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# Lipid profile and risk factors for cardiovascular diseases in older people seen in primary health care

Perfil lipídico e fatores de risco para doenças cardiovasculares em idosos acompanhados na atenção primária à saúde

Perfil lipídico y factores de riesgo de enfermedades cardiovasculares en ancianos seguidos en la atención primaria de salud

Guilherme Kunkel da Costa<sup>1</sup> <sup>(D)</sup>, Ivana Loraine Lindemann<sup>1</sup> <sup>(D)</sup>, Gustavo Olszanski Acrani<sup>1</sup> <sup>(D)</sup>, Giovana Bonessoni Felizari<sup>1</sup> <sup>(D)</sup>, Aniela Caroline Zientarski Garzella<sup>1</sup> <sup>(D)</sup>, Amauri Braga Simonetti<sup>1</sup> <sup>(D)</sup>

<sup>1</sup>Universidade Federal da Fronteira Sul – Passo Fundo (RS), Brazil.

#### Abstract

Introduction: Dyslipidemias are among the most important risk factors for the development of cardiovascular diseases (CVD), in addition to being related to other pathologies that predispose to CVD. Because of the high prevalence and incidence of complications associated with the chronicity of the disease, dyslipidemias represent high costs for the health and social security sector. This highlights the importance of the Unified Health System, represented by primary health care (PHC), in providing prevention, diagnosis and follow-up practices for dyslipidemic patients to relieve the financial system and promote healthy aging. Objective: The study aimed to describe the prevalence of altered lipid profile among older people. In addition, we sought to characterize the sample in terms of sociodemographic, health and behavioral aspects, as well as to analyze the factors associated with the distribution of the altered lipid profile and the characteristics of the sample. Methods: We conducted a cross-sectional study with secondary data, from August 2021 to July 2022, with older patients being followed up at the PHC in the city of Marau (RS) as the study population. All data were collected from the electronic medical records of the PHC network, and after double-typing and validation, the sample was characterized using descriptive statistics. The prevalence of altered lipid profile was determined with a 95% confidence interval (95%CI), and its distribution was verified according to the exposure variables, using the chi-square test and a type I error of 5%. Results: The prevalence of proportional dyslipidemia between sexes was higher in females (33%). The predominant skin color was white (76.7%). About 20% of the patients had altered total cholesterol, HDL-C and triglycerides, while about 15% had abnormal HDL-C. It was found that more dyslipidemic patients had diabetes and hypertension than non-dyslipidemic patients, with a synergy of risk factors for CVD. Conclusions: The characterization carried out in this study serves as a scientific basis for understanding the local reality and also for directing public policies in PHC that act effectively in the prevention and control of dyslipidemia and other cardiovascular risk factors.

Keywords: Dyslipidemias; Cardiovascular risk factors; Primary health care.

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Corresponding author:

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#### Resumo

Introdução: As dislipidemias estão entre os fatores de riscos mais importantes para o desenvolvimento de doenças cardiovasculares (DCV). além de estarem relacionadas a outras patologias que predispõem às DCV. Em função da elevada prevalência e da incidência de complicações associadas à cronicidade da doença, as dislipidemias representam elevados custos ao setor da saúde e da previdência social. Diante disso, ressalta-se a importância do Sistema Único de Saúde, representado pela Atenção Primária à Saúde (APS), em prover práticas de prevenção, diagnóstico e acompanhamento dos pacientes dislipidêmicos, a fim de desonerar o sistema financeiro e promover o envelhecimento saudável. Objetivo: Descrever a prevalência de perfil lipídico alterado entre os idosos. Além disso, pretendeu-se caracterizar a amostra quanto aos aspectos sociodemográficos, de saúde e de comportamento, bem como analisar os fatores associados à distribuição do perfil lipídico alterado e às características da amostra. Métodos: Estudo transversal com dados secundários, obtidos de agosto de 2021 a julho de 2022, tendo como população pacientes idosos em acompanhamento na APS do município de Marau (RS). Todos os dados foram coletados dos prontuários eletrônicos da rede de APS e, após dupla digitação e validação dos dados, a amostra foi caracterizada por meio de estatística descritiva. Foi calculada a prevalência de perfil lipídico alterado com intervalo de confiança de 95% (IC95%) e foi verificada sua distribuição conforme as variáveis de exposição, empregando-se o teste do  $\chi^2$  e admitindo-se erro tipo I de 5%. Resultados: A prevalência de dislipidemia proporcional entre os sexos foi maior no feminino (33%). A cor de pele predominante foi a branca (76,7%). Cerca de 20% dos pacientes apresentavam colesterol total, colesterol HDL-c e triglicerídeos alterados, enquanto cerca de 15% apresentavam o colesterol HDL-c anormal. Constatou-se que os pacientes dislipidêmicos apresentam mais diabetes e hipertensão em relação aos não dislipidêmicos, ocorrendo a sinergia de fatores de risco para as DCV. Conclusões: A caracterização exercida neste estudo serve de base científica para a compreensão da realidade local e, também, para o direcionamento de políticas públicas na atenção primária que atuem de forma efetiva na prevenção e no controle das dislipidemias e demais fatores de risco cardiovascular.

Palavras-chave: Dislipidemias; Fatores de risco para doenças cardiovasculares; Atenção primária à saúde.

#### Resumen

Introducción: las dislipidemias se encuentran entre los factores de riesgo más importantes para el desarrollo de enfermedades cardiovasculares (ECV), además de estar relacionadas con otras patologías que predisponen a ECV. Debido a la alta prevalencia e incidencia de complicaciones asociadas a la cronicidad de la enfermedad, las dislipidemias representan altos costos para los sectores de salud y seguridad social. Frente a eso, se destaca la importancia del Sistema Único de Salud, representado por la Atención Primaria de Salud (APS), en la provisión de prácticas de prevención, diagnóstico y seguimiento de pacientes dislipidémicos, con el fin de descongestionar el sistema financiero y promover el envejecimiento saludable. Objetivo: El estudio tiene como objetivo describir la prevalencia del perfil lipídico alterado entre los ancianos. Además, se pretende caracterizar la muestra en cuanto a aspectos sociodemográficos, de salud y conductuales, así como analizar los factores asociados a la distribución del perfil lipídico alterado y las características de la muestra. Métodos: estudio transversal con datos secundarios, de agosto de 2021 a julio de 2022, con pacientes ancianos en seguimiento en la APS del municipio de Marau (RS) como población. Todos los datos fueron recolectados de la historia clínica electrónica de la red de la APS y, luego de doble digitación y validación, la muestra fue caracterizada mediante estadística descriptiva. Se calculó la prevalencia de perfil lipídico alterado con un intervalo de confianza del 95% (IC95%) y se verificó su distribución según las variables de exposición, utilizando la prueba de chi-cuadrado y admitiendo un error tipo I del 5%. Resultados: la prevalencia de dislipidemia proporcional entre sexos fue mayor en el sexo femenino (33%). El color de piel predominante fue el blanco (76,7%). Alrededor del 20% de los pacientes tenían colesterol total, colesterol HDL-C y triglicéridos alterados, mientras que alrededor del 15% tenían colesterol HDL-C anormal. Se encontró que los pacientes dislipidémicos tienen más diabetes e hipertensión que los pacientes no dislipidémicos, con una sinergia de factores de riesgo para ECV. Conclusiones: la caracterización realizada en este estudio sirve de base científica para comprender la realidad local y también para orientar políticas públicas en atención primaria que actúen de manera efectiva en la prevención y control de la dislipidemia y otros factores de riesgo cardiovascular.

Palabras clave: Dislipidemias; Factores de riesgo de enfermedad cardiovascular; Atención primaria de salud.

#### INTRODUCTION

Dyslipidemias are characterized by an imbalance in lipid metabolism, which may result from increased production or decreased degradation of atherogenic lipoproteins, as well as decreased synthesis or increased degradation of protective lipoproteins.<sup>1</sup> These disorders are highly prevalent nationally and internationally and are directly related to the development of cardiovascular disease (CVD).<sup>1,2</sup>

Among the main risk factors associated with dyslipidemia are advanced age (over 65 years old), family history of dyslipidemia, diet, smoking, alcohol consumption, lack of physical activity, sex, race and genetic components.<sup>3,4</sup>

Regarding the prognosis of the disease, it was found that diagnosed and treated patients, with stabilization of the dyslipidemic condition, showed a reduction in morbidity and mortality rates due to CVD and, therefore, should be the focus of public policies.<sup>1,5</sup> On the other hand, it is known that, in untreated patients, dyslipidemia increases the risk of developing CVD, which is among the main causes of morbidity and mortality in the population.<sup>2,6</sup>

Given the high prevalence and incidence of complications associated with the chronicity of the disease, dyslipidemia represents high costs for the health and social security sector,<sup>6,7</sup> requiring primary, secondary and tertiary prevention measures in the context of public health. Thus, in Brazil, under the guidance of the Ministry of Health, the highest management body of the Unified Health System (SUS), early diagnosis of dyslipidemia, pharmacological and non-pharmacological treatment, and also continuous follow-up and monitoring of patients, are the responsibility of primary health care (PHC) professionals, especially those linked to the Family Health Strategy (ESF) teams. Therefore, for these programs to be effective, strict collaboration between public health professionals is necessary.<sup>7</sup>

In the municipality of Marau (RS), PHC through ESF teams covers 100% of the population. Therefore, it is important to know the aspects related to the prevalence of dyslipidemia and its implications for patients treated in the health network, aiming to provide indicators for the evaluation and adequacy of measures with the aim of qualifying care and positively impacting health levels of the population.

# METHODS

We conducted an observational, cross-sectional, descriptive and analytical study, with a quantitative approach to secondary data. The study was carried out from August 2021 to July 2022, with the population being older patients seen in PHC in Marau. The probabilistic sample was made up of patients treated in 2019, in 12 health units. Individuals of both sexes and aged 60 years or over were included. Participants who did not have electronic medical records available were excluded from the study. The list of patients treated from January 1 to December 31, 2019 was obtained from the Municipal Health Department (SMS), and the final sample was then composed.

Data collection was carried out through access, using a specific login and password provided by SMS, to the electronic medical records available in the integrated medical records system of the city's ESF, G-MUS – Municipal Health Management, transcribing them into a form prepared for this purpose. Participants were identified by sequential numbers according to the collection order and no identification data was collected. Data were obtained on sociodemographic characteristics (sex, skin color/race, education and labor market status), health (service unit, body mass index, blood pressure levels, morbidities, laboratory tests, medications in use, etc.) and behavior (practice of physical activity, use of tobacco, alcohol and other drugs).

The data were double-entered and validated in the EpiData software version 3.1 (free distribution). Statistical analyzes were carried out using the PSPP software (free distribution) and included the absolute and relative frequencies of categorical variables in order to characterize the sample. Furthermore, the prevalence of dyslipidemia was calculated, with a 95% confidence interval (95%CI), and its distribution was verified according to the exposure variables (independent), as well as the relationship between dyslipidemia and CVD, using the  $\chi^2$  test and assuming a type I error of 5%.

Furthermore, it is emphasized that, for the classification of cholesterol and triglyceride levels, the update of the Brazilian guideline on dyslipidemia and prevention of atherosclerosis was used as a reference.<sup>4</sup> The following serum cholesterol levels were considered altered: total cholesterol  $\geq$ 190 mg/dL; low-density lipoprotein cholesterol (LDL-C)  $\geq$ 160 mg/dL; high-density lipoprotein (HDL-C) <40 mg/dL ( $\geq$ 60 mg/dL were values considered normal and values between 40 and 59 mg/dL regular) and triglycerides  $\geq$ 200 mg/dL (low/borderline if <200 mg/dL and very high if  $\geq$ 500 mg/dL).

To classify individuals according to body mass index (BMI), the Lipschitz criteria were used.<sup>8</sup> In this classification, older people with a BMI  $\leq$ 22 were considered underweight, values >22 and <27 were considered normal weight and values  $\geq$ 27 were considered overweight.

Finally, the reference values of the 7th Brazilian guideline on arterial hypertension were adopted for the classification of blood pressure levels.<sup>9</sup> In this sense, older people with systolic and diastolic blood pressure  $\geq$ 140 and  $\geq$ 90 mmHg, respectively, were categorized as hypertensive.

This study was conducted in accordance with Resolution 466/2012 of the National Health Council (CNS), which provides for ethics in research involving human beings in Brazil. After acknowledgment and agreement from the Municipal Health Department of Marau, the study protocol was submitted to the UFFS Human Research Ethics Committee, following the determinations of relevant laws.

#### RESULTS

During the study period, a total of 1,728 patients were seen at the PHC in Marau, of which 1,038 (60.1%) were female and 690 (39.9%) were male. Of these, 551 (31.9%) individuals were diagnosed with dyslipidemia and selected for further analysis.

Of the dyslipidemic patients, 100% were Brazilian, with 453 (82.2%) born in Marau. Among them, 208 (37.7%) patients were male and 343 (62.3%) were female. However, when comparing male and female dyslipidemia patients to the total number of patients treated, proportionally to sex, it was seen that 30.1% of male patients had some type of dyslipidemia, while 33% in females.

The predominant skin color among dyslipidemic patients was white (76.7%), followed by brown (20.6%) and yellow (0.5%); no information was obtained regarding the skin color of 2.2% of the participants. More than half of the sample had incomplete primary education, and only 5.7% had completed secondary and/or higher education. Around 11% of individuals were active in the job market; 69.7% were retirees/pensioners, while 18.7% of participants did not have information about their work situation (Table 1).

Regarding lifestyle habits, only 3.1% of dyslipidemic participants stated that they practiced physical activity, 6.2% were smokers and 5.1% drank alcohol. There were no participants who used illicit drugs.

Regarding laboratory tests carried out in 2019, 300 patients had a total cholesterol test during this period, 21.7% of them showing values above normal. 318 patients underwent HDL-C testing, 21.7% showing values <40 mg/dL. LDL-C was tested in 294 participants, finding 14.6% of patients with abnormal values. Regarding triglycerides, of the 305 patients, 24.5% had values above normal limits (Table 2).

It was found that 434 (78.7%) of dyslipidemic patients had hypertension (HT) and 231 (41.9%) type 2 diabetes mellitus (DM2). Furthermore, it was noted that 109 (19.7%) patients had some type of heart disease; 25 (4.5%) had already had an episode of acute myocardial infarction (AMI); 26 (4.7%) had a stroke; and 29 (5.2%) had kidney problems (Table 3).

	n	%
Nationality		
Brazilian	551	100
Place of birth		
Marau	453	82.2
Other	98	17.8
Sex		
Male	208	37.7
Female	343	62.3
Skin color		
While	423	76.7
Other	128	23.3
Education		
Primary, incomplete	318	59.6
Primary, complete	30	5.4
Secondary, complete	31	5.6
Higher education	11	0.1
Not informed	161	29.3
Situation in the job market		
Employed	56	10.1
Unemployed	8	1.5
Retired, pensioner or not active	384	69.7
Not informed	103	18.7

 Table 1. Socioepidemiological factors related to older, dyslipidemic patients seen by primary health care in the city of Marau,

 Rio Grande do Sul, in 2019 (n=551).

Source: Municipal Health Department of Marau (RS).

**Table 2.** Lipid profile of older people seen by primary health care, with records in 2019, in the city of Marau, Rio Grande do Sul (n=551).

	n	%
Total cholesterol (n=300)		
Low/borderline (<190 mg/dL)	235	78.3
High (≥190 mg/dL)	65	21.7
HDL-C (n=318)		
Low (<40 mg/dL)	69	21.7
Average (40–59 mg/dL)	168	52.8
High (≥60 mg/dL)	81	25.5
LDL-C (n=294)		
Low/borderline (<160 mg/dL)	251	85.4
High (≥160 mg/dL)	43	14.6
TG (n=306)		
Low	231	75.5
High (≥200 mg/dL)	68	22.2
Very high (≥500 mg/dL)	7	2.3

Source: Municipal Health Department of Marau (RS).

Regarding risk factors for the development of CVD, statistically significant differences were noted regarding the presence of HT (p<0.01), DM2 (p<0.01) and overweight (p<0.01) in dyslipidemic patients compared to non-dyslipidemic patients. Furthermore, it was found that dyslipidemic patients had a higher incidence of AMI (p<0.01), kidney problems (p=0.02), heart disease (p<0.01) and problems with mental health (p<0.01). Furthermore, a higher prevalence of smoking was identified in non-dyslipidemic patients (p=0.02).

Variable	With dislipidemia (n=551)	Without dislipidemia	Total	p-value
		(n=1,177)	(n=1,728)	
Smoking, n (%)				0.02
Yes	34 (6.2)	110 (9.3)	144 (8.3)	
No	517 (93.8)	1,067 (90.7)	1,584 (91.7)	
HT, n (%)				0.01
Yes	434 (78.8)	715 (60.7)	1,149 (66.5)	
No	117 (21.2)	462 (39.3)	579 (33.5)	
DM2, n (%)				0.01
Yes	231 (41.9)	220 (18.7)	451 (26)	
No	320 (58.1)	957 (81.3)	1,277 (74)	
Sedentary				0.14
Yes	534 (97)	1,154 (98)	1,688 (97.7)	
No	17 (3)	23 (2)	40 (2.3)	
Heart disease, n (%)				0.01
Yes	109 (19.8)	132 (11.2)	241 (13.9)	
No	442 (80.2)	1,045 (88.8)	1,487 (86.1)	
AMI, n (%)				0.01
Yes	25 (4.5)	25 (2.1)	50 (2.9)	
No	526 (95.5)	1,152 (97.9)	1,678 (97.1)	
CVA, n (%)				0.15
Yes	26 (4.7)	39 (3.3)	65 (3.7)	
No	525	1,138	1,663 (96.3)	
BMI, n (%) (n=1,129)				0.01
Normal	118 (38.5)	312 (43.2)	430 (38)	
Overweight	288 (61.5)	411 (56.8)	699 (72)	
Renal problem, n (%)				0.02
Yes	29 (5.3)	36 (3.1)	65 (3.7)	
No	522 (94.7)	1,141 (96.9)	1,663 (96.3)	
Mental health problem, n (%)				0.01
Yes	153 (27.8)	184 (15.6)	337 (19.5)	
No	398 (72.2)	993 (84.4)	1,391 (80.5)	

**Table 3.** Comorbidities and risk factors observed in dyslipidemic and non-dyslipidemic older people, recorded in the city of Marau, Rio Grande do Sul, in 2019 (n=1,728) (continued).

HT: hypertension; DM2: type 2 diabetes mellitus; AMI: acute myocardial infarction; CVA: cerebrovascular accident; BMI: body mass index.

Source: Municipal Health Department of Marau (RS).

## DISCUSSION

Dyslipidemia is a public health problem and is directly related to the development of cardiovascular diseases.<sup>4,5</sup> In this sense, the present study aimed to describe the socio-epidemiological, as well as clinical and laboratory, situation of patients diagnosed with dyslipidemia, together with the CVD risk factors present among individuals in the city of Marau (RS).

In this study, we found that 31.9% of patients were dyslipidemic, which is in line with the national<sup>10</sup> and international literature.<sup>11</sup> A higher prevalence was observed in females compared to males, in agreement with a national study.<sup>12</sup> However, other studies show a higher prevalence of males.<sup>13</sup> The most prevalent skin color was white, in line with another epidemiological study carried out in the Southeast Region. This can be explained by the predominance of individuals of European origin (mainly Italian) in the northern region of Rio Grande do Sul, where the study was conducted.<sup>14</sup>

Regarding education, it is noted that the majority of the sample had incomplete primary education (57.8%); however, there was a substantial portion of the sample that did not report their education (29.3%), thus, not measuring the level of education was statistically significant for this variable. However, studies highlight that the level of education is not related to the development of dyslipidemia.<sup>15,16</sup>

Regarding the lipid profile of dyslipidemic patients, the following changes were found: 21.7% had changes in total cholesterol; 21.7% in HDL-C; 14.6% in LDL-C; and 24.5% in triglycerides. A similar study observed high values of total cholesterol in 51.2%, LDL-C in 43.7%, triglycerides in 27.6% and low HDL-C in 28.2% of participants.<sup>17</sup> Other Brazilian studies found higher values to those of this investigation.<sup>18,19</sup> It is noteworthy that, while our study worked with patients already diagnosed with dyslipidemia and, therefore, subject to previous treatment, the two studies cited included patients with and without dyslipidemia in the sample.

It is known that low values of HDL-c, as well as high values of triglycerides, LDL-c and total cholesterol are directly related to the risk of developing atherosclerotic cardiovascular diseases and worse clinical health conditions.<sup>2,5,17</sup> This is reinforced by this study, which demonstrated that patients with dyslipidemia are more affected by AMI compared to those without dyslipidemia (p<0.01). Therefore, it is necessary to control the lipid profile to mitigate risk factors for the development of CVD and provide aging with a higher quality of life, in addition to reducing costs to the public health sector.<sup>1</sup>

Physical activities directly affect the lipid profile of individuals and are closely related to the development of dyslipidemia.<sup>20-22</sup> In this aspect, our study observed a high percentage of sedentary lifestyle among dyslipidemic (97%) and non-dyslipidemic (98%) patients. In total, only 2.3% were not sedentary. In one study, an increase in HDL-C was observed in individuals who practiced physical activity compared to those who did not have this habit.<sup>23</sup> Furthermore, national and international research demonstrates the direct relationship between physical activity and the decrease in LDL-C and total cholesterol.<sup>23,24</sup> Therefore, emphasis should be placed on promoting primary prevention – in this case based on encouraging physical activity – to promote healthy aging and mitigate the risks of CVD.<sup>25,26</sup>

In parallel with physical activities – which play a significant role in establishing a controlled body mass index – overweight is a predictive factor for CVD,<sup>27</sup> given its influence on predisposing risk factors, such as dyslipidemia, HT, development of diabetes, inflammatory markers, obstructive sleep apnea and/ or hypoventilation and inflammatory and pro-thrombotic state.<sup>28</sup> We found in this study that 61.5% of dyslipidemic patients were overweight. These numbers are in line with those in the literature, which reports values close to 50%.<sup>5,10</sup> Furthermore, dyslipidemic patients are more overweight (p<0.01) compared to non-dyslipidemic patients, which is in line with national and international studies, reinforcing this notion.<sup>16,29</sup>

Another factor that is related to the development of CVD is smoking,<sup>29</sup> given that tobacco, combined with the inhalation of carbon monoxide present in cigarettes, negatively alters myocardial metabolic function and causes endothelial damage to blood vessels.<sup>30</sup> In this aspect, this study found that only 8.3% of participants were smokers. Furthermore, in relation to dyslipidemic and non-dyslipidemic individuals, there was a prevalence of 6.2 and 9.3%, respectively, with p=0.02, indicating a greater relationship between non-dyslipidemic and smoking. However, what was observed is not in line with the literature, which shows a greater relationship between dyslipidemia and smoking.<sup>29</sup> Furthermore, the percentages of smokers found in this study are in line with the literature, which points out – nationally – the value of 9% and, internationally, values ranging from 7 to 29%.<sup>31,32</sup>

The prevalence of DM2 was observed in 26% of patients, finding a statistically significant difference (p<0.01) between dyslipidemic and non-dyslipidemic patients, with the first group showing a prevalence of 41.9% and the second, 18.7%. There is several pieces of evidence that support this relationship.<sup>16</sup> It was observed in an American study that, in a sample of diabetic patients, 70% had dyslipidemia.<sup>33</sup> National studies corroborate this statement.<sup>34,35</sup> It is important to control this condition because of its pathophysiological characteristics (vascular inflammation, vasoconstriction, thrombosis and atherogenesis) being involved in CVD.<sup>15,29</sup>

Furthermore, the presence of hypertension was found in 66.5% of the sample evaluated. These values are close to, but higher than, those described in the Brazilian Guidelines for Arterial Hypertension, which indicate values between 44 and 55% in the elderly population. Finally, the difference between dyslipidemic and non-dyslipidemic patients was significant (p<0.01), with more than 78% of patients with dyslipidemia having hypertension, which agrees with literature data.<sup>16</sup>

It is concluded that dyslipidemia is a serious public health problem, having a high prevalence and being related to the development of CVD and the burden on the financial system. In this study, a higher prevalence of dyslipidemia was observed in females and those with white skin color. Changes were found in the levels of total cholesterol, HDL-C, LDL-C and triglycerides in patients with dyslipidemia, which indicates the importance of controlling these parameters for the prevention of CVD, with values found close to, but lower than those in the literature. Furthermore, it was identified that risk factors for CVD are present, mostly, in dyslipidemic patients, acting synergistically with dyslipidemia for the development of such pathologies. The results obtained provide important perspectives on the socio-epidemiological, clinical and laboratory situation of patients with dyslipidemia in the city of Marau, contributing to the recognition of the local reality, serving as a scientific basis for future management decisions related to the prevention and treatment of dyslipidemia and reducing the risk of CVD in the PHC of Marau.

As a limitation of the study, it is noteworthy that the assessment of the LDL-C level was not considered in light of cardiovascular risk factors. Furthermore, it is understandable to consider a possible selection bias, since the sample could not be made up of the entire older population, but rather of those who sought care during the data collection period. Furthermore, it is emphasized that future qualitative and quantitative studies are needed to explore adherence to pharmacological therapy, to understand the relationship between adherence and lipid levels in this specific group of patients.

### **AUTHORS' CONTRIBUTIONS**

GKC: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. ILL: Conceptualization,

Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – review & editing. GOA: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – review & editing. GBF: Formal analysis, Data curation, Software, Validation, Visualization, Writing – review & editing. ACZG: Formal analysis, Data curation, Validation, Visualization, Writing – review & editing. ACZG: Formal analysis, Data curation, Validation, Visualization, Writing – review & editing. ABS: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – review & editing.

# **CONFLICT OF INTERESTS**

Nothing to declare.

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