

# The Prevalence of Diabetes Mellitus Type 2 in HIV-1 Infected Patients and Antiretroviral Treatment Utilization in Ukraine – the Results of Observational Multi-center Cross-sectional Retrospective Study

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## BACKGROUND

- Based on published data 4.3% – 12.6% of patients with human immunodeficiency virus (HIV) have Diabetes Mellitus Type 2 (T2DM)<sup>1</sup>, which is the second most prevalent co-morbidity in people living with HIV (PLWH)<sup>2</sup>
- Patients with T2DM belong to a high cardiovascular risk (CVR) group<sup>3,4</sup>
- Antiretroviral (ARV) regimens need to be carefully tailored in HIV-infected patients with T2DM and high CVR due to potential drug-drug interactions (DDI), tolerability and long-term adverse effects
- For instance, protease inhibitor (PI) and efavirenz (EFV) based regimens may negatively affect lipids profile<sup>5,6</sup>, lopinavir (LPV) may facilitate the development of insulin resistance<sup>7</sup> and dolutegravir (DTG) has DDI with metformin<sup>8</sup>, which is the most commonly used treatment in T2DM patients
- There is no epidemiological data regarding the prevalence of T2DM in PLWH in Ukraine
- The burden of T2DM as well as ARV regimens utilization in this patient population are unclear

## OBJECTIVES

- Primary objective:
  - To assess the prevalence of T2DM in PLWH
- Secondary objectives:
  - To assess the percentage of PLWH with undiagnosed T2DM among a subgroup of patients with elevated fasting glucose above 7 mmol/L
  - To assess the percentage of patients with T2DM among PLWH who are not receiving hypoglycemic drugs
  - To describe the current patterns of antiretroviral therapy (ART) regimens utilization in HIV-1 infected patients with T2DM

## MATERIALS AND METHODS

- This was an observational multi-center cross-sectional retrospective study
- 2 400 patients with HIV-1 infection, who were under care in 3 large urban HIV centres in Ukraine in 2017, were randomly enrolled in the study:
  - Clinic of the Gromashevsky Institute of Epidemiology and Infectious Diseases, Kiev
  - Vinnitsya Regional Clinical AIDS Centre, Vinnitsya, Medgorodok
  - Municipal Clinical Hospital No 5, Kiev
- An equal number of patients (800) in each medical centre was enrolled
- Medical records were used as the primary source documents
- Patients were categorized as having T2DM if they were already diagnosed with T2DM or had fasting glucose level elevated above 7 mmol/L or received hypoglycemic drugs

## RESULTS

### Participants

- 2 400 patients with HIV-1 infection were included in this analysis (Table 1)

Table 1. Demographic and clinical characteristics of HIV-1 infected patients

Parameter	Patients (N=2 400)
Male, n (%)	1 385 (57.71)
Female, n (%)	1 015 (42.29)
Age (years), Mean (SD)	39.29 (8.22)
BMI, Mean (SD)	23.92 (4.21)
CD4+ T-cell count (cells per $\mu$ L), Mean (SD)	526.11 (281.56)
HIV-1 RNA ( $\log_{10}$ copies per mL), Mean (SD)	4.40 (5.42)

### T2DM Prevalence

- The prevalence of T2DM among PLWH was **4.75%** (114 out of 2 400 patients) (Table 2)

Table 2. Demographic and clinical characteristics of HIV-1 infected patients with T2DM and without T2DM

Parameter	Patients, Mean (SD)	
	With T2DM (N=114)	Without T2DM (N=2 286)
Age (years)	43.84 (9.86)	39.08 (8.07)
BMI	25.56 (5.94)	23.83 (4.04)
CD4+ T-cell count (cells per $\mu$ L)	480.03 (285.49)	528.38 (281.24)
HIV-1 RNA ( $\log_{10}$ copies per mL)	4.56 (5.52)	4.39 (5.41)

- Patients with HIV-1 infection and T2DM were significantly older than patients with HIV-1 infection and without T2DM ( $p < 0.0001$ )
- BMI in patients with T2DM was significantly higher than in patients without T2DM ( $p = 0.009$ )
- Both mean CD4+ T-cell count and mean plasma HIV-1 RNA concentration were not significantly different between the patients with T2DM and the patients without T2DM,  $p = 0.079$  and  $p = 0.065$  respectively
- 87.72%** ( $n = 100$ ) of patients with elevated fasting glucose above 7 mmol/L were not previously diagnosed with T2DM (Table 3A)
- 88.60%** ( $n = 101$ ) of patients with T2DM did not receive hypoglycemic drugs (Table 3B)

Table 3. The percentage of PLWH with undiagnosed T2DM among a subgroup of patients with elevated fasting glucose above 7 mmol/L (A) and the percentage of patients with T2DM among PLWH who are not receiving hypoglycemic drugs (B)

Patients with elevated fasting glucose above 7 mmol/L	Patients, n (%) (N=114)
<b>A</b>	
T2DM was diagnosed	14 (12.28)
T2DM was not diagnosed	100 (87.72)
<b>B</b>	
T2DM was treated	13 (11.40)
T2DM was not treated	101 (88.60)

- Metformin was the most commonly prescribed hypoglycemic drug (**53.85%**, 7 out of 13 patients)

P-value was derived from Mann-Whitney-U-tests.

HIV, human immunodeficiency virus; T2DM, diabetes mellitus type 2; PLWH, people living with HIV; CVR, cardiovascular risk; ARV, antiretroviral; DDI, drug-drug interactions; PI, protease inhibitor; EFV, efavirenz; LPV, lopinavir; DTG, dolutegravir; ART, antiretroviral therapy; AIDS, acquired immune deficiency syndrome; SD, standard deviation; BMI, body mass index; CD4+, T-lymphocyte cell bearing the CD4 receptor; RNA, ribonucleic acid; LPV/r, lopinavir/ritonavir; NNRTI, non-nucleoside reverse-transcriptase inhibitor; INI, integrase inhibitor; NVP, nevirapine; ETR, etravirine; DRV, darunavir; RAL, raltegravir; AZT, zidovudine; TDF, tenofovir disoproxil fumarate; 3TC, lamivudine; NRTI, nucleoside reverse-transcriptase inhibitor; ABC, abacavir; FTC, emtricitabine.

## ART Regimens Utilization

- 60.00%** of HIV-1 infected patients with T2DM received EFV containing regimens, **24.55%** LPV/r and **8.18%** DTG (Table 4)

Table 4. ART regimens utilization in HIV-1 infected patients with T2DM

Three-component ART regimen (classic)	Three-component ART regimen (classic)	Stratified into components		Total per group		
		n	%	n	%	
NNRTI	EFV contains regimen	66	60.00	68	61.82	
	NVP contains regimen	2	1.82			
	ETR contains regimen	0	0			
PI	LPV contains regimen	27	24.55	27	24.55	
	DRV contains regimen	0	0			
INI	DTG contains regimen	9	8.18	15	13.63	
	RAL contains regimen	6	5.45			
Total three-component ART regimens (classic)				110	100.00	
Other ART regimen	LPV + RAL				2	
	AZT + TDF + 3TC				1	
	DTG + 3TC				1	
	Total other ART regimens				4	
Total ART regimens				114		

- The most frequently used dual-NRTI combination was TDF + FTC (**52.73%**) (Table 5)

Table 5. The distribution of dual-NRTI combinations among three-component ART regimens in HIV-1 infected patients with T2DM

Dual-NRTI combination	Regimens, n (%) (N=110)
TDF + FTC	58 (52.73)
TDF + 3TC	6 (5.45)
ABC + 3TC	14 (12.73)
ABC + FTC	0 (0)
AZT + 3TC	32 (29.09)
AZT + FTC	0 (0)

## CONCLUSIONS

- This study is the first, national, epidemiological, cross-sectional study on the prevalence of T2DM in PLWH in Ukraine
- The prevalence of T2DM among PLWH in Ukraine was comparable to that described in the literature
- Almost 90% of identified T2DM patients were not under T2DM-related medical care including treatment
- Based on the results of this study we may conclude that diagnosis and management of patients with HIV and T2DM must be improved, including considerations about the optimal ARV regimens and T2DM treatment

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