhema, J., & Shapiro, R. L. (2022). High risk of adverse birth outcomes among adolescents living with HIV in Botswana compared to adult women living with HIV and adolescents without HIV. *BMC Pregnancy and Childbirth*, *22*(1), 1–9. https://doi.org/10.1186/s12884-022-04687-y

20. Joseph, O., Biodun, O., & Michael, E. (2011). Pregnancy outcome among HIV positive women receiving antenatal HAART versus untreated maternal HIV infection. *J Coll Physicians Surg Pak*, *21*(6).
21. Kebede, T., Dayu, M., & Girma, A. (2022). The Burden of HIV Infection among Pregnant Women Attending Antenatal Care in Jimma University Specialized Hospital in Ethiopia: A Retrospective Observational Study. *Interdisciplinary Perspectives on Infectious Diseases*, *2022*. https://doi.org/10.1155/2022/3483767
22. Kiser, J. J., Carten, M. L., Aquilante, C. L., Anderson, P. L., Wolfe, P., King, T. M., Delahunty, T., Bushman, L. R., & Fletcher, C. V. (2008). The effect of lopinavir/ritonavir on the renal clearance of tenofovir in HIV-infected patients. *Clinical Pharmacology and Therapeutics*, *83*(2), 265–272. https://doi.org/10.1038/sj.clpt.6100269
23. Kochanek, K. D., Murphy, S. L., Xu, J., Arias, E., Ph, D., Evans, C., Jones, C. E., Prendergast, A. J., Larsen, A., Magasana, V., Dinh, T. H., Ngandu, N., Lombard, C., Cheyip, M., Ayalew, K., Chirinda, W., Kindra, G., Jackson, D., Goga, A., … Glass, R. M. (2019). treatment in sub-Saharan Africa (POISE Study). *PLoS ONE*, *13*(1), 1–10. https://doi.org/10.1097/QAI.0000000000001875.Pregnancy
24. Li, H., Liu, J., Tan, D., Huang, G., Zheng, J., Xiao, J., Wang, H., Huang, Q., Feng, N., Zhang, G., & Bakir, M. (2020). Maternal HIV infection and risk of adverse pregnancy outcomes in Hunan province, China: A prospective cohort study. *Medicine (United States)*, *99*(8). https://doi.org/10.1097/MD.0000000000019213
25. Lokken, E. M., Mathur, A., Bunge, K. E., Fairlie, L., Makanani, B., Beigi, R., Noguchi, L., & Balkus, J. E. (2021). Pooled Prevalence of Adverse Pregnancy and Neonatal Outcomes in Malawi, South Africa, Uganda, and Zimbabwe: Results From a Systematic Review and Meta-Analyses to Inform Trials of Novel HIV Prevention Interventions During Pregnancy. *Frontiers in Reproductive Health*, *3*(November). https://doi.org/10.3389/frph.2021.672446
26. Macdonald, E. M., Ng, R., Bayoumi, A. M., Raboud, J., Brophy, J., Masinde, K. I., Tharao, W. E., Yudin, M. H., Loutfy, M. R., Glazier, R. H., & Antoniou, T. (2015). Adverse Neonatal Outcomes Among Women Living With HIV: A Population-Based Study. *Journal of Obstetrics and Gynaecology Canada*, *37*(4), 302–309. https://doi.org/10.1016/S1701-2163(15)30279-6
27. Moodley, T., Moodley, D., Sebitloane, M., Maharaj, N., & Sartorius, B. (2016). Improved pregnancy outcomes with increasing antiretroviral coverage in South Africa. *BMC Pregnancy and Childbirth*, *16*(1), 1–10. https://doi.org/10.1186/s12884-016-0821-3
28. Moyer, C. A., Kolars, C. K., Oppong, S. A., Bakari, A., Bell, A., & Busingye, P. (2016). International Journal of Gynecology and Obstetrics Predictors of stillbirths and neonatal deaths in rural western Uganda. *Internat*, *134*, 190–193.
29. Odongkara, B., Nankabirwa, V., Ndeezi, G., Achora, V., Arach, A. A., Napyo, A., Musaba, M., Mukunya, D., Tumwine, J. K., & Thorkild, T. (2022). Incidence and Risk Factors for Low Birthweight and Preterm Birth in Post-Conflict Northern Uganda: A Community-Based Cohort Study. *International Journal of Environmental Research and Public Health*, *19*(19), 12072. https://doi.org/10.3390/ijerph191912072
30. Olusanya, B. O., & Solanke, O. A. (2009). *Predictors of term stillbirths in an inner-city maternity hospital in Lagos , Nigeria*. *April*, 1243–1251. https://doi.org/10.3109/00016340903287474
31. Phanuphak, N., & Phanuphak, P. (2016). History of the prevention of mother-to-child transmission of HIV in Thailand. *Journal of Virus Eradication*, *2*(2), 107–109. https://doi.org/10.1016/s2055-6640(20)30470-2
32. Pons-Duran, C., Casellas, A., Bardají, A., Valá, A., Sevene, E., Quintó, L., Macete, E., Menéndez, C., & González, R. (2021). Adolescent, pregnant, and hiv-infected: Risk of adverse pregnancy and perinatal outcomes in young women from southern mozambique. *Journal of Clinical Medicine*, *10*(8). https://doi.org/10.3390/jcm10081564
33. Rempis, E. M., Schnack, A., Decker, S., Braun, V., Rubaihayo, J., Tumwesigye, N. M., Busingye, P., Harms, G., & Theuring, S. (2017). Option B+ for prevention of vertical HIV transmission has no influence on adverse birth outcomes in a cross-sectional cohort in Western Uganda. *BMC Pregnancy and Childbirth*, *17*(1), 1–12. https://doi.org/10.1186/s12884-017-1263-2.
34. Riemer, L. J., Le Roux, S. M., Harrison, M. C., & Tooke, L. (2020). Short-term outcomes of HIV-exposed and HIV-unexposed preterm, very low birthweight neonates: a longitudinal, hospital-based study. *Journal of Perinatology*, *40*(3), 445–455. https://doi.org/10.1038/s41372-019-0541-4
35. Santosa, W. B., Staines-urias, E., Tshivuila-matala, C. O. O., & Norris, S. A. (2019). *Perinatal outcomes associated with maternal HIV and antiretroviral therapy in pregnancies with accurate gestational age in South Africa. October 2018*. https://doi.org/10.1097/QAD.0000000000002222.

36. Sharp, P. M., & Hahn, B. H. (2011). Origins of HIV and the AIDS pandemic. *Cold Spring Harbor Perspectives in Medicine*, *1*(1), 1–22. https://doi.org/10.1101/cshperspect.a006841
37. Shava, E., Moyo, S., Zash, R., Diseko, M., Dintwa, E. N., Mupfumi, L., Mabuta, J., Mayondi, G., Chen, J. Y., Lockman, S., Mmalane, M., Makhema, J., & Shapiro, R. (2019). Brief Report: High Rates of Adverse Birth Outcomes in HIV and Syphilis Coinfected Women in Botswana. *Journal of Acquired Immune Deficiency Syndromes*, *81*(5), E135–E140. https://doi.org/10.1097/QAI.0000000000002082
38. Sikakulya, F. K., Kiyaka, S. M., Masereka, R., & Ssebuufu, R. (2021). Alobar Holoprosencephaly with Cebocephaly in a Neonate Born to an HIV-Positive Mother in Eastern Uganda. *Case Reports in Otolaryngology*, *2021*, 1–4. https://doi.org/10.1155/2021/7282283

CITE AS: Bataringaya Geoffrey Tabu, Fernando Perez Ramirez, Ddamulira Adam, Eilu Emmanuel and Ugwu Okechukwu Paul-Chima (2024). Incidence and Determinants of Adverse Neonatal Outcomes among HIV-Positive Pregnant Women: A Prospective Cohort Study at Regional Referral Hospitals in Uganda. NEWPORT INTERNATIONAL JOURNAL OF PUBLIC HEALTH AND PHARMACY, *5* (2): 21-35. https://doi.org/10.59298/NIJPP/2024/523942135