ORIGINAL ARTICLE

Prevalence of impaired fasting glucose and dyslipidemia among Mexican HIV antiretroviral-naïve patients

Prevalencia de glucosa alterada en ayuno y dislipidemia entre pacientes mexicanos con VIH naïve a tratamiento antirretroviral

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Abstract

Background: *Metabolic complications have become more relevant in the care of patients with HIV. However, little is known about the incidence and risk factors for these disorders among HIV-infected antiretroviral treatment naïve (ARTn) patients.* **Objective:** *To recognize the prevalence of Impaired Fasting Glucose (IFG) and dyslipidemia among HIV-infected ARTn Mexican individuals and identify associated risk factors.* **Method:** *A retrospective study was conducted in HIV-1-infected ART-N patients, referred for attention to a general hospital in Mexico City, between 2009 and 2019. We collected information for anthropometric, clinical, biochemical and HIV status variables.* **Results:** *We included 221 patients, 97% were males, mean age 30 years (interquartile range [IQR]: 25-38); median CD4 count was 250 cells/mm3 (IQR: 120.25-391) and median log10 HIV viral load was 4.69 HIV-1 RNA copies/ml (IQR: 3.64-5.25). Prevalence of IFG was 22.6% and was associated with overweight-obesity (odds ratio [OR]: 2.75; 95% confidence interval [95%CI]: 1.36-5.55; p-value < 0.05). Hypoalphalipoproteinemia was the most frequent dyslipidemia: 69.46%. An association between count CD4 < 250 and lower HDL cholesterol levels was found (OR, 3.23; 95CI%: 1.61-6.5; p- value < 0.05).* **Conclusions:** *IFG and dyslipidemia are highly prevalent among HIV-infected ART-naïve Mexican patients, therefore, screening for glucose and lipids abnormalities always should be considered among ARTn patients.*

Keywords: *Dyslipidemia. Pre-diabetes. Prevalence. HIV infection. Antiretroviral naïve.*

Resumen

Antecedentes: *Las alteraciones metabólicas se han vuelto más relevantes en el cuidado de los pacientes con infección por el virus de la inmunodeficiencia humana (VIH). Existe poca información sobre estas alteraciones en pacientes naïve a tratamiento antirretroviral (nART).* **Objetivo:** *Identificar la prevalencia de glucosa alterada en ayuno y dislipidemia entre individuos mexicanos con VIH nART e identificar los factores asociados.* **Método:** *Estudio retrospectivo en pacientes con VIH nART valorados en un hospital general de la Ciudad de México de 2009 a 2019. Se recabaron datos antropométricos, clínicos, bioquímicos y relacionados con el estado del VIH.* **Resultados:** *Se incluyeron 221 pacientes, el 97% hombres, con mediana de edad 30 años (rango intercuartil [RIC]: 25-38), cuenta de linfocitos CD4 250 células/mm3 (RIC: 120.25-391) y carga viral log10 4.69 copias/ml (RIC: 3.64-5.25) de VIH-1 ARN. La prevalencia de glucosa alterada en ayuno fue del 22.6% y presentó asociación con sobrepeso-obesidad (razón de momios [RM]: 2.75; intervalo de confianza del*

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95% [IC95%]: 1.36-5.55; p < 0.05). La dislipidemia más frecuente fue la hipoalfalipoproteinemia (69.46%), asociada con CD4 < 250 (RM: 3.23; IC95%: 1.61-6.5; p < 0.05). **Conclusiones:** *Las alteraciones en el metabolismo de los lípidos y de la glucosa son frecuentes entre individuos mexicanos con VIH nART; por lo tanto, es importante una adecuada evaluación antes de iniciar el tratamiento.*

Palabras clave: *Dislipidemia. Prediabetes. Prevalencia. Infección por VIH. Naïve tratamiento antirretroviral.*

Introduction

Over the past two decades, lower morbidity and mortality rates have been documented in patients infected with the human immunodeficiency virus (HIV) due to the effectiveness of antiretroviral therapy (ART)[1-3], leading to a significantly higher life expectancy. Consequently, patients with HIV are more commonly affected by chronic diseases[4]. In fact, currently, over half of the deaths reported in these patients do not account for infection-related complications[5,6]. Therefore, the evaluation of chronic diseases, such as type 2 diabetes mellitus (T2DM) and dyslipidemias, has become more relevant in the management of these patients[7-10]. However, most epidemiological data on HIV-related metabolic disorders come from studies conducted among patients treated with ART[11,12]. Nonetheless, these changes have also been described in treatment-naïve HIV patients (nART)[13,14]. On the other hand, impaired fasting glucose (IFG) is considered an intermediate condition in the transition from normal glucose to T2DM[15]. Few studies have discussed the prevalence of IFG and dyslipidemia in nART HIV patients. Also, it has been proposed that the prevalence of metabolic abnormalities in these patients may vary depending on the population studied[16].

The objective of this study was to assess the prevalence of IFG and dyslipidemia in nART HIV patients and their association with age, body mass index (BMI), smoking status, CD4 lymphocyte count (CD4c), viral load (VL), and disease duration in a population of patients treated in a general hospital of Mexico City, Mexico.

Method

This was a retrospective study conducted in adult nART patients infected with HIV treated in a general hospital of Mexico City, Mexico from July 1, 2009 through August 31, 2019. The study was approved by the hospital research and ethics committees. Patients who had been hospitalized or had an active HIV-related infection 3 months prior to their initial assessment at the hospital were excluded.

Population

The following data were collected: age, sex, previous diagnoses, anthropometric parameters (weight and height), lab test results (fasting glucose, total cholesterol [TC], high-density lipoproteins [HDL-C], low-density lipoproteins [LDL-C], and triglycerides [TG]), as well as parameters associated with the HIV infection status (approximate disease duration in months, CD4c, and HIV-1 RNA VL). The BMI was calculated by dividing the weight in kilograms squared by the height in centimeters and then stratified into 4 different categories according to the World Health Organization classification: underweight (BMI $\leq$ 18.4 kg/m^2), normal weight (BMI = 18.5-24.9 kg/m^2), overweight (BMI = 25-30 kg/m^2), and obesity (BMI $\geq$ 30 kg/m^2). The diagnosis of IFG was achieved following the criteria established by the American Diabetes Association: fasting glucose levels between 100 mg/dL and 125 mg/dL. This was the definition of dyslipidemia used: hypercholesterolemia if TC > 200 mg/dL, hypertriglyceridemia if TG > 150 mg/dL, and hypoalphalipoproteinemia if HDL-C < 50 mg/dL in women and < 40 mg/dL in men. Patients were divided based on disease duration (> or < 6 months).

Statistical analysis

Data were analyzed using the statistical software package SPSS (IBM Corp, Armonk, NY, United States), version 24. The distribution of quantitative data was determined using the Kolmogorov-Smirnov test. Variables with parametric distribution were expressed as mean ± standard deviation, and those with non-parametric distribution as median and interquartile range. Categorical variables were expressed as percentages. Continuous variables with non-parametric distribution were transformed using the natural logarithm function. The continuous variables comparison regarding BMI categories, disease duration, presence of IFG, and presence of dyslipidemia was performed using the Student t test and the ANOVA test. The association

Table 1. Characteristics of the population

Variable	All patients (n = 221)	Subgroup with lipid values (n = 167)
Men (%)	97.28	98.2
Age	30 (25-38)	30 (25-35)
Weight (kg)	65.96 (± 11.7)	66.9 (± 11-31)
Height (cm)	170.08 (± 7.79)	170.82 (± 7.57)
Body mass index	22.73 (± 3.21)	22.82 (± 3.09)
Disease duration (months)	2.43 (1.08-9.52)	3.07 (1.17-10.83)
Viral load log10 (copies/mL)	4.69 (3.64-5.25)	4.62 (3.37-5.11)
CD4 Lymphocyte Count (cells/mL)	250 (120.25-391)	286 (169-434.5)

Data are expressed as mean ± standard deviation, median and interquartile range or frequency.

between the characteristics of participants with IFG and dyslipidemia was determined using the chi-square test or Fisher's exact test. Bonferroni correction was used for the BMI-stratified analysis. The odds ratio (OR) and 95% confidence interval (CI) were estimated to evaluate the strength of the association. P values < 0.05 were considered statistically significant ($p < 0.0083$ for Bonferroni correction). To identify variables independently associated with IFG, a binary logistic regression analysis with the "backward stepwise" method, by blocks, was used, with IFG as the dependent variable, eliminating variables that did not contribute to the model. The variables included in the model were age, BMI, disease duration, VL, and the CD4c.

Results

A total of 221 patients were included in the study. Since the patients' lipid values were not available entirely, the analysis of dyslipidemia was conducted in a subgroup of 167 patients. The population characteristics are shown on table 1. The prevalence of IFG was 22.6% (95%CI, 17.07-28.18). No association among the VL, the CD4c, smoking, and age with IFG was reported (Table 2). A total of 153 participants (69.2%) had normal weight; 21 (9.5%), low weight; 42 (19%), overweight; and 5 (2.3%), obesity. Due to the low prevalence of obesity, these participants were included in the same overweight group (overweight-obesity group). The CD4c was significantly higher in the overweight-obesity group, while the low-weight group had a significantly higher VL (Table 3). After Bonferroni correction, a significantly higher prevalence of IFG was seen in the overweight-obesity group (OR, 2.75; 95%CI, 1.36-5.55). Table 4 shows the overall and age-stratified prevalences of both IFG and dyslipidemia. Among the studied population, 76.05% of participants (95%CI, 6.51-82.59) presented with some form of dyslipidemia. The most common impairment was hypoalphalipoproteinemia (69.46% [95%CI, 62.4-76.52]) with hypertriglyceridemia as the second most common impairment (32.9% [95%CI, 25.73-40.14]). A total of 11.8% of the patients had elevated LDL-C levels (95%CI, 6.51-16.24) while 7.2% (95%CI, 3.23-11.11) had hypercholesterolemia (Table 4). Patients with low weight had significantly lower TG and TC levels (Table 5). A relationship was found between a low CD4c (cut-off value, 250 cells/mm^3) and hypoalphalipoproteinemia (OR, 3.23; 95%CI, 1.61-6.5). Patients with disease durations > 6 months had significantly lower HDL-C and triglyceride levels, and lower CD4c (Table 6). In the multivariate analysis, the variable independently associated with IFG was the BMI category of overweight-obesity (OR, 2.75; 95%CI, 1.36-5.55; p = 0.007).

Discussion

There is limited information on metabolic changes in Mexican nART HIV patients. In our study, the low prevalence of obesity found was similar to the one reported by Faurholt-Jepsen et al.[17] in nART patients. However, the prevalence of IFG in our population was higher, while Srivanich et al.[18] reported a 27.5% prevalence in a heterogeneous population of patients with and without ART.

Data on the prevalence of prediabetes in Mexico are also limited. Guerrero-Romero et al.[19] reported a rate of 24.6% in the adult population, while in subgroups

Table 2. Characteristics of the population based on glucose status

Variable	Normal glucose (n = 171)	IFG (n = 50)	p
Men (%)	97.1	98	0.892
Age (years)	30 (25-37)	31.5 (27.7-40)	0.188
Smoking (%)	49.8	50.2	0.391
Weight (kg)	65.5 (± 11.56)	67.52 (± 12.14)	0.155
Height (cm)	170.5 (± 7.99)	168.5 (± 6.88)	0.103
Body Mass Index	22.44 (± 3.0)	23.74 (± 3.7)	0.011
Viral load log10 (copies/mL)	4.73 (3.96-5.25)	4.32 (3.10-5.11)	0.177
CD4 lymphocyte count (cells/mL)	239 (109-394)	304 (209.5-389.5)	0.268

IFG: impaired fasting glucose.
Data are expressed as mean ± standard deviation, median and interquartile range or frequency.

Table 3. Characteristics of the population based on different body mass index categories

	Low weight (n = 21)	Normal weight (n = 153)	Overweight-Obesity (n = 47)	p
Age (years)	27 (24-36.5)	30 (25-37.5)	31 (28-40)	0.319
Smoking (%)	42.9%	49%	57.4%	0.582
Viral Load log10 (copies/mL)	4.87 (3.62-5.25)	4.86 (3.88-5.83)	4.28 (3.31-4.77)	0.045
CD4 lymphocyte count (cells/mL)	76 (31.5-245.5)	229 (121-370)	334 (248-576)	< 0.0001
IFG, n (%)	4 (19)	28 (18.3)	18 (38.3)	0.015

BMI: body mass index; IFG: impaired fasting glucose.
Data are expressed as mean ± standard deviation, median and interquartile range or frequency.

Table 4. Overall prevalence of metabolic changes, stratified by age

	IFG, n (%)	Elevated TC[a] (%)	Elevated TG[b], n (%)	Low HDL-C[c], n (%)	Elevated LDL-C[d], n (%)
All Patients	50 (22.6%)	12 (7.2%)	55 (32.9%)	116 (69.46%)	19 (11.38%)
18-30 years	23 (19.9%)	4 (4.4%)	24 (26.4%)	55 (60.4%)	7 (7.7%)
30-40 years	16 (24%)	6 (10.9%)	22 (40%)	46 (83.6%)	10 (18.2%)
≥ 40	11 (29.8%)	11 (9.5%)	9 (42.9%)	15 (71.4%)	2 (9.5%)

HDL-C: high-density lipoprotein cholesterol; IFG: impaired fasting glucose; LDL-C: low-density lipoprotein cholesterol; TC: total cholesterol; TG: triglycerides.
Data is presented as frequencies.
[a]TC > 200 mg/dL.
[b]TG > 150 mg/dL.
[c]HDL-C < 40 mg/dL in men and < 50 mg/dL in women.
[d]LDL-C > 100 mg/dL.

with normal weight and aged 30 to 40 years, the rates were 16.7% and 22.1%, respectively. On the other hand, Ureña-Bogarín et al.[20] reported a rate of 14.6% in adults aged 18 to 30 years. Therefore, the prevalence of IFG in our population is higher than that reported in the overall population with similar characteristics.

On the other hand, the prevalence of dyslipidemia is higher than that reported by Ekrikpo et al.[14] and more similar to the one described by Muyanja et al.[11] in patients with ART. Consistent with our results, hypoalphalipoproteinemia has been reported as the most common type of dyslipidemia among individuals with HIV[21,22], and in our patients, it was associated

Table 5. Plasma lipid values and frequency of dyslipidemia based on body mass index

	BMI categories			
	Low Weight (n = 14)	**Normal weight (n = 118)**	**Overweight-Obesity (n = 35)**	**p**
TC (mg/dL)	123.35 (± 18.3)	142.7 (± 38.1)	156.48 (± 33.5)	0.006
HDL-C (mg/dL)	34.78 (± 7.87)	34.42 (± 12.19)	38 (± 8.3)	0.195
LDL-C (mg/dL)	68.35 (± 16.7)	71.3 (± 29.53)	80.88 (± 25.9)	0.101
TG (mg/dL)	93 (80.75-117.25)	128 (86-166)	137 (106-190)	0.035
TC > 200 mg/dL, n (%)	0	9 (7.6)	3 (8.5)	0.544
TG > 150 mg/dL, n (%)	1 (7.14)	38 (32.2)	16 (45.7)	0.284
HDL-C < 40 mg/dL in men or < 50 mg/dl in women, n (%)	9 (64.2)	85 (72)	22 (62.8)	0.531
LDL-C > 100 mg/dL, n (%)	0	14 (11.8)	5 (14.2)	0.237

BMI: body mass index; HDL-C: high-density lipoprotein cholesterol; IFG: impaired fasting glucose; LDL-C: low-density lipoprotein cholesterol; TC: total cholesterol; TG: triglycerides.
Data are expressed as mean ± standard deviation, median and interquartile range or frequency.

Table 6. Characteristics of the population based on disease duration

Variable	**Patients > 6 months**	**Patients < 6 months**	**p**
Age (years)	31 (26.75-40)	28 (23.75-31)	< 0.0001
Weight (kg)	65.01 (± 11.91)	68.26 (± 10.85)	0.054
BMI	23.29 (± 3.22)	22.49 (± 3.20)	0.086
Glucose (mg/dL)	91.66 (± 10.5)	92.81 (± 10.19)	0.447
TC (mg/dL)	143.98 (± 31.27)	144.26 (± 39.72)	0.783
TG (mg/dL)	101.5 (86-153.75)	136.5 (95.75-187)	0.031
HDL-C (mg/dL)	33.69 (± 10.24)	37.95 (±12.45)	0.038
LDL-C (mg/dL)	68.28 (± 28.24)	75.80 (± 27.96)	0.242
Viral load log10	4.73 (3.51-5.26)	4.49 (3.75-5.08)	0.808
CD4 lymphocyte count	229 (87-359)	314.5 (184.25-476.25)	0.004

BMI: body mass index; HDL-C: high-density lipoprotein cholesterol; IFG: impaired fasting glucose; LDL-C: low-density lipoprotein cholesterol; TC: total cholesterol; TG: triglycerides.
Data are expressed as mean ± standard deviation, median and interquartile range or frequency.

with low CD4c and disease durations > 6 months. Additionally, the prevalence in our population is higher than that reported by the National Health Survey 2012 (55.2%) in the overall Mexican population.[23] As in former studies,13 our patients with low weight had higher VL and lower TC and TG levels.

The development of metabolic changes in HIV-infected patients has been associated with a series of factors: inflammation, immune system activation, traditional risk factors, and the action of the virus. Some studies suggest that HIV infection affects the physiology of adipose tissue even before starting ART[24,25] through mechanisms of inflammation and accelerated fibrosis associated with the immune response[26].

These changes are associated with the so-called lipodystrophy syndrome (loss of subcutaneous fat in face and extremities, and gain of central and visceral fat)[27]. Although this syndrome has been described mainly in patients on ART[28], it has also been identified in nART patients[29] and is associated with an increase in the secretion of inflammatory mediators, such as tumor necrosis factor-alpha and leptin, potential mediators of insulin resistance[30,31]. It has been reported that in HIV-infected men, fat redistribution contributes

to hyperinsulinemia[32], while in women, increased abdominal fat is associated with insulin resistance[33]. Abdominal fat has also been associated with elevated TG and low HDL-C levels in both men and women with HIV[34,35]. Additionally, it has been speculated that nART patients have different degrees of inflammation and associated metabolic changes[36,37]. According to this concept, our study demonstrated that there was an association between decreased CD4c and hypoalphalipoproteinemia, as well as an association between disease duration > 6 months and high viral replication, low weight, and decreased levels of TC and TG.

In the population studied, an independent association was found between IFG and BMI, a traditional risk factor for glucose metabolic changes. On the other hand, the high prevalence of IFG in young individuals with normal weight from our population suggests that HIV-infected people may have a tendency to develop prediabetes and dyslipidemia at younger ages compared to uninfected individuals, as suggested in former studies[38]. However, we did not find an association between CD4c, VL, and IFG.

Prospective studies are needed to identify the impact of treatment and other factors in the progression to diabetes and cardiovascular diseases in Mexican subjects infected with HIV. Nonetheless, based on our findings, a careful evaluation of metabolic changes in HIV patients prior to the start of ART is advised to guide the type of initial drug that should be used, considering that new ART regimens are associated with significant weight gain[39].

The study has some limitations: predominantly, our population consists of men meaning that our conclusions cannot be extrapolated to women. Additionally, because of the study retrospective design, we could not include other variables associated with adiposity and the HIV infection status, such as waist circumference, body fat percentage, CD8c or the CD4/CD8 ratio.

Conclusions

In our study, we found a higher prevalence of IFG and dyslipidemia in Mexican nART HIV patients compared to the overall population. Overweight or obesity (according to the BMI) was independently associated with IFG. Additionally, low CD4c and disease duration > 6 months were associated with the presence of hypoalphalipoproteinemia. Therefore, we should assess the metabolic status of patients before putting them on ART while considering traditional risk factors such as BMI and the HIV infection status.

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Conflicts of interest

None reported.

Ethical disclosures

Protection of human subjects and animals in research. The authors declare that no experiments were performed on humans or animals for this study.

Patients' data protection. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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