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Diabetesamong HIV-Infected Patients on Antiretroviral Therapy at MulagoNational Referral Hospital in Central Uganda

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Abstract:-This researchaimed at determining the prevalence of diabetes and factors associated among HIV patients on ART admitted at Mulago national referral hospital ART clinic, and a total of 200 HIV-infected adults were enrolled in the study. To determine prevalence and factors associated with diabetes, a questionnaire, was used to collect socio-demographic data, participants underwent assessment of Random blood sugar levels at enrolment and returned the following morning for fasting blood sugar (FBS) to be measured and diabetes was defined as FBG ≥ 7.0 mmol/L. A multivariate logistic analysis was applied to assess factors associated with diabetes.The overall diabetes prevalence was 7.5% (95%CI: 3.5, 11.5), with males at 5.3% (95%CI: 1.3, 12.0), and females at 8.8% (95%CL: 4.8, 13.6), 7.8% (95%CI: 3.9, 12.2) among urban residents, and 5.3% (95%CI: 0.0, 15.8) among rural residents, with those on second line treatment at 23.9% (95%CI: 13.0, 39.1) and 2.6% (95%CI: 0.6, 5.2) among participants on first line drugs. Those on second line drugs were significantly more likely to have diabetes (AOR 3.420(95%CI 2.053, 25.314) *P*=0.005), compared to first line users. Overweight, and Obese participants were also more likely to have diabetes (AOR 2.94375 (95%CI 2.915, 123.562) *P*=0.002) compared to those with normal weight. Participants with systolic pressure >139mmHg were almost 2 times more likely to have diabetes (AOR 1.529 (95%CI 1.223, 17.400) *P*=0.024), compared to those with a normal blood pressure. Diabetes prevalence among HIV patients in Uganda is high compared to what is reported in the general population. Body Mass Index (BMI), Use of Second Line drugs and Hypertension were found to be the factors associated with diabetes among HIV patients on ART.

Keywords:- *Diabetes, Uganda, Antiretroviral Therapy, Human Immunodeficiency Virus, Fasting Blood Sugar, Mulago National Hospital.*

I. INTRODUCTION

Diabetes mellitus (DM) is one of debilitating non communicable disease in which a person has a high blood sugar level, either resulting from the failure of the body to produce enough insulin, or failure of body cells to properly respond to the insulin that is produced(Rother,*et al.*, 2009). Commonly there 3 types of diabetes (Tierny,*et al.*,201), Type 1 diabetes: which results from the body's failure to produce insulin. Type 2 diabetes: which results from insulin resistance, a condition in which cells fail to use insulin properly, sometimes combined with an absolute insulin deficiency, and Gestational diabetes (high blood glucose level during pregnancy). The later may precede development of type 2 diabetes mellitus.Diabetes is a common metabolic disorders in the world, prevalence in adults(Whitin,*et al.*, 2011).Globally, in relationship with other non-communicable diseases (NCD), mainly cardiovascular diseases, cancers and chronic respiratory diseases, the prevalence of diabetes has increased [WHO 2014].

In the year 2013, the world prevalence of diabetes among adults aged 20-79 years was estimated at 8.3% [IDF 2013]. In Uganda, the prevalence of diabetes mellitus is estimated at 2.7% (Bahendeka,*et al.;* 2016). The burden of diabetes in the Human Immunodeficiency Syndrome (HIV/AIDS) sub-population is undocumented. Globally, more than 33 million people are living with HIV with the greatest burden of the disease being concentrated in developing countries (Mohamed *et al.*, 2015). Currently, HIV is one of the common recognized risk factor of diabetes. Patients on Antiretroviral Treatment (ART) are more likely to have Non Communicable Diseases (NCD) due to the effects of some drugs which induce metabolic disorders [16]. Diabetes mellitus among HIV-infected patients may result from metabolic disorders and it is worsened with the use of antiretroviral drugs(Florescu,*et al.*, 2007 &Samoras, et al 2009). Traditional risk factors, such as obesity, ageing and male sex, are also important determinants of diabetes in HIV-positive patients(Capeau,*et al.*, 2012).Diabetes can result into cardiovascular diseases such as hypertension, heart attack, stroke contributing to morbidity and mortality among HIV-infected persons (Shankalala,*et al.*, 2017).

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II. MATERIALS AND METHODS

A. Design and Selection of Participants

This was a cross-sectional study of 200 HIV-infected patients aged 18 years and above, admitted at Mulago national referral hospital ART-Clinic for medical assessment and had been on ART for a period of 1 year and above.

B. Study Site Description

Mulago national referral hospital is located in Kampala, the capital city of Uganda and serves a population of about 2.5 million people. It has about 2000 beds serving as a national referral hospital and teaching hospital for Makerere University College Health Sciences (CHS), Uganda.

C. Inclusion Criteria

Only HIV positive patient aged 18 years and above, who had been on ART for a period of 1 year and above admitted at the Hospital ART-Clinic and willing to participate were enrolled in the study

D. Exclusion Criteria

All HIV positive patients below the age of 18 years, those with Hepatitis B/C co-infection since drugs for these infections can also have side effects on the internal organs like the Liver, those whose diabetes status was known, and pregnant mothers who can be with gestational diabetes were all excluded from the study.

E. Data Collection

All Data was collected by Nurses after undergoing a one week training and a structured questionnaire was used to gather information on socio-demographic variables, use of ARTs, duration on ARTs, and use of Anti-hypertensive medication, Sex, age, location. Anthropometric measurements including weight, and height were measured from which BMI was calculated. The weight was recorded in kilograms using a weighing scale, and the height was recorded in meters. BMI was calculated as weight in kilograms divided by squared height in meters. BMI was categorized as underweight (<18.5 kg/m2), normal (18.5-24.9 kg/m2), overweight (25-29.9 kg/m2), and obesity (≥30 kg/m2). Blood pressure was measured using a standardized sphygmomanometer. Two blood pressure readings were taken and hypertension was defined as systolic pressure level ≥140mmHg and/or diastolic pressure ≥ 90mmHg, or taking medication for high blood pressure. All patients known to have diabetes mellitus were excluded from the study. Participants underwent assessment of Random blood sugar (RBS) levels at enrolment stage and returned the following morning for fasting blood sugar (FBS) measured using Cera1070-One touch glucometer manufactured by Green Cross Medis Corp. The primary outcome was proportion with normal blood sugar, and diabetes mellitus. Only HIV positive patient aged 18 years and above, who had been on ART for a period of 1 year and above admitted at the Hospital ART-Clinic and willing to participate were enrolled in the study.

F. Data Management and Data Analysis

All collected data was cross-checked for errors and then entered into a computer using microsoft excel version 2016 and later analyzed using Statistical Package for Social Scientists (SPSS version 23.0), where a descriptive statistics analysis was carried out to determine the prevalence of diabetes and categorical measurements were presented in percentages, and To determine the associations between the different factors and RBS level, the outcome variable analyses using Chi-square test was performed to find the significance of the study parameters on categorical scale between two or more groups, and $P<0.05$ was taken statistically significant.

G. Ethical Considerations

The study was approved by Makerere University (COVAB) Research Ethics Committee, Mulago Hospital Research Ethics Committee and Clearance to conduct the study was obtained from the Executive Director Mulago Hospital and also the Director Kiruddu Hospital. All the ethical principles of informed consent, autonomy, non-maleficence and beneficence, as well as confidentiality were duly observed. All data collection procedures were done under supervision of medical doctors following the standard protocol.

III. RESULTS

A. Social Demographics and Clinical Factors of HIV-Infected Patients

A total of 200 HIV-infected adults who had been on ART for 1 year and above were enrolled, of which 125 (62.5%) were females. Overall the median age was 41 years (IQR: 34.3–49). The median age for females was 40 years (IQR; 33-47 years) and 44 years (IQR; 34-49 years) for males. 50 (25%) of the patients were aged between 20 to 34 years, 71 (35.5%) were of age 35 to 44 years, and 79 (39.5%) had 45 years and above. The median body mass index (BMI) was 24.35 kilograms/m^2 (IQR: 21.6-26.6), and the distribution of BMI among patients was as follows; 11 (5.5%) were underweight, 105 (52.5%) with normal BMI, 61 (30.5%) were overweight, and 23 (11.5%) were obese as shown in table 1 below. The mean systolic pressure was 123.8 ±19.9mmHg, and 79.3 ±13.1mmHg for diastolic pressure. On measuring Blood pressure 46 (23%) were found to be having hypertension and 154(77%) with normal blood pressure. History of using anti-hypertensive drugs was given by 39 (19.5%) of the patients. Majority 163 (81.5%) of the patients were on first line treatment, and 83 (41.5%) of the patients had been on ART for a period of 1 to 5 years, while 117(58.5%) for 6 years and above with the median ART duration of 5 years (IQR; 2-7.8). The median random blood sugar level was 5.1mmol/L (IQR: 4.6-5.6mmol/L). The distribution of the participants by location was as follows; 180 (90%) were living in urban areas of Kampala, and 20 (10%) from rural as shown in table 1.

Characteristics	Frequency	Percentage (%)
Gender		
Female	125	62.5
Male	75	37.5
Age (years)		
20-34	50	25.0
35-44	71	35.5
45 and above	79	39.5
Body mass index (kg/m2)		
Underweight (<18.5)	11	5.5
Normal weight (18.5 to 24.5)	105	52.5
Overweight (25 to 29.9)	61	30.5
Obese (≥30)	23	11.5
Blood pressure (mmHg)		
Normal	154	77.0
Hypertension	46	23.0
Use of anti-hypertensive drugs		
On medication	39	19.5
Not on medication	161	80.5
Current ART-Line		
First line	163	81.5
Second line	37	18.5
Time on ART		
1 to 5 years	83	41.5
6 years and above	117	58.5
Blood sugar status		
Normal (<6.0mmol/L)	185	92.5
Diabetes (≥7.0mmol/L)	15	7.5
Location		
Urban	180	90.0
Rural	20	10.0
Total	**200**	**100**

Table 1:- Socio-Demographic and Clinical Characteristics of 200 HIV-Infected Adults on ART at MulagoNational Referral Hospital ART-Clinic Uganda.

B. Prevalence of Diabetes Mellitus among HIV-Infected Patients on Art

The overall prevalence of diabetes mellitus was 7.5% (95%CI: 3.5, 11.5), with males at 5.3% (95%CI: 1.3, 10.7) and 8.8% (95%CL: 4.0, 14.4) among females, 6% (95%CI: 0, 14) among patients aged 20 to 34 years, 2.8% (95%CI: 0, 7) among those aged 35 to 44 years and 12.7% (95%CI: 3.9, 18.1) among patients aged 45 years and above, 20.5% (95%CI:7.7, 35.9) among patients who use both ART and Anti-hypertensive drugs, and 4.3% (95%CI:1.9, 7.5) among those who don`t use anti-hypertensive drugs. Basing on the time on ART, the prevalence was 4.8% (95%CI: 1.2, 12.0) among those who have been on ART for 1 to 5 years, and 9.6% (95%CI: 3.5, 14.8) among patients who have been on ART for a period of 6 years and above. The prevalence was 5.2% (95%CI: 1.3, 9.1) among those who had a normal blood pressure, and as high as 15.2% (95%CI: 4.4, 23.9) among patients with high blood pressure. The prevalence of diabetes was 18.2% (95%CI: 0.0, 45.5) among patients who were underweight, 2.9% (95%CI: 0.0, 5.7) among those with normal weight, 8.2% (95%CI: 1.7, 16.4) among overweight patients and as high as 21.7% (95%CI: 4.3, 43.5) among obese patients. The prevalence was 7.8% (95%CI: 3.9, 12.2) among urban residents, and 5.3% (95%CI: 0.0, 15.8) among rural residents as shown in table 2 below.

Characteristics	Number(%) with Diabetes	95CI	Fisher`s exact *P*value
Sex			
Male	4(5.3)	[1.3, 10.7]	0.421
Female	11(8.8)	[4.0, 14.4]	
Age (years)			
20 – 34	3(6)	[0, 14]	
35 – 44	2(2.8)	[0, 7]	0.124
45 and above	10(12.7)	[3.9, 18.1]	
Body mass index			
Underweight	2(18.2)	[0.0, 45.5]	
Normal weight	3(2.9)	[0.0, 5.7]	0.006
Overweight	5(8.2)	[1.7, 16.4]	
Obese	5(21.7)	[4.3, 43.5]	
Use of Anti-hypertensive			
Yes	8(20.5)	[7.7, 35.9]	0.002
No	7(4.3)	[1.9, 7.5]	
Blood Pressure			
Normal	8(5.2)	[1.3, 9.1]	0.048
Hypertension	7(15.2)	[4.4, 23.9]	
Time on ART			
1 to 5 years	4(4.8)	[1.2, 12.0]	0.283
6 years and above	11(9.6)	[3.5, 14.8]	
Current ART-Line			
1st Line	4(2.6)	[0.6, 5.2]	0.001
2nd Line	11(23.9)	[13.0, 39.1]	
Location			
Urban	14(7.8)	[3.9, 12.2]	1.000
Rural	1(5.3)	[0.0, 15.8]	

Table 2:- Prevalence of Diabetes Mellitus among HIV-Infected Adults on ART by Background Characteristics at Mulago National Hospital ART Clinic Uganda

C. Risk Factors of Diabetes Mellitus among HIV-Infected Adults on ART

Obese and overweight patients were found to be 2 times more likely to have diabetes mellitus compared to those with normal BMI or underweight while those who had high blood pressure were also almost 2 times more likely to havediabetes. Patients on second line treatment were 3 times more likely to have diabetes mellitus compared to those who were on first line drugs, as shown in table 3 below. History of anti-hypertensive drug use was found to be independently associated with diabetes mellitus among HIV-infected adults on ART.

Characteristics	Adjusted OR [95%CI]	*P*value
BMI		
Underweight/Normal	1	
Overweight	2.943[2.9, 123.6]	0.002
Obese	1.935[1.2, 40.3]	0.031
Blood pressure		
Normal	1	
Hypertension	1.529[1.2, 17.4]	0.024
Current ART-Line		
1st Line	1	
2nd Line	3.420[2.1, 25.3]	0.005

Table 3; Risk Factors Associated with Diabetes Mellitus among HIV-Infected patients on ART at Mulago National Referral Hospital ART-Clinic in Uganda.

IV. DISCUSSION AND CONCLUSION

This is the first study to report diabetes among HIV patients on ART in Uganda, we aimed to determine the prevalence and potential factors for diabetes among HIV-infected patients on ART at Mulago national referral hospital Uganda. The overall prevalence estimate for diabetes mellitus was 7.5%. We have found a high prevalence of diabetes among HIV-infected adults on ART compared to what was reported in the general population-based study done by (Bahendeka, *et al.,* 2016) and this could be as a result oflittle or missed attention, care and support opportunities associated with metabolic imbalance management among these patients.

According to the study done by (Hernandez *et al.,* 2017)in USA reported a higher diabetes prevalence estimate of 10.3%, while (Abebe,*et al.,* 2016), reported the diabetes prevalence estimate of 5.1% among the HIV-infected patients receiving ART in follow-up care at University of Gondar Hospital, Northwest Ethiopia and the difference that exits with our study could be as a result of the heterogenecity of diabetes across the communities, and also from differences in health determinants such as life style across the populations and also the larger sample size used in these studies. When compared our results with those reported from the study done by (Shankalala,*et al.,* 2017) who reported a slightly lower diabetes prevalence of 5.0% in their study among patients on ART, the difference that exists with our results could be because the different studies may have used different ways of measuring and defining diabetes, and also different diagnosis methods in HIV settings.

In this study we also observed that overweight or obese patients were significantly more likely to have diabetes compared to normal and underweight patients and this is because insulin resistance correlates with increased weight gain and obesity and yet initiation of ART itself is associated with rapid weight gain which leads many patients to become overweight thereby putting them at a greater risk of getting diabetes, and also greater weight means a higher risk of insulin resistance, because fat interferes with the body's ability to use insulin. Another observation was the relationship between treatments and diabetes, in this study we also observed that patients on second line drug combination with ritonavir-boosted atazanavir (ATV/r-protease inhibitor) were 3 times more likely to have diabetes compared to those on first line and this could be as a result of much effects exerted on the liver and the pancreas by these drugs, and due to drug failure, patients end up administering very many drug types with a wide range of side effects on their internal system. The study also showed that patients using both ART especially second line regimen and Anti-hypertensive drugs were at a very greater risk of getting diabetes mellitus compared to those who were only ART and this could be as a results of multiple metabolic effects of combinatorial drug therapy (ART) for HIV infection exerted on the internal organs during drug metabolism most especially in the liver and the pancreas where insulin is secreted. We also observed a higher prevalence of diabetes mellitus among patients from urban areas around Kampala compared to those from rural areas and this could be due to the fact that the selectedstudy site was in an urban area where medical information suggests presence of higher burden of metabolic disorders even among groups without HIV-infection, and also the sedentary lifestyle that most of these people live.

According to this studyDiabetes mellitus prevalence among HIV-infected sub-population on ART is high compared to what is reported in the general population of Uganda, suggesting little attention, care and support opportunities associated with metabolic imbalance management among patients on ART.

BMI, Hypertension, second line drugs and use of Anti-hypertensive drugs were found to be the major factors associated with Diabetes mellitus among HIV-infected adults receiving anti-retroviral therapy.

RECOMMENDATION

Based on the result obtained from this study early screening of patients who use both ART and Anti-hypertensive drugs, as well as those that are overweight and obese must be included into regular HIV clinical care set up as part of the overall care and support strategy for early management of diabetes mellitus, and clinicians must also consider the metabolic effects of multiple drug therapy for HIV infection and its outcome. Nonetheless there is still need to invest in additional research with larger sample size so as to increase the evidence critical in primary care strategies which directly impact on secondary care and support programmes.

REFERENCES

[1]. Abebe SM, Getachew A, Fasika S, Bayisa M, Demisse AG, Mesfin N. Diabetes mellitus among HIV-infected individuals in follow-up care at University of Gondar Hospital, Northwest Ethiopia. BMJ open. 2016 Aug 1; 6(8):e011175.
[2]. Bahendeka S, Wesonga R, Mutungi G, Muwonge J, Neema S, Guwatudde D. Prevalence and correlates of diabetes mellitus in Uganda: a population-based national survey. Tropical Medicine & International Health. 2016 Mar; 21 (3):405-16
[3]. Bi Y, Wang T, Xu M, Xu Y, Li M, Lu J, Zhu X, Ning G. Advanced research on risk factors of type 2 diabetes. Diabetes/metabolism research and reviews. 2012 Dec; 28:32-9.
[4]. Capeau J, et al. Ten-year diabetes incidence in 1046 HIV-infected patients started on a combination antiretroviral treatment. AIDS. 2012; 26 (3):303–14.
[5]. Florescu D, Kotler DP. Insulin resistance, glucose intolerance and diabetes mellitus in HIV-infected patients. AntivirTher 2007; 12:149–162.
[6]. Hernandez-Romieu AC, Garg S, Rosenberg ES, Thompson-Paul AM, Skarbinski J. Is diabetes prevalence higher among HIV-infected individuals compared with the general population? Evidence from MMP and NHANES 2009–2010. BMJ Open Diabetes Research and Care. 2017 Jan 1; 5(1):e000304.
[7]. International Diabetes Federations. IDF Diabetes Atlas, 2013. (Available from: http://www.idf.org/diabetesatlas) [5May 2015].
[8]. Mohammed M, Mengistie B, Dessie Y, Godana W. Prevalence of depression and associated factors among HIV patients seeking treatments in ART clinics at Harar Town, Eastern Ethiopia. Journal of AIDS & Clinical Research. 2015; 6(6):474.
[9]. ROTHER KI. Diabetes treatment-bridging the divide. N Engl J Med 2007; 15: 1499-1501
[10]. Samaras K. Prevalence and pathogenesis of diabetes mellitus in HIV-1 infection treated with combined antiretroviral therapy. J Acquir Immune DeficSyndr 2009; 50:499–505.
[11]. Shankalala P, Jacobs C, Bosomprah S, Vinikoor M, Katayamoyo P, Michelo C. Risk factors for impaired fasting glucose or diabetes among HIV infected patients on ART in the Copperbelt Province of Zambia. Journal of Diabetes & Metabolic Disorders. 2017 Dec; 16(1):29.
[12]. Shaw JE, Sicree RA, Zimmet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res ClinPract 2010; 87 (January (1)):4–14.
[13]. TIERNEY LM, MCPHEE SJ, PAPADAKIS MA. Current medical Diagnosis & Treatment. 40th Ed. New York: Lange Medical Books/McGraw-Hill; 2001.
[14]. Whiting DR, Guariguata L, Weil C, and Shaw J. IDF Diabetes Atlas: global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes Res ClinPract 2011; 94 (December (3)):311–21.
[15]. World Health Organization. Global report on diabetes. World Health Organization; 2016.
[16]. World Health Organization. Global status report on non-communicable diseases 2014. Geneva, 2014. (Available from: http://www.who.int/nmh/publications/ncd-statusreport- 2014/en/pdf) [5 May 2015].