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Hyperglycemia and its associated factors among people living with HIV on dolutegravir-based antiretroviral therapy in Ethiopia: a cross-sectional study

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Abstract

Background: In many low- and middle-income countries, including Ethiopia, dolutegravir (DTG)-based regimens are the preferred first-line regimens for people living with HIV (PLWH). However, there are concerns about hyperglycemia and, in certain circumstances, diabetes mellitus in individuals who have switched to DTG.

Objective: To assess the prevalence and factors associated with hyperglycemia among PLWH on DTG-based antiretroviral therapy (ART).

Design: An institutional-based cross-sectional study.

Methods: The study was carried out from December 1, 2021 to February 30, 2022, and included 423 participants who were recruited via a simple random sampling technique. We enrolled PLWH aged 18 years or older who had been on DTG-based ART for more than 6 months. Data were collected by using an interviewer-administered structured questionnaire, medical card review, physical measurement, and biochemical measurements. Hyperglycemia was defined as a fasting blood glucose level ⩾110 mg/dl. Multivariable logistic regression was used to identify factors associated with hyperglycemia, using SPSS version 26.0 software. Variables with a p-value of <0.05 were considered statistically significant.

Results: The prevalence of hyperglycemia among PLWH receiving DTG-based ART was 12.1% (95% CI: 9.2–15.1). Age (AOR = 1.04, 95% confidence interval (CI): 1–1.08, $p = 0.036$), BMI (AOR = 1.09, 95% CI: 1.01–1.17, $p = 0.022$), and triglyceride level (AOR = 2.44, 95% CI: 1.28–4.64, $p = 0.006$) were significant predictors of hyperglycemia among PLWH on DTG-based ART.

Conclusion: Overall, our study revealed a high prevalence of hyperglycemia (12.1%) among PLWH receiving DTG-based ART. Age, BMI, and triglyceride levels were significant predictors of hyperglycemia. These findings underscore the importance of monitoring blood glucose levels in PLWH receiving DTG-based ART, with a special emphasis on patients with advanced age, increased BMI, and increased triglyceride levels.

Keywords: ART, dolutegravir, Ethiopia, HIV, hyperglycemia

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Background

The increased availability of antiretroviral therapy (ART) has resulted in decreased deaths related to acquired immunodeficiency syndrome (AIDS) and a longer life expectancy for people living with HIV (PLWH) worldwide.[1,2] Despite the recognized advantages of ART, its use is not without adverse effects. PLWH are at a greater risk of

developing long-term noncommunicable diseases such as diabetes mellitus (DM) and cardiovascular disease (CVD).[3,4] A study has shown that men living with HIV on ART are four times more likely to develop DM than those without HIV.[5] Protease inhibitors, and to a lesser degree, nucleoside/nucleotide reverse transcriptase inhibitors and nonnucleoside reverse transcriptase inhibitors (NNRTIs), disrupt the metabolism of glucose and lipids, resulting in hyperglycemia, dyslipidemia, and insulin resistance.[6,7] Integrase strand transfer inhibitor (INSTI)-based regimens are advised as the first-line ARTs for the majority of PLWH, according to several recent clinical guidelines.[8]

Dolutegravir (DTG), a more recent and prominent second-generation INSTI, works by blocking the HIV integrase enzyme, which stops the virus from integrating its genetic material into host DNA and ultimately prevents viral replication.[9] The World Health Organization (WHO) has endorsed DTG as the primary drug of choice for both first- and second-line ART for all PLWH because of its effectiveness, strong resistance barriers, positive safety and tolerance attributes, and affordability.[10] As a result of the WHO's endorsement, the 2018 HIV treatment guidelines issued by the Ethiopian Ministry of Health also advocated for the implementation of DTG-based ART as the preferred first- and second-line treatment in the country.[11]

Despite its advantages, recent findings from clinical studies, case reports, and case series have indicated a link between DTG and glucose metabolism disorders, such as hyperglycemia.[12–15] Although the evidence is equivocal, the potential cause of DTG-associated hyperglycemia is that DTG suppresses insulin secretion and signaling, possibly via magnesium chelation.[16,17] According to research carried out in the USA among PLWH on a DTG-based regimen, 1.4% of patients developed DM, and 13% of patients had prediabetes.[16] Studies in Uganda indicate varying prevalence rates of hyperglycemia among DTG-treated patients, with rates of 19.8%,[18] 12.8%,[19] and 7.3%[20] at different hospitals and a case-control study finding that DTG use increases the risk of hyperglycemia sevenfold.[21] Two comparative cross-sectional studies in Ethiopia reported varying prevalence rates of hyperglycemia among PLWH on DTG-based ART, with rates of 17.2% in Northeast Ethiopia[22] and 35.9% in Southwest Ethiopia.[23] The exact rate of hyperglycemia among PLWH receiving DTG-based ART in Ethiopia is currently unknown. Therefore, there is a significant need to research this gap, especially as the majority of PLWH in Ethiopia are receiving DTG-based ART. Thus, this study aimed to determine the prevalence and factors associated with hyperglycemia among PLWH on DTG-based ART at the ART clinic of Debre Markos Comprehensive Specialized Hospital (DMCSH), Northwest Ethiopia.

Methods and materials

Study design, settings, and period

An institutional-based cross-sectional study was conducted at DMCSH from December 1, 2021 to February 30, 2022. DMCSH is located in the Debre Markos City Administration, approximately 299 km from Addis Ababa, the capital of Ethiopia, and 264 km from Bahir Dar, the capital of the Amhara Regional State. The hospital serves over 3.5 million individuals in the town and surrounding districts. Besides offering general services, it has been providing HIV/AIDS interventions, including diagnosis, treatment, and monitoring, since 2005. The hospital has been serving more than 3574 PLWH. DTG-based ART was initially introduced at the DMCSH in April 2019.

Population and eligibility criteria

We enrolled all PLWH aged 18 years or older who had been on DTG-based ART for more than 6 months. Patients with known DM, renal problems, thyroid problems, chronic liver disease, mental health problems, or any other serious health problems (e.g., those with active cancer, heart failure, or who require immediate intensive care), and patients who were not able to provide appropriate information were excluded.

Sample size and sampling technique

In this study, the sample size was calculated via a single population proportion formula with the following assumptions: 50% prevalence of hyperglycemia because of no previous study in the area, 5% margin of error, 95% confidence interval (CI), 10% nonresponse rate, and the total sample became 423. The study subjects were recruited via a simple random sampling technique.

Data collection procedure

Both the data collectors and supervisors were trained for 1 day on the research's objective and methodology, as well as the data collection approach. The principal investigator oversaw the data collection, and the collected information was reviewed for thoroughness, accuracy, and comprehensibility. Nurse professionals used a structured questionnaire to gather sociodemographic and relevant clinical information. Data on demographic, behavioral, and clinical characteristics were collected directly from participants and from medical records by nurse professionals using a structured questionnaire modified from the WHO stepwise approach to chronic disease risk factor surveillance questions.[24] Nurse professionals gathered anthropometric measurements such as height, weight, waist circumference (WC), and hip circumference with a standard balance and a SECA meter. Body mass index (BMI) was calculated by dividing weight in kilograms (kg) by height in meters squared (m^2). Nurse professionals in ART services determine blood pressure (BP) with an automated sphygmomanometer. The participant's final BP was calculated by averaging three measurements that were taken at 5-min intervals.

Laboratory tests

A laboratory technologist collected approximately 9 ml of fasting venous blood from each participant. Blood samples in vacutainer tubes were clearly labeled and transported immediately to the laboratory for analysis in a cooler box. Sample for fasting blood glucose (mmol/l) was collected by finger pricking and analyzed using an Accu-Chek glucometer manufacturer's specifications care machine. In this study, we used a single fasting blood glucose measurement to diagnose hyperglycemia.[22,25] The lipid profile was analyzed using a Cobas C111 analyzer after centrifugation for 10 min at 10,000 relative centrifugal force. CD4 count (cells/μl) samples were collected in ethylenediaminetetraacetic acid (EDTA) containers and assayed via a Becton Dickinson flow cytometer. Viral load (VL) (copies/ml) samples were collected in EDTA containers and analyzed via a COBAS® Ampliprep/COBAS® (Roche Diagnostics, Ltd., Rotkruez, Switzerland) TaqMan PCR analyzer. Blood collection, serum separation, and laboratory analysis were performed by experienced medical laboratory technologists.

Data processing and analysis

The collected data were checked and cleaned before being entered and analyzed with SPSS version 26.0 software. Categorical data were summarized using frequencies and proportions. Continuous variables are presented as median and interquartile range (IQR). The chi-square test was used to test for statistically significant associations between two categorical variables. A binary logistic regression model was employed to determine the independent variables associated with hyperglycemia. The variables with p-values < 0.25 in the bivariable logistic regression analysis were incorporated into a multivariable logistic regression model to control for the effect of confounding variables. Crude and adjusted odds ratios with 95% CI are reported, and a p-value < 0.05 was considered statistically significant. Hosmer and Lemeshow tests were used to assess the goodness of fit of the final logistic model.

Definition of terms

Diabetes mellitus was defined as a fasting blood glucose level of ⩾126 mg/dl.[26]

Hyperglycemia was defined as a fasting blood glucose level ⩾110 mg/dl.[22,26,27]

Prediabetes was defined as a fasting glucose level between 110 and 125 mg/dl.[26,28]

Dyslipidemia was defined according to the National Cholesterol Education Program Adult Treatment Panel III guidelines as having LDL-C levels of ⩾130 mg/dl, total cholesterol (TC) levels of ⩾200 mg/dl, triglycerides (TG) of ⩾150 mg/dl, and high-density lipoprotein cholesterol (HDL-C) levels of < 40 mg/dl for men and < 50 mg/dl for women, either in isolation or in combination.[29]

Hypertension was defined as systolic BP ⩾ 140 mmHg and/or diastolic BP ⩾ 90 mmHg.[30]

BMI was classified as underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), and obese (⩾30 kg/m^2).[31]

Waist circumference: a normal WC is ⩽80 cm for females and ⩽94 cm for males, according to WHO categorization. Abnormal WC was

defined as WC >80 cm for females and >94 cm for males.[32]

Waist-to-hip ratio: a normal WHR is <0.90 for males and <0.85 for females, according to WHO categorization. Abnormal WHR was defined as WHR ⩾ 0.9 in males and ⩾0.85 in females.[32]

Viral load: VL ⩽ 1000 copies/ml was categorized as suppressed, and VL > 1000 copies/ml was categorized as nonsuppressed.[33]

CD4+ T-cell count: a CD4+ T-cell count of ⩾500 cells/mm^3 is within the normal range for a competent immune system and a CD4+ T-cell count of <500 cells/mm^3 indicates a compromised immune system[34]

Adherence to ART: an adult's recent adherence to ART is considered poor if they take less than 85% of the prescribed dose, fair if they take 85%–94%, and good if they take 95% or more of the dose.[35]

Opportunistic infections refer to the list of opportunistic diseases recorded in the national comprehensive HIV prevention, care, and treatment guidelines.[35]

Sufficient physical exercise: adults should perform at least 150–300 min of moderate-intensity aerobic physical activity, or at least 75–150 min of vigorous-intensity aerobic physical activity, or an equivalent combination of moderate-intensity and vigorous-intensity activity per week and otherwise insufficient.[36]

Smoking status: "smoker" for participants who had smoked at least one cigarette within the last 1 year.[37,38]

Alcohol drinking status: "alcohol drinker" for participants who consumed any type of alcoholic beverage more than once per week in the past year regardless of the amount.[39,40]

Results

Sociodemographic characteristics of the participant

Among the 423 participants, 73.3% were female. The median age of the study participants was 41 years (IQR: 37, 49), with 43.5% of the participants aged between 31 and 40 years. Among the participants, 51.8% lived in rural areas, 37.6% could not read and write, and 35.7% were farmers (Table 1).

Behavioral characteristics of the participant

About 13% of the participants had a history of alcohol consumption, 5% had a history of smoking cigarettes, and 42.1% had insufficient physical activity (Table 2).

Clinical characteristics of the participants

Nearly half of the participants (49.6%) had been living with HIV for more than 7 years and 56.5% had been using ART for more than 5 years. A total of 60.3% of the participants had been using DTG-based ART for at least 2 years, 53.9% had CD4+ T-cell counts <500 cells/mm^3, 6.6% had a history of opportunistic infections in the last 6 months, and 11.3% had a family history of DM (Table 3).

Anthropometric and biochemical characteristics

A total of 25.8% and 10.2% of the patients were overweight and obese, respectively. A total of 22.9% had increased WC, 34.75% had increased waist-to-hip ratios, 8.5% had increased BP, and 61.2% had low HDL-C levels (see Table 4).

Hyperglycemia among PLWH on dolutegravir-based ART

Among the 423 study participants, 51 had fasting blood glucose levels ⩾110 mg/dl, resulting in an overall prevalence of hyperglycemia of 12.1% (95% CI: 9.2–15.1) as indicated in Figure 1.

Among these individuals, 8.5% (36/423) were identified as prediabetics, while 3.6% (15/423) were identified as diabetics.

Factors associated with hyperglycemia among PLWH on dolutegravir-based ART

Age, gender, residence, physical activity, alcohol consumption, VL, WHO clinical stage, duration of HIV/AIDS diagnosis, duration of DTG-based ART, family history of DM, BMI, waist-to-hip ratio, TC, and TG levels had a p-value ⩽ 0.25. However, in the multivariable logistic regression, age (AOR = 1.04, 95% CI: 1–1.08, $p = 0.036$),

Table 1. Sociodemographic characteristics of the study participants.

Variables	Category	Frequency	%
Age (years)	18–30	17	4
	31–40	184	43.5
	41–50	152	35.9
	51–60	54	12.8
	>60	16	3.8
Gender	Male	113	26.7
	Female	310	73.3
Residence	Rural	219	51.8
	Urban	204	48.2
Marital status	Single	9	2.1
	Married	270	63.8
	Divorced	81	19.1
	Widowed	63	14.9
Education	Cannot read and write	159	37.6
	Reading and writing only	90	21.3
	Primary school	84	19.9
	Secondary school	35	8.3
	College and above	55	13.0
Occupation	Employee	46	10.9
	Farmer	151	35.7
	Merchant	62	14.7
	Labor	27	6.4
	Housewife	65	15.4
	Others*	72	14.7
Income	<4000 ETB	264	62.4
	⩾4000 ETB	159	37.6

*Students, drivers, and pensioners.
ETB, Ethiopian birr.

BMI (AOR = 1.09, 95% CI: 1.01–1.17, $p = 0.022$), and TG level (AOR = 2.44, 95% CI: 1.28–464, $p = 0.006$) were predictors of hyperglycemia among PLWH on DTG-based ART (Table 5).

Discussion

This study was designed to determine the prevalence of hyperglycemia and its associated factors among PLWH on DTG-based ART. The overall

Table 2. Behavioral characteristics of the study participants.

Variables	Category	Frequency	%
Physical activity	Insufficient	178	42.1
	Recommended	245	57.9
Smoking status	No	402	95
	Yes	21	5
Alcohol	No	368	87
	Yes	55	13

Table 3. Clinical characteristics of the study participants.

Variables	Category	Frequency	%
Duration of HIV	⩽7 years	213	50.4
	>7 years	210	49.6
Duration on ART	⩽5 years	188	44.4
	>5 years	235	55.6
Duration on DTG	⩽2 years	168	39.7
	>2 years	255	60.3
WHO clinical staging	WHO stage I	339	80.1
	WHO stage II	84	19.9
Viral load (cp/ml)	Suppressed	405	95.7
	Nonsuppressed	18	4.3
CD4+ T-cell count (cell/mm^3)	<500	228	53.9
	⩾500	195	46.1
History of OIs in last 6 months	Yes	28	6.6
	No	395	93.4
Drug adherence level	Good	372	88
	Fair	34	8
	Poor	17	4
Family history of DM	No	375	88.7
	Yes	48	11.3
Family history of hypertension	No	382	90.3
	Yes	41	9.7
Family history of CVD	No	397	93.9
	Yes	26	6.1

ART, antiretroviral therapy; CD4, cluster of differentiation 4; CVD, cardiovascular disease; DM, diabetes mellitus; DTG, dolutegravir; HIV, human immunodeficiency virus; OIs, opportunistic infections; WHO, World Health Organization.

Table 4. Anthropometric and biochemical characteristics of the study participants.

Variables	Category	Frequency	%
BMI	Underweight	63	14.9
	Normal	208	49.2
	Overweight	109	25.8
	Obesity	43	10.2
Waist circumference	Normal	326	77.1
	Raised	97	22.9
Waist-to-hip ratio	Normal	276	65.25
	Raised	147	34.75
Blood pressure	Normal	387	91.5
	Raised	36	8.5
TC (mg/dl)	<200	320	75.7
	⩾200	103	24.3
HDL-C (mg/dl)*	<40/50	259	61.2
	⩾40/50	164	38.8
LDL-C (mg/dl)	<130	313	74.0
	⩾130	110	26.0
TG (mg/dl)	<150	253	59.8
	⩾150	170	40.2

*<40 mg/dl for men and <50 mg/dl for women.
BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride.

prevalence of hyperglycemia among PLWH on DTG-based ART was 12.1% (95% CI: 9.2–15.1). About 8.5% (36/423) had prediabetes, while 3.6% (15/423) had DM. We also found that age, BMI, and TG levels were significant predictors of hyperglycemia among PLWH on DTG-based ART.

The prevalence of DM in our study was comparable to the 2021 International Diabetes Federation (IDF) report,[41] which indicated a national prevalence of 3.3% among the adult population in Ethiopia, as well as to the 2016 WHO report,[42] which noted a national prevalence of 3.8% of DM in the general population of Ethiopia. The prevalence rate of hyperglycemia in this study was consistent with other published data from the USA[16] and Central Uganda,[19] which reported prevalences of 13% and 12.8%, respectively. However, the prevalence of hyperglycemia in this study was higher than that reported in a study conducted at a regional referral hospital in Uganda (7.3%).[20] The observed variation could be due to differences in sociodemographic and lifestyle characteristics, genetic predispositions, study methodologies, and HIV and ART management protocols.[19,43] For example, a study conducted at a regional referral hospital in Uganda included those who had been exposed to DTG-based ART for at least 12 weeks; however, our

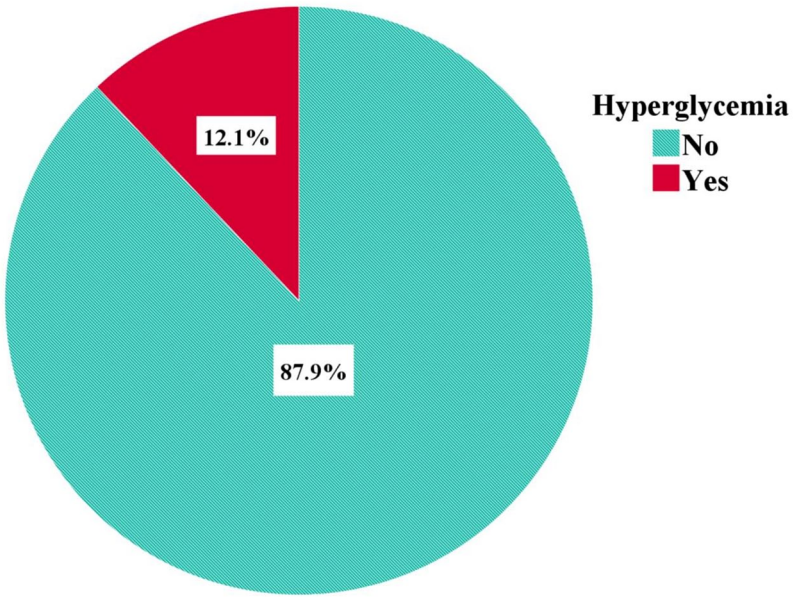

Figure 1. Prevalence of hyperglycemia among PLWH on DTG-based ART at DMCSH.
ART, antiretroviral therapy; DMCSH, Debre Markos Comprehensive Specialized Hospital; DTG, dolutegravir; PLWH, people living with HIV.

study included those who had been exposed to DTG-based ART for at least 6 months. These factors could explain the discrepancy.

On the other hand, the prevalence of hyperglycemia in this study is lower than the previous findings reported in Eastern Uganda (19.8%),[18] Northeast Ethiopia (17.2%),[22] and Southwest Ethiopia (35.9%).[23] The observed discrepancies may be attributed to several factors. For instance, variations in the ART exposure history among participants could play a role, as our study included individuals with prior ART experience, while the studies conducted in Northeast Ethiopia and Eastern Uganda focused on ART-naïve participants. In addition, there was a difference in sample sizes; studies from Eastern Uganda, Southwest Ethiopia, and Northeast Ethiopia used a smaller sample size, whereas our study used a larger sample size. Furthermore, differences in blood glucose testing methods may have contributed to the discrepancies; we used fasting blood sugar tests, while the study from Southwest Ethiopia used random blood sugar tests.

Our results support earlier evidence from case reports, case series, and randomized controlled trials that indicate a relationship between DTG and disrupted glucose metabolism.[13,14,44,45] The exact mechanism through which DTG induces disrupted glucose metabolism is not fully known, but it is speculated that DTG triggers insulin resistance by chelating magnesium ions, which are required as cofactors for insulin to operate effectively.[16,17]

Age, BMI, and TG levels were found to be significantly associated with hyperglycemia in PLWH receiving DTG-based ART. For every year of age increase, patients were 4% more likely to have hyperglycemia. This finding aligns with previous investigations in Uganda,[19] Iran,[46] and Malawi.[47] The possible reason could be the age-related deterioration of pancreatic islet cell function and increased insulin resistance, which in turn increases the likelihood of developing hyperglycemia.[48] Prior research has also indicated that the risk of insulin resistance increases as PLWH continue to live longer while on ART.[34]

BMI was also another predictor of hyperglycemia among PLWH on DTG-based ART. For a kg/m^2 increase in BMI, the odds of hyperglycemia among DTG-treated patients increased by 9%. This finding is supported by research from Zimbabwe,[49] Ethiopia,[50] and Senegal[51] and could be attributed to the fact that increased BMI causes insulin resistance in body cells, resulting in

Table 5. Factors associated with hyperglycemia among PLWH on dolutegravir-based ART at DMCSH.

Variables	Category	Hyperglycemia		Bivariable analysis		Multivariable analysis	
		Yes	No	COR (95% CI)	*p*-Value	AOR (95% CI)	*p*-Value
Age (year)				1.05 (1.01, 1.08)	0.016	1.04 (1, 1.08)	0.036*
Gender	Male	10	103	1		1	
	Female	41	269	1.57 (0.76, 3.25)	0.224	2.12 (0.88, 5.12)	0.094
Residence	Urban	32	187	1.67 (0.91, 3.05)	0.097	1.44 (0.74, 2.81)	0.290
	Rural	19	185	1		1	
Physical activity	Insufficient	29	149	1.97 (1.09, 3.57)	0.024	1.89 (0.99, 3.58)	0.053
	Recommended	22	223	1		1	
Alcohol consumption	No	40	328	1		1	
	Yes	11	44	2.05 (0.98, 4.29)	0.057	1.62 (0.7, 3.73)	0.258
Duration of HIV/AIDS diagnosis	⩽7 years	21	192	1		1	
	>7 years	30	180	1.52 (0.84, 2.76)	0.164	1.29 (0.67, 2.47)	0.447
WHO clinical staging	WHO stage I	44	295	0.61 (0.26, 1.41)	0.246	1.66 (0.67, 4.08)	0.273
	WHO stage II	7	77	1		1	
Viral load	Suppressed	46	359	0.33 (0.11, 0.98)	0.045	0.27 (0.07, 1.03)	0.055
	Nonsuppressed	5	13	1		1	
Duration of DTG-based ART	⩽2 years	16	152	1		1	
	>2 years	35	220	1.51 (0.81, 2.83)	0.196	1.33 (0.66, 2.66)	0.422
Family history of DM	No	41	334	1		1	
	Yes	10	38	2.14 (0.99, 4.62)	0.052	2.11 (0.91, 4.91)	0.082
BMI (kg/m^2)				1.12 (1.01, 1.24)	0.028	1.09 (1.01, 1.17)	0.022*
Waist-to-hip ratio	Normal	29	247	1		1	
	Raised	22	125	1.5 (0.83, 2.72)	0.182	1.54 (0.8, 2.96)	0.197
Total cholesterol (mg/dl)	<200	34	320	1		1	
	⩾200	17	86	1.66 (0.89, 3.122)	0.114	1.23 (0.61, 2.5)	0.560
Triglyceride (mg/dl)	<150	21	232	1		1	
	⩾150	30	140	2.37 (1.31, 4.3)	0.005	2.44 (1.28, 4.64)	0.006*

*Statistically significant at $p < 0.05$.
AOR, adjusted odd ratio; ART, antiretroviral therapy; BMI, body mass index; COR, crude odd ratio; DM, diabetes mellitus; DMCSH, Debre Markos Comprehensive Specialized Hospital; DTG, dolutegravir; PLWH, people living with HIV; WHO, World Health Organization.

hyperglycemia.[49] Weight gain has been shown to have a greater effect on the risk of hyperglycemia in PLWH than in the general population.[52] Moreover, some studies have shown that using DTG leads to increased weight gain,[53] but the potential long-term metabolic implications of this outcome remain incompletely understood. Growing data suggest that DTG-associated weight gain leads to an increased risk of hyperglycemia, hypertension, and metabolic syndrome, along with increased cardiovascular risk.[54]

In addition, TG levels were predictors of hyperglycemia among PLWH on DTG-based ART. The odds of having hyperglycemia were 2.44 times more likely among those who had a TG level ⩾150 mg/dl as compared to those who had a TG level < 150 mg/dl. This finding is supported by studies carried out in Malaysia,[55] Ethiopia,[25] and Nigeria.[56] A possible explanation could be that hypertriglyceridemia can increase insulin resistance in peripheral tissues.[57] The metabolites of TGs, such as free fatty acids, diacylglycerol, and others, can regulate insulin signaling pathways through the activation of several serine/threonine kinases, which suppress insulin receptor and tyrosine phosphorylation of insulin receptor substrates, resulting in peripheral insulin resistance.[58,59]

Strengths and limitations

Regarding strength, this is one of the first studies in Ethiopia that attempted to assess hyperglycemia among PLWH receiving DTG-based ART, hence ultimately adding to the limited data and laying the groundwork for future studies. Despite this strength, this study has several limitations. As a cross-sectional study, we cannot establish causal relationships between hyperglycemia and the factors. In addition, the self-reported responses for certain items may be influenced by recall bias due to their subjective nature. Furthermore, participants' baseline fasting blood glucose measurements were unavailable because they were not part of routine clinical practice in Ethiopia. The study also lacked data on participants' use of lipid-lowering or BP medications, which could potentially confound the observed prevalence of hyperglycemia. Moreover, because the study population was drawn from a single institution and blood glucose levels were determined using a one-time sampling method, the results should be interpreted with caution.

Conclusion

Overall, our study revealed a high prevalence of hyperglycemia (12.1%) among PLWH receiving DTG-based ART at the ART clinic of a hospital in Northwest Ethiopia. Age, BMI, and TG levels were significant predictors of hyperglycemia among PLWH on DTG-based ART. These findings underscore the importance of monitoring blood glucose levels in PLWH receiving DTG-based ART, with a special emphasis on patients with advanced age, increased BMI, and increased TG levels. In addition, given the widespread utilization of DTG-based ART, health policies should encourage glucose monitoring as a basic aspect of HIV care. Furthermore, we propose that researchers conduct a large-scale prospective cohort study to determine cause–effect relationships.

Declarations

Ethics approval and consent to participate

An ethical clearance letter was obtained from Debre Markos University, School of Medicine, Ethics Committee, with reference number SOM/31/11/21 and date 11/20/2021. A collaboration letter for data collection was also obtained from DMCSH. The Ethics Committee of Debre Markos University, School of Medicine (SOM/31/11/21) approved the procedure for obtaining informed consent. Before enrolling eligible participants, the study's aim, potential effects, and the significance of the data collected were briefly outlined to each individual. We collected samples and data after obtaining informed consent from the participants. A thumbprint or signature was used on the consent form. Participants who were illiterate provided informed consent with a thumbprint, which was observed and signed by a witness. Throughout the study, confidentiality, anonymity, neutrality, and accountability were preserved by methods such as using codes.

Consent for publication

Not applicable.

Author contributions

Enyew Fenta Mengistu: Conceptualization; Data curation; Investigation; Methodology; Software; Writing – original draft.

Adane Adugna: Data curation; Investigation; Methodology; Supervision; Visualization; Writing – review & editing.

Mamaru Getinet: Investigation; Methodology; Software; Supervision; Validation; Writing – review & editing.

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References

1. Wandeler G, Johnson LF and Egger M. Trends in life expectancy of HIV-positive adults on antiretroviral therapy across the globe: comparisons with general population. *Curr Opin HIV AIDS* 2016; 11(5): 492–500.
2. Palella FJ Jr, Delaney KM, Moorman AC, et al. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. *N Engl J Med* 1998; 338(13): 853–860.
3. Casper C, Crane H, Menon M, et al. HIV/AIDS comorbidities: impact on cancer, noncommunicable diseases, and reproductive health. In: Holmes KK, Bertozzi S, Bloom BR, et al. (ed). *Major infectious diseases*. Washington (DC): The International Bank for Reconstruction and Development/The World Bank©2017 International Bank for Reconstruction and Development/The World Bank, 2017.
4. Cheza A, Tlou B and Zhou DT. Incidence of non-communicable diseases (NCDs) in HIV patients on ART in a developing country: case of Zimbabwe's Chitungwiza Central Hospital-a retrospective cohort study (2010–2019). *PLoS One* 2021; 16(5): e0252180.

5. Brown TT, Cole SR, Li X, et al. Antiretroviral therapy and the prevalence and incidence of diabetes mellitus in the multicenter AIDS cohort study. *Arch Int Med* 2005; 165(10): 1179–1184.

6. 2.Classification and diagnosis of diabetes: standards of medical care in diabetes-2020. *Diabetes Care* 2020; 43(Suppl 1): S14–S31.

7. Thet D and Siritientong T. Antiretroviral therapy-associated metabolic complications: review of the recent studies. *HIV/AIDS (Auckland, NZ)* 2020; 12: 507–524.

8. Council AJP. Guidelines for the use of antiretroviral agents in adults and adolescents living with HIV. 2017.

9. Fantauzzi A and Mezzaroma I. Dolutegravir: clinical efficacy and role in HIV therapy. *Ther Adv Chronic Dis* 2014; 5(4): 164–177.

10. World Health Organization. Updated recommendations on first-line and second-line antiretroviral regimens and post-exposure prophylaxis and recommendations on early infant diagnosis of HIV: interim guidelines: supplement to the 2016 consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Geneva: World Health Organization, 2018.

11. Kebede W. *National guidelines for comprehensive HIV prevention, care and treatment*. Addis Ababa: Federal Ministry of Health, 2018.

12. McLaughlin M, Walsh S and Galvin S. Dolutegravir-induced hyperglycaemia in a patient living with HIV. *J Antimicrob Chemother* 2018; 73(1): 258–260.

13. Hailu W, Tesfaye T and Tadesse A. Hyperglycemia after dolutegravir-based antiretroviral therapy. *Int Med Case Rep J* 2021; 14: 503–507.

14. Hirigo AT, Gutema S, Eifa A, et al. Experience of dolutegravir-based antiretroviral treatment and risks of diabetes mellitus. *SAGE Open Med Case Rep* 2022; 10: 2050313x221079444.

15. Lamorde M, Atwiine M, Owarwo NC, et al. Dolutegravir-associated hyperglycaemia in patients with HIV. *Lancet HIV* 2020; 7(7): e461–e462.

16. Bahamdain F. Effect of dolutegravir on plasma glucose among human immunodeficiency virus patients in a community health center setting. *Cureus* 2022; 14(10): e30556.

17. Kamal P and Sharma S. SUN-187 dolutegravir causing diabetes. *J Endocr Soc* 2019; 3(Suppl 1): SUN-187.

18. AnnetMugoya IAO. Prevalence of hyperglycemia in HIV patients on dolutegravir art regimen receiving care at Jinja Regional Referral Hospital. a cross-sectional study. *SJ Diabetes, Hypertension Cancer Res Africa* 2024; 1(6): 7.

19. Byereta LH, Olum R, Mutebi EI, et al. Prevalence and factors associated with hyperglycemia among persons living with HIV/AIDS on dolutegravir-based antiretroviral therapy in Uganda. *Ther Adv Infect Dis* 2024; 11: 20499361241272630.

20. Namulindwa A, Wasswa JH, Muyindike W, et al. Prevalence and factors associated with adverse drug events among patients on dolutegravir-based regimen at the Immune Suppression Syndrome Clinic of Mbarara Regional Referral Hospital, Uganda: a mixed design study. *AIDS Res Therapy* 2022; 19(1): 18.

21. Namara D, Schwartz JI, 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): 1158–1164.

22. Jemal M, Shibabaw Molla T, Tiruneh GMM, et al. Blood glucose level and serum lipid profiles among people living with HIV on dolutegravir-based versus efavirenz-based cART; a comparative cross-sectional study. *Annal Med* 2023; 55(2): 2295435.

23. Waritu NC, Nair SKP, Birhan B, et al. Serum lipid profiles, blood glucose, and high-sensitivity C-reactive protein levels among people living with HIV taking dolutegravir and ritonavir-boosted atazanavir-based antiretroviral therapy at Jimma University Medical Center, Southwest Ethiopia, 2021. *HIV/AIDS (Auckland, NZ)* 2024; 16: 17–32.

24. World Health Organization. WHO STEPS instrument (core and expanded). The WHO STEPwise approach to noncommunicable disease risk factor surveillance (STEPS). Geneva: World Health Organization, 2015.

25. Gebrie A, Tesfaye B, Gebru T, et al. Diabetes mellitus and its associated risk factors in patients with human immunodeficiency virus on anti-retroviral therapy at referral hospitals of Northwest Ethiopia. *Diabetol Metab Syndr* 2020; 12(1): 20.

26. World Health Organization. Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia: report of a WHO/IDF consultation. World Health Organization, 2006.

27. U.S. Department of Health and Human Services, National Institutes of Health, National

Institute of Allergy and Infectious Diseases, Division of AIDS. Division of AIDS (DAIDS) Table for Grading the Severity of Adult and Pediatric Adverse Events Corrected Version 2.1, https://rsc.niaid.nih.gov/sites/default/files/daidsgradingcorrectedv21.pdf (2017, accessed 15 April 2024).

28. Echouffo-Tcheugui JB and Selvin E. Prediabetes and what it means: the epidemiological evidence. *Annu Rev Public Health* 2021; 42(1): 59–77.
29. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third report of the National Cholesterol Education Program (NCEP) Expert Panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III): The Program, 2002.
30. Williams B, Mancia G, Spiering W, et al. 2018 ESC/ESH guidelines for the management of arterial hypertension. *Eur Heart J* 2018; 39(33): 3021–3104.
31. World Health Organization. *Obesity: preventing and managing the global epidemic: report of a WHO consultation*. Geneva: World Health Organization. 2000.
32. World Health Organization. *Waist circumference and waist-hip ratio: report of a WHO expert consultation*. Geneva: World Health Organization, 2008.
33. Federal Ministry of Health. *Guidelines for management of opportunistic infections and anti-retroviral treatment in adolescents and adults in Ethiopia*. Federal Ministry of Health, 2008.
34. Moncivaiz A and Alexander D. CD4 vs. Viral load: what's in a Number?. https://www.healthline.com/health/hiv-aids/cd4-viral-count#cd-count (2019, accessed 15 April 2024)
35. Worku K. *National comprehensive HIV prevention, care and treatment training for health care providers, participant manual*. Ethiopia: Ministry of Health, 2017, vol. 27, pp. 29–35.
36. Bull FC, Al-Ansari SS, Biddle S, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. *Br J Sports Med* 2020; 54(24): 1451–1462.
37. Gebrie A. Hypertension among people living with human immunodeficiency virus receiving care at referral hospitals of Northwest Ethiopia: a cross-sectional study. *PLOS One* 2020; 15(8): e0238114.
38. Tesfaye F, Byass P, Wall S, et al. Peer reviewed: association of Smoking and Khat (Catha edulis Forsk) use with high blood pressure among adults in Addis Ababa, Ethiopia. *Perv Chronic Dis*; 2008; 5(3): A89.
39. Beyene Kassaw A, Tezera Endale H, Hunie Tesfa K, et al. Metabolic syndrome and its associated factors among epileptic patients at Dessie Comprehensive Specialized Hospital, Northeast Ethiopia; a hospital-based comparative cross-sectional study. *PLoS One* 2022; 17(12): e0279580.
40. Ethiopian Public Health Association. On alcohol, substance, khat and tobacco. In: *22nd annual conference of EPHA*, April 2012.
41. IDF. IDF Africa members Ethiopia. IDF, 2021.
42. WHO. *Diabetes Ethiopia 2016 country profile*. WHO. 2016.
43. Ngu RC, Choukem S-P, Dimala CA, et al. Prevalence and determinants of selected cardio-metabolic risk factors among people living with HIV/AIDS and receiving care in the South West Regional Hospitals of Cameroon: a cross-sectional study. *BMC Res Notes* 2018; 11: 1–8.
44. Raffi F, Rachlis A, Stellbrink H-J, et al. Once-daily dolutegravir versus raltegravir in antiretroviral-naive adults with HIV-1 infection: 48 week results from the randomised, double-blind, non-inferiority SPRING-2 study. *Lancet* 2013; 381(9868): 735–743.
45. ViiV Healthcare. Tivicay (dolutegravir tablets). Full Prescribing Information. Viiv Healthcare, Research Triangle Park, NC 27709, 2018.
46. Rasoolinejad M, Najafi E, Hadadi A, et al. Prevalence and associated risk factors of hyperglycemia and diabetes mellitus among HIV positive patients in Tehran, Iran. *Infect Disorders Drug Targets* 2019; 19(3): 304–309.
47. Mathabire Rücker SC, Tayea A, Bitilinyu-Bangoh J, et al. High rates of hypertension, diabetes, elevated low-density lipoprotein cholesterol, and cardiovascular disease risk factors in HIV-infected patients in Malawi. *AIDS (London, England)* 2018; 32(2): 253–260.
48. Suastika K, Dwipayana P, Siswadi M, et al. *Glucose tolerance*. InTech, 2012.
49. Chireshe R, Manyangadze T and Naidoo K. Diabetes mellitus and associated factors among HIV-positive patients at primary health care facilities in Harare, Zimbabwe: a descriptive

cross-sectional study. *BMC Primary Care* 2024; 25(1): 28.

50. Mesfin Belay D, Alebachew Bayih W, Yeshambel Alemu A, et al. Diabetes mellitus among adults on highly active anti-retroviral therapy and its associated factors in Ethiopia: systematic review and meta-analysis. *Diabetes Res Clin Pract* 2021; 182: 109125.
51. Diouf A, Cournil A, Ba-Fall K, et al. Diabetes and hypertension among patients receiving antiretroviral treatment since 1998 in Senegal: prevalence and associated factors. *ISRN AIDS* 2012; 2012(1): 621565.
52. Herrin M, Tate JP, Akgün KM, et al. Weight gain and incident diabetes among hiv-infected veterans initiating antiretroviral therapy compared with uninfected individuals. *J Acquir Immune Defic Syndr* 2016; 73(2): 228–236.
53. Norwood J, Turner M, Bofill C, et al. Brief report: weight gain in persons with HIV switched from efavirenz-based to integrase strand transfer inhibitor-based regimens. *J Acquired Immune Defic Syndr (1999)* 2017; 76(5): 527–531.
54. Jemal M. A review of dolutegravir-associated weight gain and secondary metabolic comorbidities. *SAGE Open Med* 2024; 12: 20503121241260613.
55. Hejazi N, Rajikan R, Kwok Choong CL, et al. Metabolic abnormalities in adult HIV infected population on antiretroviral medication in Malaysia: a cross-sectional survey. *BMC Public Health* 2013; 13: 758.
56. Adewole O, Eze S, Betiku Y, et al. Lipid profile in HIV/AIDS patients in Nigeria. *Afr Health Sci* 2010; 10(2): 144–149.
57. Ye X, Kong W, Zafar MI, et al. Serum triglycerides as a risk factor for cardiovascular diseases in type 2 diabetes mellitus: a systematic review and meta-analysis of prospective studies. *Cardiovasc Diabetol* 2019; 18(1): 48.
58. Grundy SM. Hypertriglyceridemia, insulin resistance, and the metabolic syndrome. *Am J Cardiol* 1999; 83(9b): 25f–29f.
59. Han T, Cheng Y, Tian S, et al. Changes in triglycerides and high-density lipoprotein cholesterol may precede peripheral insulin resistance, with 2-h insulin partially mediating this unidirectional relationship: a prospective cohort study. *Cardiovasc Diabetol* 2016; 15(1): 154.