

PREVALENCE OF DYSLIPIDEMIAS IN ANTIRETROVIRAL THERAPY PATIENTS SERVED IN A SPECIALIZED CARE SERVICE IN CUIABÁ (MT)

PREVALÊNCIA DE DISLIPIDEMIAS EM PACIENTES EM TERAPIA ANTIRRETROVIRAL ATENDIDOS EM UM SERVIÇO DE ASSISTÊNCIA ESPECIALIZADA EM CUIABÁ (MT)

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ABSTRACT

Introduction: Although associated with improved quality of life for people with human immunodeficiency virus (HIV), the antiretroviral therapy (ART) has brought changes in cardiovascular manifestations. Antiretroviral therapy has been related with dyslipidemia, insulin resistance and diabetes mellitus, which constitute risk factors for cardiovascular disease. **Objective:** This study aimed at determining the prevalence of dyslipidemia in patients with HIV/acquired immunodeficiency syndrome (AIDS) treated at the specialized care center in Cuiabá (MT), according to the duration of treatment, the stage of the disease and the drug used for treatment. **Methods:** This is a retrospective study using data collected from medical records of adult patients of both sexes, positive for HIV/AIDS treated at the specialized care center in Cuiabá. To collect the data, we used an instrument consisting of demographic, personal, anthropometric and biochemical data. The biochemical tests analyzed the presence of abnormal total cholesterol (TC), total triglycerides (TG) and low-density lipoprotein (LDL). The stage of the disease was found in accordance with CD4. **Results:** A total of 124 patients were evaluated, of which 54.8% were male. The most prevalent age group (50.8%) was between 40 and 60 years old. Regarding education, 36.8% reported having incomplete higher education. In terms of marital status, 40.2% declared to be married. With respect to the time of exposure to antiretroviral therapy, there was a 44.2% prevalence of dyslipidemia in patients with 1.0 to 4.9 years of treatment. Concerning the stage of the disease, the prevalence of dyslipidemia was found in 53.4% of patients in the early stage ($CD4 \geq 500 \text{ cells}/\mu\text{L}$). However, there was progressive worsening of lipid profile with the advance of the disease. About the type of drug used, 29.3% of the patients in our study used the scheme "NNRTI + 2ITRN." **Conclusion:** The risk of dyslipidemia may increase with the time of treatment, the severity of the disease and the type of drug used in therapy.

Keywords: AIDS; antiretroviral agents; Dyslipidemias.

RESUMO

Introdução: Embora associada à melhoria da qualidade de vida dos portadores do vírus da imunodeficiência humana (HIV), a terapia antirretroviral (TARV) trouxe alterações nas manifestações cardiovasculares. A TARV tem sido relacionada à dislipidemia, à resistência à insulina e ao diabetes *mellitus*, que se constituem como fatores de risco para doença cardiovascular. **Objetivo:** Determinar a prevalência de dislipidemia em pacientes com HIV/síndrome de imunodeficiência adquirida (AIDS) atendidos no serviço de assistência especializada (SAE) de Cuiabá (MT), de acordo com o tempo de tratamento, o grau da doença e a droga utilizada no tratamento. **Métodos:** Trata-se de um estudo retrospectivo, por meio de dados coletados em prontuários de pacientes adultos, de ambos os sexos, portadores do HIV, acompanhados pelo SAE. Para coleta de dados informados, foi utilizado um instrumento composto de dados demográficos, pessoais, antropométricos e bioquímicos. Com base nos exames bioquímicos, foi analisada a presença de alterações de colesterol total (CT), triglicerídeos totais (TG) e lipoproteína de baixa densidade (LDL). O estágio da doença foi considerado conforme a contagem de células CD4. **Resultados:** Foram avaliados 124 indivíduos, sendo 54,8% do sexo masculino. A faixa etária mais prevalente (50,8%) esteve entre 40 e 60 anos. No tocante à escolaridade, 36,8% relataram ter ensino superior incompleto. Quanto ao estado civil, 40,2% declararam-se casados. Com relação ao tempo de exposição ao tratamento antirretroviral, observou-se 44,2% de prevalência de dislipidemia nos pacientes com 1,0 a 4,9 anos de tratamento. Quanto ao estágio da doença, foi verificada prevalência de 53,4% de dislipidemia nos pacientes no estágio inicial ($CD4 \geq 500 \text{ cells}/\mu\text{L}$), porém houve piora progressiva do perfil lipídico com o avançar da doença. Concernente ao tipo de droga utilizada, 29,3% dos pacientes de nosso estudo utilizam o esquema "ITRN + 2ITRN". **Conclusão:** O risco de dislipidemias pode aumentar com o tempo de tratamento, com a gravidade da doença e com o tipo de droga utilizada na terapia.

Palavras-chave: AIDS; antirretrovirais; dislipidemias.

INTRODUCTION

The Acquired Immunodeficiency Syndrome (AIDS) represents one of the major health issues in our days, due to its pandemic aspect and severity. The history of this infection has been changing since 1996, especially in Western countries, with the implementation of the antiretroviral therapy (ART), which led to reduced rates of morbidity and mortality⁽¹⁾.

In Latin America, Brazil is the country that is most affected by AIDS in absolute numbers. The estimation is that 1.8 million people are living with the human immunodeficiency virus (HIV) in this region, and one third of them are in Brazil⁽²⁾.

Data from the epidemiological journal AIDS/DST⁽³⁾ show that, considering the regions of the country, from 1980 and June 2008 19,155 cases were notified in the North region (4%); 58,348 in the Northeast region (12%); 305,725 in the Southeast region (60%); 95,552 in the South region (19%); and 28,719 in the Center-West region.

Since the onset of the epidemic, the age group that has been most affected, in both genders, has been 20 to 39 years old, and that systematically represents more than 60% of the AIDS cases, accounting for about 70% of the total number of cases notified until June, 2000⁽⁴⁾. According to Dourado et al.⁽²⁾, it is possible to observe more cases in the segments of society with lower schooling and worse socioeconomic status.

Brazil was one of the first developing countries to guarantee universal and free access to antiretroviral medication in the Unified Health System (SUS), after 1996⁽²⁾.

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Even though ART is associated with improved quality of life for people with HIV, it has caused changes in cardiovascular manifestations⁽⁵⁾, due to the increasing number of cases of coronary syndrome and peripheral vascular events related both to the increased survival rates of the patients and to the toxicity of the therapy^(6,7).

ART, and especially the class of protease inhibitors (PIs), has been associated with dyslipidemia, insulin resistance and diabetes mellitus, which constitute risk factors for cardiovascular conditions. According to some authors, the use of this class of drugs corresponds to 60% of the aforementioned metabolic changes⁽⁸⁾.

Scientific evidence shows that the main risk factors for the development of metabolic abnormalities in people with HIV are: the duration of the treatment, the more advanced stages of the disease, and especially the use of some drugs, such as PIs⁽⁹⁾.

Dyslipidemias are found in about 50 to 70% of the individuals undergoing PI therapy. Some studies have found serum triglyceride concentrations 7 to 15 times higher, and cholesterol concentrations 5 to 19 times higher than normal. Such an increase is associated with this drug⁽¹⁰⁾.

According to the IV Brazilian Guideline on Dyslipidemia and Prevention of Atherosclerosis⁽¹¹⁾, dyslipidemia is characterized by increasing levels of low-density lipoprotein (LDL) (isolated hypercholesterolemia), reduced high-density lipoprotein (HDL), increasing levels of triglycerides (TG) (isolated hypertriglyceridemia) and increased values of LDL and TG (mixed hyperlipidemia). Hyperlipidemia affects more than 60% of the patients using ART, turning the increased cardiovascular risk into a major complication in the treatment for HIV infection⁽¹²⁾.

Besides the adverse effects of antiretrovirals, especially with medications in the PI group, researchers believe that the chronic infection caused by HIV and other life habits that are common among people with HIV, such as smoking and sedentary lifestyle, contribute with the increased number of atherosclerotic diseases.

Considering the impact of the antiretroviral treatment on lipid profile, it is important to conduct a study to assess the presence of dyslipidemia induced by the use of this medication, in order to provide better clinical management of the patients with HIV.

OBJECTIVE

General Objective

To determine the prevalence of dyslipidemia in patients with AIDS assisted at the specialized care service (SAE) of Cuiabá (MT).

Specific objectives

- To characterize the patients according to sociodemographic variables;
- To determine the prevalence of dyslipidemia according to duration of treatment;
- To determine the prevalence of dyslipidemia according to the stage of the disease;
- To determine the prevalence of dyslipidemia according to the drug used in treatment.

METHODS

This is a retrospective study including data collected from medical records of adult patients, of both genders, with HIV, followed-up at a SAE in the city of Cuiabá from January 2011 to August 2012.

The study included patients aged more than 18 years old, of both genders, undergoing ART and whose lipid profile was followed-up in the 12 months prior to the appointment.

For the collection of the informed data, an instrument composed of demographic, personal, anthropometric and biochemical data was used.

Based on biochemical tests, there were changes in total cholesterol (TC), total triglycerides (TT) and LDL, as well as a relationship with sociodemographic variables, stage of the disease, duration of treatment and type of medication.

The analysis of blood lipids used the reference values for the diagnosis of dyslipidemias in adults aged more than 20 years old, according to the National Cholesterol Education Program (NCEP) Adult Treatment Panel (2001) (**Chart 1**).

The stage of the disease was considered according to the CD4 count, using the values established by the Center for Disease Control and Prevention (CDC)⁽¹³⁾ (**Chart 2**).

Chart 1 – Reference values for the diagnosis of dyslipidemia among adults older than 20 years old.

Lipids	Values	Category
TC (mg/dL)	<200	Good
	200–239	Borderline
	≥240	High
LDL-C (mg/dL)	<100	Good
	100–129	Desirable
	130–159	Borderline
	160–189	High
TG (mg/dL)	≥190	Very high
	<150	Good
	150–200	Borderline
TG (mg/dL)	201–499	High
	≥500	Very high

Source: III Brazilian Guideline on Dyslipidemia and Prevention of Atherosclerosis at the Department of Atherosclerosis of the Brazilian Society of Cardiology, 2001.

TC: total cholesterol; LDL-C: low-density lipoprotein; TG: total triglycerides.

Chart 2 – Classification of adults infected by the human immunodeficiency virus.

CD4 count	Stage of the disease
≥500 cells/ μ L	Early
200–499 cells/ μ L	Intermediate
<200 cells/ μ L	Final

Source: Centers for Disease Control and Prevention, 1992.

CD4: clusters of differentiation 4.

Statistical analysis was conducted with the software Epi Info, version 3.6. Prevalence rates were compared using the qui-square test, considering a 95% confidence interval.

The study was in accordance with the rules established by the National Health Council (CNS) resolution. 196/96. The Ethics Research Committee of the University Hospital Júlio Müller approved it, report n. 08197212.7.0000.5541. The patients presenting changes in lipid profile were assisted at the Nutrition Service of SAE in the follow-up period.

With the study results, the expectation was to characterize the profile of patients assisted at the service, leading to the creation of a set of actions that would generate an improved health status of the participants.

RESULTS AND DISCUSSION

This study evaluated 124 individuals, being 56 (45.2%) female and 68 (54.8%) male participants. This is in agreement with the average in Brazil, whose ratio is 1.7 new case affecting men for one case affecting women⁽¹⁴⁾.

The most prevalent age group (50.8%) was 50 to 60 years old. The mean age of the patients involved in this study represents the cases of AIDS notified in Brazil, as demonstrated by the Epidemiological Journal AIDS – DST in 2011. It shows that the highest proportion (24.8%) of AIDS cases notified at the Notifiable Diseases Information System (Sinan), declared in the Mortality Information System (SIM) and registered at the Medication Logistics Control System and the Viral Load Laboratory Tests Control System (Siscel/Siclom) in 2010 was present in the age group of 40 to 49 years old, with increasing incidence rates in the age groups of 50 to 59 years old and older than 60 between 1998 and 2010⁽¹⁴⁾.

In 2010, regarding the Center-West region, 31.0% of the total number of people notified in Sinan had incomplete elementary school (between the 5th and 8th grades); 19.1% had incomplete or complete high school, and only 8.6% had complete or incomplete higher education (5.5% - complete). In 28.4% of the cases, this data was ignored⁽¹⁴⁾. Even though the percentage of patients who had incomplete elementary school was similar, those who got to higher education was higher.

As to origin, we observed that the highest percentage of patients comes from other states. This fact can be explained because we analyzed a reference service, or because our city is inhabited by people coming from other locations. The sociodemographic characterization of the patients is presented in **Chart 3**.

High prevalence of hypercholesterolemia (34.4%) and hypertriglyceridemia (69.7%) was found in the patients of this analysis. These data are in accordance with those mentioned in the IV Brazilian Guideline on Dyslipidemia and Prevention of Atherosclerosis⁽¹⁵⁾, which show that lipid abnormalities become more evident among people with HIV after the introduction of ART, and that hypercholesterolemia and hypertriglyceridemia are the most remarkable disorders.

Farhi et al.⁽¹⁶⁾, in an investigation conducted with the objective of establishing the prevalence of dyslipidemia among adults of both genders with HIV, found a 44.7% prevalence of high blood TG. Hypercholesterolemia, which, in our study, was observed in 34.9% of the patients, is in accordance with the analysis by Leite & Sampaio⁽¹⁷⁾, which found a 35.0% prevalence of this change in patients undergoing ART assisted at a SAE unit in the city of Rio de Janeiro.

Regarding the time of exposure to an antiretroviral treatment, the prevalence of dyslipidemia was higher among patients who had been undergoing treatment for 1.0 to 4.9 years (44.2% of the cases); 45.5% had "very high" triglycerides, 41.7% had "high" cholesterol, and 80.0% had "very high" LDL, as shown in **Table 1**. Similar results were found by Falcão et al.⁽¹⁸⁾ in a cross-sectional study conducted in Pernambuco about cardiovascular disease and metabolic disorders in individuals with HIV. Of the 122 patients included in the study, 99 (81.1%) underwent ART with median and 3.3 years of therapy.

Farhi et al.⁽¹⁶⁾ showed that the mean time of ART use was longer among patients with changes in blood lipids (66.4 months *versus* 53.0 months), and this variable was positively associated with dyslipidemia.

As to the stage of the disease, there was a reduced number of patients with normal lipids when the condition got worse; however, the prevalence of "high" or "very high" blood lipids was higher among patients at the early stage, showing the onset of dyslipidemia even when patients still have a low viral load. Possibly, with

Chart 3 – Sociodemographic characterization of patients assisted at the specialized care center of Cuiabá, Mato Grosso.

Variable	n	%
Sex		
Female	56	45.2
Male	68	54.8
Total	124	100.0
Age Group		
Up to 40	53	42.7
From 40 to 60	63	50.8
More than 60	08	6.5
Total	124	100.0
Schooling		
Incomplete elementary	37	31.6
Incomplete high school	26	22.2
Incomplete higher educat.	43	36.8
Complete higher educat.	11	9.4
Total	117	100.0
Marital Status		
Single	41	36.6
Married	45	40.2
Divorced	16	14.3
Widow(er)	10	8.9
Total	112	100.0
Origin		
Cuiabá–Várzea Grande	40	33.1
Countryside of Mato Grosso	39	32.2
Other states	42	34.7
Total	121	100.0

the evolution of the disease, other factors may interfere in blood biochemistry (**Table 2**). However, when considering the initial and final means of TG and TC (**Table 3**), there is a statistically significant difference between results. This change shows that both the duration of treatment and the stage of the disease can lead to worse lipid profile.

A cross-sectional study conducted by Godoi et al.⁽¹⁹⁾, aiming at identifying the prevalence of atherosclerosis among individuals with HIV undergoing ART, showed that 84% of the patients evaluated had mean viral load of 670.6 (early stage). That is, when these patients present dyslipidemia (35.7% with hypercholesterolemia and 45.7% with hypertriglyceridemia) they are mostly clinically stable.

Table 1 – Prevalence of changes in blood lipids in relation to duration of treatment.

Blood Lipid	Duration Of Treatment						P value	
	From 1.0 to 4.9 years		From 5.0 to 9.9 years		From 10.0 to 20.0 years			
	n	%	n	%	n	%		
TG								
Good	07	50.0	05	35.7	02	14.3		
Borderline	04	50.0	02	25.0	02	25.0	0.853	
High	33	41.8	20	25.3	26	32.9		
Very high	05	45.5	02	18.2	04	36.4		
TC								
Good	14	36.8	10	26.3	14	36.8	0.430	
Borderline	19	51.4	11	29.7	07	18.9		
High	15	41.7	08	22.2	13	36.1		
LDL								
Good	12	48.0	05	20.0	08	32.0		
Desirable	09	50.0	04	22.2	05	27.8	0.526	
Borderline	10	47.6	06	28.6	05	23.8		
High	04	25.0	07	43.8	05	31.3		
Very high	04	80.0	0	0.0	01	20.0		

TG: total triglycerides; TC: total cholesterol; LDL: low-density lipoprotein.

Table 2 – Change in blood lipids of the patients analyzed according to the stage of the disease.

Blood Lipid	Stage of Disease						P value	
	Early		Intermediate		Final			
	n	%	n	%	n	%		
TG								
Good	09	60.0	06	40.0	0	0.0		
Borderline	05	62.5	03	37.5	0	0.0	0.518	
High	41	51.9	28	35.4	10	12.7		
Very high	07	53.8	06	46.2	0	0.0		
TC								
Good	18	47.4	14	36.8	06	15.8	0.350	
Borderline	21	55.3	14	36.8	03	7.9		
High	23	59.0	15	38.5	01	2.6		
LDL								
Good	11	45.8	09	37.5	04	16.7		
Desirable	10	50.0	07	35.0	03	15.0	0.655	
Borderline	14	63.6	08	36.4	0	0.0		
High	09	56.3	06	37.5	01	6.3		
Very high	04	66.7	02	33.3	0	0.0		

TG: total triglycerides; TC: total cholesterol; LDL: low-density lipoprotein.

Both the infection with HIV and ART may cause or aggravate dyslipidemia. The acknowledged hypertriglyceridemia associated with the progression of the retroviral infection probably constitutes the reflection of a chronic inflammatory state or a consequence of emaciation⁽¹²⁾. According to Safrin & Grunfeld *apud* Seidl & Machado⁽²⁰⁾, the lipodystrophy syndrome (dyslipidemia, abnormal fat redistribution, changes in glycemic metabolism and insulin resistance) in seropositive people for HIV is a progressive condition, whose severity seems to be directly proportional to time of treatment with antiretroviral medication.

Advanced age and low T CD4+ cell count, associated with the beginning of ART, seem to be related to its development. Metabolic dysfunction can also depend on age and on the genetic context of the individual, as well as on other environmental factors or concomitant medication⁽¹²⁾.

The benefit of a highly active antiretroviral therapy has been clearly demonstrated in patients with advanced symptomatic disease and in those who, despite being asymptomatic, presented severe immunodeficiency expressed in the T-CD4+ lymphocyte count, below 200/mm³. Nowadays, in our country, there are four classes of antiretrovirals; they are more powerful, less toxic and with comfortable posology, so it is possible to take only one or two daily doses⁽²¹⁾.

This treatment, whose history began with the use of monotherapy with zivovudine (AZT), from 1994 to 1996, is now consolidated by the double therapy as a therapeutic pattern, and, after 1996, by the triple therapy, introducing the PIs⁽²²⁾.

Antiretroviral drugs work by blocking the action of enzymes, which are important for the replication and function of the HIV. The drugs should be used in standardized combinations. Monotherapy is not recommended, due to the unavoidable resistance to medication⁽²³⁾. The action of each class of medication is exposed in **Chart 4**.

The initial therapy should always include three combined drugs: two nucleoside analog reverse transcriptase inhibitors (NtRTIs) associated with one non-nucleoside analog reverse transcriptase inhibitor (NNRTI) or with ritonavir-boosted PI (PI/r)⁽²⁰⁾. This practice has been used in SAE, where 29.3% of the patients in our study use the scheme "NNRTI + 2NtRTI", and 22.8% use the scheme "NtRTI + PI", as shown in **Chart 5**.

According to Godoi et al.⁽¹⁹⁾, among the antiretrovirals, PIs are more frequently associated with dyslipidemia and insulin resistance, even though medications from other classes, such as NtRTI and NNRTI, are present in metabolic disorders and in acute coronary events.

A major prospective and multinational study conducted with 17,852 patients registered the presence of hypercholesterolemia in 27% of the patients using PI, and 23% of those using NtRTI⁽²⁴⁾. These findings corroborate the data in our study, in which the highest prevalence of dyslipidemia was found in patients using the scheme NNRTI + 2NtRTI.

Even if less frequently than observed with PIs, NNRTI and NtRTIs also produce hypertriglyceridemia and increase the levels of TC and LDL cholesterol fraction⁽¹²⁾.

The mechanism in charge of inducing dyslipidemia among people with HIV is not completely clear yet. It is not clear if dyslipidemia occurs due to a direct effect of ART or if it is a result of the interaction between several factors, such as antiretroviral treatment, genetic predisposition, environmental factors like diet and physical

Table 3 – Evolution of the mean value of blood lipids during treatment.

Blood lipids	n	Early	Final	P value
TG	114	209.7±122.2	297.6±170.2	0.0019
TC	111	196.2±50.6	219.3±42.9	0.0034
LDL	76	114.7±40.6	129.2±52.3	0.0630

TG: total triglycerides; TC: total cholesterol; LDL: low-density lipoprotein.

Chart 4 – Class of antiretroviral medication and its respective actions.

Class of medication	Action
Protease inhibitors	Act on protease, blocking its action and preventing the production of new copies of cells infected with HIV.
Nucleoside analog reverse transcriptase inhibitors	Act on reverse transcriptase, incorporating it to the DNA chain created by the virus. They make this chain defective, preventing the reproduction of the virus.
Non-nucleoside analog reverse transcriptase inhibitors	They block the action of the enzyme directly, as well as the multiplication of the virus.

Source: Brazil, 2013.

HIV: human immunodeficiency virus.

Chart 5 – Antiretroviral schemes used by patients assisted at the specialized care service, Cuiabá, Mato Grosso.

ART	Classification	%
EFZ, ABV	NNRTI + 2NtRTI	29.3
LPV/r, ABV	NtRTI + PI	22.8
ATV, RTV, ABV	PI + 2NtRTI	13.8
Others		34.1

ART: antiretroviral therapy; EFZ: Efavirenz; ABV: Abacavir; LPV/r: Lopinavir; ATV: Atazanavir; RTV: Ritonavir; NNRTI: non-nucleoside analog reverse transcriptase inhibitor; 2NtRTI: nucleoside analog reverse transcriptase inhibitors; NtRTI: nucleoside analog reverse transcriptase inhibitors; PI: protease inhibitor.

activity, or other factors — possibly the response of the host to the HIV infection⁽²⁵⁾. However, regardless of the causing mechanism, the presence of dyslipidemia always requires the attention of health professionals, especially the nutritionist, who is essential to prevent and control blood lipids using an adequate diet therapy.

CONCLUSION

The use of antiretroviral therapy, which radically changed the treatment of patients infected with HIV, is associated with metabolic changes, such as dyslipidemia and insulin resistance, which constitute risk factors for the development of cardiovascular disease. The mechanism leading to dyslipidemia is not completely clear yet, so further ongoing studies are necessary.

Our investigation concluded that the risk of dyslipidemia increases with the duration of treatment, the severity of the disease and the type of drug used in therapy.

In order for the therapy not to cause any risk to the patient, changes in lifestyle, a balanced diet and physical activities should be implemented. The last resort for treatment would be pharmacological interventions.

It is also essential to raise awareness of the medical community for the increasing incidence of heart disease among patients with HIV undergoing antiretroviral therapy or not, once this incidence tends to grow because of the increasing life expectancy of infected patients.

Conflict of interest

The authors declare there is no conflict of interests in this paper.

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