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Comorbidities in pregnant South African women living with HIV and associations with adverse birth outcomes: a prospective cohort study

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Abstract

Background Despite improved health and survival due to lifelong antiretroviral therapy (ART), women living with HIV (WHIV) still face lower life expectancy, partly due to increased non-communicable disease (NCD) risk. Both HIV and NCDs are linked to adverse birth outcomes, yet data on their combined impact are limited. We investigated NCD burden by HIV status and compared adverse birth outcomes in pregnant WHIV only versus HIV-NCD comorbidity in Cape Town, South Africa.

Methods Pregnant WHIV ($n=479$) and without HIV ($n=510$) were enrolled and prospectively followed for pregnancy outcome. Weight and height measurements were serially collected by a study nurse, and diagnoses of hypertension and diabetes mellitus (DM) were made by healthcare providers as part of routine care (ANC). Birth outcomes were abstracted from health records. Proportions described adverse outcomes between groups. Logistic regression was used to estimate associations between HIV and HIV-NCD with small for gestational age (SGA), large for gestational age (LGA), preterm delivery (PTD), low birthweight (LBW), and high birthweight (HBW) (reference: group with neither HIV nor NCDs).

Results Among 989 pregnant women, 48% ($n=479$) with HIV (median age 29 years, IQR 25–34), the prevalence of obesity (BMI ≥ 30 kg/m^2) was 43%, hypertension 15% and DM 2%. The NCD prevalence did not differ by HIV status. HIV co-occurred with obesity in 31% of pregnancies, with hypertension in 5% and with DM in 0.2%. HIV with hypertension and HIV with hypertension and obesity were associated with increased odds of PTD compared to those with neither HIV-NCD (aOR 3.03, 95% CI 1.01, 8.05 and aOR 2.67, 95% CI 1.08, 6.23, respectively). However, HIV and obesity together were associated with lower odds of SGA (aOR 0.39, 95% CI 0.16, 0.97). Likewise, in women without HIV, obesity protected against SGA and LBW, but hypertension increased PTD and LBW.

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Conclusion There was no difference in the prevalence of NCD in pregnant women by HIV status. Increased risk of adverse birth outcomes was demonstrated with concurrent NCD regardless of HIV status. Integration of NCD screening and management within ANC could minimise excess adverse outcomes in high HIV burden settings.

Keywords Pregnancy, Obesity, Hypertension, Diabetes, HIV, Adverse birth outcomes

Background

The global nutritional transition and urbanization have led to higher population body mass index (BMI) and an increased risk of non-communicable diseases (NCDs) such as obesity, hypertension (HTN) and DM [1, 2]. In South Africa (SA), approximately 68% of women ≥ 15 years are overweight/obese [3]. For women of childbearing age, pregnancy is a window for the development of NCDs over a life course. For example, gestational weight gain is associated with postpartum weight retention, which is increasingly being recognised as a contributor to obesity [4, 5]. In addition, gestational hypertension and DM are associated with an increased risk of overt HTN and DM in later life [6, 7]. In a large Denmark population-based cohort study, a history of gestational DM was associated with 3 times the hazard of HTN and 7 times the risk of type 2 DM during the 39-year follow-up period [8]. Another large survey found that women with hypertensive disorders of pregnancy, including gestational HTN and pre-eclampsia, had a substantially increased risk of developing chronic HTN in the years following delivery. Specifically, within 10 years postpartum, 21% of women with gestational HTN and 22.9% with pre-eclampsia developed HTN, compared to just 10.5% of women with normotensive pregnancies [9].

Despite improved health outcomes and higher survival rates among women living with HIV (WHIV) due to lifelong antiretroviral therapy (ART), this population still has lower life expectancy compared to their HIV-negative counterparts, in part due to heightened risk of NCDs [10, 11]. In Africa, in WHIV, the prevalence of DM is estimated to be 3.19% higher than the general population [12, 13]. Pregnant WHIV have also been reported to have an increased risk of DM during pregnancy [13, 14]. In Zambia, pregnant women on ART were shown to have a higher risk of gestational HTN than both those without HIV and treatment-naïve WHIV [15]. In addition to the putative impact of HIV on the risk of NCDs, growing evidence suggests that newer ART classes such as integrase strand transfer inhibitors (INSTI) are associated with excessive weight gain, which would compound the risk of NCDs in WHIV [16, 17]. There are limited data comparing the burden of NCDs among pregnant WHIV and those without HIV in sub-Saharan Africa.

Independently, HIV and NCDs are among the leading obstetric risks associated with adverse birth outcomes [18–20]. Specifically, HIV/ART exposures in pregnancy have been shown to be associated with spontaneous preterm delivery (PTD), low birth weight (LBW), and small size for gestational age (SGA) [21–23]. In contrast, adverse birth outcomes associated with maternal obesity include large for gestational age (LGA) and high birthweight (HBW) infants and medically indicated PTD [24, 25]. DM in pregnancy is associated with HBW, LGA, PTD and risk of caesarean sections [26, 27], whereas hypertensive pregnancies have been reported to be associated with stillbirth, PTD, SGA and neonatal death [28–31]. However, there are limited data on the interplay of HIV/ART and these NCDs on adverse birth outcomes in sub-Saharan Africa, where HIV is most common.

To address this evidence gap, we conducted a cohort study in pregnant WHIV and without HIV enrolled at the first antenatal care (ANC) visit in Cape Town, South Africa, to compare the burden of NCDs (obesity, DM and HTN) in pregnant WHIV and without HIV. We also investigated the association between having HIV with or without NCDs and adverse birth outcomes vs. having neither HIV/NCDs.

Methods

Study design and population

In this prospective cohort study, we enrolled consecutive pregnant women with and without HIV (1:1 ratio) attending ANC services at the Gugulethu Community Health Centre, a primary healthcare facility, in Cape Town, South Africa, from January 2017 to July 2018. Eligibility criteria included women aged ≥ 18 years who were attending their first ANC visit, regardless of gestational age. The majority of WHIV were on efavirenz-based ART (73%) (see **Maternal HIV and ART History questionnaire**). The integrase inhibitor, dolutegravir (DTG), was only introduced to first-line ART regimens in 2020 in South Africa [32]. Gugulethu is an urban community with approximately 300,000 residents and is characterized by predominantly low socioeconomic status (SES). The participants were followed prospectively through face-to-face interviews. We collected self-reported diagnoses of HTN and DM during their ANC visits, which were confirmed on folder review (see **Maternal Medication Use and Side Effect Questionnaire**). The study aimed to collect data across four visits; however, for very late-booked pregnancies, only two data collections were conducted. Efforts were made to track the outcomes of women who were referred to higher levels of care for their routine ANC visits through folder reviews. According to the most recent data, ANC HIV Sentinel Survey,

HIV seroprevalence among pregnant women in the Western Cape remained relatively consistent, changing only modestly from 15.9% in 2017 to 16.3 in 2022 [33].

Data on infant gestational age and birth weight were abstracted from the birth records at the delivery facilities. For the birth outcomes analysis, we included women with live singleton pregnancies. We excluded 101 pregnancies (multiple births, women who withdrew from the study, women without HIV at enrolment who seroconverted to HIV during pregnancy and those without a birth outcome) (Fig. 1a**)** and (Fig. 1b)The study was approved by the University of Cape Town (UCT) Faculty of Health Sciences Human Research Ethics Committee (HREC 541/2015, 345/2022) and the Western Cape Department of Health (WC_2016RP6_286). All participants provided written informed consent prior to study participation.

Exposure assessment (HIV and HIV- NCD comorbidity)

Maternal HIV status was self-reported at enrolment and confirmed by HIV rapid testing as per standard of care. Women without HIV at enrolment who seroconverted during the study (i.e. having a positive HIV rapid assay after a previous negative test) were excluded. Three NCDs were included: obesity, HTN and diabetes. Weight and height measurements were taken by trained nurses as part of routine clinical care. Measured weight was corrected for gestational age (GA) to allow for the estimation of pre-conception BMI as described by Santos et al. [34]. Briefly, standard gestational weight gain (GWG) charts, which account for estimated GA during measurement and corresponding BMI categories, were utilized to adjust the weight measured at the first ANC visit. The estimated pre-conception BMI was then calculated

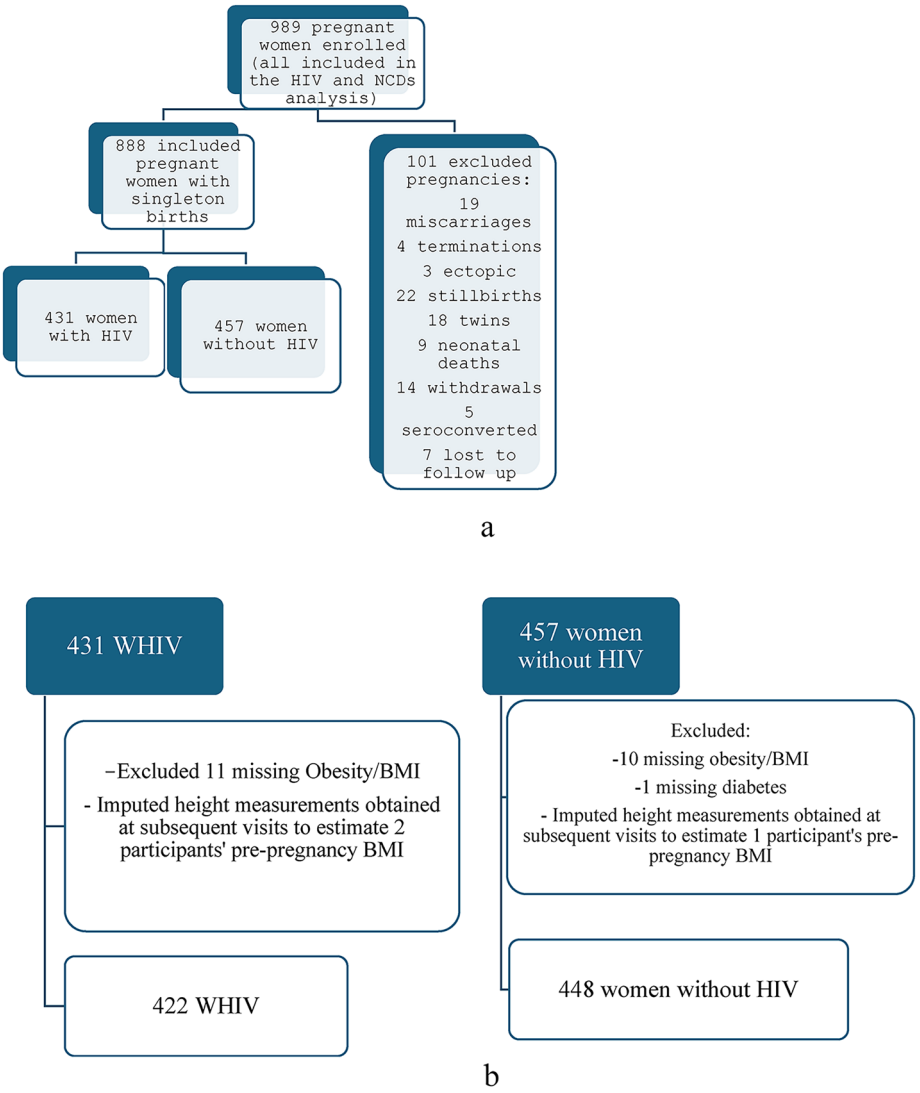


Fig. 1 (**a**) Flow diagram showing the selection of pregnant women with and without HIV (**b**)Flow diagram showing the selection of pregnant women with and without HIV included in the adverse birth outcomes analysis

by dividing the GA-corrected weight by the square of the height and categorized as underweight (< 18.5 kg/m²), normal weight (18.5–24.9 kg/m²), overweight (25–29.9 kg/m²), and obese (≥ 30 kg/m²) [35].

For incident HTN, blood pressure measurements were taken by healthcare providers as part of routine care during the four ANC visits. Blood pressure was classified: normotensive for systolic/diastolic < 120/80 mmHg, and hypertensive for systolic ≥ 120mmHg or diastolic ≥ 80 mmHg. In addition, data on chronic HTN were obtained from medical records.

Chronic DM data were obtained from medical records, and incident DM was self-reported throughout ANC visits and checked against medical records. Chronic and gestational/incident HTN and DM were considered together in the analysis because there was insufficient data to consider each individually. We defined HIV-NCD comorbidity as living with HIV and one NCD (i.e., HIV with obesity OR HTN OR DM); two NCDs (HIV with obesity AND HTN; HIV with obesity AND DM; and HIV with HTN AND DM) or three NCDs (HIV with obesity AND HTN AND DM).

Outcome assessment (adverse birth outcomes)

Gestational age (GA) was assessed by obstetric ultrasound at enrolment. We calculated delivery GA by adding the weeks between enrolment and delivery to the GA recorded at the first ANC visit. Preterm delivery was defined as birth at < 37 completed weeks of gestation [36]. We obtained the birthweight from medical records. Birthweight was categorized as low (< 2500 g), normal (2500–3999 g) and high (≥ 4000 g) [37]. Size for gestational age was categorized in percentiles according to the INTERGROWTH-21st Project norms using GA at birth, birthweight and sex [38] as follows: small for gestational age (SGA) (< 10th percentile weight for gestational age at birth), appropriate for gestational age (AGA) (10-90th percentile) and large for gestational age (LGA) (> 90th percentile weight for gestational age at birth) (see **Obstetrics Abstraction Form** for all birth outcomes).

Covariables

Questionnaires administered by trained study staff were used to obtain demographic and clinical data, substance use and timing of ART initiation. SES was determined using a composite score based on education level, employment status, housing type, and availability of amenities such as a toilet, running water, electricity, fridge, telephone, and television (see **Maternal Demographics and Clinical History Questionnaire**). Participants were then categorized into tertiles representing the lowest, middle, and highest SES groups. Education status was assessed in categories of 'completed high school' or 'did not complete high school'. We assessed alcohol consumption using the **Alcohol Use Disorders Identification Test (AUDIT)** and added the Xhosa and Afrikaans translations, and 'yes' referred to the participants who reported alcohol use after discovering the pregnancy [39]. Gravidity was categorised as 1 for a single past pregnancy, 2 for having been pregnant twice before and ≥ 3 for three or more past pregnancies. Parity (number of previous births where pregnancy was known to have reached viable GA) was categorised as 0 for those who had never given birth before, 1 for having given birth once and ≥ 2 for two or more past births. Relationship status was self-reported and categorized as 'not in a relationship,''not cohabiting/married but in a relationship,' and 'cohabiting/married'. ART initiation timing was determined by combining recorded maternal ART history with gestational age at the first ultrasound. Women were classified as initiating ART "pre-conception" if ART start dates preceded the dates of conception, or as initiating "during pregnancy" if ART was commenced thereafter.

Data analysis

All data were analysed using R Studio 4.1.1 (R Foundation, Vienna, Austria). We summarised baseline characteristics in the overall samples by HIV status, and in WHIV we further summarised characteristics by NCD status. Continuous variables were presented using the medians and interquartile ranges (IQR), and categorical variables were presented in proportions. Differences between variables were assessed using the Wilcoxon test for continuous variables and the Chi-squared test for categorical variables. To examine the burden of individual NCDs and comorbid NCDs (e.g. HTN AND obesity, HTN AND diabetes) by HIV status, we used proportions. Among WHIV, we studied NCD prevalence by ART initiation timing.

In the second analysis, we compared the proportion of adverse birth outcomes (LBW, HBW, SGA, LGA and PTD) in WHIV only (without NCDs) vs. WHIV plus one or more NCDs.

To compare the associations between having HIV only and HIV-NCD comorbidity with adverse birth outcomes, we used binomial and multinomial logistic regression; women living with neither HIV nor NCDs (disease-free) were a reference group across all models. We repeated the same analyses in women without HIV to examine whether NCDs had a similar impact on adverse birth outcomes. All models were adjusted for a minimally sufficient set of confounders i.e. maternal age, parity and SES, identified a priori. Regression data were reported using adjusted odds ratios (aOR) and 95% confidence intervals (CI).

Results

This analysis included 989 participants, 48% of whom were WHIV ($n = 479$). At the first ANC visit, the median age was 29 years (IQR 25–34), GA at first ANC presentation was 17 weeks (IQR 13, 22), and 21% were primigravid (Table 1.). The median pre-conception BMI was 29 kg/m^2 (IQR 24, 34), with 24% overweight and 43% obese. Among WHIV, 61% initiated ART pre-conception ($n = 291$) and 39% post-conception ($n = 188$). WHIV were older compared to those without HIV (62% >30 years vs. 38%, $p < 0.001$), had higher gravidity (59 vs. 42%, $p < 0.001$) and parity (49 vs. 34%, $p < 0.001$), and were more likely to not to have completed high school (71 vs. 60%, $p = 0.001$) compared to women without HIV.

The overall prevalence of obesity (pre-conception BMI ≥ 30 kg/m^2) was 43%, 15% for HTN, and 2% for diabetes. There were no statistically significant differences in the proportions of obesity, HTN or DM in women with and without HIV (Table 1.) and when all NCDs and NCD combinations were studied exclusively (Fig. 2**).**

Among WHIV, WHIV + NCDs were older (73% vs. 60% ≥30 years) compared to those with HIV only (Table 2). A greater proportion of WHIV + NCDs presented earlier in pregnancy (41% in the first trimester for HIV + obesity + HTN, 30% WHIV + HTN) compared to WHIV only (7%). Employment rates were lower in some HIV + NCDs groups (e.g. HTN + obesity, 44%) compared to those with HIV only (57%). 58% vs. 41% of WHIV + HTN were married/cohabiting compared to WHIV with no NCDs.

The prevalence of HIV with one NCD was observed at 31% for HIV + obesity, 5% for HIV + HTN, and 0.2% for HIV + DM (Fig. 2). When examining the prevalence of HIV with two NCDs, the rates were 9% for HIV + obesity + HTN, 0.2% for HIV + obesity + diabetes, and 0.4% for HIV + HTN + diabetes. Lastly, the prevalence of HIV in conjunction with all three NCDs was found to be 0.6%. Among WHIV, we studied NCDs by looking at whether ART was started pre-conception or during pregnancy. In this cohort, most WHIV had initiated ART pre-conception, regardless of whether they also had an NCD. Approximately 62% of WHIV without NCDs were on ART before conception, compared to similar proportions among those with NCDs. There was 54% in WHIV with obesity only, 79% in WHIV with HPT only and 66% in WHIV + obesity + HTN (Table 2). It also follows that NCDs were more common in those who started ART pre-conception compared to during pregnancy, for example, 79% vs. 0% in HTN, 54% vs. 3% in obesity and 66% vs. 2% in 3% in HTN + obesity.

In women without HIV, women with NCDs were generally older, with medians ranging from 28 to 29 years compared to a median of 24 years in women without NCDs (Table 3). Those with obesity tended to be 30 years or more (48% in obesity only, and 37% in HTN only). Women with NCDs had a slightly higher gravidity and parity with women in NCD groups having 3 or more past pregnancies and births than those without NCDs (gravidity ≥ 3: 46% obesity only, 60% HTN + obesity, vs. 31% in those without NCDs). Education and SES indicators showed mixed trends. In most NCD groups, a higher proportion of women had completed high school (up to 81% – 100% vs. 56% in those without NCDs). Alcohol use was low and did not vary across all groups. Gestational age at booking was similar across groups, with most women in both categories presenting in the second semester.

Adverse birth outcomes

Overall, we found a total of 10% PTD, 10% LBW, 4% HBW, 11% SGA and 10% LGA. PTD proportions were consistently elevated in pregnancies with both HIV and one NCD compared to those with HIV alone (e.g., HIV + hypertension: 26% vs. 12%, $p = 0.023$) and in pregnancies with HIV and 2 NCDs compared with HIV alone (e.g., HIV + HTN + obesity: 23% vs. 12%, $p = 0.026$) (Fig. 3). The prevalence of PTD was even lower among individuals with neither HIV nor NCDs (10%) (Fig. 4).

Having HTN only was associated with 16% PTD. The prevalence of LBW tended to be higher in pregnancies with HIV and one NCD relative to HIV alone (HIV + HTN: 17% vs. 13%, $p = 0.077$) but not different, neither in pregnancies with HIV + 2 NCDs compared with HIV alone (HIV + HTN + obesity: 15% vs. 13%, $p = 0.898$). The prevalence of LBW was even lower among individuals without HIV or NCDs (12%), but was more common in women with HTN only (28%).

HBW and LGA were both more frequently observed in pregnancies with HIV and one NCD compared to WHIV only. Specifically, in WHIV + obesity, the prevalence of HBW was 8% compared to 4% in HIV alone ($p = 0.032$), and the prevalence of LGA was 15% compared to 7% in HIV alone ($p = 0.031$). HBW was even lower in women with neither HIV nor NCDs (5%). In women without HIV, LGA prevalence was common in those with HTN + obesity (19%) and obesity only (17%) (Fig. 4). However, the prevalence of LBW and SGA was lower in WHIV + obesity (LBW: 13% in WHIV only vs. 6% in WHIV + obesity, $p = 0.032$; SGA: 14% in WHIV only vs. 6% in WHIV + obesity, $p < 0.033$) compared to WHIV only.

Adjusting for maternal age, parity and SES using those with neither HIV nor NCDs as a reference, having HIV alone was not significantly associated with adverse birth outcomes (Table 4). In WHIV, ART initiation timing was not significantly associated with any adverse birth outcomes (Additional Table 1). However, in WHIV, NCDs were associated with some adverse birth outcomes in comparison to women without either. In WHIV,

Table 1 Maternal characteristics among study participants, overall and by HIV status (n = 989)

Maternal characteristics	Total n = 989 (%)	HIV status		*Chi²P-value*
		WHIV n = 479 (%)	Without HIV = 510 (%)	
GA at presentation (weeks)				
Median (IQR)	17 (13, 22)	17 (12, 21)	18 (13, 23)	
(≤13)1st trimester	292 (23)	159 (33)	138 (27)	0.03
(14-28) 2nd trimester	621 (63)	296 (72)	334 (65)	
(>28) 3rd trimester	60 (6)	22 (5)	38 (7)	
Missing	2 (0)	2 (0)	0	
Age (years)				
Median (IQR)	29 (25, 34)	31 (26, 35)	27 (23, 32)	
≤24	210 (21)	59 (12)	151 (30)	<0.001
≥25-29	289 (29)	124 (26)	165 (32)	
≥30	490 (50)	296 (62)	194 (38)	
Gravidity				
Median (IQR)	2 (2, 3)	3 (2, 3)	2 (1, 3)	
1	205 (21)	69 (14)	136 (27)	< 0.001
2	287 (29)	126 (26)	161 (32)	
≥3	497 (50)	284 (59)	213(42)	
Parity				
Median (IQR)	1 (0, 2)	1 (1, 2)	1 (0, 2)	< 0.001
1	205 (21)	69 (14)	136 (27)	
2	287 (29)	126 (26)	161 (32)	
≥2	407 (41)	234 (49)	173 (34)	
Pre-conception BMI				
Median (IQR)	29 (24, 34)	29 (24, 34)	29 (24, 35)	< 0.001
Missing	26 (3)	10 (2)	16 (3)	
Education				
Completed high school	319 (32)	133 (28)	186 (36)	0.001
Did not complete	646 (65)	341 (71)	305 (60)	
Missing	24 (2)	5 (1)	19 (4)	
*SES				
Lower	325 (33)	173 (36)	152 (30)	0.071
Middle	274 (28)	132 (28)	142 (28)	
Higher	388 (39)	173 (36)	215 (42)	
Missing	2 (0.2)	1 (0.2)	1 (0.2)	
Employment status				
Yes	423 (43)	202 (42)	221 (43)	0.761
No	566 (57)	277 (58)	289 (57)	
*Alcohol use				
Yes	89 (9)	435(91)	46 (9)	0.982
No	898 (91)	1 (0.2)	463 (91)	
Missing	2 (0.2)		1 (0.2)	
Relationship status				
No relationship	46 (5)	23 (5)	23 (5)	0.874
Not Cohabiting/marrie but in a relationship	509 (51)	242 (51)	267 (52)	
Cohabiting/married	428 (43)	210 (44)	218 (43)	
Missing	6 (1)	4 (1)	2 (0.4)	
*Maternal morbidity				
HTN	145 (15)	71 (15)	74 (15)	0.961

Table 1 (continued)

Maternal characteristics	Total n = 989 (%)	HIV status		*Chi²P-value*
		WHIV n = 479 (%)	Without HIV = 510 (%)	
DM	21 (2)	7 (1)	14 (3)	0.237
Obesity	428 (43)	192 (40)	236 (46)	0.556

Missing data: obesity n=11 (1%) DM and obesity n=1 (0.1%). Values for some characteristics may not be equal to 100 because of rounding.*Alcohol use "yes" is based on drinking after finding out about pregnancy*Maternal morbidity is based on ever meeting the criteria for a condition at any point during the data visits i.e. obesity = pre-conceptio BMI ≥30 kg/m^2, hypertension = systolic ≥120mmHg or diastolic ≥ 80 mmHg, DM= obtained from medical records and self-reported throughout antenatal visits and checked against medical records.* SES was determined using a composite score based on education level, employment status, housing type, and availability of amenities. Abbreviations: GA = Gestational age, WHIV = Women with HIV, IQR = Interquartile range, BMI = Body-mass index, SES =Socio-economic status, DM = Diabetes mellitus, HTN = Hypertension

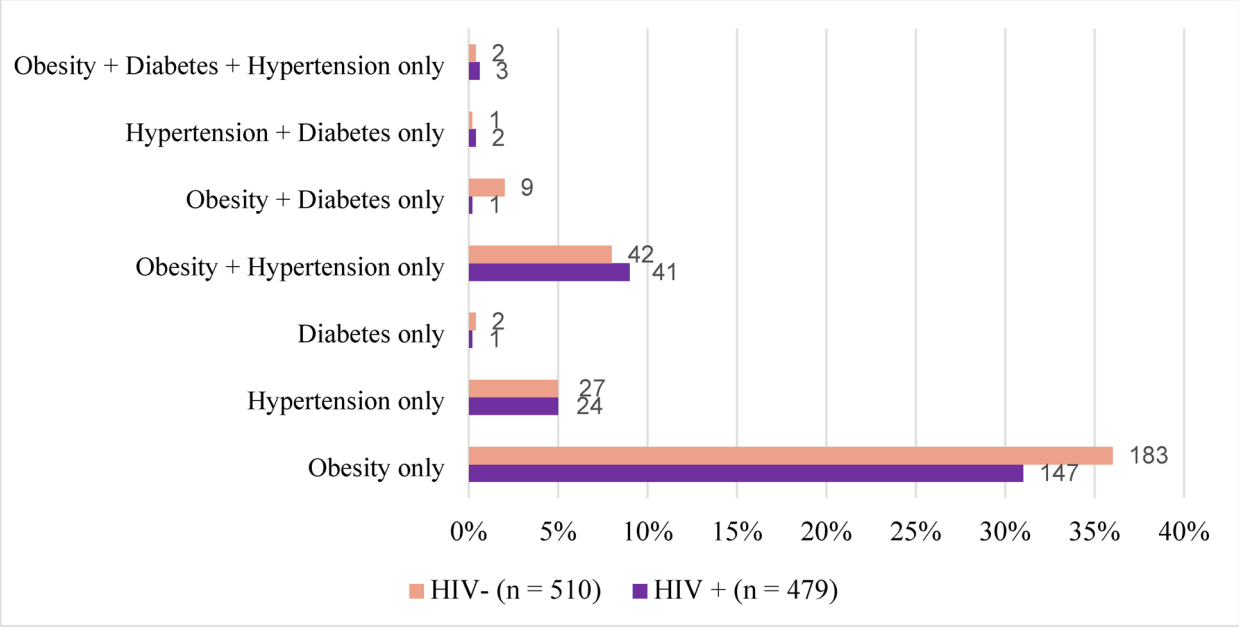


Fig. 2 Non-communicable diseases proportions by HIV status in the study (n = 989).Diabetes and hypertension were combined irrespective of chronicity due to their small proportions. Maternal morbidity is based on ever meeting the criteria for a condition at any point during the data visits i.e. obesity = pre-conception BMI ≥30 kg/m^2, hypertension = systolic ≥120mmHg or diastolic ≥ 80 mmHg, Diabetes= obtained from medical records and self-reported throughout antenatal visits and checked against medical records

hypertension was associated with increased odds of PTD compared to those with neither NCDs nor HIV (aOR 3.01, 95% CI 1.01, 8.05), with a similar increase for those who also had obesity (aOR 2.67, 95% CI 1.08, 6.23) (Table 4).

Adjusting for the same variables in WHIV, obesity was significantly associated with lower odds of SGA (aOR 0.39, 95% CI 0.16, 0.97) compared to those with neither NCD nor HIV.

In women without HIV, HTN + obesity was associated with more PTD (aOR 3.18, 95% CI 1.21, 7.90) (Table 5). Obesity alone was associated with less LBW and SGA compared to those with neither HIV nor NCDs (LBW aOR 0.24, 95% CI 0.14, 0.78; SGA aOR 0.41, 95% CI 0.19, 0.92). In women without HIV, LBW was significantly higher in women with HTN (aOR 2.74, 95% CI: 1.03, 7.24).

When comparing WHIV with NCDs to those with the same NCDS but without HIV, we found no statistically significant differences in adverse birth outcomes (Table 6). For PTD, aOR ranges from 0.72 (95% CI 0.24–2.15) for HIV + HTN + obesity to aOR 2.28 (95% CI 0.46–12.8) for HIV + HTN. All with p values > 0.55. Similar patterns were observed for LBW, where estimates ranged from 0.51 to 2.02, none, reaching statistical significance.

Discussion

In an urban community in Cape Town, we found no difference in the prevalence of NCDs (HTN, DM and obesity) in pregnancy by HIV status, with approximately one-third of WHIV having obesity. In WHIV, having one or two NCDs increased the risk of some adverse birth outcomes relative to those who had HIV alone. In particular, HTN only and HIV + HTN + obesity were associated with more PTD. However, obesity seemed

Table 2 Maternal non-communicable disease morbidity in women living with HIV (*n* = 468)

Maternal characteristics	WHIV without NCDs	NCDs		
	HIV only *n* = 249 (%)	HTN only *n* = 24 (%)	Obesity only *n* = 147 (%)	HTN + obesity only *n* = 41 (%)
GA at presentation (weeks)				
Median (IQR)	17 (12, 21)	18 (12, 21)	18 (12, 21)	16 (13, 21)
1st trimester (≤13)	81 (7)	9 (38)	44 (30)	17 (41)
2ndtrimester (14-28)	10 (4)	4 (17)	6 (40)	2 (5)
3rdtrimester (>28)	158 (63)	11 (46)	95 (65)	22 (54)
Missing	0	0	2 (1)	0
Age (years)				
Median (IQR)	31 (26, 35)	30 (26, 35)	32 (26, 35)	31 (27, 35)
≤24	33 (13)	3 (13)	18 (12)	4 (10)
≥25 – 29	66 (27)	8 (33)	38 (26)	7 (17)
≥30	150 (60)	13 (54)	91 (62)	30 (73)
Gravidity				
Median (IQR)	3 (2, 3)	3 (1, 3)	2 (2, 3)	3 (2, 3)
1	33 (13)	3 (13)	25 (17)	5 (12)
2	75 (30)	6 (25)	34 (23)	7 (17)
≥3	141 (57)	15 (62)	88 (60)	29 (22)
Parity				
Median (IQR)	1 (1, 2)	1 (1, 2)	1 (0, 2)	1 (1, 2)
0	44 (18)	3 (13)	27 (18)	5 (12)
1	91 (37)	7 (29)	48 (33)	11 (27)
≥2	114 (46)	14 (58)	72 (49)	25 (61)
Education				
Completed high school	179 (72)	19 (79)	100 (68)	29 (71)
Did not complete	67 (27)	5 (21)	46 (31)	11 (27)
Missing	3 (1)	0	1 (1)	1 (2)
*SES				
Lower	91 (37)	9 (38)	49 (33)	13 (32)
Middle	66 (27)	9 (38)	40 (27)	13 (32)
Higher	91 (37)	6 (25)	58 (39)	15 (37)
Missing	1 (0.4))		0	0
Employment status				
Yes	143 (57)	15 (104)	84 (57)	23 (56)
No	106 (43)	9 (38)	63 (43)	18 (44)
*Alcohol use				
Yes	226 (91)	18 (75)	136 (93)	37 (90)
No	23 (9)	5 (25)	11 (7)	4 (10)
Missing	1 (0.4)	1 (0.4)	0	0
Relationship status				
No relationship	9 (4)	0	11 (7)	2 (5)
Not Cohabiting/married	137 (55)	8 (33)	70 (48)	18 (44)
Cohabiting/married	101 (41)	14 (58)	66 (45)	21 (51)
Missing	2 (0.6)	2 (9)	0	0
ART initiation timing				
During pregnancy	18 (7)	0	5 (3)	1 (2)
Pre-conception	154 (62)	19 (79)	95 (54)	27 (66)
Missing	77 (31)	5 (21)	47 (32)	13 (32)

Values for some characteristics may not be equal to 100 because of rounding.Missing data: BMI n=11, removed from the total WHIVDM groups: DM only (n=1), HPT + DM only (n=2), DM + obesity only (n=1) and HPT + DM + obesity (n=3) were excluded from the table due to small sample sizes. Abbreviation: NCD = Non-communicable disease, HTN = Hypertension, DM = Diabetes mellitus, IQR = Interquartile range, BMI = Body-mass index*Alcohol use "yes" is based on drinking after finding out about pregnancy* SES was determined using a composite score based on education level, employment status, housing type, and availability of amenities

Table 3 Maternal non-communicable disease morbidity in women without HIV (*n* = 499)

Maternal characteristics	Without HIV/NCDs	NCDs		
	***n* = 233 (%)**	**HTN only *n* = 27 (%)**	**Obesity only *n* = 183 (%)**	**HTN + Obesity only *n* = 42 (%)**
GA at presentation (weeks)				
Median (IQR)	16 (13, 21)	17 (14, 21)	18 (12, 21)	16 (13, 22)
(≤13) 1st trimester	59 (25)	7 (32)	50 (27)	16 (38)
(14-28) 2nd trimester	156 (67)	18 (67)	121 (66)	22 (52)
(>28) 3rd trimester	18 (7)	2 (1)	12 (7)	4 (18)
Missing	0	0	0	0
Age (years)				
Median (IQR)	24 (23, 33)	28 (26, 35)	28 (26, 34)	29 (27, 33)
≤24	99 (42)	8 (30)	35 (19)	7 (17)
≥25 – 29	78 (33)	9 (33)	61 (33)	11 (26)
≥30	56 (24)	10 (37)	87 (48)	24 (57)
Gravidity				
Median (IQR)	3 (2, 3)	3 (1, 3)	2 (2, 3)	3 (2, 3)
1	85 (36)	6 (25)	32 (17)	9 (21)
2	75 (32)	7 (26)	66 (36)	8 (19)
≥3	73 (31)	14 (52)	85 (46)	25 (60)
Parity				
Median (IQR)	1 (1, 2)	1 (1, 2)	1 (0, 2)	1 (1, 2)
0	102 (44)	7 (26)	42 (23)	11 (26)
1	72 (31)	10 (37)	70 (38)	10 (24)
≥2	57 (24)	10 (37)	71 (49)	21 (50)
Education				
Completed high school	131 (56	22 (81)	115 (63)	26 (62)
Did not complete	93 (40)	5 (19)	60 (33)	15 (36)
Missing	9 (4)	0	8 (4)	1 (2)
*SES				
Lower	66 (28)	9 (33)	54 (30)	16 (38)
Middle	63 (27)	9 (33)	52 (28)	10 (24)
Higher	103 (44)	12 (44)	77 (42)	16 (38)
Missing	1 (0.4))	0		0
Employment status				
Yes	102 (44)	9 (33)	85 (46)	15 (36)
No	131 (56)	18 (67)	98 (54)	27 (64)
*Alcohol use				
Yes	21 (9)	4 (15)	14 (8)	3 (7)
No	211 (91)	23 (85)	169 (92)	39 (93)
Missing	0	0	0	0
Relationship status				
No relationship	15 (6)	0	3 (2)	5 (5)
Not Cohabiting/married	136 (58)	18 (67)	89 (49)	12 (29)
Cohabiting/married	80 (34)	9 (33)	91 (50)	25 (60)
Missing	2 (1)		0	0

Values for some characteristics may not be equal to 100 because of rounding.Missing data: BMI n=10, obesity n=1, removed from the total women without HIVDM groups: DM only (n=2), HPT + DM only (n=1), DM + obesity only (n=9) and HPT + DM + obesity (n=2) were excluded from the table due to small sample sizes. Abbreviation: NCD = non-communicable disease, HTN = hypertension, DM = diabetes mellitus, IQR = interquartile range, BMI = body-mass index*Alcohol use "yes" is based on drinking after finding out about pregnancy* SES was determined using a composite score based on education level, employment status, housing type, and availability of amenities

protective against SGA. We observed that NCDs had a similar impact in women without HIV. Having HTN only produced approximately 3 times more LBW compared to having no disease, whereas HTN + obesity produced over 3 times more PTD. Having obesity only protected against SGA and LBW. Our additional analysis comparing WHIV with NCDs to those with NCDs alone did not show a statistically significant differences in the risk of adverse outcomes. This suggests that the elevated risk of adverse outcomes such as PTD or LBW were primarily

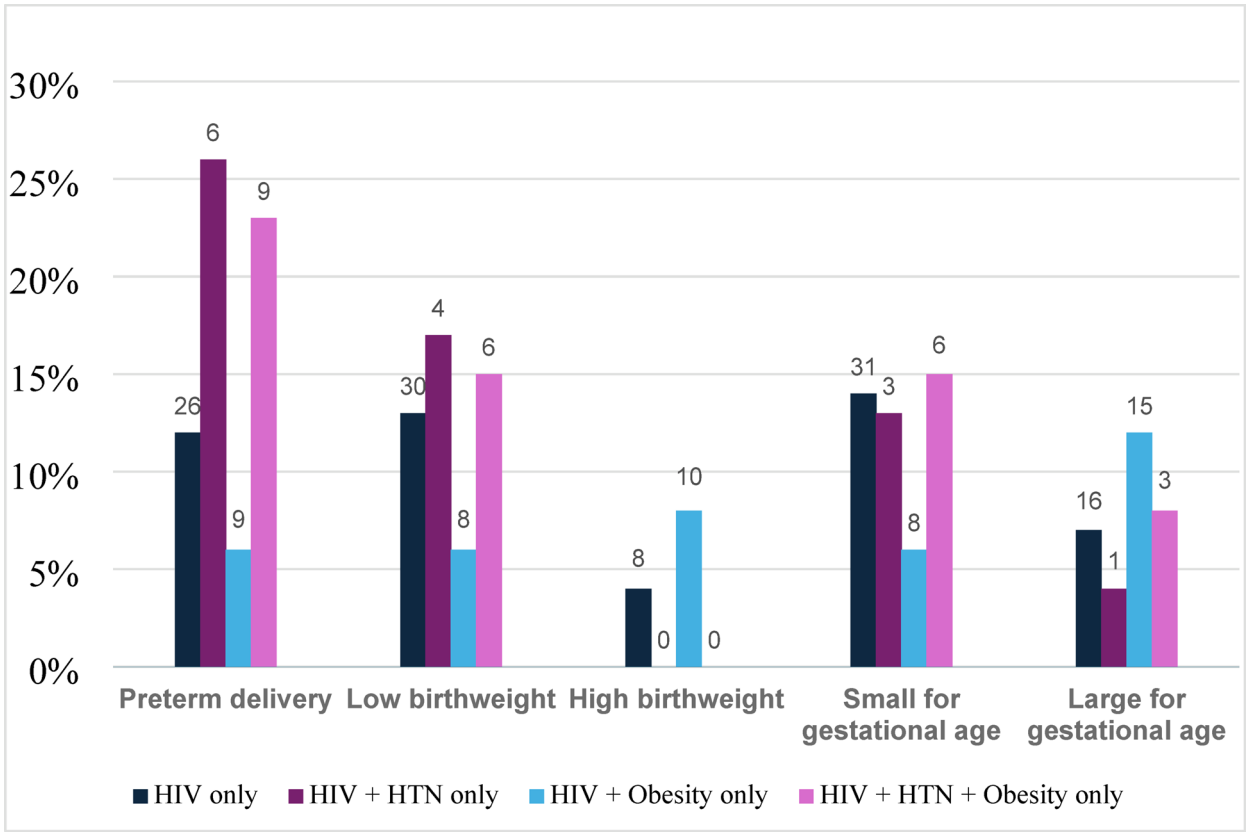


Fig. 3 Proportions of adverse outcomes in WHIV and HIV-NCD comorbidity (n = 422). Abbreviation: NCD = Non-communicable disease, HTN = Hypertension, ANC = Antenatal care, WHIV = Women with HIV, PTD = Preterm delivery, LBW = Low birthweight, HBW = High birth weight, SGA = Small for gestational age, LGA = Large for gestational age. Maternal morbidity is based on ever meeting the criteria for a condition at any point during the data visits i.e. obesity = pre-conception BMI ≥30 kg/m^2, hypertension = systolic ≥120mmHg or diastolic ≥ 80 mmHg, DM obtained from medical records and self-reported throughout antenatal visits and checked against medical records. Groups that included DM were excluded from the graphical birth outcome analyses due to very small numbers, which limited meaningful interpretation and impaired the clarity of visual presentations

associated with the presence of NCDs themselves, irrespective of HIV status.

We found that HTN prevalence was similar in WHIV and in those not living with HIV. While there was a higher prevalence of HTN + obesity, HTN + DM and HTN + obesity + DM in WHIV than in those not living with HIV, the results were not significantly different. These findings contrast with the literature that reports a higher occurrence of HTN, DM and obesity in WHIV than in the general population, due to ART use and HIV-related inflammation [40–43]. Recent literature has shown links between the elevated prevalence of NCDs such as HTN in WHIV and the mediative role of ART-related weight gain since the switch to dolutegravir-based ART [43, 44]. A study in China documented abdominal fat accumulation during ART follow-up, correlating with incident HTN [45]. However, our study data were collected before the transition to dolutegravir-based ART, where efavirenz-based ART predominated.

While the HIV-NCDs comorbidity in our study diverged from the trends indicative of more NCDs in WHIV, our results may have been influenced by the high proportion of overweight and obesity in the study population [46]. Regardless of HIV status, elevated BMI in the population may be a key factor underlying the distribution of NCDs observed in the results. With a median BMI of 29 kg/m^2, most participants, regardless of their HIV status fell in the top end of overweight, with nearly half of the participants having obesity. Other South African studies indicate that most women present at ANC with an unhealthy BMI and an overall elevated prevalence of obesity [3, 47]. Urbanization and its accompanying dietary transition in the low-middle income countries (LMICs) may explain the high obesity prevalence observed in low-income settings such as ours [2].

The high prevalence of pre-conception ART initiation across WHIV, regardless of NCD status, highlights the success of HIV treatment programs in this urban South African setting. Chronic immune activation and inflammation from HIV, exacerbated by ART, have been shown to lead to vascular and metabolic dysfunctions, increasing the risk of immune-mediated conditions such as

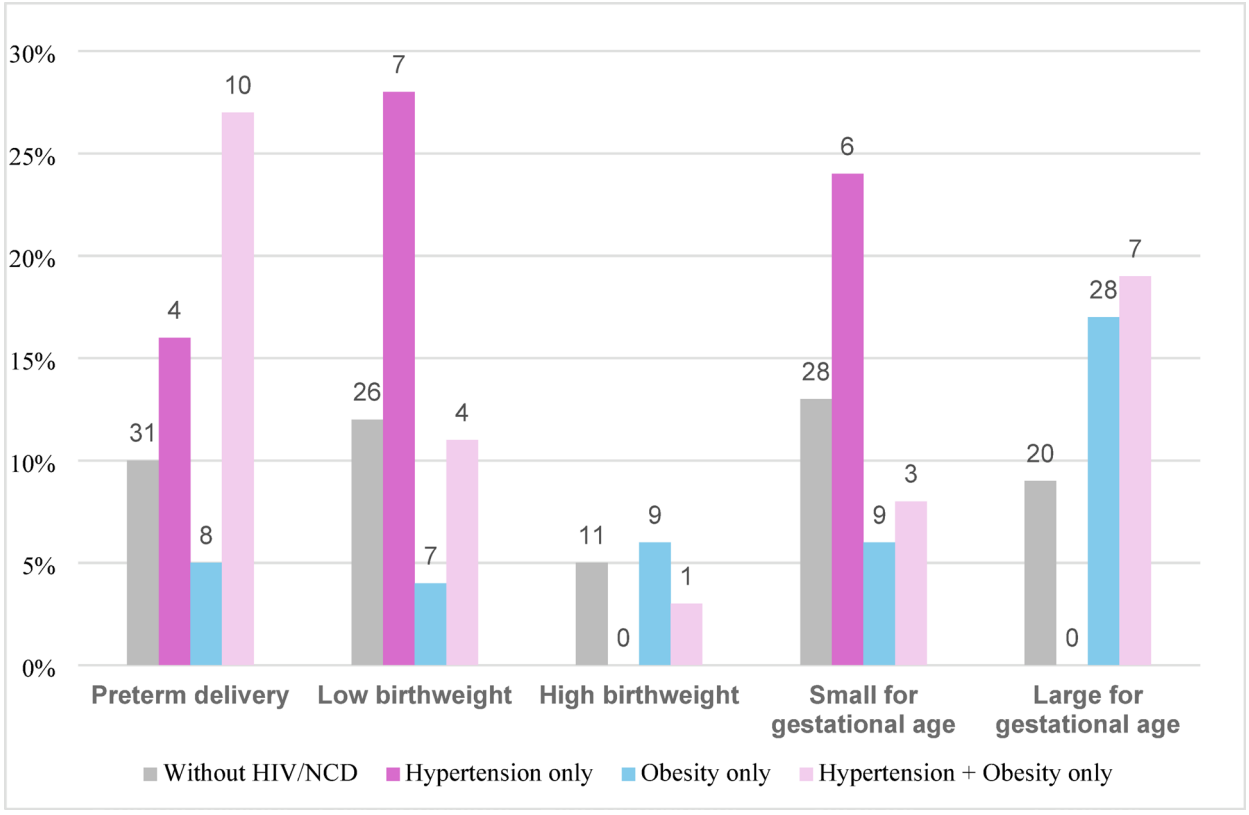


Fig. 4 Proportions of adverse outcomes in women without HIV with/without NCDs (n = 448). Abbreviation: NCD = Non-communicable disease, PTD = Preterm delivery, LBW = Low birthweight, HBW = High birth weight, SGA = Small for gestational age, LGA = Large for gestational age. Maternal morbidity is based on ever meeting the criteria for a condition at any point during the data visits i.e. obesity = pre-conception BMI ≥30 kg/m^2, hypertension = systolic≥120mmHg or diastolic ≥ 80 mmHg, DM = obtained from medical records and self-reported throughout antenatal visits and checked against medical records. Groups that included DM were excluded from the graphical birth outcome analysis due to very small numbers, which limited meaningful interpretation and impaired the clarity of visual presentations

Table 4 Association between HIV-NCD comorbidity and adverse birth outcomes

	HIV only[1] Ref. without HIV/NCD		**HIV + HTN only[1] Ref. without HIV/NCD**		**HIV + Obesity only[1] Ref. without HIV/NCD**		**HIV + HTN + Obesity only[1] Ref. without HIV/NCD**	
Birth outcome	aOR (95% CI)	*P*	aOR (95% CI)	*P*	aOR (95% CI)	*P*	aOR (95% CI)	*P*
Term delivery	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Preterm < 37weeks	1.27 (0.66, 2.47)	0.471	3.01 (1.01, 8.05)	0.032	0.82 (0.33, 1.93)	0.664	2.67 (1.08, 6.23)	0.026
Appropriate for GA	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Small (< 10th percentile)	1.12 (0.63, 2.02)	0.698	1.04 (0.31, 3.45)	0.955	0.39 (0.16, 0.97)	0.043	1.30 (0.49, 3.45)	0.597
Large (> 90th percentile)	1.02 (0.50, 2.08)	0.952	0.44 (0.05, 3.65)	0.449	1.25 (0.58, 2.69)	0.567	0.76 (0.20, 2.95)	0.691
Normal birth weight	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Low (< 2500 g)	1.11 (0.61, 2.04)	0.728	1.74 (0.60, 5.04)	0.305	0.58 (0.24, 1.40)	0.228	1.57 (0.52, 3.59)	0.528
High (≥ 4000 g)	1.08 (0.42, 2.77)	0.874	- *	- *	1.54 (0.58, 4.10)	0.387	- *	- *

[1]Adjusted for parity, SES and maternal age.*Results converged due to low outcome frequency. Abbreviation: NCD = non-communicable disease; GA = gestational age, aOR = adjusted odds ratios

HTN and DM, which were more common in those who initiated ART pre-conception in our study [48]. While ART effectively controls HIV, it may accelerate immune-mediated processes that increase cardiometabolic risks in people on treatment compared to treatment-naïve people [48, 49]. Our findings should be interpreted in the light of possible selection bias inherent in observational studies. As Springer et al. have highlighted, women who initiate ART before pregnancy may systematically differ from those starting during pregnancy in ways that influence NCD prevalence and birth outcomes [50]. For example, pre-conception ART users are often older, may have

Table 5 Association between NCDs and adverse birth outcomes in women without HIV

	HTN only[1] Ref. without HIV/NCD		**Obesity only[1] Ref. without HIV/NCD**		**HTN + Obesity only[1] Ref. without HIV/NCD**	
Birth outcome	aOR (95% CI)	*P*	aOR (95% CI)	*P*	aOR (95% CI)	*P*
Term delivery	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Preterm < 37weeks	1.77 (0.48, 5.28)	0.338	0.46 (0.18, 1.06)	0.080	3.18 (1.21, 7.90)	0.015
Appropriate for GA	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Small (< 10th percentile)	1.85 (0.67, 5.08)	0.233	0.41 (0.19, 0.92)	0.031	0.44 (0.10, 1.99)	0.284
Large (> 90th percentile)	- *	- *	1.78 (0.94, 3.36)	0.076	1.00 (0.91, 1.10)	0.987
Normal birth weight	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Low (< 2500 g)	2.74 (1.03, 7.24)	0.043	0.24 (0.14, 0.78)	0.012	0.67 (0.19, 2.43)	0.544
High (≥ 4000 g)	- *	- *	0.99 (0.88, 1.10)	0.797	0.95 (0.82, 1.10)	0.510

[1]Adjusted for parity, SES and maternal age.*Results converged due to low outcome frequency. Abbreviation: NCD = non-communicable disease; GA = gestational age, aOR = adjusted odds ratio

Table 6 Association between HIV and NCDs vs. NCDs and adverse birth outcomes

	HIV + HTN only[1] Ref. HTN only		**HIV + Obesity only[1] Ref. obesity only**		**HIV + Obesity + HTN only[1] Ref. HTN + Obesity only**	
Birth outcome	aOR (95% CI)	*P*	aOR (95% CI)	*P*	aOR (95% CI)	*P*
Term delivery	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Preterm < 37weeks	2.28 (0.46, 12.8)	0.992	1.31 (0.477, 3.67)	0.594	0.72 (0.24, 2.15)	0.554
Appropriate for GA	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Small (< 10th percentile)	0.45 (0.883, 2.30)	0.338	0.88 (0.31, 2.52)	0.816	3.14 (0.60,16.5)	0.178
Large (> 90th percentile)	- *	- *	0.71 (0.35, 1.42)	0.326	0.37 (0.08, 1.76)	0.214
Normal birth weight	Ref.	Ref.	Ref.	Ref.	Ref.	Ref.
Low (< 2500 g)	0.51(0.11, 2.39)	0.394	1.42(0.49, 4.15)	0.521	2.02 (0.47, 8.73)	0.348
High (≥ 4000 g)	- *	- *	1.46 (0.55, 3.91)	0.448	- *	- *

[1]Adjusted for parity, SES and maternal age.*Results converged due to low outcome frequency. Abbreviation: NCD = non-communicable disease; GA = gestational age, aOR = adjusted odds ratio

a longer duration of HIV infection and more frequent interaction with the healthcare system, increasing the chances of NCD detection.

The intersection of NCDs with ART in the context of maternal health among pregnant WHIV remains a persistent concern. Addressing this issue may necessitate strict NCD interventions, particularly considering the switch to dolutegravir-based regimens, which have been associated with an increased risk of obesity [44, 51, 52].

Adverse birth outcomes

Adverse birth outcomes did not differ between WHIV relative to those with neither HIV nor NCDs nor by ART initiation timing. However, NCDs accounted for increased adverse birth outcomes in WHIV, except for obesity, which had varying effects on adverse birth outcomes. Likewise, in women without HIV, NCDs inflated some birth outcomes while reducing others.

In WHIV, there was a strong association between PTD and HTN. About three times the odds of PTD were found in WHIV with HTN compared to the disease-free control group, and 2.67 times the odds in WHIV with both HTN + obesity compared to the disease-free control group. The proportion of PTD was even lower in pregnancies with neither HIV nor NCDs. Additionally, we found NCDs had similar adverse effects in women without HIV. HTN and obesity comorbidity had over 3 times the odds of PTD and approximately 3 times LBW compared to the disease-free group.

The implications of this study are of clinical concern, particularly with a high prevalence of obesity in South Africa. The coexistence of high obesity rates, a significant HIV burden, and an increasing prevalence of HTN in the LMICs underscores the potential for compounded health risks and the need for comprehensive medical attention and interventions to address these complex health challenges in this population [53]. Maternal and neonatal health morbidity carries a substantial economic burden in both the short and long term. Adverse birth outcomes, including PTD and LBW, can lead to a heightened risk of health conditions such as congenital hearing loss, poor vision, developmental delays, cerebral palsy and intellectual difficulties [54, 55]. LGA and HBW can increase the risks of conditions such as respiratory distress, low blood pressure and birth injuries in neonates [56]. Since the time of our study, the first-line ART guidelines have shifted, particularly with the 2020 rollout of dolutegravir-based regimens. However, our findings remain important for establishing baseline patterns of maternal and birth outcomes concerning the intersection of HIV-NCD,

prior to these changes, a largely under-researched area in Southern Africa. This information is valuable for evaluating the effects of more recent treatment strategies.

A positive note in our study is having no association between HIV only and adverse outcomes, which contradicts other findings elsewhere. Associations between LBW, PTD and SGA in WHIV on ART have been reported by other studies [57–59]. The mechanisms implicated in these outcomes include reduced assimilation of nutrients due to HIV, thus resulting in intrauterine growth restrictions that lead to fetal microsomia, inflammatory responses that trigger preterm births and ART-related hormonal imbalances such as reduced progesterone [60–62]. Our results may be due to a higher prevalence of pre-conception ART, which may protect against poor assimilation or a spike in inflammatory response during pregnancy.

Notably, we observed that obesity was associated with a reduced risk of SGA and LBW compared to the disease-free group. This pattern was evident in both WHIV and without HIV, suggesting that the protective association is more closely linked to maternal body mass index than HIV status. This is consistent with established evidence that higher pre-conception BMI reduces the risk of fetal growth restrictions, likely by supporting greater nutrient availability for fetal development [25, 63]. While obesity may lower the likelihood of SGA and LBW, it is widely recognised to increase the risk of delivering LGA or HBW babies [25], carrying its own set of neonatal risks. Our results reinforce the complex role of maternal adiposity in pregnancy outcomes and underscore the importance of integrated care that balances risks across the spectrum of fetal growth.

Strengths and limitations

Our study was able to compare birth outcomes using different exposure combinations: HIV only, HTN only, obesity only, HIV and HTN, HIV and obesity, and ART initiated during pregnancy and pre-conception. A strength of this study is the use of ultrasound to determine gestational age, ensuring accurate assessment of birth outcomes allowing for calculation of gestational weight gain and pre-conception BMI.

This study has several limitations. We could not disentangle the effects of gestational versus chronic HTN and DM on birth outcomes due to a small prevalence of HTN and diabetes. Additionally, we could not meaningfully assess the impact of DM on birth outcomes due to the very low prevalence in our cohort. Due to missing data, the study does not distinguish by ART regimen, CD4 counts, or viral load to assess HIV severity. Missing data could have influenced the analysis of our ART initiation timing effect of NCDs, and these should be interpreted with caution. We were unable to distinguish between type 1 and type 2 DM in this analysis as the dataset did not capture subtype information.

Conclusion

We found no meaningful differences in the prevalence of obesity, hypertension or DM between pregnant WHIV and those without HIV attending a primary care obstetric facility, although the overall burden of obesity was high at nearly 50% of the cohort. Regardless of HIV status, hypertension, especially when combined with obesity, was associated with increased odds of PTD, while obesity alone appeared protective against SGA and LBW. These findings highlight the complex interplay of maternal NCDs on birth outcomes, independent of HIV infection. In a setting like South Africa, where high rates of obesity coexist with a substantial HIV burden and rising hypertension prevalence, these results underscore the urgent need for integrated ANC care models that address both infectious and non-infectious diseases to optimize maternal and neonatal outcomes.

Abbreviations

ANC	Antenatal Care
ART	Antiretroviral Therapy
AGA	Appropriate Gestational Age
aOR	Adjusted Odds Ratio
BMI	Body Mass Index
CI	Confidence Interval
DM	Diabetes Mellitus
GA	Gestational Age
HIV	Human Immunodeficiency Virus
HTN	Hypertension
IQR	Inter-Quartile Range
LBW	Low Birth Weight
LGA	Large for Gestational Age
LMIC	Low-Middle Income Countries
MOU	Midwife Obstetric Unit
MCR	Maternity Case Records
NCD	Non-Communicable Disease
OR	Odds Ratio
PTD	Preterm Delivery
SGA	Small for Gestational Age
SSA	Sub-Saharan Africa
WHO	World Health Organization
WHIV	Women living with HIV
WNLHIV	Women not living with HIV

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12884-025-08086-x.

Supplementary Material 1.

Supplementary Material 2.

Supplementary Material 3.

Supplementary Material 4.

Supplementary Material 5.

Supplementary Material 6.

Supplementary Material 7.

Supplementary Material 8.

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Author contributions
AJL conceptualised the research question, conducted the design and analysis of data, and wrote the manuscript under the supervision and guidance of HPM. Additionally, HPM gave access to the primary data analysed in this study. All authors reviewed, edited, and approved the final manuscript.

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Data availability
All data generated or analysed during this study are included in this published article (and its supplementary information files). In addition, the datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study followed the guidelines laid down in the Declaration of Helsinki, and all procedures involving research study participants were approved by relevant ethical bodies. The current study analysed data from a parent study titled B Positive. Since the study is a secondary research analysis, there was no requirement for obtaining informed consent, as participants had already consented that their information could be used for research and academic purposes. The University of Cape Town Human Research Ethics Committee had approved the parent study (HREC 541/2015) as well as the Western Cape Department of Health (REFWC_2016RP6_286). This current study sought ethical clearance from the University of Cape Town Human Research Ethics Committee (HREC 345/2022). All participants provided written informed consent prior to study participation.

Consent for publication
Not applicable

Competing interests
The authors declare no competing interests.

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