https://repository.uaeh.edu.mx/revistas/index.php./MJMR/issue/archive

Mexican Journal of Medical Research ICSa

Biannual Publication, Vol. 12, No. 23 (2024) 33-38

ISSN: 2007-5235

Development of dyslipidemias in a cohort of Mexican adult patients with HIV/AIDS under highly active antiretroviral therapy

Desarrollo de dislipidemias en una cohorte de pacientes adultos mexicanos con VIH/SIDA bajo terapia antirretroviral altamente activa

Guadalupe López-Rodríguez[a], *Marcos Galván*[b], *Liliana Arias-Castelán*[c]

Abstract:

Dyslipidemias are comorbidities in seropositive patients under highly active antiretroviral therapy (HAART), which increase their complications risk and reduce their life expectancy. Objective: to evaluate the frequency and development of dyslipidemias in seropositive Mexican patients with highly active antiretroviral therapy (HAART). Material and method: retrospective cohort study, in recently diagnosed HIV+ patients: 366 men and 59 women. Serum concentrations of total cholesterol (TC), triglycerides (TGC), HDL cholesterol (HDL-c) and LDL cholesterol (LDL-c) were evaluated before starting and at month 6, 24, 36 and 48 with HAART. Results: in both sexes at the beginning of the HAART, 67.1% of low HDL-c levels were obtained. Dyslipidaemia due to TGC and TC increased significantly in all participants after 48 months of HAART (36.9% vs. 52.7% and 7.1% vs. 22.4%, respectively, $p<0.05$). however, the HDL-c decreased in patients with nucleoside and non-nucleoside reverse transcriptase inhibitor drugs. Discussion: HIV+ patients with HAART have a higher risk of developing dyslipidaemia, an increase in concentrations occurred after 6 months of treatment, a trend that continued positive until 48 months with HAART. Conclusions: dyslipidemias due to TG and TC, as well as low HDL-c are the most frequent in HIV+ patients, which change depending on the time and the type of drug indicated in the HAART.

Keywords:

Dyslipidemias, highly active antiretroviral therapy, HIV infections, acquired immunodeficiency syndrome

Resumen:

Las dislipidemias son comorbilidades en pacientes seropositivos bajo terapia antirretroviral altamente activa (TARAA), lo que incrementan su riesgo de complicaciones y reducen su esperanza de vida. Objetivo: evaluar la frecuencia y desarrollo de dislipidemias en pacientes mexicanos seropositivos con TARAA. *Material y método:* estudio de cohorte retrospectivo, en pacientes VIH+ de reciente diagnóstico: 366 hombres y 59 mujeres. Se evaluaron concentraciones séricas de colesterol total (CT), triglicéridos (TGC), colesterol HDL (c-HDL) y colesterol LDL (c-LDL), antes de iniciar y al mes 6, 24, 36 y 48 con TARAA. *Resultados:* en ambos sexos al inicio de la TARAA se registró un 67.1% de niveles bajos de c-HDL. En todos los participantes las dislipidemias por TGC y CT aumentaron significativamente después de 48 meses de TARAA (36.9% vs. 52.7% y 7.1% vs. 22.4%, respectivamente, $p<0.05$), sin embargo, disminuyó la de c-HDL, en los pacientes con fármacos inhibidores de la transcriptasa reversa nucleósidos y no nucleósidos. *Discusión:* Los pacientes VIH+ con TARAA tienen un mayor riesgo de desarrollar dislipidemias, un aumento en las concentraciones se presentó desde los 6 meses de tratamiento, tendencia que continuó positiva hasta los 48 meses con TARAA. *Conclusiones:* las dislipidemias por TG y CT, así como c-HDL bajo son las más frecuentes en los pacientes VIH+, las cuales cambian dependiendo del tiempo y el tipo de fármaco indicado en la TARAA.

Palabras Clave:

Dislipidemias, terapia antirretroviral altamente activa, infecciones por VIH, síndrome de inmunodeficiencia adquirida

INTRODUCTION

[a] Corresponding autor, Universidad Autónoma del Estado de Hidalgo, https://orcid.org/0000-0001-5432-0382; Email. glopez@uaeh.edu.mx

[b] Universidad Autónoma del Estado de Hidalgo, https://orcid.org/0000-0002-3254-4470; Email: marcos_galvan3112@uaeh.edu.mx

[c] CAPASITS-Hidalgo, Universidad Autónoma del Estado de Hidalgo, https://orcid.org/0000-0003-0149-7699; Email: liliana_arias6@hotmail.com

Received: 15/08/2023, Accepted: 20/10/2023, Postprint: 24/10/2023, Published: 05/01/2024

DOI: https://doi.org/10.29057/mjmr.v12i23.11518

With the implementation of highly active antiretroviral therapy (HAART), the human immunodeficiency virus (HIV) infection has become a chronic disease, which has allowed a longer survival time in patients with acquired immunodeficiency syndrome (AIDS). However, HAART has been associated with the risk of diseases such as hypertension, diabetes, and dyslipidaemias.[1-2] Dyslipidemia is the imbalance of lipids such as cholesterol, low-density cholesterol (LDL-c), triglycerides, and high-density cholesterol HDL-c.

In patients on HAART, dyslipidemias appear after three months of starting treatment, and are mainly associated with an increased risk of atherogenic dyslipidemia.[3] The most common dyslipidemias in HIV infection are low levels of c-HDL with increases in total cholesterol (TC), LDL-c and triglycerides (TGC); these conditions in turn increase the risk of atherogenic dyslipidemia and cardiovascular disease [4] in Mexican patients [5] and in patients from other parts of the world. It has been observed that 28.8% of HIV-positive patients are at moderate risk of suffering a cerebrovascular event; the relative risk of myocardial infarction is higher in HIV-positive patients that have taken protease inhibitors (49%) or abacavir (43%).[6] The relative risk of myocardial infarction is increased by 1.26 times in HIV-positive (HIV+) persons who have taken protease inhibitor drugs.[7] The aim of this study was to evaluate the frequency and development of dyslipidemias in a cohort of Mexican adult patients with HIV/AIDS on HAART.

MATERIAL AND METHODS

Retrospective cohort study in clinical records of male and female patients diagnosed with HIV/AIDS at the Ambulatory Center for the Prevention and Attention of AIDS and other sexually transmitted infections of the State of Hidalgo, Mexico (CAPASITS) in the period from 2010 to 2019. All reviews to clinical records of patients adhered to Mexican laws and regulations on confidentiality, patient autonomy and data protection and health research. [8]

Inclusion criteria were applied to data from 1241 CAPASITS patients. Men and women with recent HIV diagnosis, who at admission had not received any type of antiretroviral therapy nor previous diagnosis of any dyslipidemia were included in the study (Figure 1). Fasting serum lipid data (minimum of 8 hours) recorded were: total cholesterol (TC), triglycerides (TGC), high-density lipoprotein cholesterol (c-HDL) and low-density lipoprotein cholesterol (c-LDL); before starting HAART (baseline) and at 6, 24, 36 and 48 months after initiation of this therapy.

The diagnosis of dyslipidemias was performed according to The National Cholesterol Education Program Adult Treatment Panel III (ATP III) guidelines.[9] The cut-off points for serum lipids were TC ≥ 200 mg/dL, c-HDL < 40 mg/dL, c-LDL ≥ 130 mg/dL and TGC ≥ 150 mg/dL.

The systolic and diastolic blood pressure in mmHg, CD4 T lymphocyte count^{+} (cells/mm^{3}), viral load (thousands of viruses), age, weight (kg) and height (cm) of the patients included in the study were obtained from the file. The body mass index (BMI= Kg/m^{2}) was calculated with weight and height, to classify the subjects as underweight: <18.5, normal weight: 18.5-24.9; overweight: 25.0-29.9 and obese: ≥ 30.0.[10]

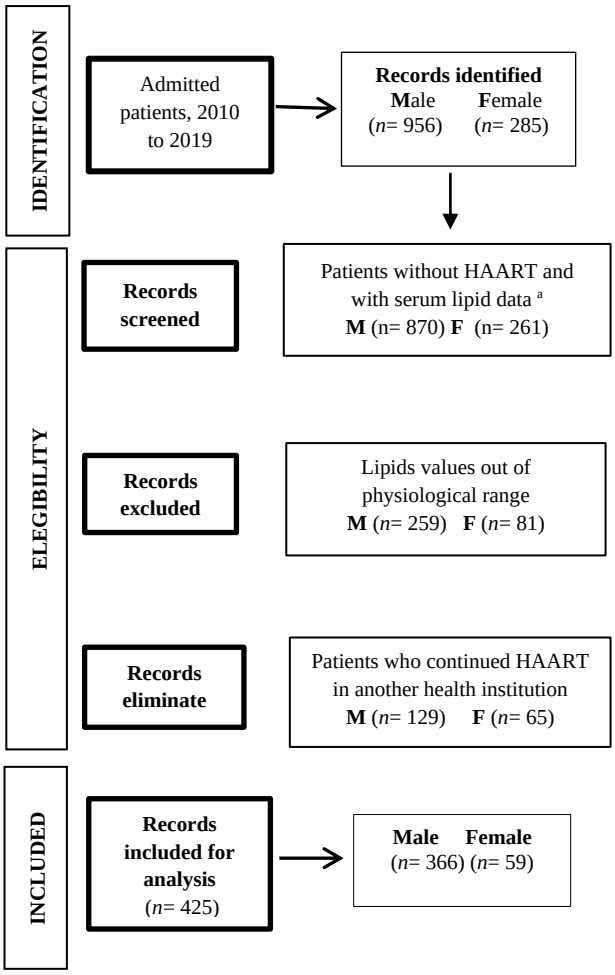

Figure 1. Selection and eligibility criteria diagram, including sample sizes in patients of the Ambulatory Center for the Prevention and Attention of AIDS and other sexually transmitted infections of the State of Hidalgo, Mexico. HAART: highly active antiretroviral therapy; n: Number of patients. [a]Fasting serum lipids: triglycerides, total cholesterol, high-density lipoprotein cholesterol, high-density lipoprotein cholesterol and low-density lipoprotein cholesterol. M=male and F= female.

For the purposes of this study the HAART drugs were stratified into groups according to the type of drugs patients were receiving in CAPASITS; scheme of HAART 1 (Efavirenz, Lamivudina/Abacavir): non-nucleoside reverse transcriptase

inhibitors (NNRTIs) with nucleoside reverse transcriptase inhibitors (NRTIs), scheme 2 (Dolutegravir, Abacavir/Lamivudina): integrase inhibitors (INSTIs) with NRTIs, and scheme 3 (Abacavir/Lamivudina, Atazavir/Ritonavir): NRTIs with protease inhibitors (PIs).

DATA ANALYSIS

The median, first quartile (25th percentile: Q1) and third quartile (75th percentile: Q3) were used to describe continuous data and percentages to describe categorical data. The Kolmogorov-Smirnov test was used to establish the normality of the data. The Wilcoxon signed-rank test was used to compare the value of the medians between groups for treatment times and the McNemar test for the related proportion. A value of $p < 0.05$ was considered statistically significant. Data analysis was performed using the IBM SPSS version 25 statistical package (IBM Corp; New York, USA).

ETHICAL ASPECTS

The present study was reviewed and approved by the ethics and research committee of the health services of the state of Hidalgo, Mexico, with registration number: FSSA2019088. In this study procedures conform to the Declaration of Helsinki. All reviews of the patients' clinical records were in accordance with the Mexican laws and regulations established in chapter I, articles 13 to 26 of the regulations of the general health law on health research, [8] and the precepts of the Declaration of Helsinki were followed.

RESULTS

Table 1 describes the general characteristics of HIV+ patients before and after 48 months of HAART initiation. Results are presented for 425 patients, of whom 366 (86%) were male. A viral load in all study subjects of 39 copies (38-40, Q1-Q3) was recorded at month 48 of treatment. In both sexes, median serum CD4 lymphocyte, TGC and TC concentrations increased after 48 months of starting HAART ($p<0.05$), but only in men increases in median c-HDL were observed ($p<0.05$, Table 1). After 48 months of HAART, there was an increase of ~2.7 points in median BMI ($p<0.05$) in men and women, with positive changes in underweight diagnoses (women) and negative changes in normal weight due to increases in the proportions of overweight in both sexes (Table 1).

The proportion of dyslipidaemias is presented in Table 2; at baseline assessment, low c-HDL concentrations was the most frequent dyslipidaemia (67.1%) followed by high TGC (36.9%) in the total subjects. In male patients, significant differences were found in the proportion of high TC and TGC levels from 6 months on HAART ($p<0.05$). At 48 months of treatment, an increase in the proportions of TC and TGC was recorded in both sexes, but the greatest magnitude of change was observed in men, Table 2. The proportion of low c-HDL figures was the only dyslipidaemia that decreased after 48 months with HAART, explained mainly by percentage changes in males.

The most frequent combination of antiretrovirals in patients was scheme 1, composed of NRTI and NRTI drugs (78.6%), followed by scheme 3, which had an NRTI drug plus a PI (19.1%), Table 3. There was a significant increase in dyslipidemias for TC and TGC, in patients with scheme 1, this was observed in the four measurements recorded (6, 24, 36 and 48 months with HAART, $p<0.05$); in contrast, low c-HDL levels at 6 and 24 months had a positive change ($p<0.05$). Percentage changes for TC, TGC and c-HDL were higher in patients prescribed scheme 2 (INSTI with NRTI); however, due to the number of subjects (n=10), these changes were not significant. For scheme 3, percentage changes were high at month 24 and 48 of starting HAART ($p<0.01$).

DISCUSSION

In Mexico, the prevalence of HIV infection is higher in men than in women, 81.2% of the cases correspond to men and 18.8% to women.[11] In our study, men represented 86.1% of the total number of participants, which is similar to that reported at national level. The disparity in the proportion between sexes has been explained by biological and sexual behavioral differences.[12]

The importance of early diagnosis of dyslipidemias in HIV-infected persons on HAART is evident, to reduce risks from the start of drug treatment. One of the main findings of this study was the high proportion of low c-HDL before all subjects started the treatment (67.1%), this proportion decreased 48 months after starting HAART (54.9%), suggesting that c-HDL returns in some cases to normal values as patients improve clinically; this same pattern of hyperlipoproteinemia (59.6%) was found in a study conducted in China, where dyslipidemias in HIV+ patients on HAART were evaluated.[13] The decrease in HDL in HIV+ patients has been related to an activation state of the immune response and chronic inflammation due to infection,[14] as well as inhibition of the ABCA1 transporter (ATP-binding cassette transporter protein A1) by the HIV Nef protein. [15]

In most studies, HIV infection has been associated with low concentrations of c-HDL TC, c-LDL and moderate hypertriglyceridemia with a positive correlation between the immunosuppression degree and these dyslipidemias.[16] Moreover, the prevalence of dyslipidaemias changes with prolonged use of HAART. In this study, hypertriglyceridemia was the second most frequent dyslipidaemia in patients (36.9%), prior to receiving treatment, which together with TC significantly increased 48 months after starting HAART, similar to what has been reported in other studies. [5,13]

Tumour necrosis factor-alpha (TNF-α) may be partly responsible for the alterations in plasma lipids, by interfering with the metabolism and oxidation of free fatty acids [17] and reducing lipolysis induced by insulin.[18] The low-grade inflammatory process continues in HIV+ patients on HAART, as the virus is in some cases undetectable, but has not been eliminated. High levels of TNF-α in HIV+ patients could cause tissue damage and have implications for the development of other diseases independent of the disease control using HAART.[19]

HIV+ patients on HAART are at increased risk of developing metabolic abnormalities including elevated TGC and c-LDL levels and reduced c-HDL.[20] A follow-up study by Zhou et al. of 57 HIV-positive Chinese patients who started HAART and had two NRTIs included in their regimen developed hypertriglyceridemia and hypercholesterolemia after 5 to 6 years of follow-up.[21]

In this study, the percentage increase in TGC and TC (15.8% and 15.3%, respectively) at 48 months with HAART consisting of NNRTIs and NRTIs occurred in both men and women. These data suggest that NRTI or NRTI drugs have negative effects on lipid concentrations in HIV+ patients, mainly in TGC and TC. In HIV+ patients, NRTI treatment regimens have been reported to produce increases in TGC and plasma cholesterol levels associated with mitochondrial toxicity.[22] In the case of NRTIs, the role of the pregnane X receptor, (PXR) in mediating adverse effects on lipid homeostasis, has been discussed.[23] However, the mechanisms by which HAART produces dyslipidaemias are not fully elucidated.

Table 1. *General characteristics of HIV patients before and after 48 months of HAART initiation, Hidalgo, Mexico*

	Men (n=366)		**Women (n=59)**		**Total (n=425)**	
	Median (Q1 and Q3)					
	Basal	**48 months**	**Basal**	**48 months**	**Basal**	**48 months**
Age	30 (25-37)	35 (29-41)	35 (28-40)	39 (32-44)	31 (26-37)	34 (28-41.7)
TGC (mg/dL)	126 (92.5-179)a	161 (108.5-221)b	140 (90-186)a	150 (107-234)b	128 (92-179)a	160 (108-222)b
CT (mg/dL)	135 (110-159)a	168 (146.5-195)b	153 (131-173)a	179 (156-204)b	137 (112-161)a	170 (149-196)b
c-HDL (mg/dL)	33 (26-41.7)a	38 (29.1-48.3)b	40.8 (26.5-59)a	40 (39.1-51)a	33.1 (26-42)a	38 (28.6-49)b
c-LDL (mg/dL)	78 (57.9-99.1)a	87 (52-111)b	89 (38.5-132)a	64.3 (60-106)a	78.8 (56.9-100)a	85 (42-110)a
SBP (mmHg)	110 (100-120)a	110 (100-120)a	100 (90-110)a	110 (100-110)a	110 (100-120)a	110 (100-120)a
DBP (mmHg)	70 (62.5-80)a	70 (70-80)a	70 (60-70)a	70 (60-70)a	70 (61.2-80)a	70 (60-80)a
Viral load (thousand)	115 (37.7-321)a	0.039 (0.038-0.040)b	84.2 (15.4-316)a	0.039 (0.03-0.039)b	110 (34.7-319)a	0.039 (0.038-0.040)b
CD4 (cells/mm^3)	146 (58-311)a	429 (302-628)b	124 (74-236)a	428 (311-678)b	146 (58-311)a	429 (302-628)b
BMI (kg/m2)	22.3 (19.8-24.5)a	25.0 (21.9-27.8)b	24.0 (22.1-26.8)a	26 (23.5-28.9)b	22.6 (19.9-24.9)a	25.3 (22.5-28.0)b
Weight (Kg)	60.7 (53.7-69.6)a	68 (59.7-77.0)b	56.6 (50-62.7)a	61.7 (54.8-67.5)b	60 (53.2-69)a	66 (58.4-76.0)b
Height (m)	1.66 (1.62-1.71)a	1.66 (1.62-1.71)a	1.52 (1.48-1.58)a	1.52 (1.48-1.58)a	1.65 (1.6-1.7)a	1.65 (1.6-1.7)a

Comparisons are between baseline and at 48 months of highly active antiretroviral therapy (HAART). TC, total cholesterol; c-HDL, high-density lipoprotein cholesterol; c-LDL, low-density lipoprotein cholesterol; TGC, triglycerides; SBP, systolic blood pressure; DBP, diastolic blood pressure. Different letters in the same row indicate p<0.05, between median at baseline and at 48 months, Wilcoxon test. BMI, body mass index; Q1 and Q3: first quartile and third quartile.

Table 2. Proportion of dyslipidemias and nutritional status in patients with HIV/AIDS under antiretroviral treatment, Hidalgo, Mexico.

	Number of months with HAART								
	Basal			6			48		
Dyslipidaemias									
	M	**F**	**T**	**M**	**F**	**T**	**M**	**F**	**T**
TC	6.3	11.9	7.1	16.5a	22 a	17.3a	20.3a	31b	22.4 a
c-HDL	68.6	42.9	67.1	49.8a	50	49.8a	54.2b	50 a	53.4 b
c-LDL	7.3	7.7	7.3	12.1b	14.3	12.3	8.3	8.6	8.4 b
TGC	35.8	44.1	36.9	47.8 a	55.2	48.8a	56.9a	50 b	52.7a
Nutritional status BMI									
Low weight	15.3	6.8	14.1	6.8 b	0 b	5.9 b	16.5	0 b	13.6
Normal weight	62.6	54.2	61.4	58.5 b	55.9	58.1 b	39.2 b	39.7 b	39.3 b
Overweight	18.9	27.1	20.0	28.4 b	33.9	29.2 b	34.4 b	43.1 b	36.0 b
Obesity	3.3	11.9	4.5	6.3 b	10.2	6.8 b	9.9 b	17.2	11.2

N=425 patients (366 men and 59 women). M: men, F: female and T: all. HAART: highly active antiretroviral therapy. TC: total cholesterol. c-HDL: high-density lipoprotein cholesterol, c-LDL: low-density lipoprotein cholesterol, TGC, triglycerides. *Letter a: p<0.01 and b: p<0.05 for McNemar's test relative to baseline measurement. Cut-off points for dyslipidemias: TC ≥200 mg/dL, c-HDL <40 mg/dL, c-LDL ≥130 mg/dL and TGC ≥150 mg/dL.*

Table 3. *Proportion of dyslipidaemias according to the type of antiretroviral scheme in patients with HIV/AIDS in Hidalgo, Mexico.*

	Number of months with HAART				
	Basal	6	24	36	48
	HAART 1 (n=334)				
CT	6.3	20.8 a	22.6a	22.6a	20.5a
c-HDL	67.7	47.3a	54.9a	42.6 b	50.0 b
c-LDL	6.8	12.7b	9.6	9.6	8.7
TGC	34.4	47.1a	44.7b	50.2a	54.8a
	HAART 2 (n=10)				
CT	10	37.5	25.0	100	100
c-HDL	66.7	80.0	75.0	50	100
c-LDL	0	40.0	0	0	0
TGC	50	75.0	75.0	100	100
	HAART 3 (n=81)				
CT	9.9	16.0	23.8b	21.8	26.6b
c-HDL	63.9	60.5	74.4b	51.0	62.0
c-LDL	8.6	5.7	4.7	15.6	7.6
TGC	47.5	53.1	60.0	59.0	57.0

HAART: highly active antiretroviral therapy; TC: total cholesterol; c-HDL: high-density lipoprotein cholesterol; c-LDL: low-density lipoprotein cholesterol; TGC: triglycerides. Different letters in the same row indicate p<0.05 according to McNemar test. Scheme 1: NNRTI with NRTI; scheme 2: INSTI with NRTI; and scheme 3: NRTI with PI. Cut-off points for dyslipidaemias: TC ≥200 mg/dL, c-HDL <40 mg/dL, c-LDL ≥130 mg/dL and TGC ≥150 mg/dL.

CONCLUSIONS

HIV infection was more frequent in males, who also had the highest underweight proportion before starting HAART. The most frequent dyslipidemia before starting HAART was low HDL-C levels, mainly in men. Antiretroviral treatment in HIV+ patients is associated with a significant increase in the BMI as of 6 months after initiating treatment. In both sexes, triglyceride and total cholesterol dyslipidemias increased significantly as of 6 months after starting HAART. The antiretroviral regimen that included NNRTI + NRTI was associated with the greatest percentage change in total cholesterol and triglycerides.

ACKNOWLEDGMENTS

To the Centro Ambulatorio de Prevención y Atención en SIDA e Infecciones de Transmisión Sexual del Estado de Hidalgo, México (CAPASITS).

FUNDING

This research has not received specific support from public, commercial, or private sector agencies.

CONFLICT OF INTERES

The authors have no conflicts of interest to declare.

REFERENCES

[1] Hammer SM, Squires KE, Hughes MD, Grimes JM, Demeter LM, Currier JS, et al. A controlled trial of two nucleoside analogues plus indinavir in persons with human immunodeficiency virus infection and CD4 cell counts of 200 per cubic millimeter or less. AIDS Clinical Trials Group 320 Study Team. N. Engl. J .Med. 1997;337(11):725-33. DOI: 10.1056/NEJM199709113371101.

[2] Ahmed D, Roy D, Cassol E. Examining relationships between metabolism and persistent inflammation in HIV patients on antiretroviral therapy. Mediators of inflammation. 2018;2018. DOI: 10.1155/2018/6238978.

[3] Estrada V, Portilla J. Dyslipidemia related to antiretroviral therapy. AIDS Rev. 2011;13(1):49-56. PMID: 21412389

[4] Chuapai Y, Kiertiburanakul S, Malathum K, Sungkanuparph S. Lipodystrophy and dyslipidaemia in human immunodeficiency virus-infected Thai patients receiving antiretroviral therapy. J. Med. Assoc. Thai. 2007;90(3):452-8. PMID: 17427520

[5] Mehta R, Loredo B, Sañudo M, Hernández Jiménez S, Rodríguez Carranza SI, Gómez Pérez FJ, et al. Epidemiología de las anormalidades metabólicas en pacientes con infección por VIH. Rev. Invest. Clin. 2004;56(2):209-21.

[6] Estrada V, Domingo P, Suarez-Lozano I, Gutiérrez F, Knobel H, Palacios R, et al. Risk of cardiovascular disease in HIV-infected patients on antiretroviral therapy. Rev. Clin. Esp. 2020;220(3):149-54. DOI: 10.1016/j.rce.2019.05.006.

[7] Group DS. Class of antiretroviral drugs and the risk of myocardial infarction. N. Engl. J .Med. 2007;356(17):1723-35. DOI:10.1056/NEJMoa062744.

[8] Health Protection. Reglamento de la ley general de salud en materia de investigación para la salud. 1987. DOF 02-04-2014.

[9] Lipsy RJ. The National Cholesterol Education Program Adult Treatment Panel III guidelines. JMCP. 2003;9(1 Suppl):2-5. DOI: 10.18553/jmcp.2003.9.s1.2

[10] World Health Organization. Obesity: preventing and managing the global epidemic: World Health Organization; 2000.

[11] CENSIDA. Personas por estado, activas en sistema con Tratamiento Antirretroviral 2023. Accessed 13/03/2023, available at: https://datos.gob.mx/busca/dataset/personas-por-estado-activas-en-sistema-con- tratamiento-antirretroviral-2023

[12] Beyrer C, Baral SD, Van Griensven F, Goodreau SM, Chariyalertsak S, Wirtz AL, et al. Global epidemiology of HIV infection in men who have sex with men. The Lancet. 2012;380(9839):367-77. DOI: 10.1016/S0140-6736(12)60821-6.

[13] Shen Y, Wang J, Wang Z, Qi T, Song W, Tang Y, et al. Prevalence of dyslipidaemia among antiretroviral-naive HIV-infected individuals in China. Medicine. 2015;94(48). DOI: 10.1097/MD.0000000000002201.

[14] Feingold KR, Grunfeld C. Effect of inflammation on HDL structure and function. Curr. Opin. Lipidol. 2016;27(5):521-30. DOI: 10.1097/MOL.0000000000000333.

[15] Mukhamedova N, Brichacek B, Darwish C, Popratiloff A, Sviridov D, Bukrinsky M. Analysis of ABCA1 and Cholesterol Efflux in HIV-Infected Cells. Methods. Mol. Biol. 2016;1354:281-92. DOI: 10.1007/978-1-4939-3046-3_19.

[16] Tadewos A, Addis Z, Ambachew H, Banerjee S. Prevalence of dyslipidaemia among HIV-infected patients using first-line highly active antiretroviral therapy in Southern Ethiopia: a cross-sectional comparative group study. AIDS Res. Ther.. 2012;9(1):31. DOI: 10.1186/1742-6405-9-31.

[17] Grunfeld C, Kotler DP, Shigenaga JK, Doerrler W, Tierney A, Wang J, et al. Circulating interferon-alpha levels and hypertriglyceridemia in the acquired immunodeficiency syndrome. Am. J. Med. 1991;90(2):154-62. PMID: 1996584.

[18] Haugaard SB AO, Pedersen SB, Dela F, et al. Tumor necrosis factor alpha is associated with insulin-mediated suppression of free fatty acids and net lipid oxidation in HIV-infected patients with lipodystrophy. Metabolism. 2006:175-82. DOI: 10.1016/j.metabol.2005.08.018

[19] De Pablo-Bernal RS, Ruiz-Mateos E, Rosado I, Dominguez-Molina B, Alvarez- Rios AI, Carrillo-Vico A, et al. TNF-alpha levels in HIV-infected patients after long- term suppressive cART persist as high as in elderly, HIV-uninfected subjects. J. Antimicrob. Chemother. 2014;69(11):3041-6. DOI: 10.1093/jac/dku263.

[20] Karthikeyan N. Prevalence of Dyslipidemia among HIV Infected Patients using First Line HAART in Coimbatore Medical College Hospital: Coimbatore Medical Collegel, Coimbatore; 2015.

[21] Zhou H-y, Zheng Y-h, He Y, Chen Z, Liu M, Yin W, et al. Evaluation of a 6- year highly active antiretroviral therapy in Chinese HIV-1-infected patients. Intervirology. 2010;53(4):240-6. DOI: 10.1159/000302762.

[22] García-Benayas T, Blanco F, Alcolea A, Cruz JJDL, González-Lahoz J, Soriano V. Benefits in the lipid profile after substitution of abacavir for stavudine: a 48-week prospective study. AIDS Res. Hum. Retrovir. 2004;20(12):1289-92. DOI: 10.1089/aid.2004.20.1289.

[23] Gwag T, Meng Z, Sui Y, Helsley RN, Park S-H, Wang S, et al. Non-nucleoside reverse transcriptase inhibitor efavirenz activates PXR to induce hypercholesterolemia and hepatic steatosis. J. Hepatol. 2019;70(5):930-40. DOI: 10.1016/j.jhep.2018.12.03