Prevalence And Predictors Of Diabetes Mellitus Among Persons Living With Hiv (PLWHIV)

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Research article

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Abstract

**Background:** Diabetes mellitus is a chronic non-infectious medical condition which is evident by raised levels of glucose in the blood, because the body cannot produce any or enough of the hormone insulin or use insulin effectively. Diabetes, if not well managed leads to complications such as neuropathy, retinopathy, nephropathy which can be fatal. Some of the factors that predispose to diabetes include older age, higher body mass index, heredity and hypertension.

With the availability of HAART for the managing HIV/AIDS infection, life span of persons living with HIV (PLWHIV) has increased significantly. With increased longevity, the aging population of PLWHIV also face chronic diseases such as diabetes in addition to HIV. The burden of both HIV and diabetes is high in South Africa, particularly in KwaZulu-Natal. Nevertheless, the prevalence of diabetes among PLWHIV in KwaZulu-Natal and its predictors is not well understood. Therefore, this study was conducted to determine the prevalence, predictors of diabetes and the outcome of managing diabetes among PLWHIV.

**Methods:** The study was conducted in four public health care facilities in KwaZulu-Natal after ethical approval and informed consent were obtained. A pretested questionnaire and hospital patient charts were used to collect data. SPSS version 26 was used to analyze the data using descriptive statistics and logistic regression.

**Results:** The prevalence of diabetes among PLWHIV was 9%. This was higher than the prevalence of diabetes of 5.4% among the general population in South Africa. Just over 47% of those who had diabetes, had uncontrolled blood sugar, with a mean fasting blood sugar (FBS) of 11.7 mmol/L. The predictors of diabetes among PLWHIV were, male gender and older age. Male PLWHIV had 65% less chances of having diabetes and those who were between the ages of 18 and 48 years were 88% less probable to have diabetes compared to those who were older than 48 years.

**Conclusion:** Public sector health care facilities in KwaZulu-Natal need to do much more to manage diabetes in PLWHIV in order to prevent diabetic complications and possible negative impact on the outcome of HIV management.

Introduction

“Diabetes is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both” [1].

Insulin is an essential hormone produced in the body's pancreas gland and carries glucose from the bloodstream into the cells of the body where the glucose is transformed into energy. Deficiency of insulin or the cell's failure to respond to insulin results in hyperglycemia, which is a key feature of diabetes.

If no intervention is done, hyperglycemia can cause damage to different body organs, resulting to the development of debilitating and life-threatening health problems such as cardiovascular disease,
neuropathy, nephropathy and eye disease, resulting in retinopathy and blindness. These complications, however, can be slowed down or avoided if diabetes is appropriately managed.

Besides the main types of diabetes, viz Type 1, type 2 and gestational, there is secondary diabetes which arises as a complication of other diseases like pancreatitis, and hormonal disturbances such as Cushing’s disease [2].

The development of combined antiretroviral therapy has led to the increase in the life span of persons living with HIV (PLWHIV) with treatment, similar to the expected age of the general population [3,4,5]. With longevity, however, PLWHIV are developing other chronic medical conditions [6,7,8,9]. One of these chronic comorbidities is diabetes mellitus.

There are identified risk factors associated with the development of diabetes in PLWHIV that are the same as those in persons without HIV; they include older age, heredity, higher Body Mass Index [BMI], higher triglyceride and hypertension. However, PLWHIV have the additional risk factors of HIV and HIV medicines [10,11,12]. Antiretroviral medications, such as nucleoside reverse transcriptase inhibitors (NRTI) and protease inhibitors (PI), have been implicated in causing disorders such as insulin resistance, hyperglycaemia and diabetes [11,13].

This study is particularly important as South Africa is among the highest diabetes prevalent nations in Africa. The convergence of HIV and diabetes in same patients makes it crucial to investigate the extent of the burden and the predictors of diabetes among persons living with HIV, especially as data on the prevalence and the predictors of diabetes in PLWHIV in KwaZulu-Natal is limited.

Understanding the magnitude of the problem and proper management are essential, not only for the prevention of diabetic complications, reduction of mortalities due to the complications or for the improvement in the quality of life but also to prevent possible negative impact on the outcomes of managing HIV. Hence, this study was conducted with the following aim.

Methods

This was a retrospective and a prospective study, aimed at determining the prevalence and predictors of diabetes among persons living with HIV (PLWHIV) and assessing the outcome of managing diabetes. The study was conducted in 4 HIV clinics at Public Sector Hospitals in the eThekwini Metro of KwaZulu-Natal (KZN), South Africa. These hospitals were selected based on the different former designated racial settlements. A total of 1,203 patients living with HIV that have been on antiretroviral therapy (ART) for at least 6 months, between 2005 and 2019 were randomly selected as follows; letters ‘Y’ and ‘N’ were written on separate folded pieces of paper. Each patient who consented to participate in the study was asked to pick a folded piece of paper. Those who picked ‘Y’ were included in the study.

The participants had to be 18 years and above, and not pregnant. Those satisfying the criteria were recruited into the study after obtaining their written consent to take part in the study. The following
statistical parameters were used to arrive at the minimum sample size of 249 per hospital: Odds ratio = 1.25, type 1 error = 0.05, type 2 error = 0.2 and statistical power = 0.80. Assuming a population variance of 1 and population mean of 0 (normal distribution). A minimum sample size of 996 was determined with a critical Z value = 1.96. Though 996 was required for this study, the number of participants that selected Y was more than the required sample size resulting in a sample size of 1203 which was accepted to allow for dropouts in the study.

Data was collected by using both pretested questionnaire and patient chart. The pretesting was done by administering the questionnaires to 4 respondents randomly selected from the 4 hospital where the study was to be done and retrieved after they filled them. The completed questionnaires were checked to determine if the respondents understood the questions as intended by the researcher based on their responses and assessed the time taken to complete the questionnaire so as to avoid designing a questionnaire that was too long that could discourage the respondents from completing it. After that, all necessary adjustments and corrections were made on the questionnaire and made ready for data collection.

The questionnaire was designed to obtain information on patient demographics, other information such as diabetes screening at the clinic, diabetes status, adherence to hypoglycemic medications by the patients, and life style modification while information on patients management outcomes such as baseline and current CD4 cell counts, baseline and current viral load, initial and current blood sugar were obtained from the hospitals’ patient charts and transcribed into a table designed using Microsoft word.

The statistical package for social sciences (SPSS) software version 26 was used to analyze the data. Descriptive statistics and logistic regression were used in the analyses of data.

Before the commencement of the study, ethics approval was obtained from the Biomedical Research Ethics Committee of the University of KwaZulu-Natal with the ethics reference number BE314/18. Approvals were also obtained from the KwaZulu-Natal Department of Health and the hospitals where the study was conducted before the commence of the study.

Each participant was given the informed consent form from the UKZN Biomedical Research Ethics Committee to read or to be read to and explained thoroughly in either English language or isiZulu according to the preference of the participant. They were given the opportunity to ask questions, the form explained that their participation was voluntary, no incentives or reimbursements for participation in the study and that their anonymity was assured, the purpose for collecting the data was explained and their right to continue or withdraw from the study at any time without any consequence whatsoever was explained to them. Every participant who so consented to participate signed the consent form before he or she was included in the study. Some participants who opted out during the data collection, were excluded from the study.

Results
A total of 1203 participants were included in this study, with about two third (64%) females while 28 (2.3%) did not indicate their gender. The majority age group was 29 – 48 years, with slightly over 60% of the participants belonging to this age group. Over 45% of the participants had a CD4 count less than 200 cell/µL at the commencement of ART. Over two third were unemployed. Besides the common opportunistic infections in PLWHIV, other comorbidities present were hypertension (1.0%), epilepsy (0.6%) and renal impairment (0.7%), totally making up 2.3% across the participants, excluding diabetes mellitus. (Table 1) Out of the eleven ART regimens prescribed for the patients, TDF/FTC/EFV was the most commonly prescribed regimen (65%). (Table 2)

Prevalence of diabetes mellitus and outcome of diabetes management.

The prevalence of diabetes among persons living with HIV (PLWHIV) was 9%, [Fig 1] Large percentage (61%) of those having diabetes were diagnosed while already on ART. Almost half (47.1%) of those with diabetes remained with uncontrolled blood sugar, having a mean FBS of 11.7 mmol/L.

Association between patient variables and diabetes mellitus among PLWHIV on ART.

Patients’ age and socio-economic status were significantly associated (CI, 95%) with diabetes among PLWHIV on ART. (Table 3)

Predictors of diabetes among PLWHIV on ART.

In a stepwise forward likelihood ratio multivariate logistic regression model, female gender and age were the predictors of diabetes in PLWHIV on ART. (table 4)

The probability for diabetes mellitus in male PLWHIV on ART was 65% less than that of females (aOR = 0.35, 95% CI= 0.15-0.82, P-value=0.016). (table 4)

The likelihood of diabetes mellitus in PLWHIV on ART who were between the ages 18 and 48 years was 88% less than those that were older than 48 years. (aOR = 0.12, 95% CI= 0.06-0.26, P-value=0.000). (Table 4)

Table 2: Distribution of ART regimens prescribed
| ART Regimen         | Percentage (%) |
|--------------------|----------------|
| ABC/3TC/EFV        | 13.5           |
| ABC/FTC/EFV        | 0.1            |
| D4T/3TC/EFV        | 0.7            |
| TDF/3TC/NVF        | 0.3            |
| TDF/FTC/ATVr       | 3.3            |
| TDF/FTC/EFV        | 65             |
| TDF/FTC/LPVr       | 4.5            |
| TDF/FTC/NVP        | 3.1            |
| ZDV/3TC/ATVr       | 1.9            |
| ZDV/3TC/EFV        | 0.4            |
| ZDV/3TC/LPVr       | 7.0            |

Figure 1: Prevalence of diabetes among persons living with HIV

**Discussion**

In this study 9% of the participants living with HIV (PLWHIV) had diabetes (figure 1). South Africa, where the study was conducted has a high HIV prevalence as 20.4% of adults between the ages of 15 and 49 live with HIV [14]. In addition, the prevalence of diabetes among South Africa's adult general population was 5.4%. [15], yet the prevalence of diabetes among PLWHIV was much higher at 9%. As shown in this study.

This high prevalence of diabetes among PLWHIV as shown in our study, is consistent with findings by some other earlier studies [16,17,18,12]. However, a study by Diabetes Focus eMag [19] indicated that prevalence of diabetes among PLWHIV is similar to that among the general population. This difference in
findings by different studies may be due to differences in the prevalence of diabetes amongst different populations, or differences in participant’s lifestyles.

Another finding from this study relating to gender has shown that the prevalence of diabetes among females PLWHIV was higher (9.5%) than that of males (7.4%). This finding is similar with a study by Hernandez-Ronieu et al, where in 2017 [20], it was shown that the prevalence of diabetes among females living with HIV was higher than that of males living with HIV. However, the same study showed that the prevalence of diabetes is higher in males among the general population. Furthermore, in this South African study it was found that female gender is a predictor for diabetes in PLWHIV, as males living with HIV were 65% less likely to have diabetes than females (table 4). This finding was similar with other studies which indicated that female who are HIV positive are more likely to have non-communicable diseases (NDC) co-morbidity. [21,22]. Hence, females living with HIV should be screened for diabetes repeatedly at close interval, in other to detect diabetes early and manage them accordingly.

Though this study found that 61% of the PLWHIV were diagnosed with diabetes after the commencement of antiretroviral therapy, there was no significant association found between when ART was commenced and the incidence of diabetes mellitus. Earlier studies vary in their findings with regards to the association between ART and diabetes, with some studies showing similar results to this study [19], while other studies were contrary to the findings of this study, in that, they showed association between ART and diabetes [23,16,17,18]. People who test positive for HIV should be tested for diabetes before the commencement of ART and periodically thereafter.

Almost half (47.1%) of the PLWHIV with diabetes in this study remained with uncontrolled blood sugar (Mean FBS of 11.7 mmol/L), this is particularly of concern, as this predisposes them to diabetic complications such as retinopathy, neuropathy, nephropathy among others. These complications, if allowed to occur will further increase the disease burden and pill burden for this group of patients. Therefore, this study further sheds light on this issue to help clinicians understand the burden of diabetes among PLWHIV and appreciate the possible impact of uncontrolled blood sugar among these patients, with a view to mitigating the impact of the convergence of these chronic conditions by ensuring effective management of diabetes among persons living with HIV.

This study also showed that older age is a predictor to diabetes in PLWHIV, such that the likelihood of diabetes for those older than 48 years of age was 88% compared to those that are younger than 48 years of age (table 4). This is similar with other studies which showed that old age is a risk factor to chronic comorbidities in PLWHIV. [21,22]. As ART increases the life span of PLWHIV, predisposing them to chronic medical conditions such as diabetes, clinicians should give adequate attention to diabetes in PLWHIV as they do to other comorbidities.

However, the current (at the time of the study) blood sugar measurement for some of the patients with diabetes were missing, this might have affected the level of accuracy of the mean fasting blood sugar found in this study (11.7 mmol/L).
Conclusion/recommendations

In KwaZulu-Natal, the prevalence of HIV among PLWHIV (9%) was higher than that of the general population (5.4%), the prevalence among females was higher (9.5%) than that of males (7.4%) and predictors of diabetes among PLWHIV were female gender and older age. About half (47.1%) of the people with diabetes had uncontrolled blood sugar with a mean FBS of 11.7 mm/L. There was no association between ART and diabetes. People who test positive to HIV should be tested for diabetes before the commencement of ART, this is to further study the possible association between ART and HIV as some studies indicated. Regular and continuous testing for diabetes should be carried out and those found to be diabetic should be adequately managed to prevent diabetic complications as well as prevent possible interference with the outcomes of managing HIV.

Abbreviations

AIDS – Acquired Immunodeficiency Syndrome
ART - Antiretroviral Therapy
BMI – Body Mass Index
BREC - Biomedical Research Ethics Committee
FBS - Fasting Blood Sugar
HAART – Highly Active Antiretroviral Therapy
HIV – Human Immunodeficiency Virus
KZN – KwaZulu-Natal
NRTI - Nucleoside Reverse Transcriptase Inhibitors
PI - Protease Inhibitors
PLWHIV – Persons Living With HIV
SPSS - Statistical Package for Social Sciences
UKZN – University of KwaZulu-Natal

Tables

Table 1. Demographic information of patients.
(Table 1 should appear below results, line 189 in the text file)
| Variable                  | Frequency | Percentage (%) |
|---------------------------|-----------|----------------|
| **Gender**                |           |                |
| Female                    | 770       | 64.0           |
| Male                      | 405       | 33.7           |
| **Age in years**          |           |                |
| 18-28                     | 145       | 12.6           |
| 29-48                     | 694       | 60.2           |
| >48                       | 313       | 27.2           |
| **Baseline CD4**          |           |                |
| ≤200 cells/µL             | 275       | 45.5           |
| 200-350 cells/µL          | 156       | 25.8           |
| 351-500 cells/µL          | 75        | 12.4           |
| >500 cells/µL             | 98        | 16.2           |
| **Socio-economic status** |           |                |
| Employed                  | 384       | 32.4           |
| Unemployed                | 801       | 67.6           |
| **Opportunistic infections** |        |                |
| Tuberculosis              | 90        | 7.5            |
| Oral candidiasis          | 6         | 0.5            |
| Hepatitis B               | 4         | 0.3            |
| Condition                | Count | Percentage |
|-------------------------|-------|------------|
| Herpes zoster           | 5     | 0.4        |
| Diarrhoea               | 3     | 0.2        |
| Septic cellulitis       | 2     | 0.2        |
| Pneumonia               | 2     | 0.2        |
| Other comorbidities     |       |            |
| Hypertension            | 12    | 1.0        |
| Epilepsy                | 7     | 0.6        |
| Renal impairment        | 8     | 0.7        |

Table 3. Association between patient variables and diabetes among PLWHIV taking ART.

(Table 3 should appear below table 2 in the text file)
| Variables               | Diabetes, n (%) | Total frequency, n (%) | Chi-square P-value |
|------------------------|-----------------|------------------------|--------------------|
|                        | No              | Yes                    |                    |
| Gender                 |                 |                        |                    |
| Male                   | 363(92.4)       | 30(7.6)                | 393(34.6)          | 0.219              |
| Female                 | 669(90.2)       | 73(9.8)                | 742(65.4)          |                    |
| Age                    |                 |                        |                    |
| 18 – 28                | 139 (99.3)      | 1(0.7)                 | 140(12.5)          | 0.000*             |
| 29-48                  | 643(95.3)       | 32(4.7)                | 675(60.5)          |                    |
| >48                    | 233(77.4)       | 68(22.6)               | 301(27.0)          |                    |
| Level of Education     |                 |                        |                    |
| No formal education    | 40(87.0)        | 6(13.6)                | 46(4.2)            | 0.109              |
| Primary                | 175(87.1)       | 26(12.9)               | 201(18.5)          |                    |
| High school            | 601(92.2)       | 51(7.8)                | 652(60.0)          |                    |
| Tertiary               | 173(92.0)       | 15(8.0)                | 188(17.3)          |                    |
| Employment Status      |                 |                        |                    |
| Employed               | 349(93.6)       | 24(6.4)                | 373(32.6)          | 0.030*             |
| unemployed             | 692(89.6)       | 80(10.4)               | 772(67.4)          |                    |
| Alcohol consumption    |                 |                        |                    |
| Yes                    | 189(92.2)       | 16(7.8%)               | 205(18.1)          | 0.505              |
| No                     | 841(90.7)       | 86(9.3)                | 927(81.9)          |                    |
| Initial CD4 count (cells/mm3) |              |                        |                    |
| <200                   | 234(88.6)       | 30(11.4)               | 264(44.9)          | 0.414              |
| 200 - 350              | 142(91.0)       | 14(9.0)                | 156(26.5)          |                    |
| 351 - 500              | 68(93.2)        | 5(6.8)                 | 73(12.4)           |                    |
| >500                   | 89(93.7)        | 6(6.3)                 | 95(16.2)           |                    |
| Current CD4 count (cells/mm3) |           |                        |                    |
| <200                   | 50(94.3)        | 3(5.7)                 | 53(8.3)            | 0.386              |
| 200 - 350              | 99(93.4)        | 7(6.6)                 | 106(16.7)          |                    |
| 351 - 500              | 133(90.5)       | 14(9.5)                | 147(23.1)          |                    |
| >500                   | 293(88.8)       | 37(11.2)               | 330(51.9)          |                    |
As can be seen from table 3 above, there was statistically significant association between the age and employment status of PLWHIV and having diabetes, at 95% confidence level.

Table 4: Predictors of diabetes in PLWHIV on ART (Multi-covariate and uni-covariate logistic regression).

(Table 4 should appear below table 3 in the text file)
| Variables                  | COR (95%CI)  | COR P-Value | aOR (95%CI)  | aOR P-Value |
|---------------------------|--------------|-------------|--------------|-------------|
| Gender                    |              |             |              |             |
| Male                      | 0.76 (0.49-1.18) | 0.220       | 0.35 (0.15-0.82) | 0.016*      |
| Female                    | 1            | 1           |              |             |
| Age                       |              |             |              |             |
| 18 – 48                   | 0.14 (0.09-0.22) | 0.000*     | 0.12 (0.06-0.26) | 0.000*      |
| >48                       | 1            | 1           |              |             |
| Duration on ART           |              |             | 1 (0.99-1.01) | 0.473       |
| Level of education        |              |             |              |             |
| No formal education       | 1.73 (0.63-4.74) | 0.286       |              |             |
| Primary                   | 1.71 (0.88-3.35) | 0.115       |              |             |
| High school               | 0.98 (0.54-1.78) | 0.944       |              |             |
| Tertiary                  | 1            |             |              |             |
| Employment Status         |              |             |              |             |
| Employed                  | 0.60 (0.37-0.96) | 0.032*     |              |             |
| unemployed                | 1            |             |              |             |
| Alcohol consumption       |              |             |              |             |
| Yes                       | 0.83 (0.48-1.44) | 0.506       |              |             |
| No                        | 1            |             |              |             |
| Baseline CD4 cells count  |              |             |              |             |
| >200 cells/µL             | 1.90 (0.91-3.98) | 0.088       |              |             |
| ≤200 cells/µL             | 1            |             |              |             |
| Current CD4 cells count   |              |             |              |             |
| >200 cells/µL             | 1.04 (0.25-4.32) | 0.957       |              |             |
| ≤200 cells/µL             | 1            |             |              |             |

Keys: 1 = the reference category; COR = Crude Odd Ratio; CI = Confidence interval; aOR = Adjusted Odd Ratio (Logistic regression).
Figures

Figure 1

Prevalence of diabetes among persons living with HIV