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The Prevalence of Overweight/Obesity and Related Comorbidities among HIV-Positive and HIV-Negative Patients Attending the Same Clinics in Gaborone, Botswana

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Abstract

Context: Antiretroviral therapy (ART) helps restore the health status of people living with HIV (PLHIV). Likewise, it increases the risk of overweight/obesity and related comorbidities among the recipients. In countries like Botswana where ±84% of PLHIV is on ART, the paucity of data comparing overweight/obesity between HIV-positive on ART and HIV-negative patients may impede clinical and policy decision-making. This study sought to estimate and compare: i) the prevalence of overweight/obesity between HIV-positive on ART and HIV-negative patients; ii) the prevalence of hypertension (HTN), diabetes mellitus (DM)/coronary heart disease (CHD) between HIV-positive patients on ART and HIV-negative patients attending same outpatient departments of general clinics in Gaborone, Botswana. **Patients and Methods:** Five hundred eighty-one (581) outpatients were recruited in four major clinics of Gaborone, Botswana, between June and July 2019; 294 or 51% of them were HIV-negative and 287 or 49% were HIV-positive on ART. The prevalence of overweight/obesity and of HTN and DM/CHD were calculated and examined using stratified analysis. Subgroups were compared using Chi-square analysis with Yates correction or Fisher exact test and t-student test for continuous data. Results: Major findings after stratification of the study population by HIV status were: i) the prevalence of all categories of (BMI), including overweight/obesity, were comparable between HIV-negative-patients and HIV-positive. In fact, there were 24 (8.0%) cases of underweight among

HIV-negative-Patients and 15(5%) cases among HIV-positive patients, p = 0.2; 145 (49%) HIV-negative-patients and 128 (45%) HIV-positive, p = 0.07 cases of normal weight; 72 (25%) HIV-negative-patients and 87 (30%) HIV-positive, p = 0.08, were overweight; 53 (18%) HIV-negative-patients and 57 (20%) HIV-positive, p = 0.12, were obese; 125 (43%) HIV-negative patients and 144 (50%) HIV-positive, p=0.06 were overweight/obese; ii) the prevalence of HTN and DM/CHD among HIV-positive-patients were significantly lower ($p < 0.05$) compared to HIV-negative patients: There were 32 (10.9%) cases of HTN among HIV-negative patients compared to 18 (6.3%) cases of HTN among HIV-positive patients, p = 0.001; 32 (11%) cases of DM/CHD HIV-negative patients compared to 4 (1.4%) cases of DM/CHD among HIV-positive patients, p = 0.001. Conclusion: the prevalence of overweight/obesity observed between HIV-negative and HIV-positive patients may suggest that the two groups shared the same exposure factors. That HTN and DM/CHD prevalence was lower among HIV-positive compared to HIV-negative patients, is possibly due to interplay factors of ART, HIV or the host population. Further studies are, however, recommended for clarifications.

Keywords

Overweight/Obesity, Related Comorbidities, HIV-Positive, HIV-Negative

1. Introduction

Persons living with human immunodeficiency virus (PLHIV) are now living longer, normal and healthier lives than before due to access to available effective antiretroviral therapy (ART) [1] [2] [3]. Recipients of ART are now achieving viral suppression (viral load of <400 copies of viral DNA per millilitre) and having better CD4 cells count, thus making them immunocompetent enough to earn a life expectancy comparable to HIV-negative persons [2] [3]. Morbidity and mortality rates among PLHIV have therefore fallen to levels similar to those in the general population [3], primarily due to the significant decline of Acquired Immune Deficiency Syndrome (AIDS) defining opportunistic pathologies, *i.e.*, cancers such as Kaposi Sarcoma, non-Hodgkin-lymphoma and invasive cervical cancer [3] [4]. Unfortunately, this significant health status improvement among PLHIV on ART has dangled new challenges. In the pre-ART era, for instance, wasting used to be the predominant clinical picture of HIV/AIDS patients [4], today overweight and obesity have taken over among these patients [2] [5] [6]; yet, overweight/obesity has long been associated with unwanted outcomes such as hypertension (HTN), coronary heart disease (CHD) and diabetes mellitus DM [7]. Some experts even consider this pattern change as a side effect of ART [8] while others see it as part of the current World epidemic of overweight/obesity [5] [6] [9]. Research at two US Navy clinics [5] [6] showed no difference in the prevalence of overweight/obesity between recipients of ART and HIV-negative patients. The authors claimed that the finding was not unexpected due to the easy access to ART. This treatment makes PLHIV live normal lives and longer [3] [4] and eventually encounter the same health challenges as the general population. While these assertions corroborate data from Botswana [10] [11], at the same time, bring up questions to whether the prevalence of overweight/obesity among ART recipients and HIV-negative patients were also comparable in Botswana. This is because what is happening elsewhere may not necessarily be the case in Botswana owing to differences in population's characteristics [12]. So far, there is a paucity of data comparing prevalence of overweight/obesity, DM, HTN and CHD between HIV patients on ART and HIV-negative patients in Botswana. Yet, such data are of great interest since ± 84% of PLHIV in the country are on ART [10]. In order to inform decisions it is imperative to ascertain whether or not the profile of overweight/obesity documented elsewhere among HIV patients on ART [13] [14] is actually similar to the Botswana profile. So far, this information is still missing. We sought in this study to estimate and compare: (i) the prevalence of overweight/obesity between HIV patients on ART and HIV-negative patients, (ii) the prevalence of HTN, DM/CHD between the two groups while attending the same outpatient departments (OPDs) of selected clinics in Gaborone at the same period.

2. Subjects and Methods

2.1. Study Design

This was a cross-sectional study employing an analytical approach to address objectives. Data were collected from June 15 to July 31, 2019. We expected the prevalence of overweight/obesity among HIV-positive patients on ART to be higher compared to HIV-negative patients; and, similarly the prevalence of comorbidities, *i.e.*, HTN, DM/CHD to be higher among HIV-positive patients on ART compared to HIV-negative patients.

VARIABLE STUDIED

Thirty-nine variables were investigated among 581 patients attending clinics in Gaborone, Botswana from June 15 to July 31, 2019 (N = 581)

Dependent variables: Overweight/obesity, HTN, DM/CHD

Exposure variables of interest: **Being HIV-positive or HIV-negative;**

Other exposure variables: A**) participants' Gender:** Male or Female; B) **Marital status:** married or single; C) **Area of residence**; Urban, semi-urban, rural; D) **Level of Education:** tertiary, secondary and primary; E) **Socioeconomic status** (SES): higher, middle-class and lower.

Biomedical Characteristics, A) Reason for clinic visit: Follow up, Sick visit, other, **B)** HIV status, **C)** ART types, mean duration on ART, **D)** duration on ART in years, **E)** parents with HTN, parents with DM, parents with CHD, **F)** Patient with comorbidities: HTN, DM, CHD.

Type of activity practiced by patients: Physical activities, Smoking Status; Alcohol consumption, Religious/Culture.

2.2. Study Site and Settings

The study was conducted in Gaborone, the capital city of Botswana. Gaborone lies on the Notwane River occupying a landmass of around 19,096 hectares, located between Kgale and Oodi Hills in Botswana's South-East District. The population of Gaborone City was estimated to be 233,135 based on the 2011 Botswana Population and Housing census. This means that Gaborone was home to about 12% of Botswana's national population by then. The study was conducted in 4 different Gaborone clinics: Julia Molefe clinic, BH3 clinic, Extension 2 clinic and Gaborone West clinic. These were selected because they received and provided services to the highest number of patients per day compared to all other clinics. All the clinics in Gaborone have an outpatient department (OPD) and Infectious Diseases Control Centre (IDCC) where HIV-positive clients were followed up for treatment and routine monitoring. All the clinics and IDCCs are linked online through an Integrated Patient Management System. General outpatient clinics also have either a stand-alone network installed or Patient Information Management System.

2.3. Study Population, Inclusion and Exclusion Criteria

HIV-positive and HIV-negative patients attending local health facilities between June and July 2019 in Gaborone constituted the study population. Outpatient clients aged 18 years and above, patients receiving ART for HIV or as therapy for any other disease, *i.e.* chronic hepatitis B virus infection, as well as HIV-positive patients not yet on ART, all met the inclusion criteria. Excluded from the study were patients below 18 years of age, of unknown HIV status, pregnant women and women visiting clinics for a 6-week post-natal visit, patients that were not mobile or were wheelchair bound, not capable of standing without support and patients with decreased mental capacity.

2.4. Sample Size and Sampling Strategy

The sample size was estimated as described by Ariya and colleagues [15], using 1.96 (Z-score) as the value of the standard normal distribution corresponding to a level of alpha that was significant (<0.05) for a two-side test or margin of error of 5%; where n is the sample size, P = the expected prevalence, d = the allowable error. Assuming that P and d, are decimal values but would hold correct if they are percentages, except that the term (1-P) will become 100-P in the numerator. P was set to 0.97 for common conditions, and d = 0.015; thus, we estimated the sample size as:

$$n = \frac{\left(Z^2\right)P\left(1-P\right)}{d^2} = \frac{\left(1.96\right)^2 \times 0.97\left(100-97\right)}{\left(0.015\right)^2} = 497$$

Considering respondents who will not meet inclusion criteria or withdraw from the study, this sample was increased by 17% or 581 patients.

Selection and enrolment of both HIV-negative and HIV-positive patients were conducted in selected sites where both HIV^- and HIV^+ were attending. Since the majorities of patients were drop-ins and did not have doctors' appointments, it was difficult to produce a sampling frame from which potential participants could have been drawn. Nevertheless, participants were randomly selected by approaching every 3rd patient when he/she finished with his/her clinic visit of the day. Those who consented were enrolled in the study. In case of non-consent, the latter was automatically replaced by the next patient. Recruitment continued until the estimated sample size was reached. The number of patients recruited in each of the four settings was proportional to the size of patients that the clinic catered for. The study was conducted in all four clinics at the same time period.

2.5. Data Collection

All selected clinics operated 24 hours over 24. Two trained research assistants were assigned to each clinic; one for the day and the other for the night shift. A structured questionnaire was used to collect data from consenting participants through face-to-face interviews. Most data values, *i.e.*, biomedical and other comorbidities were extracted from clinics databases, patient medical records, laboratory and clinical diagnosis and treatment as prescribed by attending physicians. Data collected are presented in **Tables 1 - 4**. Data on HIV status, ART exposures, date of ART initiation, type of current medication and ART adverse effects were also collected.

Data analysis: Data was analyzed using IBM SPSS version 27 (Chicago, IL). Patients' BMI were estimated by dividing their weight (in kilograms) by the square of the height (in meters). Patients with BMI < 18.5 kg per m^2 were classified as underweight, those with BMI between 18.5 - 24.9 kg per m^2 were classified as having normal BMI, those between 25-29.9 kg per m^2 were categorised as overweight, and those with BMI ≥ 30 kg per m^2 were classified as obese. Overweight and obesity were aggregated as a single variable for simplicity of analysis "overweight/obesity". Duration of exposure to ART was estimated among HIV-positive patients by subtracting the date of ART initiation from the date of data collection and was expressed in years. Participants whose major mode of transport was walking were categorised as having a low socioeconomic status (LSES), and those who used public transport had a middle-income status (MSES). Those who used private cars were considered to have a high socioeconomic status (HSES). Analysis was performed to portray patient characteristics as well as their BMI. Patients with HIV/AIDS, HTN, DM and CHD; were identified based on the diagnosis of the attending physician and in line with the International Classification of Diseases, tenth revision (ICD-10). The prevalence of overweight/obesity and HTN of HIV-positive/ART recipients and that of HIV-negative patients were estimated by dividing the number of cases in each subgroup by the subgroup's size times 100. DM and CHD were aggregated as DM/CHD to simplify analysis due to the small number of cases; similarly, their prevalence was estimated by dividing the number of cases by the number of participants times 100 in each subgroup. Patients were stratified by HIV status groups/subgroups and compared using Chi-square analysis with correction of Yates or Fisher exact test for categorical data and, t-student test for continuous data. The level of significance was set at $P < 0.05$.

3. Results

Of the 581 outpatients investigated in the clinics, 294 (51%) were HIV-negative or non-recipients of ART; 287 (49%) were HIV-positive or recipients of ART. Of those, 47.4% were on Tenofovir/Emtricitabine/Efavirenz (TDF-FTC-EFV) or (Truvada-Efavirenz/) (ATRIPLA) combination; 21.3% were on Tenofovir/Lamivudine/Dolutegravir (TDF-3TC-DTG) also known as TLD. The rest were on other combination therapies as presented in **Table 1**. All HIV-positive patients were on ART regardless of CD4 count. Those already on ART were in the process of being switched from other regimens to the recommended first-line ART (TDF-FTC-DTG) at the time of data collection except those with renal failure, cardiac toxicity and those on triple drug combinations administered only once a day, *i.e.*, ATRIPLA (TDF-FTC-EFV) as defined in the Botswana Integrated HIV Clinical Care Guidelines for adults 2016. No case of ART adverse effects (lipodystrophy, buffalo hump) was recorded among ART recipients by attending physicians.

Table 1. Proportion of HIV participants by current ART regimen (n = 287).

ART Drug Abbreviation	Antiretroviral Therapy (ART) Drug Names	ART Type	Number of Recipients	Proportion (%)
ABC-3TC-DTG	Abacavir/Lamivudine/Dolutegravir	2 NRTIs + II	1	0.3%
ABC-3 TC-LPV/r	Abacavir/Lamivudine/Lopinavir/rironavir *(ABC-3TC-Aluvia)*	2 NRTIs + PI/b	1	0.3%
ABC-3TC-NVP	Abacavir/Lamivudine/Nevirapine)	2 NRTIs + NNRTI	1	0.3%
AZT-3TC-EFV	Zidovudine/Lamivudine/Efavirenz *(Combivir-Efavirenz)*	2NRTIs + NNRTI	8	2.8%
AZT-3TC-LPV/r	Zidovudine/Lamivudine/Lopinavir/rironavir *(Combivir-Aluvia)*	2NRTIs + PI/b	6	2.1%
AZT-3TC-NVP	Zidovudine/Lamivudine/Nevirapine *(Combivir-Nevirapine)*	2NRTIs + NNRTI	17	5.9%
TDF-3TC-DTG	Tenofovir/Lamivudine/Dolutegravir *(TLD)*	2NRTIs + II	61	21.3%
TDF-FTC-DTG	Tenofovir/Emtricitabine/Dolutegravir *(Truvada- Dolutegravir)*	2NRTIs + II	44	15.3%
TDF-FTC-EFV	Tenofovir/Emtricitabine/ Efavirenz *(Truvada-Efavirenz/) {ATRIPLA}*	2NRTIs + NNRTI	136	47.4%
TDF-FTC-LPV/r	Tenofovir/Emtricitabine/Lopinavir/rironavir *(Truvada-Aluvia)*	2NRTIs + PI/b	4	1.4%
TDF-FTC-NVP	Tenofovir/Emtricitabine/Nevirapine *(Truvada-Nevirapine)*	2NRTIs + NNRTI	8	2.8%
TOTAL			**287**	**100%**

Legend: ART Drug Types: Nucleoside Reverse Transcriptase Inhibitor (NRTI): ABC, AZT, 3TC, FTC, TDF. Non-Nucleoside Reverse Transcriptase Inhibitor (NNRTI): NVP, EFV. Boosted Protease Inhibitor (PI/b): LPV/r. Integrase Inhibitor (II): DTG.

BMI status by participants' characteristics is described in Tables 2 - 4. In general, 39 (6.7%) participants were underweight, 273 (46.9%) had normal BMI, 159 (27.3%) were overweight, 110 (18.9%) were obese or 269 (46.3%) cases of overweight/obesity. Three hundred and thirty-five patients, (58.0%) were females. The mean age ± SD of patients was 35.5 ± 11.0 years; 91 (16.0%) of them were aged between 18 - 24 years old, 215 (37.0%) were between 25 - 34 years old, 155 (27.0%) between 35 - 45 years and 120 (20.0%) were >45 years old; overweight/obesity was significantly ($p < 0.05$) higher among those between

Table 2. BMI status categorized as underweight, normal weight, overweight, obesity and overweight/obesity by participants' sociodemographic characteristics (N = 581).

Characteristics	Participant BMI profile					
	Overall	Underweight	Normal BMI	Overweight	Obesity	††Overweight/obesity
Total: n (%)	**581 (100)**	**39 (6.7)**	**273 (46.9)**	**159 (27.3)**	**110 (18.9)**	**269 (46.3)**
Age (years, Mean (±SD)	35.5 (±11.0)	31.1 (±10.3)	33.6 (±10.4)	38.2 (±11.6)	37.9 (±10.4)	38.1 (±11.1)
Age groups						
18 - 24 years, n (%)	91 (16)	13 (14)	53 (58)	19 (21)	6 (7)	25 (28)
25 - 34 years, n (%)	215 (37)	15 (7)	112 (52)	47 (22)	41 (19)	88 (41)
35 - 44 years, n (%)	155 (27)	5 (3)	61 (39)	52 (34)	37 (24)	89 (58) [a]
>45 years, n (%)	120 (20)	6 (5)	47 (39)	41 (34)	26 (22)	67 (56) [b]
Gender						
Male, n (%)	246 (42)	26 (11)	151 (61)	49 (20)	20 (8)	69 (28)[a]
Female, n (%)	335 (58)	13 (4)	122 (36)	110 (33)	90 (27)	200 (60)[b]
Marital Status						
Single, n (%)	512 (88)	36 (7)	246 (48)	136 (27)	94 (18)	230 (45)[a]
Married, n (%)	69 (12)	3 (4)	27 (39)	23 (33)	16 (23)	39 (56)[b]
Area of residence						
Urban, n (%)	418 (72)	28 (7)	196 (47)	113 (27)	81 (19)	194 (46)[a]
Semi Urban, n (%)	106 (18)	6 (6)	48 (45)	31 (29)	21 (20)	52 (49)[a]
Rural, n (%)	57 (10)	5 (9)	29 (51)	15 (26)	8 (14)	23 (40) [b]
Level of Education						
Tertiary, n (%)	174 (30)	21 (12)	82 (47)	45 (26)	26 (15)	71 (41)[a]
Secondary, n (%)	338 (58)	13 (4)	168 (50)	94 (28)	63 (18)	157 (46)[a]
Primary, n (%)	69 (12)	5 (7)	23 (33)	20 (29)	21 (30)	41 (59)[b]
SES						
High SES, n (%)	120 (21.0)	6 (5)	53 (44)	33 (28)	28 (23)	61 (51)[a]
Middle-class SES, n (%)	260 (45.0)	17 (7)	121 (46)	76 (29)	46 (18)	122 (47)[a]
Low SES, n (%)	201 (34.0)	16 (8)	99 (49)	50 (25)	36 (18)	86 (43)[b]

Legend: BMI = Body mass Index, n = number, ††Overweight/obesity = the aggregate of Overweight and Obesity, SD = standard deviation; within column, [a]different superscript letters in the same column indicate significantly different values ($P < 0.05$).

Table 3. Participants' BMI status categorized as underweight, normal weight, overweight, obesity and overweight/obesity by participants' biomedical characteristics (N = 581).

Characteristics	Participant BMI profile					
	Overall	Underweight	Normal BMI	Overweight	Obesity	††Overweight/obesity
Total	**581 (100)**	**39 (6.7%)**	**273 (46.9)**	**159 (27.3)**	**110 (18.9)**	**269 (46.3)**
Reason for clinic visit						
Follow Up, n (%)	337 (58.0)	16 (5.0)	151 (45.0)	103 (31.0)	67 (20.0)	170 (51.0)[a]
Sick Visit, n (%)	205 (35.0)	21 (10.0)	99 (48.0)	49 (24.0)	36 (18.0)	85 (42.0)[b]
Other, n (%)	39 (7.0)	2 (5.0)	23 (59.0)	7 (18.0)	7 (18.0)	14 (36.0)[c]
HIV status						
Negative, n (%)	294 (51.0)	24 (8.0)	145 (49.0)	72 (25.0)	53 (18.0)	125 (43.0)
Positive, n (%)	287 (49.0)	15 (5.0)	128 (45.0)	87 (30.0)	57 (20.0)	144 (50.0)
ART type						
2NRTIs + NNRTI, n (%)	170 (59.0)	7 (4.0)	85 (50.0)	49 (29.0)	29 (17.0)	78 (46.0)[a]
2NRTIs + II, n (%)	106 (37.0)	4 (4.0)	40 (38.0)	37 (35.0)	25 (24.0)	62 (59.0)[a]
2NRTIs + PI, n (%)	11 (4.0)	4 (36.0)	3 (27.0)	1 (9.0)	3 (27.0)	4 (36.0)[b]
Duration on ART, M (±SD)	5.7 (±5.0)	5.9 (±3.6)	6.2 (±5.2)	5.6 (±5.3)	4.5 (±4.1)	5.2 (±4.9)
Duration on ART in years						
0 year, n (%)	294 (51.0)	24 (8.0)	145 (49.0)	72 (25.0)	53 (18.0)	125 (43.0)[a]
≤ 4 years, n (%)	151 (26.0)	5 (3.0)	61 (40.0)	49 (33.0)	36 (24.0)	85 (57.0)[b]
> 4 years: n (%)	136 (23.0)	10 (7.0)	67 (49.0)	38 (28.0)	21 (15.0)	59 (43.0)[a]
Parent with HTN						
No, n (%)	397 (68.0)	25 (6.0)	204 (51.0)	97 (25.0)	71 (18.0)	168 (43.0)
Yes, n (%)	184 (32.0)	14 (8.0)	69 (37.0)	62 (34.0)	39 (21.0)	101 (55.0)
Parent with DM						
No, n (%)	532 (92.0)	38 (7.0)	251 (47.0)	145 (27.0)	98 (19.0)	243 (46.0)[a]
Yes, n (%)	49 (8.0)	1 (2.0)	22 (45.0)	14 (29.0)	12 (24.0)	26 (53.0)[b]
Parent with CHD						
No, n (%)	573 (99.0)	39 (7.0)	268 (47.0)	156 (27.0)	110 (19.0)	266 (46.0)[a]
Yes, n (%)	8 (1.0)	0 (0.0)	5 (62.0)	3 (38.0)	0 (0.0)	3 (38.0)[b]
Has a comorbidity						
No, n (%)	495 (85.0)	33 (7.0)	244 (49.0)	130 (26.0)	88 (18.0)	218 (44.0)[a]
HTN, n (%)	50 (9.0)	1 (2.0)	11 (22.0)	20 (40.0)	18 (36.0)	38 (76.0)[b]
DM/CHD, n (%)	36 (6.0)	5 (14.0)	18 (50.0)	9 (25.0)	4 (11.0)	13 (36.0)[c]

Legend: BMI = Body mass Index, ††Overweight/obesity = aggregate of Overweight and Obesity, HIV = Human Immune Deficiency Syndrome, ART = Antiretroviral therapy, CHD = Coronary Heart Disease, DM = Diabetes Mellitus, HTN = hypertension, [a]different superscript letters in the same column indicate significantly different values ($P < 0.05$).

Table 4. BMI status of participants expressed as underweight, normal weight, overweight, obesity and overweight/obesity by type of activity practiced (N = 581).

Characteristics	Participant BMI profile					
	Overall	Underweight	Normal BMI	Overweight	Obesity	††Overweight/obesity
Physical activities						
Yes, n (%)	411 (71.0)	29 (7.0)	210 (51.0)	108 (26.0)	64 (16.0)	172 (42.0)[a]
No, n (%)	170 (29)	10 (6)	63 (37.0)	51 (30.0)	46 (27.0)	97 (57.0)[b]
Smoking status						
Current-smoker, n (%)	72 (12.0)	10 (14.0)	45 (63.0)	11 (15.0)	6 (8.0)	17 (23.0)[a]
Former-Smoker, n (%)	67 (12.0)	2 (3.0)	35 (52.0)	15 (22.5.0)	15 (22.5.0)	30 (45.0)[a]
Never, n (%)	442 (76.0)	27 (6.0)	193 (44.0)	133 (30.0)	89 (20.0)	222 (50.0)[b]
Alcohol consumption						
No, n (%)	274 (47.0)	14 (5.0)	127 (46.0)	81 (30.0)	52 (19.0)	133 (49.0)
Yes, n (%)	307 (53.0)	25 (8.0)	146 (48.0)	78 (25.0)	58 (19.0)	136 (44.0)
Religion/culture						
Christianity, n (%)	497 (85.0)	31 (6.0)	241 (49.0)	131 (26.0)	94 (19.0)	225 (45.0)[a]
ATR & Other, n (%)	46 (8.0)	4 (9.0)	17 (37.0)	12 (26.0)	13 (28.0)	25 (54.0)[b]
None, n (%)	38 (7.0)	4 (11.0)	15 (39.0)	16 (42.0)	3 (8.0)	19 (50.0)[b]

Legend: BMI= Body Mass Index, ††Overweight/obesity = aggregate of Overweight and Obesity, ATR = African Traditional Religion, within column, [a]different superscript letters in the same column indicate significantly different values (P <0.05).

35 - 44 years old patients and those aged >45 years old compared to the rest of age groups. Female patients were significantly ($p < 0.05$) overweight/obese compared to males. Married couples were significantly ($p < 0.05$) overweight/obese than single patients; urban and semi-urban patients had comparable levels of overweight/obesity; and, significantly ($p < 0.05$) higher than rural residents. Patients with primary school education level were significantly ($p < 0.05$) overweight/obese compared to those with some secondary and tertiary level. Higher and middle-class SES patients were significantly ($p < 0.05$) overweight/obese compared to lower SES patients; details are provided in Table 2.

Results in Table 3 indicate that 337 (58%) patients visited OPD for follow-up and 170 (51%) of them were overweight/obese, 205 (35%) visited OPD for sicknesses and 85 (42%) of them were overweight/obese. Only 39 (7%) patients visited OPD for other purposes, 14 (36%) were overweight/obese. Two hundred ninety-four (51%) patients seen at OPD during the study period were HIV-negative and 43% had overweight/obesity; of 287 (49%) HIV-positive-patients, 50% were overweight/obese. Of those, 170 (59.0%) were recipients of 2NRTIs + NNRTI, 106 (37.0%) were on 2NRTIs + II and 11 (4.0%) were on 2NRTIs + PI. A significant ($p < 0.05$) difference was noticed in overweight/obesity between groups by duration on-ART. Of those who spent ≤4-year time duration on ART, 85 (57.0%) had overweight/obesity while those who were on ART for >4 year period only 59 (43.0%) had overweight/obesity. A statistically significant ($p < 0.05$) difference in overweight/obesity was also noted between those without and those with comorbidities, namely HTN, and DM/CHD. Four hundred and ninety-five (85%) patients had no comorbidities, 218 (44%) of them were overweight/obese, of 86 (15%) patients with comorbidities, 50 (9%) had HTN and 38 (76%) of them were overweight/obese. Thirty-six (6%) patients with comorbidities had DM/CHD, 13 (36%) of them were overweight/obese; more details are given in Table 3.

Data in Table 4**,** show BMI status of participants by type of activity practiced. Those who practiced physical activities had significantly ($p < 0.05$) less cases of overweight/obesity compared to their counterparts who did not practice physical activities; patients who smoked and ex-smokers had significantly ($p < 0.05$) less cases of overweight/obesity than those who never smoked; while those who consumed and those who did not consume alcohol, had a comparable level of overweight/obesity cases.

Major findings after stratification of participants by HIV status are presented in Table 5: i) the prevalence of all categories of (BMI), including overweight/obesity, were comparable between HIV-negative-patients and HIV-positive. In fact, 24 (8.0%) HIV-negative-Patients versus 15 (5%) HIV-positive, p = 0.2, were underweight; 145 (49%) HIV-negative-patients versus 128 (45%) HIV-positive, p = 0.07 had normal weight; 72 (25%) HIV-negative-patients versus 87 (30%) HIV-positive, p = 0.08, were overweight; 53 (18%) HIV-negative-patients versus 57 (20%) HIV-positive, p = 0.12, were obese; 125 (43%) HIV-negative patients versus 144 (50%) HIV-positive, p = 0.06 were overweight/obese; ii) the prevalence of HTN and DM/CHD among HIV-positive-patients were significantly lower ($p < 0.05$) compared to HIV-negative patients: There were 32 (10.9%) HTN-HIV-negative patients compared to 18 (6.3%) HTN-HIV-positive patients, p = 0.001; 32 (11%) DM/CHD-HIV-negative patients compared to 4 (1.4%) DM/CHD-HIV-positive patients, p = 0.001.

Table 5. Prevalence of overweight/obesity, HTN and DM/CHD by HIV status among patients attending clinics in Gaborone from June 15 to July 31, 2019, Botswana (N = 581).

BMI status/comorbidity	Participants		
	HIV- negative n (%)	**HIV- positive n (%)**	**P value**
Overall/Total, n (%)	294 (51.0)	287 (49.0)	0.10
Underweight, n (%)	24 (8.0)	15 (5.0)	0.20
Normal, n (%)	145 (49.0)	128 (45.0)	0.07
Overweight, n (%)	72 (25.0)	87 (30.0)	0.08
Obesity, n (%)	53 (18.0)	57 (20.0)	0.12
Overweight/obesity, n (%)	125 (43.0)	144 (50.0)	0.06
HTN, n (%)	32 (10.9)[a]	18 (6.3)[b]	0.001*
DM/CHD, n (%)	32 (11.0)[a]	4 (1.4)[b]	0.001*

Legend: HTN = Hypertension, DM = Diabetes Mellitus, CHD = Coronary heart disease, *p < 0.05, [a]different superscript letters in the same line indicate significantly different values (P < 0.05).

4. Discussion and Conclusions

Results from this study showed similar BMI profiles (underweight, normal weight, overweight, obesity and overweight/obesity) between HIV-negative and HIV-positive-patients on-ART. Thus, lending support to previous data and evidences excluding ART as the reason for undesirable BMI profiles seen among ART recipients [5] [6]. Had BMI categories in the two study groups been mediated by different exposure factors, one group likely would have shown a different BMI profile from the other group, *i.e.*, the prevalence of overweight/obesity being higher among ART recipients compared to HIV-negative patients. Furthermore, the fact that no lipodystrophy, buffalo hump or any other metabolic abnormality linked to ART adverse effects were documented among patients on ART, it is more likely that overweight/obesity seen among patients in the two groups shared the same rather than different exposures factors. In other words, in both groups, BMI profiles are possibly the expression of the current epidemic of overweight/obesity seen in the general population. Nevertheless, one may feature ART as a remote but not an immediate mediator of overweight/obesity among the recipients. Because, after all, weight gain among ART-recipients did not occur by chance and by chance alone. Patients' exposure to ART has prompted it. The scenario being: i) ART suppressed viral load in PLHIV [16], which improved their CD4 count [17]; ii) the improvement in CD4 count, in turn, restored patients' health status; iii) thus, prolonging their life expectancy, nearing or sometimes equating that of the general population [9] [16] [17] [18]. The aftermath of improved life expectancy exposed ART recipients to health challenges comparable to the general population. A situation that logically would have barely happened without ART input. This is probably why one may consider ART as a remote but not an immediate mediator of the outcome.

Outcomes from this study bring in new input into the ongoing issue of whether or not the current surge of overweight/obesity among ART recipients is part of the overweight/obesity epidemic seen in the general population [19] [20], ART side-effects or a direct effect of ART on recipients. Indeed, the most undisputable answer to these conflicting viewpoints can only come from randomized control clinical trials, assigning a group of PLHIV to ART and another to placebo, and then following them up until the development of outcomes of interest, if any. But since this approach is ethically not feasible, scientists use alternative strategies (case control, cohort design) to address the issue. That's probably why so far, results are conflicting; some have reported ART as the immediate mediator of overweight/obesity among patients on ART [21], whereas others have reported no association between overweight/obesity and ART [5] [6]. Tshikuka and co-workers [22] even noticed that neither the first line, nor second line, third line ART regimen significantly predicted overweight/obesity more than the other among Batswana patients on ART. Suggesting that, none of the ART regimen mediated BMI profiles were documented among the recipients. Also, Crum-Cianflone and co-workers [5] [6], after reviewing data from two

USA Navy clinics, failed to find differences in prevalence rates of overweight/obesity between ART recipients and HIV-negative-patients. These findings support the present study and corroborate reports that overweight/obesity among ART-recipients seemingly is part of the current epidemic in the general population and not an aftermath of ART [5] [6]. Nevertheless, additional research is still needed for clarification.

Reports of higher prevalence of HTN, DM and CHD among HIV-positive compared to HIV-negative patients are found in the literature [23] [24]. However, results presented herein do not corroborate these assertions; HTN and DM/CHD are less prevalent among HIV-positive than in HIV-negative patients. This contradicts our expectation that the prevalence of HTN and DM/CHD be higher among HIV-positive compared to HIV-negative patients [23] [24]. Ironically, these findings are supported in the literature too. Itai Madogoro and coworkers [25] investigated 11,083 households in the South African national demographic health survey in 2016. They reported a lower prevalence of HTN, DM or CHD among HIV-positive patients with overweight/obesity in adult South Africans compared to HIV-negative patients. Likewise, Tripathi *et al* [26] studied 6816 HIV-positive patients; over 80% of them on ART had lower DM incidence rates than HIV-negative patients (11.4 vs 13.6). Nix and colleagues [27] also reported a lower incidence of DM in obese PLHIV compared to their counterparts in the general population. These reports are amenable to questions like: do HIV-positive patients on ART have some protective factors/mechanisms against HTN, DM, or DM/CHD? Do overweight/obesity, HTN, DM and DM/CHD seen in HIV-positive patients on ART and those seen among HIV-negative patients have similar exposure factors? Whatever is the answer to these questions in the affirmative or not, the reality is that there are still some blind spots on the way which need clarification. Nevertheless, there are reports that provide potential ground on conflicting relationships between (HTN, DM or DM/CHD) and HIV status, particularly those on ART. The outcome is likely not due to a common pathway; but rather to a multitude of factors' interplay, including the host, HIV and ART factors. Thus, the low DM and HTN prevalence among HIV-positive overweight/obese patients on ART compared to HIV-negative patients expressed by this data likely is from the interplay of a multitude of factors. Many may belong to the current highly active ART (HAART) combinations. These combinations are known to have fewer adverse effects as demonstrated by data from the South Carolina Medicaid system and the enhanced HIV/AIDS Reporting System surveillance database [26] which support this pathway. Findings from these studies [26] showed little difference in DM incidence between HIV-positive and HIV-negative patients from 1994 to 2003. But, from 2004 through 2011 when HAART took over as the first-line regimen, results showed significantly lower DM incidence among HIV-positive patients compared to HIV-negative. Suggesting that studies aiming to control overweight/obesity and related comorbidities (HTN, DM or DM/CHD) among

HIV-positive and negative patients should not only focus on approaches used in the general population. The use of strategies considering factors of ART, HIV and the host population in order to achieve effective control of overweight/obesity as well as related comorbidities is recommended.

On the other hand, aggregated data from HIV-negative and HIV-positive patients in our study showed a higher prevalence of overweight/obesity among female compared to male patients. These results being not new in the study setting [28] can only support previous works [28] and are in line with the global profiles of overweight/obesity epidemic seen in the general population [1] [2]. In addition, the findings showed low prevalence rates of overweight/obesity among patients who practiced physical activities compared to those who did not; current- and former-smokers with lower prevalence of overweight/obesity compared to non-smoker patients; middle-class class and low SES patients with less overweight/obesity than the higher SES class. Although all these findings are supported by the literature [29], those about smoking bring us into a never-ending conflict area; that of the relationship of smoking with overweight/obesity which, is complex and still so far not well understood. Published data have produced contradicting results; some revealed no significant association between smoking status and BMI [30], while others reported negative associations between smoking and BMI [31], then smoking cessation with increased BMI [30]. Again, more research is needed in this particular area.

Findings in this study were: i) All categories of BMI, namely underweight, normal weight, overweight, obesity and overweight/obesity were comparable between HIV-positive on ART and HIV-negative patients, suggesting that overweight/obesity seen among PLHIV on ART is part of the overweight/obesity epidemic seen in the general population; ii) The prevalence of HTN, and DM/CHD among HIV-positive patients on ART was lower than in HIV-negative patients; which, advocate for the interplay of factors of ART, HIV and the host population as a possible pathway to the occurrence of HTN, DM, DM/CVD among HIV-positive.

However, the fact that data analyzed in this work were from a cross-sectional study, is, a limiting factor. Though we used the analytical approach to compare groups/subgroups, causal relationships still cannot be readily ascertained as data on both the exposure and the outcome were collected simultaneously. But, the fact of collecting data from HIV-positive and HIV-negative patients from the same OPD of 4 major clinics of Gaborone at the same time period, plus the stratification of participants by HIV status may have somewhat minimized biases. And, though associations brought up herein may not be causal owing to the study design, they are a good start point; since to our knowledge, this is the first study in the country where overweight/obesity and related comorbidities are compared between HIV-positive and HIV-negative patients. This new insight on HIV, overweight/obesity and related comorbidities is somehow, supported by existing data and thus, opening the way for more robust research designs to reconcile ongoing conflicting reports.

5. Conclusion

The prevalence of overweight/obesity in this study was comparable between HIV-positive and HIV-negative patients; suggesting that overweight/obesity among HIV-positive patients was part of the overweight/obesity epidemic seen in the general population as reported by others [5] [6] and not a direct effect or an aftermath of ART. The fact that the prevalence of HTN and DM/CHD was lower among HIV-positive compared to HIV-negative patients, possibly was from the interplay of multiple factors namely, factors of ART, HIV and the host population. Studies seeking to control overweight/obesity and related comorbidities among HIV-patients shouldn't use only strategies used in the general population, but also approaches that take into account ART, HIV and the host population factors.

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Ethics Approval and Consent to Participate

The study was approved by the University of Botswana Ethical Review Board (IRB) and the Health Research and Development Division in the Ministry of Health (MoH). Permission was also granted by the Greater Gaborone District Health Management ethics review committee and by clinic managers. Patient information that was unique and could be traced back to the patient was not used on the data collection tools to maintain confidentiality. They were assigned unique numbers created by the research team on the data collection tool. A face-to-face interview took place in private clinic rooms. Data collected was only used for research purposes and not shared.

Data Availability

Data underlying the findings in this study are neither readily available nor publicly accessible; they are professionally managed and safeguarded to protect patient confidentiality, as they include potentially identifying demographic and clinical care information. However, the data can be requested from the corresponding author. Before sharing the data, the latter would need first to securer clearance from the management of the HIV clinics where the study was conducted.

Competing Interests

The authors have no conflict of interest to declare.

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Authors' Contributions

This study was designed by JG Tshikuka, M Boitshwarelo, and S Hamda. The three participated in all the stages of this study, from the preparation of the proposal to manuscript writing. MGMD Magafu participated in reviewing the study proposal, analyzing data and writing the manuscript. R Tapera, T Masupe, JC Mwita, NKZ Bukonda, ME Onokoko participated in data analysis and manuscript preparation. All the authors contributed to the writing of the manuscript, and all of them read and approved the final copy.

List of Abbreviations

AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral therapy
AZT	Azidothymidine, also known as zidovudine
BMI	Body mass index
CD4	Cluster of differentiation 4
CI	Confidence interval
DM	Diabetes mellitus
CHD	Coronary heart disease
HAART	Highly active ART HAART
HTN	Hypertension
HIV	Human immunodeficiency virus
HSES	High socioeconomic status or participants whose major mode of transport was private cars
IDCC	Infectious Diseases Control Centre
ICD-10	The 10^{th} revision of the international statistical classification of diseases and related health problems
MOHW	Ministry of Health and Wellness
MSES	Middle-income status or participants whose major mode of transport was public transport
LSES	Low socioeconomic status or participants whose major mode of transport was walking
PLHIV	People living with HIV
SD	Standard deviation
SES	Socioeconomic status
WHO	World Health Organization

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