HHS Public Access

Author manuscript

Diabetes Metab Res Rev. Author manuscript; available in PMC 2017 September 01.

Published in final edited form as:

Diabetes Metab Res Rev. 2016 September ; 32(6): 544–549. doi:10.1002/dmrr.2792.

Prevalence of and Factors Associated with Prediabetes and Diabetes among HIV-infected Adults in Cameroon

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Abstract

Background—HIV and certain antiretrovirals (ARVs) are associated with diabetes. Few studies have examined the prevalence of and factors associated with diabetes amongst HIV-infected individuals on combination antiretroviral therapy (cART) in sub-Saharan Africa; some report prevalence estimates between 3.5–26.5% for diabetes in Cameroon and 20.2–43.5% for prediabetes in sub-Saharan Africa.

Methods—In a cross-sectional study, HIV-infected individuals (16–65 years old) were screened for diabetes using haemoglobin A_{1C} (HbA_{1C}). We further categorized HbA_{1C} as normoglycemia (HbA_{1C} <5.7%), prediabetes (HbA_{1C} 5.7–6.4%), or diabetes (HbA_{1C}≥6.5%). Dysglycemia was defined as HbA_{1C} ≥5.7%. Logistic regression modeling was used to assess factors associated with having dysglycemia..

Results—Of 500 participants, 363 (72.6%) were female. Median age was 42.5 years [Interquartile Range (IQR):36.5–49.5]. Nineteen (3.8%) were diabetic, and 170 (34%) were prediabetic. One hundred nine (22%) had a CD4+ count ≤200 cells/mm^3, and 464 (93%) had received ≥28 days of antiretroviral therapy (ART) at time of screening. Median abdominal circumference for women was 79.5cm (IQR: 75.5–85.3) and for men, 86.5cm (IQR: 81.7–90.5). Adjusting for age, sex, socio-economic status, CD4 cell count, being on cART >28 days, BMI, hypertension, history of hypertension, abdominal circumference, and duration of HIV infection,

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Duality of Interest:
The authors have no conflicts of interest to disclose.

Ethics:
This project and manuscript are in accordance with the ethical standards of and approved by both the CBCHS and the Icahn School of Medicine at Mount Sinai IRBs.

larger abdominal circumference was associated with higher prevalence of prediabetes or diabetes [adjusted Odds Ratio (aOR)=1.07, 95% Confidence Interval (CI):1.03–1.11], while being on cART (aOR=0.46, CI:0.22–0.99) was associated with lower prevalence.

Conclusions—There was a high prevalence of Cameroonian HIV-infected adults with dysglycemia. Larger abdominal circumference was associated with higher prevalence, while cART was associated with lower prevalence.

Keywords

diabetes; HIV; prevalence; Cameroon; antiretroviral therapy

Introduction

Diabetes morbidity has increased in the past two decades at a disturbing rate worldwide and, along with HIV/AIDS, is now one of the leading causes of death in low-middle income countries. HIV infection and certain antiretrovirals (ARVs) are known to be associated with diabetes. Few studies in Africa have assessed diabetes or prediabetes among HIV-infected adults as well as the impact of combination antiretroviral treatment (cART) regimens on diabetes morbidity. However, some studies have reported prevalence estimates between 3.5–26.5% for diabetes in Cameroon [1–3] and 20.2–43.5% for prediabetes in sub-Saharan Africa [1, 4]. We conducted a cross-sectional study to assess the prevalence of and factors associated with diabetes and prediabetes in HIV-infected individuals in Cameroon.

Materials and Methods

In this cross sectional study a convenience sample of Cameroonian HIV patients were studied for dysglycemia.

Study Population and Sample Size

The Cameroon Baptist Convention Health Services (CBCHS) is a healthcare consortium that delivers primary and tertiary healthcare throughout 6 of 10 provinces in Cameroon. HIV-infected persons ≥16 years receiving care at the CBCHS's semi-rural Mbingo Family Care and Treatment Center were invited to participate in this study between June-August 2014. Pregnant individuals and those already diagnosed with diabetes were excluded. All patients provided written informed consent. This study was approved by the Institutional Review Boards of CBCHS and the Icahn School of Medicine at Mount Sinai.

Assuming a true insulin resistance prevalence rate of approximately 30% amongst HIV-infected adults in Cameroon based on previous research [1], an infinite population size, and a 95% confidence interval required, we chose a sample size of 500 participants, allowing us to improve the precision of the calculated prevalence estimate to within 4%.

Measurements

Participants were screened for diabetes using serum haemoglobin A1C (HbA_{1C}) which was measured via the Tinaquant Gen2 immunoassay and performed on the Roche® Cobas c111 automated analyzer. Participants with a $HbA_{1C} \geq 6.5\%$ were categorized as those with

previously undiagnosed diabetes; those with a HbA_{1C} < 6.5% but ≥ 5.7% were categorized as having prediabetes. Dysglycemia was defined as HbA1C ≥5.7%. [5] Data on patient medical history, family history, HIV immune status, and antiretroviral therapy (ART) regimen were collected. Height, weight, abdominal circumference, and blood pressure were measured in standardized fashion using a stadiometer, scale, tape measure, and blood pressure cuffs respectively by 2 trained staff members. High blood pressure was defined as ≥140/90 according to the World Health Organization [6].

Analysis

Characteristics were compared between those with prediabetes or diabetes and those that were diabetes free using Wilcoxon, Chi-square, or Fisher's Exact tests as appropriate. We did not impute missing data as only 16 (3%) had missing HbA_{1C} data. However, we did perform a secondary analysis and compared characteristics between those with and without HbA_{1C} data in order to assess for selection bias. Crude and adjusted odds ratios (aOR) were calculated to identify factors associated with dysglycemia (HbA_{1C} ≥ 5.7). Variables at least marginally associated with dysglycemia ($p<0.2$) were considered candidates for inclusion in multivariable modeling and entered in the initial logistic regression model. Both stepwise and backward elimination were used to determine whether both procedures arrived at the same parsimonious model at a 5% significance level. In addition, sex, CD4 cell count, and duration of HIV infection were forced into the final model since sex and measures of HIV immune status are known to be associated with dysglycemia. Statistical analyses were performed using SAS® 9.3 (Cary, NC).

Results

After excluding 16 participants with missing HbA_{1C} values, 500 participants remained for analysis.

Of 500 participants 363 (72.6%) were female. Median age was 42.5 years [Interquartile Range (IQR):36.5–49.5], and 328 (65.6%) achieved a primary school level education or less. (Table 1) One hundred nine (22%) had a CD4+ cell count ≤200 cells/mm^3 at enrollment, and 464 (93%) received >28 days of cART prior to HbA_{1C} testing. Median years of HIV infection was 4.5 years (IQR: 1.6–7.5), and the median duration of cART was 3.8 years (IQR: 1.3–6.3).

Participants receiving non-nucleoside reverse transcriptase inhibitor (NNRTI)-based cART were either on efavirenz (414/453) or nevirapine (31/453). Eleven (2.2%) received protease inhibitors (PI). Of those on cART, nucleoside reverse transcriptase inhibitor (NRTI) backbones received included: 448 (96.3%) on tenofovir (TDF)+ lamivudine (3TC), 3 (0.6%) on zidovudine (AZT)+3TC, 3 (0.6%) on abacavir (ABC)+3TC (3/465,0.6%), and 11 (2.4%) on other NRTI antiretrovirals (ARVs).

Eighty-nine (17.8%) had a blood pressure ≥140/90 mm Hg, and 200 (40%) participants were overweight or obese. Median abdominal circumference for women was 79.5cm (IQR 75.5–85.3) and for men, 86.5cm (IQR 81.7–90.5). Overall, 19 (3.8%) had diabetes; 170 (34%) had

prediabetes. Out of the 500 participants, 212 (42.4%) had a HbA_{1C} of 5.5 or greater but less than 6.0% and 91 (18.2%) had a HbA_{1C} of 6.0% or greater.

In multivariate logistic regression modeling (Table 2), larger abdominal circumference (per 1 cm increment) was associated with having prediabetes or diabetes (aOR=1.07, 95% Confidence Interval (CI):1.03–1.11, *p<0.01*), while being on cART (aOR=0.46, CI:0.22–0.99, *p=0.046*) was inversely associated. In secondary analysis, to assess whether there was selection bias in excluding participants missing HbA_{1C} data (n=16), we found no statistically significant differences in characteristics between those missing and those not missing HgA1C data.

Discussion

We observed a higher than expected prevalence of having prediabetes or diabetes (i.e., dysglycemia) in ambulatory HIV-infected individuals 16 years and older. Larger abdominal circumference was associated with a higher prevalence of prediabetes or diabetes, while cART was associated with a lower prevalence.

The prevalence of diabetes we report are consistent with the few studies published to date amongst HIV-infected adults in Cameroon where estimates have ranged from 3.5–26.5% [1–3]. One Cameroonian study of 204 subjects reported a prevalence of 26.5% using fasting plasma glucose [2]. The variability in prevalence estimates may be due to differences between studies in sample processing as well as in methods for diabetes screening between fasting plasma glucose and HbA_{1C}.

Although the prevalence of frank diabetes in our population was low, the prevalence of dysglycemia was high, consistent with other studies. Though no other studies in Cameroon have been published to date evaluating diabetes risk using HbA_{1C}, one study of 108 HIV-infected and 96 HIV-uninfected adults in Cameroon reported 43.5% HIV-infected and 28.1% uninfected to have had impaired fasting glucose (100–125 mg/dL)[1], according to 2006 WHO criteria [8]. A Ugandan study of 1,497 adults in the general population reported a prediabetes rate of 20.2% using fasting plasma glucose [4] according to the 2010 American Diabetes Association (ADA) [9] criteria.

Larger abdominal circumference was associated with prediabetes/diabetes among our study population. This has been shown in the general population [10], and in one study of 1,481 HIV-infected men and 841 HIV-infected women, higher waist circumference was associated with increased risk for metabolic syndrome as well as diabetes [11]. A study by Scherzer et al has shown waist circumference to be a strong predictor of insulin resistance among HIV-infected patients [12].

Being on cART was associated with a lower prevalence of prediabetes/diabetes in our study sample, a finding that is in direct contrast to another smaller study of HIV-infected individuals in Cameroon [3]. This may be explained in part by the differing cART regimens received by participants between the two studies. Forty-five percent of participants in the study [3] were receiving stavudine, known to be associated with an increased risk of diabetes [13]. Conversely, the overwhelming majority of our patients received TDF + 3TC which

have not been shown to be associated with prediabetes or diabetes. In addition, all but 11 of the participants in our study receiving cART were on NNRTIs, in particular, EFV, which, when compared with PIs, have been shown to be associated with decreased risk for metabolic complications [14].

Our study was limited by its cross-sectional design, precluding our ability to infer causality. The use of a single HgA_{1C} measurement to screen for dysglycemia may have reduced the specificity of our screen, since the ADA currently recommends repeat testing for abnormal HgA_{1C} results. The fact that all participants were enrolled at a single site may reduce the generalizability of our findings to the population of Cameroon as a whole, although our site does provide HIV care to a large catchment area across the northwest province in Cameroon. Our study was also 72.6% female and therefore, this may limit the generalizability of the study. However, our results likely reflect the fact that HIV prevalence in Cameroon is almost twice as high among women compared to men [15]. In addition, we were not able to properly assess insulin resistance or metabolic syndrome. Furthermore, our cohort included only small numbers of participants not on cART. Because of this we are cautious not to over-interpret our findings. In addition, we were unable to distinguish whether a participant had type I or type II diabetes mellitus which would have been important amongst the youngest participants. However, only 35 participants were <30 years old, 13 of whom (2.6% of the study sample) had prediabetes or diabetes. Lastly, because of the homogeneity in cART regimens, we were unable to assess the impact of specific ARVs on dysglycemia.

In conclusion, while the prevalence of frank diabetes may have been low in our study, we found a high prevalence of patients with dysglycemia among the HIV-infected adult population in Cameroon. Larger abdominal circumference was associated with having prediabetes or diabetes in our sample of HIV-infected adults in Cameroon. Early screening for diabetes in patients with increased abdominal circumference and the continued use of current WHO-recommended first-line cART regimens in sub-Saharan Africa may be beneficial for HIV-infected individuals in resource-limited countries. Further prospective studies are warranted to elucidate the association between HIV infection and dysglycemia in this population.

Acknowledgments

Funding:

This work was supported by the Arnhold Global Health Institute at the Icahn School of Medicine at Mount Sinai.

We would like to acknowledge the hard work of the staff at the Family Care and Treatment Center at Mbingo Baptist Hospital and thank them for helping us execute this project. J.J. is supported by NICHD K23HD070760.

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Table 1

Characteristics of study participants

	TOTAL n=500 (%)	Dysglycemic (HbA_{1C} ≥ 5.7) n=189	Normoglycemic (HbA_{1C} <5.7) n=311	*p*-value[§]
Socio-demographics				
Age (years)	42.5 (36.5–49.5)	44.8 (36.8– 50.6)	41.7 (35.8– 48.6)	*0.03*
Female	363 (72.6)	137 (72.5)	226 (72.7)	*0.97*
Marital Status				*0.57*
Single	101 (20.2)	33 (17.5)	68 (21.9)	
Married/Live w. partner	207 (41.4)	79 (41.8)	128 (41.2)	
Divorced/Separated	55 (11)	20 (10.6)	35 (11.3)	
Widowed	137 (27.4)	57 (30.2)	80 (25.7)	
Highest level of education				*0.17*
Primary school	328 (65.6)	113 (60.0)	215 (69.1)	
Secondary School	94 (18.8)	43 (22.8)	51 (16.4)	
Vocational School/University	47 (9.4)	21 (11.1)	26 (8.4)	
Graduate	31 (6.2)	12 (6.3)	19 (6.1)	
Electricity in the house	291 (58.2)	116 (61.3)	175 (56.3)	*0.26*
Refrigerator in the house	76 (15.2)	37 (19.6)	39 (12.5)	*0.03*
Water Source				*0.17*
Tap water in home	53 (10.6)	24 (12.7)	29 (9.3)	
Tap water in compound	155 (31.0)	59 (31.2)	96 (30.9)	
Community tap water	217 (43.4)	72 (38.1)	145 (46.6)	
Other	75 (15.0)	34 (18.0)	41 (13.2)	
Gainfully employed	113 (22.6)	50 (26.5)	63 (20.3)	*0.11*
Duration of HIV infection (years)	4.5 (1.6– 7.5)	4.5 (1.7– 7.5)	4.4 (1.5– 7.5)	*0.62*
Duration of cART (years)	3.8 (1.3– 6.3)	3.8 (1.4– 6.0)	3.6 (1.0– 6.7)	*0.99*
Family Medical History				
Diabetes				*0.76*
Yes	28 (5.6)	12 (6.3)	16 (5.1)	
No	397 (79.4)	147 (77.8)	250 (80.4)	
Unknown	75 (15.0)	30 (15.9)	45 (14.5)	
Heart problem				*0.56*
Yes	30 (6)	14 (7.4)	16 (5.1)	

	TOTAL n=500 (%)	**Dysglycemic (HbA_{1C} ≥ 5.7) n=189**	**Normoglycemic (HbA_{1C} <5.7) n=311**	***p*-value[§]**
No	403 (80.6)	149 (78.8)	254 (81.7)	
Unknown	67 (13.4)	26 (13.8)	41 (13.2)	
Patient Medical History				
Hypertension				*0.01*
Yes	37 (7.4)	20 (10.6)	17 (5.5)	
No	456 (91.2)	166 (87.8)	290 (93.2)	
Unknown	7 (1.4)	3 (1.6)	4 (1.3)	
CD4 at enrollment (cells/ uL)				*0.60*
0–50	26 (5.2)	9 (4.8)	17 (5.5)	
51–200	83 (16.6)	28 (14.8)	55 (17.7)	
201–350	85 (17)	37 (19.6)	48 (15.4)	
>350	306 (61.2)	115 (60.8)	191 (61.4)	
Nadir CD4 (cells/uL)				*0.26*
0–50	89 (17.8)	27 (14.3)	62 (19.9)	
51–200	227 (45.4)	89 (47.1)	138 (44.4)	
201–350	149 (29.0)	56 (29.6)	93 (29.9)	
>350	35 (7.0)	17 (9.0)	18 (5.8)	
ART regimen at time of sample >28 days				*<0.01*
None	36 (7.2)	19 (10.1)	17 (5.5)	
NNRTI-based	453 (90.6)	170 (89.9)	283 (91.0)	
PI-based	11 (2.2)	0 (0)	11 (3.5)	
Physical Measurements				
BMI (kg/m^2)				
Underweight (0–18.49)	25 (5.0)	9 (4.8)	16 (5.1)	
Normal (18.5–24.99)	275 (55.0)	90 (47.6)	185 (59.5)	*<0.01*
Overweight (25–29.99)	151 (30.2)	60 (31.7)	91 (29.3)	
Obese (≥30)	49 (9.8)	30 (15.9)	19 (6.1)	
Systolic BP (mm Hg)				*0.10*
≥140	66 (13.2)	31 (16.4)	35 (11.3)	
Diastolic BP (mm Hg)				*0.15*
≥90	68 (13.6)	31 (16.4)	37 (11.9)	
Female Median Abdominal circumference (cm)	86.5 (81.5–90.5)	86.7 (82.5–91.4)	85.0 (80.5–90.5)	*0.16*
Male Median Abdominal circumference (cm)	79.5 (75.5–85.5)	81.9 (77.5–89.4)	78.6 (74.5–83.0)	*<0.01*

ART=Antiretroviral Treatment; BMI=body mass index; BP=Blood Pressure; NNRTI=non-nucleoside reverse transcriptase inhibitor; PCP=pneumocystis pneumonia; PI=protease inhibitor;

§Data are reported as median (interquartile range) for continuous variables and number (%) for categorical variables. p-values from Wilcoxon test for continuous variables (except student t-test was done for age), Chi-square or Fisher's Exact test, as appropriate, for categorical variables.

Table 2

Characteristics associated with the prevalence of dysglycemia in HIV patients in Cameroon.

Factor		Adjusted Odds Ratio	95% CI	
Age	**1 year increment**	1.01	0.99	1.03
Female gender		0.65	0.40	1.06
Refrigerator in the home		1.40	0.82	2.39
CD4+ cells (cells/mm^3)	**0–50**	0.94	0.37	2.38
	51–200	0.78	0.44	1.38
	201–350	1.30	0.77	2.18
	350+	(ref)	--	--
On cART		0.46	0.22	0.99
BMI (kg/m^2)	**Underweight (0–18.49)**	1.64	0.63	4.25
	Normal (18.5–24.99)	(ref)	--	--
	Overweight (25–29.99)	0.82	0.49	1.38
	Obese (30+)	0.96	0.38	2.40
High blood pressure[a]		1.15	0.64	2.05
Patient history of hypertension		1.37	0.61	3.08
Abdominal circumference	**1 cm increment**	1.07	1.03	1.11
Years of HIV Infection	**1 year increment**	0.98	0.92	1.04

BMI=Body Mass Index; cART= Combination Antiretroviral Treatment; CI=Confidence Interval

[a]Defined as systolic blood pressure >140 mm Hg or diastolic blood pressure>90 mm Hg

[*]All factors listed above were retained in the final logistic regression model.