Original Article

Maternal and Obstetric Complications among HIV-infected Women Treated with Highly Active Antiretroviral Treatment at a Regional Hospital in Durban, South Africa

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Abstract

Introduction: HIV is the leading cause of maternal deaths in resource-poor countries. The use of highly active antiretroviral treatment (HAART) has been shown to almost eliminate vertical transmission and improve maternal health outcomes. Its effect on direct obstetric conditions has not been well documented. **Methods:** We conducted a retrospective study of women who delivered at a regional hospital from April 1, 2011, to April 30, 2014. We employed a stratified random selection, where the first 50 files recorded in the birth register during each calendar month were chosen, at a ratio of one HIV uninfected for every 4 infected women. **Results:** We analyzed files belonging to 302 HIV-uninfected women and 1159 HIV-infected women. The latter were further subdivided into those who used zidovudine, n = 424; those who initiated HAART prepregnancy, n = 312; and those who initiated in-pregnancy HAART, n = 423. We found that despite the use of HAART, HIV-infected women were at increased risk of both respiratory and lower genital tract infections (P = 0.009 and 0.001 respectively), compared to HIV-uninfected women. The women receiving HAART before pregnancy had an increased risk of preterm births (P = 0.004), and poor perinatal outcomes (P = 0.002); however, postpartum complications were reduced (P = 0.023). There was a trend toward an increased risk of preeclampsia (P = 0.064). **Conclusion:** The initiation of HAART before pregnancy reduces the frequency of postpartum complications. However, compared to HIV-negative women, women receiving HAART prepregnancy remained at risk of infectious morbidity, had poor perinatal outcomes, and may also be at an increased risk of preeclampsia.

Keywords: *Highly active antiretroviral treatment, maternal, obstetric, outcomes*

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Introduction

HIV-related complications are the leading cause of maternal mortality in resource-poor countries.[1,2] Reduction of global maternal mortality ratio as well as ending the AIDS epidemic are among the targets in the sustainable development goals set out by the United Nations.[3] In a review of maternal deaths in Botswana by Ray *et al*., it was found that 64% (36/56) deaths were HIV infected and that 59% had died of HIV-related causes. The initial reports of the national committee on confidential enquiries into maternal deaths (NCCEMD) in South Africa (SA) indicated that HIV accounts for 40.5% of maternal deaths, mostly secondary to tuberculosis (TB).[4] Furthermore, in a study of the maternal deaths occurring at a regional hospital in Durban, SA by Ramogale *et al*. found the 3 leading causes among HIV-infected women to be puerperal sepsis, pneumonia, and TB.[5]

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Before the introduction of highly active antiretroviral treatment (HAART) for immunocompromised pregnant women in SA, the national data on institutional maternal deaths showed a worsening trend in the 3 triennial periods spanning 2002–2010 from 55 to 66.2 and 71.3/100 thousand live births.[1,4] However, with most women now accessing HAART during pregnancy since 2010 (55% of HIV-infected women compared to 36% in the previous triennium), there was a 12.6% overall reduction in maternal deaths, and notably, a 25% reduction in deaths due to nonpregnancy-related infections, including AIDS.[1]

Thus, the use of HAART in pregnancy has been hailed as one of the most effective interventions that has led to the reduction in maternal deaths in resource-limited countries. However, it is possible that both direct and indirect effects of HAART on other pregnancy-related comorbidities may begin to emerge. The initial use of nevirapine (NVP) as part of the 3 drug regimen used as HAART for pregnant women was accompanied by increasing reports of fatal hepatotoxicity directly linked to the drug.[6] An earlier study found that the use of NVP at higher CD4 counts was associated with higher risk of hepatotoxicity.[7] Other direct side effects during pregnancy from antiretroviral drugs have been anemia mainly from zidovudine and lactic acidosis associated with stavudine.[6]

Even though the data show improved maternal mortality rates as a result of HAART, treated women may still die from the disease. The latest NCCEMD report showed that 54.7% of the HIV-infected women who died were receiving HAART.[1] In addition, the institutional maternal mortality rate (iMMR) for HIV-infected women remains high. Chweneyagae reported higher iMMR in HIV infected compared to uninfected women, for both obstetric hemorrhage (OH) and hypertensive disorders of pregnancy (HDP) (38.4 compared to 17.2 and 27.4 compared to 18.8/100,000 live births, respectively).[8] Deaths due to these 2 conditions, which are direct causes of maternal mortality, are still higher in women taking HAART than those not accessing HAART.[1]

With many reports indicating worse outcomes for HIV-infected untreated women, the literature on the use of HAART has not been matched with an equal enthusiasm in reporting expected improved outcomes. There are a limited number of publications which have tracked the improvement in maternal outcomes with the use of HAART;[9] in addition, these reports focus mainly on perinatal outcomes[10] and not on the effect of HIV or its treatment on direct obstetric complications such as preeclampsia, OH, and gestational diabetes.

Therefore, the aim of this audit was to determine maternal and obstetric complications in women receiving HAART, initiated before or during pregnancy in a resource-constraint setting.

Methods

This was a retrospective study of records of HIV infected and uninfected women delivering at King Edward VIII regional hospital, over a 3 year period (April 2011 to April 2014). This facility is one of the large metropolitan specialist-run hospitals in the city of Durban, SA, with about 600 deliveries per month. The HIV seroprevalence among obstetric patients in the hospital is 40%–45%, the highest in the province (38%), or in SA as a country (29.7%).[11] We used a stratified random sampling method where for each month during the stipulated study period, we identified the first 50 patients recorded in the birth register (i.e., the first 40 HIV-infected women and the first 10 HIV-uninfected women). Of the 1800 patients identified, we were only able to retrieve 1474 case records (due to missing files and others with incomplete data).

During the stipulated study period, the drug regimen for pregnant women infected with HIV was HAART if CD4 counts were <350 cells/mm^3; otherwise, women would receive 300 mg of zidovudine twice daily during the antenatal period and a single dose of 200 mg NVP in labor (termed dual therapy). In the period of April 2011–April 2012, HAART for women with CD4 <350 cells/mm^3 included NVP, whereas NVP was subsequently replaced by efavirenz (EFV) from April 2012 to April 2013. From the year 2013 onward, all women regardless of CD4 counts received fixed-dose combination, made up of EFV, tenofovir, and emtricitabine. All information regarding maternal condition and obstetric outcomes were recorded, and the outcomes of interest were grouped into themes according to systems. For fetal or neonatal outcomes, we recorded only the gestational age at delivery as well as whether the fetus was stillborn (above 500 g), alive, or an early neonatal death (within 7 days of birth) occurred. Routine tests performed during pregnancy were also recorded, including full blood count, syphilis serology, and HIV test with CD4 counts where applicable. TB screening is performed on verbal enquiry, and no active screening for sexually transmitted infections (apart from syphilis) is routinely performed.

Definitions

Outcomes were grouped as follows:

- Anemia was graded according to WHO classification of mild (10–10.9 g/dl), moderate (7–9.9) and severe (4–6.9), and very severe anemia (<4 g/dl)

- Thrombocytopenia was defined as a platelet count <150 cells/microliter
- Hypertensive diseases of pregnancy included all cases of gestational hypertension, preeclampsia, eclampsia, and the HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets)
- Antepartum hemorrhage included all cases recorded as antepartum hemorrhage, placenta previa, and placental abruption
- Lower genital tract infections (LGTIs) included all cases recorded as abnormal vaginal discharges, vaginal warts, and Bartholin' s abscess
- Respiratory tract infections (RTI) included all cases recorded as pneumonia (all forms), chest infection, upper and lower RTI, and pulmonary TB
- Urinary tract infections (UTI) included all cases recorded as UTI, cystitis, and pyelonephritis
- "Other medical" conditions included all other cases – meningitis, epilepsy, asthma, diabetes mellitus, renal impairment, and liver abnormalities (not related to preeclampsia)
- "Other obstetric" conditions included all other complications in pregnancy such as chorioamnionitis and twin gestations
- Postpartum complications included postpartum hemorrhage, puerperal sepsis, lower genital tract tears, and retained placenta
- Preterm birth (PTB) was defined as birth before 37 weeks, and early preterm delivery included all births above 500 g and below 34 weeks of gestation
- Stillbirths included both macerated and fresh stillbirths, with a weight of >500 g
- Early neonatal deaths included all deaths of infants >500 g, occurring within 7 days of birth
- Perinatal morality rate (PNMR) included all stillbirths, and early neonatal deaths, per 1000 births.

Statistical considerations and data analysis

For both binary and continuous endpoints, an anticipated sample size of ~960 was required to achieve a 80% power, to detect a small effect size (W) of 0.11 for a category outcome (stillbirth or postpartum bleeding) by regimen using a 1° of freedom Chi-square test with a significance level (alpha) of 0.05 or 5%. This would require 240 HIV-uninfected patients. Data were entered on an excel spreadsheet and transposed into SPSS (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp.) for statistical analysis.

Continuous variables were summarized using mean and standard deviation (SD). Categorical data are represented using frequency tables. One-way analysis of variance (ANOVA) was used to identify significant differences in continuous explanatory variables (gestational age and birth weight) across the 4 regimen groups. Where the data were not normal, then, the nonparametric equivalent of the ANOVA was used. Categorical explanatory variables were cross-tabulated against group, and significant association will be identified using the standard Pearson's Chi-square test. Statistical significance was assessed at $P < 0.05$.

The study was approved by the Biomedical Research Ethics Committee of the University of KwaZulu Natal (BE 510/14).

Results

One thousand four hundred and sixty-one case files with complete data were analyzed – 1159 infected and 302 HIV uninfected. Of the HIV infected women, 424 received "dual therapy" during pregnancy (i.e., antenatal twice daily 300 mg of zidovudine and a single dose of 200 mg NVP during labor). The remainder $n = 735$ received HAART – 423 initiated during pregnancy (termed in-pregnancy HAART group [IPH], and 312 initiated before the index pregnancy, termed prepregnancy HAART group, [PPH]).

The demographic profile of the women was significantly different, with HIV-infected women older than uninfected (mean = 28.2 years, SD = 5.7, compared to 24.4, SD = 6.33, $P = 0.001$), as shown in Table 1. HIV-infected women also had higher parity than uninfected, 1.5, SD = 1.1 compared to 0.9, SD = 1.2, $P < 0.0001$. Among HIV-infected women, the PPH group was also significantly older and also had higher parity than those falling pregnant on no treatment, as shown in Table 2.

There was no difference in the prevalence of thrombocytopenia when comparing HIV uninfected and infected, or the latter according to treatment groups, $P = 0.885$ and 0.106, respectively.

Other maternal conditions

LGTI occurred more frequently among HIV infected compared to uninfected (odds ratio [OR] =1.88, 95% confidence intervals [CI] =1.26–2.82, $P = 0.001$) and in addition were more prevalent in women who had been on HAART before pregnancy (OR = 1.61, 95% CI = 0.99–2.63, $P = 0.042$), compared to HIV uninfected. However, the HIV treatment groups were similar, $P = 0.826$.

RTI was significantly higher among HIV-infected women compared to uninfected, 3.45% compared to 0.66%, $P = 0.009$ and even higher when looking at PPH group of HIV infected compared to uninfected women, 4.5% versus 0.66%, $P = 0.0001$. In a univariate

Table 1: HIV infected versus uninfected

Clinical Characteristics	HIV negative (*n*=302)	All HIV positive (*n*=1159)	PPH (*n*=312)	OR (95% CI) *P* < 0.05	
				All versus negative	PPH versus negative
Age, mean (SD)	24.4 (6.33)	28.2 (5.7)	30.2 (5.28)	0.01	0.006
Parity, mean (SD)	0.9 (1.15)	1.5 (1.14)	1.83 (1.21)	<0.0001	0.033
Anemia <11 g/dl (at booking), *n* (%)	117/275 (42.5)	589/1094 (53.8)	139/298 (46.6)	1.58 (1.2-2.08)	1.18 (0.84-1.67)
				0.0008	0.324
Anemia <11 g/dl (at delivery), *n* (%)	104/241 (43.2)	477/944 (50.5)	125/257 (48.6)	1.35 (1-1.81)	1.25 (0.86-1.8)
				0.041	0.219
Platelets (baseline), mean (SD)	246 (78.3)	237 (74.7)	235 (78.3)	0.482	0.336
Platelets <150, *n* (%)	16/187 (8.6)	59/717 (8.3)	41/717 (5.7)	0.96 (0.52-1.78)	0.65 (0.34-1.24)
				0.885	0.155
Perinatal outcomes					
Gage at delivery, mean (SD)	37.8 (2.96)	37.2 (3.39)	37.01 (3.6)	0.023	0.029
Preterm birth <37 weeks (*n*=343; 23%), *n* (%)	51 (16.9)	291 (25)	192 (26.1)	1.65 (1.17-2.33)	1.72 (1.33-3.01)
				0.003	0.0004
Preterm <34 weeks, *n* (%)	21 (6.95)	125 (10.8)	94 (12.8)	1.62 (0.98-2.70)	1.69 (0.94-3.06)
				RR 1.09 (1.01-1.17)	0.06
				0.047	
PNMR (*n*=57) (5 NNDs + 52 SB), *n* (%)	12 (3.97)	45 (3.88)	38 (5.2)	0.98 (0.49-1.97)	1.14 (0.49-2.67)
				0.942	0.752
Cesarean section, *n* (%)	152 (50.3)	556 (47.9)	356 (48.4)	0.91 (0.7-1.18)	0.93 (0.67-1.29)
				0.465	0.631
Maternal outcomes, *n* (%)					
HDP (*n*=245; 16.7%)	65 (21.5)	180 (15.5)	112 (15.2)	0.67 (0.48-0.93)	0.68 (0.44-1/04)
				0.013	0.064
APH (*n*=63; 4.3%)	19 (6.3)	44 (3.8)	32 (4.4)	0.59 (0.33-1.06)	0.81 (0.39-1.68)
				0.057	0.534
Medical, *n* (%)					
RTI (*n*=42; 2.9%)	2 (0.66)	40 (3.45)	33 (4.5)	5.36 (1.26-32.25)	10.27 (2.29-64.17)
				0.009	0.0001
UTI (*n*=132; 9%)	31 (10.3)	101 (8.7)	63 (8.6)	0.83 (0.54-1.3)	0.60 (0.32-1.12)
				0.403	0.083
STIs (*n*=257; 17.6%)	34 (11.3)	223 (19.2)	140 (19.1)	1.88 (1.26-2.82)	1.61 (0.99-2.63)
				0.001	0.042
Other med (*n*=103)	18 (5.9)	85 (7.3)	17 (5.5)	1.25 (0.72-2.19)	0.91 (0.44-1.89)
				0.406	0.784
Postpartum complications (*n*=72)	11 (3.64)	61 (5.3)	9 (2.9)	2.39 (1.2-4.49)	0.79 (0.30-2.08)
				0.007	0.602

PPH=Prepregnancy HAART group; NNDs=Neonatal deaths; SB=Stillbirth; HDP=Hypertensive diseases of pregnancy; APH=Antepartum hemorrhage; STIs=Sexually transmitted infections; RTI=Respiratory tract infection; UTI=Urinary tract infection; HAART=Highly active antiretroviral treatment; SD=Standard deviation; CI=Confidence interval; OR=Odds ratio; PNMR=Perinatal mortality rate; RR=Relative risk

analysis, controlling for HIV status, RTIs remained significantly more prevalent in women who initiated HAART prepregnancy, $P = 0.0006$. Among the RTI cases ($n = 42$), 16 were confirmed cases of TB, giving an incidence rate of 1.09%. These were mainly among HIV-infected women (with only one case among HIV uninfected), most of whom were receiving HAART (11/15).

The prevalence of other medical conditions (other than infectious and including asthma, epilepsy, and diabetes mellitus) was not statistically different according to HIV status, $P = 0.406$.

Obstetric conditions

HDP including gestational hypertension, preeclampsia, and eclampsia were significantly lower among HIV-infected women than the uninfected group, 15.5%

Table 2: All HIV infected

	Dual (*n*=424)	IPH (*n*=423)	PPH (*n*=312)	OR (95% CI) *P*	
				PPH versus dual	PPH versus IPH
Age, mean (SD)	27.1 (5.73)	27.9 (5.68)	30.2 (5.28)	0.001	0.049
Parity	1.4 (0-5)	1.4 (1-7)	1.8 (0-9)	0.022	0.028
Anemia <11g/dl (at booking), *n* (%)	126/376 (33.5)	106/403 (26.3)	74/297 (24.9)	0.82 (0.62-1.08)	0.93 (0.65-1.33)
				0.144	0.678
Anemia <11g/dl (delivery), *n* (%)	107/336 (31.9)	94/351 (26.8)	54/256 (21.1)	0.69 (0.51-0.94)	0.73 (0.49-1.09)
				0.014	0.107
Platelets (booking), mean (SD)	251 (79.1)	250 (77.2)	235 (78.3)	0.367	0.562
TCP <150, *n* (%)	18/233 (7.7)	19/282 (6.7)	22/202 (10.9)	1.11 (0.6-2.05)	1.69 (0.85-3.37)
				0.733	0.106
CD4, mean (SD)	444 (219.9)	373 (214.1)	398 (186)	0.046	0.384
Perinatal outcomes					
Gest age delivery	37.5 (2.7)	37.1 (3.79)	37 (3.6)	0.224	0.563
Preterm birth <37 weeks (*n*=291; 25%), *n* (%)	99/417 (23.7)	103/417 (21.8)	89/308 (28.9)	0.95 (0.711.27)	1.24 (0.88-1.75)
				0.727	0.205
Preterm <34 weeks, *n* (%)	31 (7.3)	55 (13)	39 (12.5)	1.85 (1.19-2.9)	0.95 (0.60-1.51)
				0.004	0.834
PNMR (*n*=45), *n* (%)	7 (1.65)	24 (5.67)	14 (4.49)	3.25 (1.38-8.04)	0.78 (0.38-1.6)
				0.002	0.472
Cesarean section, *n* (%)	200 (47.2)	205 (48.5)	151 (48.4)	1.05 (0.82-1.35)	1.0 (0.74-1.35)
				0.677	0.985
Maternal outcomes, *n* (%)					
HDP (*n*=180; 15.5%)	68 (16)	63 (14.9)	49 (15.7)	0.94 (0.67-1.32)	1.06 (0.7-1.63)
				0.717	0.762
APH (*n*=44; 3.8%)	12 (2.8)	16 (3.8)	16 (5.1)	1.56 (0.77-3.25)	1.38 (0.64-2.95)
				0.191	0.376
Medical, *n* (%)					
RTI (*n*=42; 2.9%)	7 (1.65)	13 (3.1)	20 (6.4)	6.51 (2.71-16.36)	2.16 (1.01-4.68)
				<0.0001	0.031
UTI (*n*=132; 9%)	38 (8.9)	43 (10.2)	20 (6.4)	0.95 (0.61-1.48)	0.61 (0.34-1.08)
				0.820	0.072
STIs (*n*=257; 17.6%)	83 (19.6)	87 (20.6)	53 (17)	0.97 (0.71-1.32)	0.79 (0.53-1.17)
				0.826	0.221
Other med (*n*=103)	36 (8.5)	32 (7.6)	17 (5.5)	0.77 (0.48-.23)	0.70 (0.37-1.34)
				0.251	0.256
Postpartum complications	28 (6.6)	24 (5.7)	9 (2.9)	0.42 (0.18-0.95)	0.50 (0.21-1.14)
				0.023	0.072

IPH=In-pregnancy HAART group; PNMR=Perinatal mortality rate; TCP=Thrombocytopenia; PPH=Prepregnancy HAART group; HAART=Highly active antiretroviral treatment; SD=Standard deviation; CI=Confidence interval; OR=Odds ratio; HDP=Hypertensive diseases of pregnancy; APH=Antepartum hemorrhage; STIs=Sexually transmitted infections; RTI=Respiratory tract infection; UTI=Urinary tract infection

compared to 21.5% (OR = 0.67, 95% CI = 0.48–0.93; *P* = 0.013). However, among the HIV treatment groups, there was no difference in the prevalence of HDP, *P* = 0.717 and 0.762. Compared to HIV uninfected women, HIV-treated (PPH and IPH) women were still at lower risk for prevalence of HDP, *P* = 0.015. However, when comparing the HIV uninfected with HIV infected who received dual therapy, the reduction in prevalence was no longer significant (OR = 0.7, 95% CI = 0.47–1.03, *P* = 0.059). Furthermore, there was no difference when comparing the PPH group with dual therapy.

Although antepartum hemorrhage (APH) was lower among HIV-infected women, this was not statistically significant (3.8% compared to 6.3% in those uninfected, OR = 0.59, 95%CI = 0.33–1.06, *P* = 0.057). HAART did not also make a significant difference in prevalence of APH, among women with HIV infection.

Postpartum complications, including postpartum hemorrhage and puerperal sepsis, were significantly higher in HIV-infected women, $P = 0.007$, particularly when not receiving HAART, $P = 0.023$. Of the 9 cases of postpartum hemorrhage, one was HIV uninfected, while all the 8 cases of puerperal sepsis were among HIV-infected women.

Perinatal outcomes

The overall rate of PTBs was 23%, being higher in HIV infected than uninfected, 25% compared to 16.9%, $P = 0.003$, including when comparing HIV treated and untreated separately with HIV uninfected, $P = 0.0004$ and 0.026, respectively. The same pattern persisted when looking at early PTB below 34 weeks, which was higher in HIV-infected women, especially if receiving HAART. Among the HIV treatment groups, the rate of PTB was similar ($P = 0.727$) however was HAART before pregnancy, significantly increased the risk of very early PTB <34 weeks, $P = 0.002$. The PNMR was similar between HIV infected and uninfected (3.88% versus 3.97% for HIV positive and negative respectively, $P = 0.942$). However, among HIV infected, HAART use (before and during pregnancy) was associated with a higher PNMR, $P = 0.010$. In a subanalysis of the HIV groups, prepregnancy HAART was significantly associated with higher PNMR, when compared to women receiving <3 drugs (OR = 3.25, 95% CI = 1.38–8.04, $P = 0.002$).

Caesarean section rates were similar among all groups examined.

Discussion

The high rates of anemia (53.8%) found in the study was of a mild nature and in keeping with findings of other local studies.[12] In a comparable setting and population, Nandlal *et al*. found higher rates of anemia of 64.2% among HIV-infected women at antenatal booking, which persisted or developed postpartum in 35%–59% of patients.[12] The current study shows higher rates of anemia in women not treated with HAART, whereas those treated with HAART before pregnancy were comparable to HIV uninfected women. Adeniran *et al*. found a high prevalence of anemia in women initiating HAART during pregnancy compared to those who accessed HAART prepregnancy, 35.2% compared to 0.9%, $P < 0.01$.[9]

The study found a lower prevalence of HDP in women infected with HIV, including those who received HAART. This is in keeping with previous reports, which indicated that HIV-infected women have lower rates of preeclampsia.[13] Although no significant differences existed among the HIV treatment groups, when compared to the HIV uninfected, the risk of preeclampsia was still lower in the HAART treated group, $P = 0.015$, but not the untreated group, $P = 0.059$. Earlier studies indicated the increased risk of preeclampsia in women accessing HAART, but most of these had no HIV-uninfected controls.[14,15] In our previous analysis, we showed that HIV infection, particularly immunosuppression, was significantly associated with lowered prevalence of preeclampsia/eclampsia syndrome and that HAART seemed to increase the risk.[16] It is therefore not surprising that in this study, HDP was not significantly different between HIV-uninfected women and those women who were infected but not requiring HAART (receiving dual therapy), $P = 0.059$.

In the current study, we also found no definite differences in APH between HIV infected or uninfected. In our previous report, we found an increased risk of postpartum but not antepartum hemorrhage in HIV-infected women.[17] However, a meta-analysis by Calvert and Ronsmans showed a higher incidence of APH (which was not related to placenta abruptio or previa) but not postpartum hemorrhage.[18]

As expected, the current study further showed increased rates of infectious morbidity, particularly RTIs and LGTIs among HIV infected compared to uninfected women. The former was higher, especially in women receiving HAART, even significantly higher in those who initiated HAART before pregnancy. This could indicate the immune reconstitution inflammatory syndrome, mainly, the cases of TB, as well as other pneumonias (where TB was missed). The prevalence of TB (1.1% of maternities) in this cohort was higher than earlier reports of 0.1%–0.6% of maternities in the same institution in the pre-HAART era.[19] This is of concern as this may reflect poor screening for TB in HIV-infected women, which may be unmasked as the immune system improves. More recently, Black *et al*. found that 7.7% of women initiating HAART during pregnancy had TB.[20] Adult studies have shown that initiation of HAART at very low CD4 counts may be associated with more morbidity and even mortality.[21] Of the 396 deaths from TB in the last NCCEMD report, 50.7% were receiving HAART.[1] Delayed detection of TB may result in increased morbidity and mortality despite the use of isoniazid preventative therapy and may eventually lead to isoniazid resistance.

We also found that LGTIs during pregnancy were higher among HIV-infected women, even those who received HAART before pregnancy, and presumably immune restored. Moodley *et al*., in a similar population, but using more sensitive screening methods, found a much higher prevalence of 32% of sexually transmitted infections during pregnancy.[22] In the latter study, more

than 50% of the infections were asymptomatic, which may explain the lower rate in our study where diagnosis was made clinically.

The association between HIV and PTBs found in our study is in keeping with other reports, which have indicated that this relationship is particularly associated with the use of prepregnancy HAART.[10] A recent local study, however, did not find such associations; instead, they reported improved perinatal outcomes in women accessing HAART.[23]

The current study is unique in that it focuses on overall general maternal conditions, occurring in pregnant women receiving HAART. While previous studies have concentrated mainly on perinatal outcomes related to HAART use, there has not been many on the effect of HAART on direct obstetric conditions, such as HDP and OH. In addition, the impact of immune reconstitution in women accessing HAART on the development of infectious complications as found in this study has not been reported before and needs further research. Our attempts to further differentiate women according to the antiretroviral drugs used, as well as whether HAART was initiated before or during index pregnancy, is also an important aspect of this study.

Because of the retrospective nature of the study, we acknowledge the inherent limitation of available information that has not been specifically related to the study objectives. However, all efforts were made to ensure that the captured study data inform the objectives. Second, most of the conditions reported in the study are as in the records, and therefore, standardization of diagnostic methods and definitions was not possible.

Conclusion

Prepregnancy use of HAART improved maternal outcomes such as low rates of anemia and postpartum complications; however, the study showed an increased risk of preeclampsia, preterm deliveries, and subsequent poor perinatal outcomes. In addition, HAART may also unmask coinfections such as TB.

Recommendations

We recommend increased vigilance for obstetric complications and tighter screening methods for coinfections such as TB. Further prospective studies should control for confounding factors to document the impact of HAART use on maternal and obstetric outcomes are needed.

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Conflicts of interest

There are no conflicts of interest.

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