PREVALENCE AND PREDICTORS OF DIABETES MELLITUS AMONG PERSONS LIVING WITH HIV (PLWH)

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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 predisposes 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 (PLWH) has increased significantly. With increased longevity, the aging population of PLWH 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 PLWH 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 PLWH.

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 was used to analyze the data using descriptive statistics and logistic regression.

Results: The prevalence of diabetes among PLWH 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 PLWH were, male gender and older age. Male PLWH

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 PLWH in order to prevent diabetic complications and possible negative impact on the outcome of HIV management.

Key words: Diabetes, Patient, Factors, HIV, Predictors, Prevalence. PLWH

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 (PLWH) with treatment, similar to the expected age of the general population [3,4,5]. With longevity, however, PLWH are developing other chronic medical conditions [6,7,8,9]. One of these chronic comorbidities is diabetes mellitus

Factors associated with the development of diabetes in PLWH are the same as those in persons without HIV; they include older age, heredity, higher Body Mass Index [BMI], higher triglyceride, lower total cholesterol and hypertension. However, PLWH 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].

Irrespective of the factors linked with the development of diabetes in PLWH, 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 therefore 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 (PLWH) 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. The patients who consented to participate in the study were 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 and validated questionnaire and patient chart.

The questionnaire was designed to obtain information on patient demographics, other information such as diabetes screening at the clinic, diabetes status, diabetes medication, 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.

Results

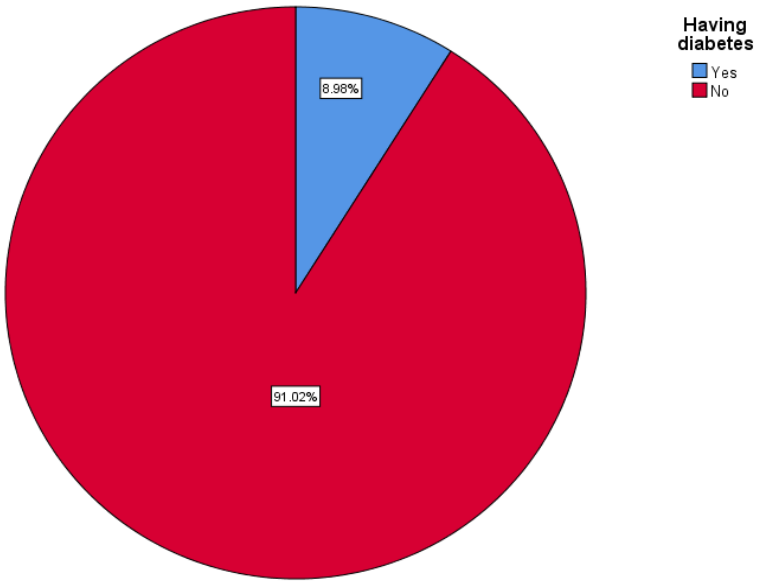
Table 1. Demographic information of patients

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

Of the 1203 participants, there were more females by close to fifty percent than males, while 28 (2.3%) did not indicate their gender. The age group 29 to 48 years was the majority age group of

the participants with just over 60%. Over 45% of the participants still had a CD4 count of less than 200.

Figure 1: Prevalence of diabetes among persons living with HIV



The prevalence of diabetes among persons living with HIV (PLWH) was 9%, [Fig 1]

Over 61% of those having diabetes were diagnosed while already on ART.

Over 47% of those with diabetes remained with uncontrolled blood sugar, having a mean FBS of 11.7 mmol/L.

Discussion

In this study 9% of the participants living with HIV (PLWH) had diabetes. 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 PLWH was much higher at 9%. As shown in this study.

This high prevalence of diabetes among PLWH 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 PLWH 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 PLWH 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 PLWH, as males living with HIV were 65% less likely to have diabetes than females. 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 PLWH were diagnosed with diabetes after the commencement of antiretroviral therapy, there was no significant association 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]. While the question whether ART predisposes PLWH to diabetes or not remain controversial, 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 PLWH 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 PLWH 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 PLWH, 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. This is similar with other studies which showed that old age is a risk factor to chronic comorbidities in PLWH. [21,22]. As ART increases the life span of PLWH, predisposing them to chronic medical conditions such as diabetes, clinicians should give adequate attention to diabetes in PLWH 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 PLWH (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 PLWH 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.

List of abbreviations

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PLWH – Persons Living With HIV

HIV – Human Immunodeficiency Virus

AIDS – Acquired Immunodeficiency Syndrome

FBS - Fasting Blood Sugar

HAART – Highly Active Antiretroviral Therapy

BMI – Body Mass Index

NRTI - Nucleoside Reverse Transcriptase Inhibitors

PI - Protease Inhibitors

KZN - KwaZulu-Natal

ART - Antiretroviral Therapy

SPSS - Statistical Package for Social Sciences

BREC - Biomedical Research Ethics Committee

Declarations

Ethics approval and consent to participate

Before the commencement of this study, ethical approval was obtained from the biomedical research ethics committee (BREC) of the University of KwaZulu-Natal (UKZN) (Reference number BE 314/18).

Each participant read or was read to, the Informed Consent Form from BREC and consented to participate in the study and signed the form before being included in the study.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

Funding

The College of Health Sciences Research office provided stipends to the corresponding author, funded logistics such as transportation to collect data and funded the cost of printing the research instruments (questionnaire and information sheet). But it was not involved in any way in the design

of the study, was not involved in the data collection. Was not involved in any way in the analysis, interpretation of data or in writing the manuscript.

Authors' contribution

DMU conceptualized the study, designed the work, collected data alongside 2 research assistants, analyzed and interpreted the data with the guidance of a statistician.

DMU has approved the submitted version of this manuscript and has agreed both to be accountable for his contributions and to ensure that questions related to the accuracy or integrity of any part of the work even ones in which he was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature

PN revised, the proposal, the questionnaire, the information sheet, draft manuscript and the final manuscript.

PN has approved the submitted version of this manuscript and has agreed both to be accountable for her contributions and to ensure that questions related to the accuracy or integrity of any part of the work even ones in which she was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature

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376 Table 2. Association between patient variables and diabetes among PLWH taking ART.

377 (Table 2 should appear below table 1 in the text file)

378

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)	
Initial viral load (copies/mm3)				

High (≥100,000)	22(95.7)	1(4.3)	23(14.6)	0.137
Low (10,000 – 99,000)	19(79.2)	5(20.8)	24(15.3)	
Lower (<10,000)	100(90.9)	10(9.1)	110(70.1)	
Current viral load (cells/mm3)				
'Detectable'	340(90.9)	34(9.1)	374(59.0)	0.587
LTDL	233(89.6)	27(10.4)	260(41.0)	

Key: * = Statistically significant

As can be seen from table 2 above, there was statistically significant association between the age and employment status of PLWH and having diabetes, at 95% confidence level.

389 Table 3: Predictors of diabetes in PLWH on ART (Multi-covariate and uni-covariate logistic

390 regression).

391 (Table 3 should appear below table 2 in the text file)

392

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	

393 Keys: 1 = the reference category; COR= Crude Odd Ratio; CI= Confidence interval; aOR =

394 Adjusted Odd Ratio (Logistic regression).

395

In a stepwise forward likelihood ratio multivariate logistic regression model (as shown in table 3 above), female gender and age were predictors of diabetes in PLWH on ART.

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

The likelihood of diabetes mellitus in PLWH 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% Cl= 0.06-0.26, P-value=0.000)