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RESEARCH ARTICLE

# Association between HIV infection, antiretroviral therapy and dysglycaemia prevalence in black South Africans: evidence from the Durban Diabetes Study

**D Perumal[1]*, FJ Pirie[1], TM Esterhuizen[2], B O'Leary[3], EH Young[4], MI McCarthy[5], MS Sandhu[6] and AA Motala[1]**

[1]*Department of Diabetes and Endocrinology, Nelson R Mandela School of Medicine, University of KwaZulu-Natal, South Africa*
[2]*Department of Global Health, Division of Epidemiology and Biostatistics, Faculty of Medicine and Health Sciences, Stellenbosch University, South Africa*
[3]*Research and Policy Department, Office of Strategy Management, eThekwini Municipality, South Africa*
[4]*Wellcome Trust Sanger Institute, UK*
[5]*Oxford Centre for Diabetes, Endocrinology and Metabolism, University of Oxford, UK*
[6]*Department of Public Health and Primary Care, University of Cambridge, UK*
**Correspondence: daneperumal18@gmail.com*



**Aims** To determine the association between HIV infection, antiretroviral therapy (ART), and dysglycaemia in urban black South Africans in the Durban Diabetes Study (DDS).
**Methods** In a population-based cross-sectional study, adult participants without a history of diabetes mellitus (DM) were included for analysis. The prevalence of dysglycaemia (total, impaired fasting glucose [IFG], impaired glucose tolerance [IGT], or diabetes ), using oral glucose tolerance test (OGTT), and its relationship to HIV and ART use was assessed.
**Results** In the total group (*n*: 1 067, 749 women), 45.6% (*n*: 487) were HIV+; 35.3% (*n*: 172) of the HIV+ group were on ART. The overall prevalence of total dysglycaemia was 8.1%; IFG 0.8%, IGT 3.8%, and diabetes 3.5%. IGT and diabetes prevalence was higher in women than in men. The prevalence of all categories of dysglycaemia peaked in the ≥ 65-year age group and was higher in the HIV– vs. HIV+ group ($p = 0.001$). There was no significant difference between HIV+ART– and HIV+ART+ for prevalence of total dysglycaemia and its subsets. Traditional risk factors (BMI, age) but not HIV or ART were associated with increased risk of dysglycaemia.
**Conclusion** In this population, HIV infection and ART are not associated with a higher prevalence of dysglycaemia.

**Keywords:** antiretroviral therapy, dysglycaemia, epidemiology, HIV infection, South Africa

## Introduction

Health systems planning in sub-Saharan Africa (SSA) faces several challenges, in particular, the significant dual burden of infectious and non-communicable diseases (NCDs).[1–4] The World Health Organization (WHO) reports that NCDs, including diabetes mellitus (diabetes), accounted for an estimated 3.1 million deaths in the Africa region in 2021, with a projected increase to over 5 million in 2030.[2,4]

There is a rise in the burden of diabetes in SSA. In 2021, the International Diabetes Federation (IDF) estimated that there were 537 million adults living with diabetes globally, with a projected increase of 46% to 783 million in 2045; the greatest increase is expected for the Africa region, by 134%, from 24 to 55 million. For South Africa, in 2021, there were an estimated 4.23 million adults with diabetes of whom approximately 45% were undiagnosed.[5,6] The increasing prevalence of diabetes in South Africa, as in the rest of SSA, is thought to be multifactorial and includes population growth and epidemiologic transition (increased longevity, changes in lifestyle and diet, economic development) induced by rapid urbanisation.[3–6]

In 2024, the Joint United Nations Programme on HIV/AIDS (UNAIDS) reported that SSA remained the worst-hit region with 52.1% (20.8 million) of the 39.9 million people living with HIV (PLWH) in the world being from the eastern/Southern Africa region.[7] With improved healthcare systems and access to antiretroviral therapy (ART), life expectancy in HIV–positive people has increased and has been accompanied by an increase in the burden of NCD in this population.[7,8]

Disorders of glucose tolerance/glycaemia (dysglycaemia) are defined as one or more of impaired fasting glucose (IFG), impaired glucose tolerance (IGT), or diabetes (D).[9,10] While there is emerging information on diabetes prevalence in Africa, data on other components of dysglycaemia from epidemiology studies are limited.[6] The IDF has projected greater increases for IGT than diabetes in Africa (by 124%, from 52.2 million in 2021 to 116.7 million by 2045), with concern for further increases in the burden of diabetes and, therefore, healthcare expenditure. In 2021, Africa had the highest proportion of people with undiagnosed diabetes (53.6%; 12.7 million).[6]

Dysglycaemia has been reported to be associated with HIV infection, although the true pathophysiological processes regarding the diabetogenic effects of HIV and ART remain to be elucidated and the relationship appears complex. However, traditional risk factors remain important in the development of dysglycaemia.[11] HIV itself may be diabetogenic: HIV–1 accessory proteins have been implicated in the development of insulin resistance, viral protein R (Vpr) interferes with insulin transcriptional activity, and trans-activator of transcription (Tat) proteins activate nuclear factor kappa B and induce a pro-inflammatory cascade with the final common pathway being suppressed insulin signalling at the insulin receptor level.[11] Antiretroviral agents have long been implicated in insulin

resistance and the development of dysglycaemia.[12,13] Nucleoside reverse transcriptase inhibitors (NRTIs) have been reported to induce mitochondrial toxicity via inhibition of DNA polymerase-γ and, at a muscle level, to induce insulin resistance. Protease inhibitors (PIs) and their effect on fat metabolism, insulin resistance, and diabetes remain to be fully understood. Studies have reported intra-class differences in their effects on insulin and glucose metabolism interplay.[11] A clinic-based study from South Africa reported an increased likelihood of dysglycaemia in HIV seropositive patients on a PI-containing ART regimen (OR 4.1, 95% CI 2.54–6.61) when compared with those who were ART naive or on a non-PI-containing ART regimen.[14] The study reported that total dysglycaemia was increased in all HIV groups (ART naive 26%, first-line ART 29.9%, and second-line ART 34.3%), when compared with a historical population-based study control group (15%), presumed to be HIV–, and this was largely contributed to by increased rates of IFG; of note, HIV tests were not done in the control group.[14]

There is a paucity of studies on the association of HIV with dysglycaemia from epidemiology studies from Africa;[5,15] most reports are from clinic studies.[14,16–19] UNAIDS rates the data available from the SSA region as poor for analysis and extrapolation on dysglycaemia.[7,20] The Durban Diabetes Study (DDS) was a population-based study undertaken to determine the prevalence of diabetes and to ascertain its associations with cardiometabolic, infective and genetic risk.[20, 21] In the total group (*n*: 1 209), there was a high age-standardised prevalence of diabetes (12.9%); prevalence was moderate for IGT (3.5%) and low for IFG (0.8%).[21] This sub-analysis of the DDS was done to determine the association between HIV infection, ART use, and dysglycaemia in urban black Africans.

## Subjects, materials, and methods

### Study design

The DDS was a population-based, cross-sectional study on non-pregnant, urban black South African adults aged 18 years and older in the eThekwini municipality conducted between November 2013 and November 2014. A detailed description of the study design and methods have been previously published.[20,21] The DDS was approved by the University of KwaZulu-Natal Biomedical Research Ethics Committee (Ref: BF030/12 & BE007/19) and the UK National Research Ethics Service (Ref: 14/WM/1061).

## Methods

### Data collection

In brief, following informed consent, an electronic questionnaire, adapted from the standardised WHO STEPwise approach to surveillance (STEPS) tool, was administered by trained study personnel and collected health and lifestyle data (demographic data, education, occupation and socioeconomic indices, tobacco use, dietary behaviours, physical activity, medical and family history).[22] Anthropometric measurements included height, weight, waist circumference (WC) and hip circumference, body mass index (BMI) and waist-to-hip ratio (WHR). Venous blood samples were drawn for glycaemic biomarkers (75 g oral glucose tolerance test [OGTT], glycated haemoglobin [HbA1c]), fasting serum lipids (LDL, HDL, triglycerides, total cholesterol). Samples for HIV were stored and tested according to standard WHO methodology.[9, 23]

The following analytic methods were used: plasma glucose was measured using the glucose oxidase method (Abbott ARCHITECT 2: ci8200, Abbott Laboratories, Chicago, IL, USA), serum lipids were measured with an autoanalyser (Abbott ci 6200), HbA1c using high-performance liquid chromatography (HPLC) (BioRad VARIANT II TURBO 2.0, Bio-Rad Laboratories, Inc., Hercules, CA, USA), an instrument certified by the National Glycohaemoglobin Standardization Program (NGSP) and International Federation of Clinical Chemistry and Laboratory Medicine (IFCC). HIV status was determined using HIV ELISA (Roche Cobas e601). Confirmatory HIV tests were also performed with ELISA (Vironostika bioMerieu HIV Ag/Ab Microelisa system).

### Definitions

Participants were categorised by HIV and ART status as follows: no HIV (HIV–), HIV infected/ positive (HIV+), ART naive (HIV + ART–), treated HIV (HIV + ART+), or treatment details unknown ("don't know"). Current ART use was obtained on history. WHO criteria were used for OGTT classification: normoglycaemia, IFG, IGT, or diabetes.[9,10] Total dysglycaemia was defined as the sum of IFG, IGT, and diabetes. Prevalence of glycaemia categories was determined for the total group and then stratified by sex, HIV, and ART status. WHO criteria were used to interpret HbA1c results.[23] Anthropometry results were classified using WHO criteria.[24] Dyslipidaemia was defined according to South African lipid guidelines which are based on the European guidelines.[25]

### Statistical analysis

Statistical analysis was undertaken using Stata v17 software package (StataCorp LLC, College Station, TX, USA). Analysis was restricted to participants with no history of known diabetes and for whom complete data were available for HIV and glycaemia variables. A chi-square test was used for categorical data and categorical variables were presented as a percentage. Continuous variables were presented as mean ± SD, and comparison between groups undertaken using a *t*-test. A $p$-value < 0.05 was considered statistically significant. Age standardisation was calculated with the direct method using the WHO world standard population as the reference.[26] The prevalence of dysglycaemia and its individual components (IFG, IGT, diabetes) are presented as crude, age-specific, and age-standardised. Multivariable logistic regression analysis was undertaken for estimation of associations between risk factors and dysglycaemia. Sex, age, BMI, and family history were controlled for as they are among the most commonly identified predictors in epidemiology studies on diabetes and dysglycaemia and were significant on univariate analysis. The results are presented as odds ratios (ORs) and 95% CIs.

## Results

### Total study group

A total of 1 067 participants (749/62.1% women) were included in the analysis. The mean (SD) age was 38 ± 16 years. The prevalence of HIV (HIV+) was 45.6% (*n*: 487) of whom, 35.3% (*n*: 172) were on ART (HIV + ART+). The majority (*n*: 145; 84.3%) of participants on ART were on first-line therapy (non-PI-based, NNRTI/NRTI-based therapy); only 3 (1.7%) were on second-line (PI-based) treatment and in 14% (*n*: 24) therapy details were unknown ("don't know"). The peak prevalence of HIV was in the 35–44-year age group (68%) and the age-standardised prevalence of HIV was 48.9%. The mean duration of ART therapy was 2.1 years (95% CI 1.96–2.19).

Table 1 presents the general characteristics of the group by sex. When compared with men, women were significantly older ($p = 0.0011$), had significantly higher mean BMI ($p < 0.001$) and WC ($p < 0.001$), and had a higher prevalence of total ($p < 0.001$) and central adiposity ($p < 0.001$). Mean FPG ($p = 0.006$), 2-hour plasma glucose ($p < 0.001$), HbA1c ($p = 0.0024$), and serum lipids (total and LDL cholesterol, triglycerides) were also higher in women, while mean systolic blood pressure ($p = 0.0008$) and HDL cholesterol ($p = 0.0094$) were lower.

Clinical and laboratory characteristics of the total group by HIV and ART status are given in Table 2. When compared with the HIV– group the prevalence of elevated WC was significantly higher ($p = 0.047$), while mean total cholesterol ($p < 0.001$), LDL ($p < 0.001$) and HDL ($p = 0.023$) were significantly lower in the HIV + group. Systolic ($p < 0.001$) and diastolic ($p = 0.035$) blood pressure, as well as FPG ($p = 0.025$) and 2-hour plasma glucose, ($p = 0.001$) were lower in the HIV+ group.

When the HIV+ group was stratified by ART status, a higher WHR in men ($p = 0.004$) and women ($p = 0.026$) and serum lipids (total cholesterol [$p < 0.001$], triglycerides [$p = 0.0179$], LDL [$p = 0.036$], and HDL [$p < 0.001$]) were found in those on ART.

## Dysglycaemia prevalence

### *Total group*

In the total group, the crude prevalence of IFG was 0.8%, IGT 3.8%, and diabetes 3.5%; total dysglycaemia prevalence was 8.1%. The prevalence of IGT, diabetes and total dysglycaemia was higher in women (4.3%, 4.1% and 9.1%, respectively) than in men (2.8%, 1.9%, and 5.6%, respectively) (Table 3). Using age-specific rates, the peak prevalence of total dysglycaemia was in the oldest age group (≥ 65 years) (Supplementary Table 1). The age-standardised prevalence of IFG was 0.6%, IGT 2.8%, of diabetes 2.6% and of total dysglycaemia 6.1% (Table 3). The crude prevalence of diabetes by HbA1c was 3.8%, higher in women (4.5%) than in men (2.2%) ($p = 0.037$).

### By HIV and ART status

Table 4 indicates the prevalence of dysglycaemia by HIV and ART status. The crude prevalence of IGT, diabetes, and total dysglycaemia was significantly higher ($p = 0.001$) in HIV– compared with the HIV+ group: IGT 5.5% vs. 1.8%; diabetes 4.7% vs. 2.1%; total dysglycaemia 8.3% vs. 5.3%. In both HIV– and HIV+ there was a low prevalence of IFG (0.7% and 0.8% respectively). In the HIV– group the most prevalent category was IGT, while diabetes was the most prevalent category in the HIV+ group. The age-standardised prevalence of total dysglycaemia was higher in HIV– group (8.3%) than in the HIV+ group (5.3%). The crude prevalence of diabetes by HbA1c was 5.7% in HIV– group, and 1.4% in the HIV+ group ($p < 0.0001$) (Table 4).

When stratified by ART status (HIV + ART– vs. HIV + ART+) the groups did not differ significantly: IFG 1.0% vs. 0.6%, IGT 2.2% vs. 1.2%, diabetes 1.6% vs. 2.9%. Age-standardised prevalence of total dysglycaemia was higher in the ART– group (6.2%) than the ART+ group (2.7%). In the case of HbA1c, diabetes prevalence was similar by ART status (ART– 1.6%; ART+ 1.2%) ($p = 0.707$).

## Association: dysglycaemia and HIV/ART

In multivariate analysis, only the traditional risk factors (age and BMI) were significantly associated with increased risk of dysglycaemia after adjusting for other confounders (Table 5). Relative to the HIV– group, there was a non-significantly decreased risk of dysglycaemia in the HIV + ART+ group (OR 0.47; 95% CI 0.21–1.08, $p = 0.077$).

**Table 1:** Clinical and laboratory characteristics of total group by sex (*n*: 1 067)

| Item | All (*n*: 1 067) | Men (*n*: 318) | Women (*n*: 749) | *p*-value |
|---|---|---|---|---|
| Age (years) | 38.0 ± 16.0 | 35.6 ± 14.4 | 39.1 ± 16.6 | 0.0011 |
| Weight (kg) | 73.6 ± 20.4 | 65.7 ± 12.9 | 76.9 ± 22.0 | < 0.001 |
| BMI (kg/m$^2$) | 28.6 ± 8.4 | 23.2 ± 4.5 | 30.9 ± 8.6 | < 0.001 |
| Overweight[a] (%) | 23.3 | 18.2 | 25.5 | |
| Obese[b] (%) | 35.3 | 6.3 | 47.7 | |
| Overweight/obese (%) | 58.7 | 24.5 | 73.2 | |
| Waist circumference (WC) (cm) | 94.0 ± 17.2 | 84.4 ± 10.3 | 98.0 ± 17.9 | < 0.001 |
| Elevated WC[c] (%) | 62.7 | 15.1 | 82.9 | |
| WHR | 0.86 ± 0.1 | 0.86 ± 0.1 | 0.86 ± 0.1 | 0.3004 |
| Systolic BP (mmHg) | 116.2 ± 20.6 | 119.5 ± 18.1 | 114.9 ± 21.5 | 0.0008 |
| Diastolic BP (mmHg) | 77.1 ± 13.1 | 76.3 ± 12.6 | 77.5 ± 13.3 | 0.1714 |
| Lipids (mmol/l) | | | | |
| TC | 4.18 ± 1.02 | 3.92 ± 0.94 | 4.30 ± 1.03 | < 0.001 |
| TG | 1.17 ± 0.76 | 1.08 ± 0.63 | 1.20 ± 0.80 | 0.0112 |
| LDL | 2.23 ± 0.78 | 1.97 ± 0.68 | 2.33 ± 0.79 | < 0.001 |
| HDL | 1.28 ± 0.32 | 1.32 ± 0.36 | 1.27 ± 0.30 | 0.0094 |
| FPG (mmol/l) | 4.7 ± 1.5 | 4.6 ± 1.0 | 4.8 ± 1.6 | 0.0061 |
| 2HPG (mmol/l) | 5.35 ± 2.6 | 4.75 ± 2.0 | 5.6 ± 2.8 | < 0.001 |
| HbA1c (%) | 5.5 ± 0.8 | 5.4 ± 0.6 | 5.5 ± 0.9 | 0.0024 |
| (mmol/mol) | 36.3 ± 8.8 | 35.2 ± 6.3 | 36.8 ± 9.6 | 0.0046 |

Data are mean (±SD) or percentage (%); BMI: body mass index, WC: waist circumference, WHR: waist-to-hip ratio, BP: blood pressure, TC: total cholesterol, TG: triglycerides, LDL: low-density lipoprotein, HDL: high-density lipoprotein, FPG: fasting plasma glucose, 2HPG: 2-hour plasma glucose, HbA1c: glycated haemoglobin [a]: BMI 25–29.9 kg/m$^2$, [b]: BMI ≥ 30 kg/m$^2$, [c]: ≥ 94 cm in men and ≥ 80 cm in women.

**Table 2:** Clinical and laboratory characteristics of the total group by HIV and ART status (*n*: 1 067)

| Item | HIV– 580 (54.4%) | HIV+ 487 (45.6%) | *p*-value | ART- 315 (64.7%) | ART+ 172 (35.3%) | *p*-value |
|---|---|---|---|---|---|---|
| Weight (kg) | 75.0 ± 20.9 | 71.9 ± 19.7 | 0.014 | 71.8 ± 20.5 | 72.2 ± 18.2 | 0.841 |
| BMI (kg/m$^2$) | 29.2 ± 9.0 | 28.0 ± 7.6 | 0.015 | 27.9 ± 8.0 | 28.0 ± 7.0 | 0.906 |
| Overweight* (%) | 21.0 | 26.1 | 0.101 | 27.0 | 24.4 | 0.753 |
| Obese** (%) | 38.3 | 31.8 | | 30.2 | 34.9 | |
| WC (cm) | 94.9 ± 18.3 | 92.9 ± 15.7 | 0.056 | 91.9 ± 16.2 | 94.7 ± 14.6 | 0.061 |
| Male | 84.6 ± 10.6 | 84.1 ± 9.7 | 0.641 | 83.0 ± 8.9 | 86.2 ± 10.9 | 0.094 |
| Female | 100.6 ± 19.2 | 95.4 ± 16.2 | <0.001 | 94.6 ± 17.0 | 97.0 ± 14.7 | 0.162 |
| Elevated WC+ (%) | 60.0 | 65.9 | 0.047 | 63.5 | 70.4 | 0.127 |
| WHR | 0.86 ± 0.10 | 0.85 ± 0.09 | 0.076 | 0.84 ± 0.08 | 0.87 ± 0.09 | 0.002 |
| Male | 0.86 ± 0.09 | 0.87 ± 0.08 | 0.462 | 0.85 ± 0.06 | 0.89 ± 0.06 | 0.004 |
| Female | 0.86 ± 0.11 | 0.85 ± 0.09 | 0.027 | 0.83 ± 0.09 | 0.86 ± 0.10 | 0.026 |
| Systolic BP (mmHg) | 119.5 ± 21.2 | 112.4 ± 19.2 | <0.001 | 112.3 ± 19.3 | 112.5 ± 19.1 | 0.893 |
| Diastolic BP (mmHg) | 77.9 ± 13.2 | 76.2 ± 13.0 | 0.035 | 75.8 ± 12.8 | 76.9 ± 13.4 | 0.340 |
| Lipids (mmol/l) | | | | | | |
| TC | 4.29 ± 1.09 | 4.06 ± 0.91 | <0.001 | 3.93 ± 0.89 | 4.30 ± 0.92 | <0.001 |
| TG | 1.15 ± 0.75 | 1.18 ± 0.76 | 0.569 | 1.12 ± 0.64 | 1.29 ± 0.94 | 0.0179 |
| LDL | 2.32 ± 0.84 | 2.12 ± 0.67 | <0.001 | 2.07 ± 0.66 | 2.21 ± 0.70 | 0.036 |
| HDL | 1.31 ± 0.30 | 1.26 ± 0.35 | 0.023 | 1.21 ± 033 | 1.34 ± 0V.37 | <0.001 |
| FPG (mmol/l) | 4.8 ± 1.5 | 4.6 ± 1.4 | 0.025 | 4.6 ± 1.6 | 4.7 ± 0.8 | 0.291 |
| 2HPG (mmol/l) | 5.6 ± 2.8 | 5.1 ± 2.3 | 0.001 | 5. ± 2.5 | 5.1 ± 1.9 | 0.959 |
| HbA1c (%) | 5.56 ± 0.9 | 5.37 ± 0.6 | <0.001 | 5.39 ± 0.6 | 5.35 ± 0.7 | 0.591 |
| (mmol/mol) | 37.2 ± 9.9 | 35.3 ± 7.1 | <0.001 | 35.4 ± 7.1 | 35.0 ± 7.1 | 0.556 |

Data are mean (±SD) or percentage (95% CI), ART–: untreated HIV, ART+: treated HIV, BMI: body mass index, * BMI 25–29.9 kg/m$^2$, ** BMI ≥ 30 kg/m$^2$, WC: waist circumference, ≥ 94 cm in men and ≥ 80 cm in women, WHR: waist-to-hip ratio, BP: blood pressure, TC: total cholesterol, TG: triglycerides, LDL: low-density lipoprotein, HDL: high-density lipoprotein, FPG: fasting plasma glucose, 2HPG: 2-hour plasma glucose, HbA1c: glycated haemoglobin.

## Discussion

In this urban black South African population, using WHO criteria, dysglycaemia prevalence was higher in HIV– than in HIV + participants, and similar in HIV+ ART treatment groups. Moreover, HIV infection and ART were not associated with an increased risk of dysglycaemia.

In this study, when compared with HIV– participants, the HIV+ group had a lower prevalence of diabetes (2.1% vs. 4.7%), IGT (1.8% vs. 5.5%), and total dysglycaemia (4.7% vs. 10.9%). This is in contrast to several studies from Africa, which have reported high prevalence of total dysglycaemia or total prediabetes.[14,16,19,27,28] However, those studies were clinic-based trials that focused on HIV participants and used widely variable biomarkers for the diagnosis of dysglycaemia (FPG alone, OGTT alone, or HbA1c) or diagnostic cut-points for IFG/prediabetes (WHO/ADA).[16,19] The DDS, to our knowledge, is the first population-based diabetes epidemiology study in Africa to assess the relationship between dysglycaemia and HIV using all three biomarkers with validated analytic methods.

Regarding diabetes, the finding in this study are compatible with those of a recent analysis of a national study (South African Demographic and Health Survey 2016/SADHS16), which showed that diabetes prevalence was higher in HIV– (20.4%) than HIV+ (18.4%) participants; that there was no

**Table 3:** Prevalence (%) of dysglycaemia in the total group (*n*: 1 067)

| Item | *n* | All *n*: 1 067 | % All* *n*: 1067 | % Men *n*: 318 | % Women *n*: 749 | *p*-value |
|---|---|---|---|---|---|---|
| By OGTT | | | | | | |
| | | | | | | 0.173 |
| IFG | 8 | 0.8 (0.4–1.5) | 0.6 | 0.9 (0.3–2.9) | 0.7 (0.2–1.6) | |
| IGT | 41 | 3.8 (2.8–5.2) | 2.8 | 2.8 (1.5–5.4) | 4.3 (3.0–6.0) | |
| Diabetes | 37 | 3.5 (2.5–4.8) | 2.6 | 1.9 (0.8–4.1) | 4.1 (2.9–5.8) | |
| Total dysglycaemia | 86 | 8.1 | 6.1 | 5.6 | 9.1 | |
| By HbA1c | | | | | | |
| Diabetes | 40 | 3.8 (2.8–5.2) | – | 2.2 (1.1–4.5) | 4.5 (3.2–6.3) | 0.037† |

Data are % (±95% CI). * Age-standardised. IFG: impaired fasting glucose, IGT: impaired glucose tolerance, diabetes: diabetes mellitus, HbA1c: glycated haemoglobin †*p*: men vs. women.

**Table 4:** Prevalence of dysglycaemia by HIV and ART status (*n*: 1 067)

| Item | % HIV– *n*: 580 | % HIV+ *n*: 487 | *p*-value | % ART- : 315 | % ART+ *n*: 172 | *p*-value |
|---|---|---|---|---|---|---|
| By OGTT | | | | | | |
| | | | 0.001 | | | 0.614 |
| IFG | 0.7 (0.3–1.8) | 0.8 (0.3–2.2) | | 1.0 (0.3–2.9) | 0.6 (0.1–4.0) | |
| IGT | 5.5 (3.9–7.7) | 1.8 (1.0–3.5) | | 2.2 (1.1–4.6) | 1.2 (0.3–4.5) | |
| Diabetes | 4.7 (3.2–6.7) | 2.1 (1.1–3.8) | | 1.6 (0.7–3.8) | 2.9 (1.2–6.8) | |
| Total dysglycaemia | 10.9 | 4.7 | | 4.8 | 4.7 | |
| Age-standardised dysglycaemia | 8.3 | 5.3 | | 6.2 | 2.7 | |
| By HbA1c | | | | | | |
| Diabetes | 5.7 (4.1–7.3) | 1.4 (0.7–3.0) | < 0.001 | 1.6 (0.6–3.8) | 1.2 (0.3–4.6) | 0.707 |

Data are % (95% CI). ART –: untreated HIV, ART+: treated HIV, IFG: impaired fasting glucose, IGT:– impaired glucose tolerance, diabetes: diabetes mellitus, HbA1c: glycated haemoglobin.

significant association between HIV and any increased risk of diabetes; and that PLWH have better cardiometabolic profiles than the general population.[29] However, in the SADHS16, the diagnosis of diabetes was based solely on the use of point of care finger-prick HbA1c, which has not been validated for the diagnosis of diabetes. By contrast, most other studies from SSA reporting on dysglycaemia in PLWH largely represent clinic studies or convenience sampling or were HIV-focused epidemiology studies.[14–19,28] In the Ugandan HIV epidemiology study, a very low prevalence of diabetes (0.4%) was reported.[15] The SADHS16 perhaps represents one of the few African studies that can be directly compared with the DDS as its primary aim was the determination of the association between HIV/ART exposure and diabetes and hypertension.[29]

In the DDS, the prevalence of IGT was lower and IFG higher in the HIV+ (vs. HIV–) group. Direct comparison with available reports is not possible, because in most clinic-based HIV studies the comparison was between HIV– vs. HIV+ by ART status.[14,16,19] Notwithstanding, IGT prevalence, which was lower in the HIV+ group in this study, is similar to that found in the clinic-based South African study, in which IGT was found in 11.6% in the "HIV–" group, 4.3% in HIV+ ART–, and 2.5% in HIV ART+ on first-line ART, but higher (12.0%) in HIV+ ART+ on second-line (PI-based) ART.[14] It is important to note, though, that in that study the "HIV–/control" group were drawn from a historical population-based study and presumed to be HIV–, and did not have HIV tests. By contrast, in the large Tanzanian clinical trial, IGT (termed prediabetes) prevalence was significantly higher in HIV+ groups regardless of ART status.[16] The higher prevalence of IGT in the HIV + ART– group in that study may be accounted for by the fact that the participants were newly diagnosed with HIV, with low levels of screening for dysglycaemia in the general population (i.e., undetected dysglycaemia).

**Table 5:** Logistic regression analysis: independent factors associated with dysglycaemia (IFG, IGT, diabetes combined)

| Variable | aOR (95% CI) | *p*-value |
|---|---|---|
| Sex (F vs. M) | 1.00 (0.52–1.95) | 0.988 |
| Family history of diabetes | 0.80 (0.47–1.37) | 0.416 |
| BMI | 1.03 (1.00–1.06) | 0.016 |
| Age | | |
| < 35 | Reference | |
| 35–< 45 | 12.93 (3.55–47.10) | < 0.001 |
| 45–< 55 | 31.07 (9.12–105.87) | < 0.001 |
| 55–< 65 | 37.00 (10.56–129.64) | < 0.001 |
| ≥ 65 | 55.35 (15.67–195.59) | < 0.001 |
| HIV | | |
| HIV– | Reference | |
| HIV + ART- | 0.83 (0.43–1.61) | 0.16 |
| HIV + ART+ | 0.47 (0.21–1.08) | 0.077 |

Data are adjusted odds ratio (95% CI). HIV+ ART–: untreated HIV, HIV+ ART+: treated HIV.

Regarding IFG, of interest is that, in the Cape Town study,[14] prevalence was higher in all HIV+ groups (ART– and ART+), but low (1.5%) in the population study, and similar to that found in our study. This may be due to differences in epidemiological transition in South Africa, i.e., that in the general population, the prevalence of IFG is low, while moderate to high prevalence of IGT and diabetes is seen.[21,30] Comparison with the Ghanian clinical HIV study, which reported significantly lower prediabetes prevalence in HIV + ART+ (13.2%) when compared with HIV + ART– (27.9%) and HIV– (27.3%) groups, is difficult, given that in that study the diagnosis of "prediabetes" was based on lower (ADA) diagnostic cut-points (FPG ≥ 5.6–< 7.0 mmol/l).

In the DDS, there was no significant difference in the prevalence of total dysglycaemia and its subsets by ART status ($p = 0.614$). Although not directly comparable, due to differences in design, methods, and criteria employed, variable findings have been reported from clinic studies from Africa, with some showing higher prevalence in ART+ (vs. ART–) groups, and others reporting no difference.[14,19,27] Studies using only FPG also report variable results.[31,32]

The prevalence of diabetes based on HbA1c in our study was similar to that found using OGTT, i.e., significantly higher in HIV– (vs. HIV+) and similar when stratified by ART status. In the Ghanaian study, in which FPG and HbA1c were done, there was a similar prevalence of diabetes in HIV– (7.4%) and HIV+ (6.6% in ART-; 7.4% in ART+) ($p = 0.91$) participants, and prevalence was higher than in the DDS; however, the diabetes

group in that study included those with known diabetes and the diagnosis of diabetes was based on a combination of FPG and HbA1c results.[19] In the Tanzanian study, by HbA1c, diabetes prevalence was significantly higher in the HIV + ART– (17.7%) vs. HIV– (9.3%) or HIV + ART+ (7.8%) groups, probably related to the same factors as discussed for IGT, i.e., low levels of screening for dysglycaemia in the general population.[16] In a smaller Cameroonian study, diabetes prevalence using HbA1c was 3.8%, similar to the DDS, and to that found in population studies in Cameroon.[33]

There are only a few reported studies that have examined HIV, ART exposure, and dysglycaemia risk using both OGTT and HbA1c.[16] In the Tanzanian study, as stated earlier, the HIV + ART– group had a higher prevalence of both diabetes and IGT using OGTT and diabetes by HbA1c when compared with HIV– and HIV + ART+ participants ($p < 0.001$).[16] Additionally, there existed differences in prevalence of categories of dysglycaemia, which was higher by HbA1c than OGTT for diabetes, and lower by HbA1c than OGTT for "PreD". In the total study population, diabetes prevalence based on OGTT (6%) was lower than by HbA1c (13%), with partial overlap, i.e., OGTT and HbA1c identified different participants as having diabetes or prediabetes.

In our study, multivariate analysis showed that traditional risk factors (BMI, age) and not ART status were associated with dysglycaemia.

In the DDS, there was a female preponderance of enrolled participants; this is similar to other epidemiology studies in South Africa and may reflect the historic effects of the migrant worker system.[20,30,34,35]

The strength of the DDS was its design as a population-based epidemiology study, compared with the facility-based sampling reported from most other African studies. There was no upper age limit, allowing for analysis of geriatric populations. Data were collected using a standardised framework allowing for comparison with other studies with similarly aligned methodology.[36]

An inherent limitation is the cross-sectional nature restricting the assessment of causality. Small numbers of those on second-line ART precluded reliable analysis of PI-based regimens and dysglycaemia. The data collection occurred at a time when South African health policies regarding HIV care differed from the current ones with the advent of "test-and-treat" strategies ensuring wider rollout of ART and the encouraged first-line use of an integrase inhibitor (dolutegravir), a drug that has several adverse metabolic effects including dysglycaemia.[37]

## Conclusion

In this analysis of the DDS, dysglycaemia prevalence was higher in HIV– than in HIV+ participants and was similar between those on ART and those who were ART naive in the HIV+ group, suggesting that HIV infection and exposure to ART were not associated with an increased risk of dysglycaemia in this population. To our knowledge, our study represents the first diabetes epidemiology study in Africa to examine that association. These findings may have implications for health systems planning and reflect that, in contrast to high-income countries, NCDs in South Africa are not largely impacted by HIV and ART use. Clearly, there is a need for further studies from SSA, both cross-sectional and prospective studies, to confirm these findings.

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## ORCID

*D Perumal* http://orcid.org/0000-0002-2528-0331
*Fj Pirie* http://orcid.org/0009-0009-6420-3855
*Aa Motala* http://orcid.org/0000-0003-0517-1784

## References

1. Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the global burden of disease study 2010. Lancet. 2012;380(9859):2095–2128. https://doi.org/10.1016/S0140-6736(12)61728-0
2. World Health Organization. Global health estimates 2021: deaths by cause, age, sex, by country and by region, 2000-2021. 2024. Available from: https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-leading-causes-of-death. Accessed 24 January 2025.
3. Motala AA, Mbanya JC, Ramaiya K, et al. Type 2 diabetes mellitus in sub-Saharan Africa: challenges and opportunities. Nat Rev Endocrinol. 2022;18(4):219–229. https://doi.org/10.1038/s41574-021-00613-y
4. World Health Organization. Global health estimates 2015 summary tables: deaths by cause, age, sex. 2015.
5. Gouda HN, Charlson F, Sorsdahl K, et al. Burden of non-communicable diseases in sub-saharan Africa, 1990-2017: results from the global burden of disease study 2017. Lancet Glob Health. 2019;7(10):e1375–e1e87. https://doi.org/10.1016/S2214-109X(19)30374-2

6. International Diabetes Federation. IDF diabetes atlas, 10th edn. International Diabetes, 2021. Available from:https://diabetesatlas.org/atlas/tenth-edition/.
7. Joint United Nations Programme on HIV. Global HIV/AIDS statistics: 2024 Fact Sheet 2024. Available from: https://www.unaids.org/en/resources/fact-sheet. Accessed 21 January 2025.
8. McDonald CL, Kaltman JR. Cardiovascular disease in adult and pediatric HIV/AIDS. J Am Coll Cardiol. 2009;54(13):1185–1188. https://doi.org/10.1016/j.jacc.2009.05.055
9. Alberti KGMM, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part; 1, diagnosis and classification of diabetes mellitus. Provisional report of a WHO consultation. Diabetic Med. 1998;15(7):539–553. https://doi.org/10.1002/(SICI)1096-9136(199807)15:7<539::AID-DIA668>3.0.CO;2-S
10. World Health Organization. Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia: report of a WHO/IDF consultation. 2006. Available from: https://iris.who.int/handle/10665/43588.
11. Samaras K. Prevalence and pathogenesis of diabetes mellitus in HIV–1 infection treated with combined antiretroviral therapy. JAIDS J Acquir Immune Defic Syndr. 2009;50(5):499–505. https://doi.org/10.1097/QAI.0b013e31819c291b
12. Dave JA, Lambert E, Badri M, et al. Effect of nonnucleoside reverse transcriptase inhibitor-based antiretroviral therapy on dysglycemia and insulin sensitivity in South African HIV–infected patients. J Acquir Immune Defic Syndr. 2011;57(4):284–289. https://doi.org/10.1097/QAI.0b013e318221863f
13. Gutierrez AD, Balasubramanyam A. Dysregulation of glucose metabolism in HIV patients: epidemiology, mechanisms, and management. Endocrine. 2012;41:1–10. https://doi.org/10.1007/s12020-011-9565-z
14. Levitt NS, Peer N, Steyn K, et al. Increased risk of dysglycaemia in South Africans with HIV; especially those on protease inhibitors. Diabetes Res Clin Pract. 2016;119:41–47. https://doi.org/10.1016/j.diabres.2016.03.012
15. Maher D, Waswa L, Baisley K, et al. Distribution of hyperglycaemia and related cardiovascular disease risk factors in low-income countries: a cross-sectional population-based survey in rural Uganda. Int J Epidemiol. 2011;40(1):160–171. https://doi.org/10.1093/ije/dyq156
16. Jeremiah K, Filteau S, Faurholt-Jepsen D, et al. Diabetes prevalence by HbA1c and oral glucose tolerance test among HIV–infected and uninfected Tanzanian adults. PLoS One. 2020;15(4):e0230723. https://doi.org/10.1371/journal.pone.0230723
17. Julius H, Basu D, Ricci E, et al. The burden of metabolic diseases amongst HIV positive patients on HAART attending The Johannesburg hospital. Curr HIV Res. 2011;9(4):247–252. https://doi.org/10.2174/157016211796320360
18. Mutimura E, Stewart A, Rheeder P, et al. Metabolic function and the prevalence of lipodystrophy in a population of HIV–infected African subjects receiving highly active antiretroviral therapy. J Acquir Immune Defic Syndr. 2007;46(4):451–455. https://doi.org/10.1097/QAI.0b013e318158c0a6
19. Sarfo FS, Norman B, Nichols M, et al. Prevalence and incidence of pre-diabetes and diabetes mellitus among people living with HIV in Ghana: evidence from the EVERLAST study. HIV Med. 2021;22(4):231–243. https://doi.org/10.1111/hiv.13007
20. Hird TR, Young EH, Pirie FJ, et al. Study profile: the Durban Diabetes Study (DDS): a platform for chronic disease research. Glob Health Epidemiol Genom. 2016;1:e2. https://doi.org/10.1017/gheg.2015.3
21. Hird TR, Pirie FJ, Esterhuizen TM, et al. Burden of diabetes and first evidence for the utility of HbA1c for diagnosis and detection of diabetes in urban black South Africans: the durban diabetes study. PLoS One. 2016;11(8):e0161966. https://doi.org/10.1371/journal.pone.0161966
22. World Health Organization. WHO STEPS surveillance manual: the WHO STEPwise approach to chronic disease risk factor surveillance. 2005, World Health Organization. Available from: https://iris.who.int/handle/10665/43376.
23. World Health Organization. Use of glycated haemoglobin (HbA1c) in diagnosis of diabetes mellitus: abbreviated report of a WHO consultation. 2011, World Health Organization. Available from: https://www.who.int/publications/i/item/use-of-glycated-haemoglobin-(-hba1c)-in-diagnosis-of-diabetes-mellitus.
24. World Health Organization. Obesity: preventing and managing the global epidemic. 2000. Available from: https://iris.who.int/handle/10665/42330.
25. Klug EQ. South African heart association (S A heart); South African dyslipidaemia guideline consensus statement. S Afr Med J. 2012;102(3):178–187. https://doi.org/10.7196/SAMJ.5502
26. Ahmad OB, Boschi-Pinto C, Lopez AD, et al. Age standardization of rates: a new WHO standard. Geneva: World Health Organization. 2001;9(10):1–14. Available from: https://www.researchgate.net/publication/203609941_Age_Standardization_of_Rates_A_New_WHO_Standard.
27. Manuthu EM, Joshi MD, Lule GD, et al. Prevalence of dyslipidemia and dysglycaemia in HIV infected patients. East Afr Med J. 2008;85(1):10–17. https://doi.org/10.4314/eamj.v85i1.9600
28. Nguyen KA, Peer N, De Villiers A, et al. Glycated haemoglobin threshold for dysglycaemia screening, and application to metabolic syndrome diagnosis in HIV–infected Africans. PLoS One. 2019;14(1):e0211483. https://doi.org/10.1371/journal.pone.0211483
29. Magodoro IM, Okello S, Dungeni M, et al. Association between HIV and prevalent hypertension and diabetes mellitus in South Africa: analysis of a nationally representative cross-sectional survey. Int J Infect Dis. 2022;121:217–225. https://doi.org/10.1016/j.ijid.2022.05.035
30. Peer N, Steyn K, Lombard C, et al. Rising diabetes prevalence among urban-dwelling black South Africans. PLoS One. 2012;7(9):e43336. https://doi.org/10.1371/journal.pone.0043336
31. Ngala RA, Fianko F. Dyslipidaemia and dysglycaemia in HIV–infected patients on highly active anti-retroviral therapy in Kumasi metropolis. Afr Health Sci. 2013;13(4):1107–1116. https://doi.org/10.4314/ahs.v13i4.35
32. Salami AK, Akande AA, Olokoba AB. Serum lipids and glucose abnormalities in HIV/AIDS patients on antiretroviral therapies. West Afr J Med. 2009;28(1):10–15. https://doi.org/10.4314/wajm.v28i1.48417
33. Rhee JY, Bahtila TD, Palmer D, et al. Prediabetes and diabetes among HIV–infected adults in Cameroon. Diabetes Metab Res Rev. 2016;32(6):544–549. https://doi.org/10.1002/dmrr.2792
34. Peer N, Lombard C, Steyn K, et al. High prevalence of metabolic syndrome in the black population of Cape Town: The Cardiovascular Risk in Black South Africans (CRIBSA) study. Eur J Prev Cardiol. 2015;22(8):1036–1042. https://doi.org/10.1177/2047487314549744
35. Motala AA, Esterhuizen T, Gouw E, et al. Diabetes and other disorders of glycemia in a rural South African community: prevalence and associated risk factors. Diabetes Care. 2008;31(9):1783–1788. https://doi.org/10.2337/dc08-0212
36. Ekoru K, Young EH, Adebamowo C, et al. H3Africa multi-centre study of the prevalence and environmental and genetic determinants of type 2 diabetes in sub-Saharan Africa: study protocol. Glob Health Epidemiol Genom. 2016;1:e5. https://doi.org/10.1017/gheg.2015.6
37. Namara D, Schwartz J, Tusubira AK, et al. The risk of hyperglycemia associated with use of dolutegravir among adults living with HIV in Kampala, Uganda: A case-control study. Int J STD AIDS. 2022;33(14):1158–64. https://doi.org/10.1177/09564624221129410.


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