

# The Prevalence of Non-AIDS Comorbidities Among People Living with HIV in Tbilisi, Georgia

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## Abstract

**Background:** Georgia has made significant accomplishments in the effective delivery of HIV treatment and care. However, little is known about the burden of non-AIDS comorbidities (NACM) in Georgia. The objectives of the study were to estimate the burden of NACM among people living with Human Immunodeficiency Virus (HIV) infection in Georgia, establish a Georgian NACM cohort, and estimate the prevalence of NACM.

**Methods:** A cross-sectional study was conducted to assess the burden of NACM among people living with HIV infection receiving care at the Infectious Diseases, AIDS, and Clinical Immunology Research Center (IDACIRC). Statistical software R version 4.1.2, along with its packages for statistical analysis was used to conduct statistical analysis.

**Results:** Overall, 1200 patients were included in the study. The prevalence of hypertension was 65% in male participants. Other comorbidities, such as cardiovascular disease (CVD) -- 55 (65%), chronic kidney disease (CKD) -- 8 (73%), diabetes mellitus (DM) -- 67 (83%), and dyslipidemia -- 120 (58%) -- were more prevalent in female participants. The risk of NACM increases with age.

**Conclusions:** Long-term healthcare management and long-term health outcomes could be improved for people living with human immunodeficiency virus infection by careful HIV management according to current recommendations with optimal selection of antiretrovirals and early management of comorbidities through recommended lifestyle improvements and preventative measures. (TCM-GMJ March 2023; 8 (1):P7-P15)

**Keywords:** NACM; CVD; CKD; Diabetes mellitus; Dyslipidemia; Eastern Europe; Georgia.

## Introduction

Georgia has made significant accomplishments in the effective delivery of HIV treatment and care. Universal access to antiretroviral therapy (ART) in the country has led to a significant reduction in mortality among people living with HIV infection (PLHIV). Patterns of cause-specific mortality have been changing following the universal availability of antiretroviral therapy, with more people dying from non-AIDS-related causes (1,2). However, little is known about the burden of non-AIDS comorbidities (NACM) in Georgia. People living with HIV in Georgia are at increased risk of NACM due to the aging of the population following successful ART provision, high rates of smoking (up to 74%) among HIV-positive MSM, and high rates of late presentation. It is known that uncontrolled HIV may lead to more than a 12-fold increased risk of non-AIDS-related complications, such as cardiovascular problems and metabolic disturbances(1).

## Methods

### Study design

A cross-sectional study has been conducted to assess the burden of NACM among people living with human

immunodeficiency virus infection receiving care at the Infectious Diseases, AIDS, and Clinical Immunology Research Center (IDACIRC), Georgia's referral institution for HIV, which provides HIV care services to 64% of all people living with human immunodeficiency virus infection in Georgia.

The study enrolled 1,200 people living with HIV through age- and gender-stratified random sampling to estimate the prevalence of cardiovascular disease (CVD), chronic kidney disease (CKD), diabetes mellitus (DM), and dyslipidemia.

## Definitions

CVD: hypertension was defined as a blood pressure of 140/90 mmHg or receiving antihypertensive drugs (3); clinical CVD events included myocardial infarction (4), stroke (5), and any invasive cardiovascular procedure. Dyslipidemia as a major risk factor for CVD was evaluated based on a standard lipid panel (6). DM was defined as a confirmed fasting blood glucose level of 7 mmol/L (126 mg/dL) or a random blood glucose level of 11.1 mmol/L (200 mg/dL) or taking anti-diabetic medication, including insulin (7,8).

CKD was defined as an eGFR of 60 mL/min for 3 months using the 2009 CKD-EPI creatinine equations (9).

The Data Collection on Adverse Events of Anti-HIV Drugs (D: A: D) risk scores for CVD and CKD were

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calculated using online tools available at <https://www.chip.dk/Tools-Standards/Clinical-Risk-Scores> (10,11).

### Sources of data

Routinely available data collected as part of the standard of care was used for the study. Data on clinical events, appropriately documented in accordance with national regulations on medical record-keeping, were extracted from the medical charts. Data on patient demographics, mode of HIV transmission, weight, height, ART use, co-infections with viral hepatitis and tuberculosis, and laboratory examinations (CD4 cell count, plasma HIV RNA, lipid panel, and serum creatinine) were extracted from the National AIDS Health Information System.

### Variables and sources of information

Socio-demographic data (age, sex, race, and country of origin), addictive behaviors (smoking, i.e., currently smoking or past/never smoking; alcoholism; and illicit drug use), HIV-1 infection characteristics (mode of transmission, duration of infection, plasma HIV RNA, and CD4 count at presentation), and ART data (regimen, duration, previous regimens) were obtained from the medical records and through patient interviews. The duration of infection was defined as the time elapsed from the year of diagnosis to the year of the study appointment.

The diagnosis of NACM of interest was obtained from the medical records and included diabetes mellitus, hypercholesterolemia, arterial hypertension, acute myocardial infarction, stroke, renal failure, and renal lithiasis. Comedications of interest included lipid-lowering agents, antihypertensives,

insulin or oral antidiabetics, antiplatelets, or anticoagulants. The study was approved by the ethics committee, and all participants provided written informed consent before enrolment.

### Statistical analysis

Methods of descriptive and analytical statistics were used to analyze the data. The prevalence of CVD and other non-AIDS comorbidities was calculated for each condition. A bivariate and multivariate analysis was conducted to identify associations between risk factors and outcomes. Statistical software R version 4.1.2 and its packages for statistical analysis were used to conduct statistical analysis.

### Results

Overall, 1200 patients were included, of whom 825 (68.7%) were male. The mean age of the study patients was 47 +/- 8.4 years (Table 1). 501 (41.7%) patients were current smokers, 33 (2.8%) were current alcohol users, and 758 (63.2%) (chronic, compulsive drinking) were past or

current users of injection drugs (people who inject non-medical and controlled medical drugs (and may have substance use disorder) for non-medical purposes) [31] (12). The mean duration of HIV-1 infection was 12.0 +/- 6.2 years, and the most frequent mode of transmission was injection drug use (61.7%). The median CD4 count was 589 cells/mm<sup>3</sup> (IQR 608 + 313.5). An AIDS diagnosis was made in 44.6% of patients (Table 1). The cART has never been started by more than four people (0.3%). The overall prevalence of NACM was 427 (35.6%). The prevalence of hypertension was 65% in male participants. Other comorbidities, such as CVD-55 (65%), CKD-8 (73%), DM-67 (83%), and dyslipidemia (the imbalance of

Lipids such as cholesterol, low-density lipoprotein cholesterol (LDL-C), triglycerides, and high-density lipoprotein (HDL) 120 (58%) were more prevalent in female participants. The risk of NACM increases with age. The distribution of NACM among non-smoker participants was as follows: CVD: 117 (52%), CKD: 34 (40%), DM: 30 (37%), and dyslipidemia: 107 (52%). Detailed information about the burden and prevalence of non-AIDS comorbidities Stratified by possible risk factors are provided in Tables 2 and 3. The age (P 0.001) and the smoking status (P 0.010) were significantly associated with CVD (table 4).

### Discussion

In this study, we found that people living with HIV aged 50 years and older had at least one co-morbidity. The most common NACM was dyslipidemia (hypercholesterolemia). The prevalence found is disproportionately higher when compared to reports from other countries (6,13–17).

It is known that hypercholesterolemia is commonly associated with long-term use of ART (6,13,16,17) and that both protease inhibitors and nucleoside reverse transcriptase inhibitors (NRTI) are associated with metabolic syndrome, which is highly prevalent in people living with HIV (6,13,16,18). Some studies conducted in Georgia showed the prevalence of hypercholesterolemia among the general population to be 31%. The prevalence of hyperlipidemia is lower in the general population compared to people living with HIV (31% vs. 70.9%). Contributing factors of dyslipidemia are not only HIV and ART but also an unhealthy diet, low physical activity, smoking, and heavy alcohol consumption. In general, these factors are linked to elevated blood pressure, high serum cholesterol, and obesity (19); according to a WHO report about the Georgian Profile of Health and Well-Being, 58.5% of males are using tobacco in Georgia, which is one of the highest tobacco consumption rates in Europe (where the average rate is 38.5%) and higher than in the CIS (51.8%). In our cohort, the rate of current smokers is 40.6%, which is lower compared to the general population.

Arterial hypertension was another common NACM in this study. Arterial hypertension was associated with a higher body mass index, hyperlipidemia, and familial history of high cholesterol (3,4,16,20,21). We found that the prevalence of arterial hypertension was higher in the general population compared to our study cohort (56% vs.

48%, respectively). In addition, a higher prevalence was found in the Georgian population compared to people living with HIV (11.6% vs. 3.6%, respectively) (22). The higher distribution of arterial hypertension and diabetes rates among the general population than among people living with HIV is a non-typical finding of this study and needs further investigation.

This study also focused on hyperglycemia, which was the third NACM obtained in this study. Abnormal glucose metabolism, which occurs during the course of HIV infection and its treatment, is a prevalent condition (13,18,23,24). Diabetes is a well-known complication of ART, and it is associated with exposure to some antiretroviral drugs (25,26). The reported prevalence of diabetes among people living with HIV ranges from 2% to 14%. In our cohort, the prevalence of impaired fasting glucose was higher than previously reported and ranges from 5 to 17, or 7%, according to increasing age.

For an understanding of kidney disease prevalence in our cohort, we performed analyses of the GFR rates. It's well known that HIV infection is associated with several types of renal dysfunction, including HIV-associated nephropathy (HIVAN), immune complex kidney disease, acute renal failure, and chronic kidney disease (CKD), which itself may be related to the nephrotoxicity of antiretrovirals 3, 11, and 19. According to the Chronic Kidney Disease Collaboration article "Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis of the Global Burden of Disease Study 2017," the global all-age prevalence of CKD increased by 29.3% (95% UI 26.4 to 32.6) since 1990, whereas the age-standardized prevalence remained stable (1.2% –1.1 to 3.5). The findings of our study showed that the prevalence of abnormal GFR rates was higher among elderly persons, and on average, in our cohort, it was 2.4 %.

## Conclusions

People living with HIV aged 50 years and older had at least one co-morbidity. The most common NACM for the Georgian cohort was dyslipidemia (hypercholesterolemia). The prevalence of hyperlipidemia among people living with HIV is higher than among the general population. Arterial hypertension was another common NACM in this study. We found a higher prevalence of arterial hypertension in the general population compared to people living with HIV. In addition, a higher prevalence of diabetes was found in the general population (11.6% vs. 3.6%, respectively). The higher distribution of arterial hypertension and diabetes rates among the general population compared to people living with HIV is a non-typical finding of this study and needs to be addressed.

further investigation. was found to have a high prevalence of impaired fasting glucose in our cohort.

Overall, the NACM burden was high in the cohort, but higher in the obese and smoker groups. The findings of our study showed that the prevalence of abnormal GFR rates on average in our cohort was 2.4%, which is twice

higher than the age-standardized prevalence of CKD among the global general population.

Long-term healthcare management and long-term health outcomes could be improved for people living with human immunodeficiency virus infection by careful HIV management according to current recommendations with optimal selection of antiretrovirals and early management of comorbidities through recommended lifestyle improvements and preventative measures.

**Table 1.** Demographic and Clinical Characteristics

Dialysis due to CKD, n (%)	4, (0.3%)
<b>GFR values</b>	
<b>Age group, n (%)</b>	
<40 y	201, (16.7%)
40–49 y	529, (44.1%)
50–59 y	361, (30.1%)
≥60 y	109, (9.1%)
<b>Gender</b>	
Male	825 (68.7%)
female	375 (31.3%)
<b>BMI, n (%)</b>	
Normal 18.5 -24.9 kg/m <sup>2</sup>	533, (44.4%)
Overweight 25- 30 kg/m <sup>2</sup>	508, (42.3%)
Obese ≥30	159, (13.3%)
<b>CVD prevalence</b>	
Hypertension ever diagnosed by doctor	227, (18.9%)
SBP (measured during interview), mmHg	112, ± 11.21
DBP (measured during interview), mmHg	70, ± 8.12
Use any anti-hypertension pills during last 2 weeks, n (%)	129, (10.7%)
Myocardial infarction n (%)	83, (6.9%)
Stent or cardiac bypass, n (%)	13, (1.1%)
Receiving aspirin pills, n (%)	36, (3.0%)
Receiving statins pills for prophylactic reasons, n (%)	27, (2.2%)
Cardiac event among ancestors, n (%)	490, (40.8%)
CKD (Chronic Kidney Disease), n (%)	11, (0.9%)
Dialysis due to CKD, n (%)	4, (0.3%)
<b>GFR values</b>	
GFR <90, n (%)	31, (2.6%)
GFR 90+, n (%)	1157, (97.4%)
<b>Diabetes prevalence</b>	
Diabetes ever diagnosed by doctor	81, (6.7%)
Use any anti-diabetic medicine during last 2 weeks, n (%)	46, (3.5%)
Insulin (anti-diabetic) use current, n (%)	14, (1.2%)

**Table 1.** Demographic and Clinical Characteristics (Cont.)

<b>Elevated cholesterol prevalence</b>	
Elevated blood cholesterol level diagnosed by doctor, n (%)	206, (17.2%)
Use any lipid-lowering medication during last 2 weeks, n (%)	43, (3.6%)
<b>Cigarette use, n (%)</b>	
Never	524, (43.6 %)
Current	501, (41.7%)
Former	177, (14.7%)
<b>Current alcohol use, n (%)</b>	33, (2.8%)
<b>Injection drug use</b>	
Yes, n (%)	785(63.2%)
No, n(%)	414(36,8%)
<b>CD4 Count, cells/mm3</b>	
CD4 count median	608 $\pm$ 313.5
CD4 nadir	177 $\pm$ 194.1
<b>HIV viral load, n (%)</b>	
<200 cop/ml	1099, (91.8%)
200–999 copies/mL	39, (3.3%)
$\geq$ 1000 copies/mL	59, (4.9%)
<b>Year initiated cART, n (%)</b>	...
2004–2013	415, (34.6%)
2013-2021	781, (65.1%)
Never initiated cART, n (%)	4, (0.3%)
Overall prevalence of Non-AIDS comorbidities, n (%)	427, (35.6%)

**Table 2.** Burden and Prevalence of Non-AIDS Comorbidities Stratified by possible risk factors

	Total N	Hypertension		CVD		CKD		DM		Dyslipidemia	
		n (%)	p value	n (%)	p value	n (%)	p value	n (%)	p value	n (%)	p value
Total co-hort	1200										
Age categories			<0.001		<0.001		0.7		0.002		<0.001
<40	201	11 (5)		2 (3)		2 (18)		7 (9)		22 (11)	
40–49	528	50 (22)		16 (19)		3 (27)		35 (43)		74 (36)	
50–59	361	107 (47)		39 (46)		5 (45)		23 (28)		86 (42)	
≥60	107	59 (55.1)		27 (32)		1 (9)		16 (20)		24 (12)	
Gender			0.3		0.8		>0.9		0.018		0.002
Women	375	80 (35)		55 (65)		8 (73)		67 (83)		120 (58)	
Men	825	147 (65)		29 (35)		3 (27)		14 (17)		86 (42)	
BMI			< 0.001		0.4		0.2		< 0.001		<0.001
<25	533	63 (28)		37 (44)		2 (18)		20 (25)		57 (28)	
25 - <30	159	56 (25)		15 (18)		3 (27)		23 (28)		62 (30)	
30+	508	108 (48)		32 (38)		6 (55)		38 (47)		87 (42)	

**Table 2.** Burden and Prevalence of Non-AIDS Comorbidities Stratified by possible risk factors

Smoking			0.026		0.003		0.4		0.4		0.017
Never Smoked	517	117(52)		34(40)		7(64)		30(37)		107 (52)	
Former Smoker	177	34(15)		23(27)		1(9)		15(19)		29(14)	
Current Smoker	501	75(33)		27(32)		3(27)		36(44)		70(34)	
Alcohol			0.5		0.4		>0.9		0.021		0.14
No use	1167	218(96)		80(95)		11 (100)		75(93)		204 (99)	
>4 times a Week	33	9(4)		4(5)		0(0)		6(7)		2(1)	
Injection drug use			0.8		0.9		>0.9		0.3		0.39
	317	58(26)		21(25)		3(27)		26 (32)		42 (20)	
	883	169(74)		63 (75)		8(73)		55 (68)		164 (80)	
CD4 (nadir)			0.051		0.04		0.031		0.4		0.2
	1200	152 (49,305 )		128 (29, 294)		44 (16, 176)		151 (74, 269)		160 (62, 298)	
HIV viral load			0.8		0.4		0.6		0.5		0.7
< 200	1099	209 (92)		80 (95)		11 (100)		75(93)		191 (93)	
200 – 999	39	5 (2)		1 (1.4)		0		1(1)		7(3)	
>1000	59	13 (6)		3 (3.6)		0		5(6)		8(4)	

**Table 3.** MULTIVARIATE ANALYSIS FOR CVD RISK FACTORS

Characteristic	N	OR <sup>1</sup>	95% CI <sup>1</sup>	p-value
<b>Age group</b>	1166			<b>&lt;0.001</b>
<i>&lt;40</i>		—	—	
<i>40-49</i>		3.17	0.87, 20.3	
<i>50-59</i>		12.4	3.60, 78.2	
<i>60+</i>		35.6	9.92, 229	
<b>Smoking Status</b>	1166			<b>0.010</b>
<i>Never smoked</i>		—	—	
<i>Former smoker</i>		2.76	1.39, 5.45	
<i>Current smoker</i>		1.27	0.65, 2.51	
<b>Gender</b>	1166			0.26
<i>F</i>		—	—	
<i>M</i>		0.68	0.35, 1.32	
<b>CD4 nadir</b>	1166	1.00	1.00, 1.00	0.91
<b>cd4last</b>	1166	1.00	1.00, 1.00	0.83
<b>Viral Load Categories</b>	1166			0.59
<i>&lt;200</i>		—	—	
<i>200-999</i>		0.44	0.02, 2.23	
<i>&gt;1000</i>		0.70	0.16, 2.14	
<b>HIV transmission</b>	1166			0.57
<i>Injection drug use</i>		—	—	
<i>Heterosexual transmission</i>		1.03	0.54, 1.98	
<i>Homosexual transmission</i>		1.16	0.39, 3.09	
<i>other</i>		2.69	0.62, 10.1	
<b>Cholesterol</b>	1166			0.24
<i>Cholesterol</i>		—	—	
<i>1</i>		209,384	0.00, NA	
<i>2</i>		334,519	0.00, NA	
<b>BMI categories</b>	1166			0.26
<i>&lt;25</i>		—	—	
<i>&gt;30</i>		1.20	0.58, 2.40	
<i>25-30</i>		0.71	0.42, 1.21	

<sup>1</sup>OR = Odds Ratio, CI = Confidence Interval

**Table 4.** MULTIVARIATE ANALYSIS FOR CKD RISK FACTORS

Characteristic	N	OR <sup>1</sup>	95% CI <sup>1</sup>	p-value
<b>Age group</b>	1161			0.64
<i>&lt;40</i>		—	—	
<i>40-49</i>		0.39	0.06, 3.15	
<i>50-59</i>		0.83	0.15, 6.63	
<i>60+</i>		0.39	0.02, 4.75	
<b>Smoking Status</b>	1161			0.30
<i>Never smoked</i>		—	—	
<i>Former smoker</i>		0.29	0.01, 2.01	
<i>Current smoker</i>		0.33	0.06, 1.55	
<b>Gender</b>	1161			0.44
<i>F</i>		—	—	
<i>M</i>		2.07	0.32, 14.0	
<b>CD4 nadir</b>	1161	0.99	0.99, 1.00	<b>0.018</b>
<b>cd4last</b>	1161	1.00	1.00, 1.00	0.53
<b>Viral Load Categories</b>	1161			0.39
<i>&lt;200</i>		—	—	
<i>200-999</i>		0.00		
<i>&gt;1000</i>		0.00		
<b>HIV transmission</b>	1161			0.40
<i>Intravenous drug users</i>		—	—	
<i>Heterosexual transmission</i>		0.58	0.10, 3.45	
<i>Homosexual transmission</i>		1.83	0.20, 13.4	
<i>other</i>		3.83	0.15, 46.2	
<b>GFR categories</b>	1161			0.38
<i>90+</i>		10,160,810	0.00, NA	
<b>BMI categories</b>	1161			0.16
<i>&lt;25</i>		—	—	
<i>&gt;30</i>		5.61	0.84, 46.6	
<i>25-30</i>		3.20	0.69, 22.8	

<sup>1</sup>OR = Odds Ratio, CI = Confidence Interval



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