














ORIGINAL ARTICLE

Factors associated with hypercholesterolemia in older adults: A cross-sectional investigation

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Abstract

Objective: To investigate the factors associated with hypercholesterolemia in older adults residing in a small municipality in northeastern Brazil.

Methods: This is a population-based cross-sectional epidemiological study conducted with 232 older adults (women: 58.60%; men: 41.40%) in Aiquara, Bahia, Brazil. Independent variables included socioeconomic, behavioral, and health-related factors. The outcome was self-reported hypercholesterolemia (yes or no). Poisson regression with a robust estimator was used to calculate Prevalence Ratios (PR) and their respective 95% Confidence Intervals (CI) in the inferential analysis. Gross models were initially developed, followed by a hierarchical multiple explanatory model (Level 1: socioeconomic variables; Level 2: behavioral aspects; Level 3: health conditions).

Results: The observed prevalence of hypercholesterolemia was 34.50% (men: 21.90%; women: 43.40%). Additionally, a higher probability of hypercholesterolemia was observed in women (PR: 1.94; 95% CI: 1.27–2.97); participants with high sedentary behavior (PR: 1.47; 95% CI: 1.03–2.09); those with abdominal obesity (PR: 1.65; 95% CI: 1.06–2.57); and those with diabetes mellitus (PR: 1.54; 95% CI: 1.04–2.29).

Conclusion: The main results showed that female sex, high sedentary behavior, abdominal obesity, and diabetes mellitus were positively associated with hypercholesterolemia in the older population of the study.

KEYWORDS

aging, dyslipidemias, epidemiology, older people

1 | INTRODUCTION

Dyslipidemias, characterized by alterations in lipid transport or metabolism, tend to disproportionately affect older adults due to genetic factors, lifestyle, medication use, and the prevalence of chronic diseases at advanced ages.^{1,2} Among these, hypercholesterolemia, resulting from elevated total cholesterol levels due to increased low-density lipoprotein (LDL) cholesterol or triglycerides and/or a reduction in high-density lipoprotein (HDL) cholesterol, is particularly prevalent.² This condition can have environmental or genetic origins, as exemplified by familial hypercholesterolemia.³

In Brazil, the prevalence of hypercholesterolemia increases with age. Malta et al.,⁴ analyzing data from the National Health Survey, reported a prevalence of 41.90% (95% CI: 39.10%–44.80%) in older adults. This is a significant public health concern, as hypercholesterolemia can lead to the accumulation of lipoproteins in endothelial tissues, causing inflammatory damage and promoting the development of atherosclerotic plaques. These plaques can obstruct blood flow and contribute to cardiovascular diseases.⁵

Given the multifactorial nature of hypercholesterolemia,⁴ it is plausible to hypothesize that socioeconomic, behavioral, and health-related aspects may influence its likelihood. However, there is a dearth of population-based epidemiological studies focusing on these aspects in localities with low socioeconomic indicators, particularly in smaller urban centers with rural characteristics and populations under 5000 inhabitants. This is relevant as 22.50% of Brazilian cities fit this description,⁶ making the investigation of hypercholesterolemia in older adults residing in these areas crucial for expanding scientific knowledge.

Brazil's continental dimensions and social inequalities underscore the importance of conducting epidemiological research that considers regional disparities.⁷ The Northern and Northeastern regions, characterized by lower socioeconomic conditions and limited healthcare access,⁸ have been underrepresented in studies on hypercholesterolemia in older adults, which have primarily been conducted in the Southern and Southeastern regions.^{9,10}

Considering the potential health implications of hypercholesterolemia, research in localities with low socioeconomic levels can provide valuable evidence to guide professionals and managers in Primary Health Care (PHC). This evidence can inform screening practices, surveillance, promotion, and health recovery actions, ultimately strengthening the right to comprehensive health care. To address this need, this study aimed to investigate the factors associated with hypercholesterolemia in older adults residing in a small municipality in northeastern Brazil.

2 | MATERIALS AND METHODS

2.1 | Study design, setting, and population

This cross-sectional epidemiological study was conducted in accordance with the Strengthening the Reporting of Observational Studies

in Epidemiology statement.¹¹ It was based on baseline data from the population-based research "Health conditions and lifestyle of older adults residing in a small municipality," conducted with all older adults residing in the urban area of Aiquara, Bahia, Brazil, registered in the Family Health Strategy (FHS). The city, located in the south-central region of Bahia, has a population of 4447 inhabitants, ranks 410th in population among the municipalities of the state (out of a total of 417), and has a Human Development Index of 0.583.¹²

2.2 | Ethical aspects

The research was conducted in accordance with the Declaration of Helsinki of the World Medical Association and Resolution no. 466/2012 of the National Health Council. It was approved by the Research Ethics Committee of the State University of Southwest Bahia, under opinion no. 171.464 and CAAE no. 10786212.30000.0055. All participants were informed about the study objectives, procedures, and voluntary nature of participation. After the explanation, they signed the Informed Consent Form.

2.3 | Eligibility criteria

Given the research's focus on older adults in Brazil, a developing country, we adopted age 60 or over as an inclusion criterion. Additionally, participants had to be non-institutionalized, live in an urban area, and sleep at least four nights in the same household.¹³ Exclusion criteria included: cognitive deficit, identified by the short version of the Mini-Mental State Examination (MMSE)¹⁴ with a cut-off point <13¹⁵; being bedridden or having hearing problems.¹⁶

2.4 | Data collection

Data collection was divided into two stages: (1) a household interview, in which information related to socioeconomic profile, behavior, and health conditions was obtained; and (2) anthropometric measurements. More information about the description of the procedures adopted and stages of data collection was previously published and can be verified in Santos et al.¹⁷

2.5 | Independent variables

2.5.1 | Socioeconomic aspects

Sex (male or female); age group (60–69, 70–79, ≥ 80 years); skin color (white or non-white [black, brown, and indigenous]); education (with or without education [never attended school and/or cannot write their own name]); marital status (with or without partner); and income (≤ 1 minimum wage or >1 minimum wage).¹⁸

2.5.2 | Behavioral aspects

Level of physical activity (PA), assessed by the first four domains of the long version of the International Physical Activity Questionnaire (IPAQ),¹⁹ an instrument validated for the Brazilian older population.^{20,21} Older individuals who reported a weekly time of <150 min of moderate to vigorous PA were considered insufficiently active.²² Sedentary behavior (SB) was quantified by the fifth domain of the IPAQ, which considers the time spent sitting on a typical weekday and weekend day.¹⁹ The weighted average of SB was calculated as follows: $(5 \times \text{min/weekday}) + (2 \times \text{min/weekend day} / 7)$. The cutoff point adopted for high SB was based on the 75th percentile of the weighted average, which corresponded to 342.85 min/day (5.71 h/day).¹⁶ Additionally, the following were considered as behavioral aspects: tobacco use (yes or no); alcohol consumption in the last 30 days before data collection (yes or no); consumption of fruits, vegetables, or legumes (consumption at least twice a day: yes or no); consumption of eggs, beans, lentils, or soy (consumption at least once a week: yes or no); consumption of meat, chicken, or fish (three times a week: yes or no).¹⁸

2.5.3 | Health conditions

Diagnosis of hypertension (yes or no); diabetes mellitus (yes or no); self-perceived health (positive or negative)¹⁸; suspicion of common mental disorders, verified by the Self-Reporting Questionnaire-SRQ-20 with a cutoff point ≥ 7 positive responses²³; occurrence of falls in the last 12 months before collection (yes or no); and abdominal obesity, determined from elevated waist circumference values (women: ≥ 88 cm; men: ≥ 102 cm).²⁴

2.6 | Dependent variable

The outcome analyzed was assessed through self-reported diagnosis by the older adults, based on the following question: "Has any doctor ever told you that you have hypercholesterolemia, that is, that you have high cholesterol?" According to the answer, this variable was categorized dichotomously (hypercholesterolemia: yes or no).

2.7 | Statistical analysis

The description of the population characteristics was conducted based on the calculation of frequencies (absolute and relative) and the percentage of response for each variable analyzed. In addition, for the descriptive analysis, means and standard deviations were also considered.²⁵ For inferential analyses, gross models were initially constructed using Poisson regression with a robust estimator, through which Prevalence Ratios (PR) and their respective 95% Confidence Intervals (CI) were calculated.²⁶

The independent variables that showed a "p-value" of less than or equal to 20% ($p \leq 0.20$) in the gross analyses were considered for multivariate analysis in a hierarchical model, where socioeconomic aspects constituted the most distal level (Level 1), behavioral aspects the intermediate level (Level 2) and health conditions the most proximal level (Level 3),¹⁸ as shown in Figure 1.

The development of the model began with the variables of the most distant level, gradually adding the subsequent levels. In this way, intra and inter-level adjustments were made, where the effect of each independent variable on the outcome was controlled by the variables of the same level and by the variables of the previous

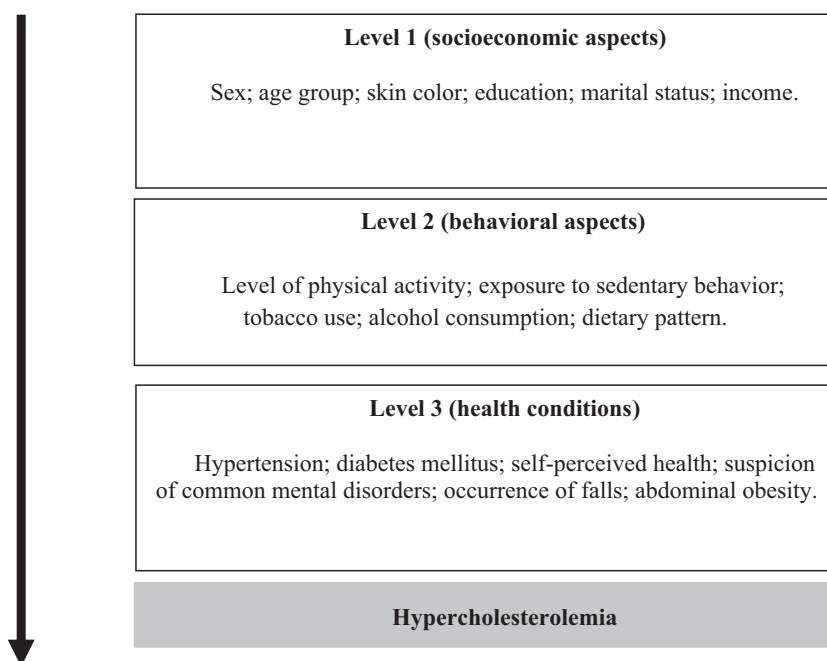


FIGURE 1 Hierarchical model used to identify factors associated with hypercholesterolemia in older adults.

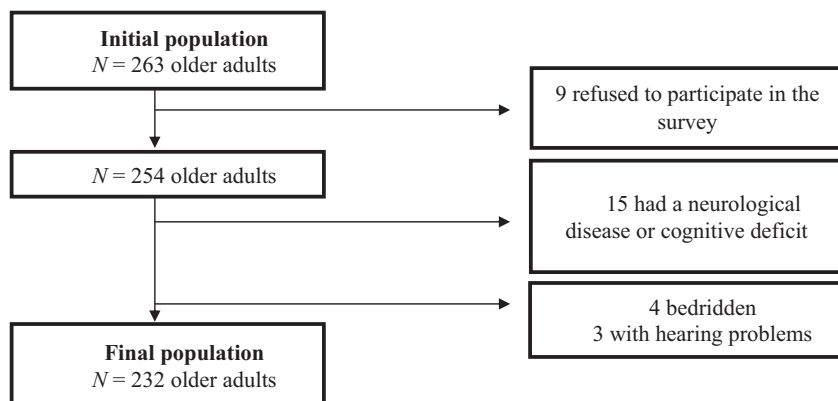


FIGURE 2 Flowchart describing the eligibility process for the older adults participating in the study.

levels, positioned hierarchically. In the final model, only the independent variables that maintained a “p-value” ≤ 0.20 , as observed by the Wald test for heterogeneity, remained.¹⁸ Finally, the variables that demonstrated a significance level of 5% ($p \leq 0.05$) were considered factors associated with hypercholesterolemia. Data analyses were performed using the Statistical Package for the Social Sciences (IBM-SPSS 21.0, 2013, Inc., Chicago, IL).

3 | RESULTS

Initially, a census was conducted to identify all older adults residing in Aiquara, Bahia, Brazil, with the help of community health workers working in the FHS, which covers 100% of the municipality's population. Thus, all households in the urban area were visited, resulting in the identification of 263 older adults.²⁷ Of these, 232 adults (women: 58.60%; men: 41.40%) comprised the study population, as illustrated in Figure 2.

The mean age of older men was 72.08 ± 8.06 years, while that of older women was 71.26 ± 7.02 years. Among the participants, the observed prevalence of hypercholesterolemia was 34.50% (older men: 21.90%; older women: 43.40%). Furthermore, it was found that 83.60% of participants self-identified as non-white; 61.10% had no formal education; 86.60% had an income equal to or less than one minimum wage; 53.90% were insufficiently active; and 45.20% had abdominal obesity. More population characteristics can be found in Table 1.

Table 2 presents the bivariate analyses between the independent variables and hypercholesterolemia. The variables sex; education; alcohol consumption; consumption of eggs, beans, or lentils; sedentary behavior; abdominal obesity; diabetes mellitus; hypertension; and self-perceived health showed a “p-value” ≤ 0.20 ; therefore, they were selected for multivariate analysis.

After intra- and inter-level adjustments, variables that did not meet the established criterion for remaining in the hierarchical model were removed. Thus, through the final explanatory model, it was found that the following independent variables were associated with the outcome: female sex (PR: 1.94; 95% CI: 1.27–2.97); high exposure to sedentary behavior (PR: 1.47; 95% CI: 1.03–2.09);

abdominal obesity (PR: 1.65; 95% CI: 1.06–2.57); and diabetes mellitus (PR: 1.54; 95% CI: 1.04–2.29) (Table 3).

4 | DISCUSSION

This study aimed to investigate factors associated with hypercholesterolemia in older adults residing in a small municipality in northeastern Brazil. The main results showed that female sex, high exposure to sedentary behavior, abdominal obesity, and diabetes mellitus were independent factors that increased the probability of the outcome investigated.

In a cross-sectional study, Richter et al. found that women had a mean total cholesterol value of 219.50 ± 43.00 mg/dL, while men had 184.80 ± 52.40 mg/dL ($p = 0.001$). In addition, the authors found a higher prevalence of hypercholesterolemia in women (24.70%) compared to men (9.40%) ($p = 0.002$).¹³ In fact, data from the National Health Survey, conducted by the Brazilian Ministry of Health, shows that hypercholesterolemia is more prevalent in women.⁴

The higher prevalence of hypercholesterolemia in older women compared to older men is likely due to sex-specific hormonal changes.²⁸ These changes are a consequence of ovarian aging and occur throughout menopause, becoming more severe after menopause, with a notable decrease in the production of sex steroid hormones, such as estrogen.^{28,29}

17 β -estradiol, a form of estrogen, plays a crucial role in the hypothalamus, influencing energy expenditure and body thermogenesis. This hormone interacts with the AMP-activated protein kinase, modulating its activity and impacting the physiological response to hypoglycemia. Moreover, 17 β -estradiol acts through various molecular pathways, modulating the action of specific neurons in the hypothalamus, such as leptin, cholecystokinin, and ghrelin, as well as neurotransmitters like serotonin, which are key regulators of appetite and body weight.²⁹

Thus, the decrease in 17 β -estradiol levels during female aging can lead to a reduction in basal metabolism and an increase in caloric intake. These factors, together, can promote excessive adipose tissue accumulation, resulting in metabolic disturbances, such as hypercholesterolemia.³⁰

TABLE 1 Descriptive analysis of the socio-economic behavioral and health-related characteristics of the study population.

Variables	% response	N	%
Sex	100.00		
Male		96	41.40
Female		136	58.60
Age group	100.00		
60–69 years		98	42.20
70–79 years		93	40.10
≥80 years		41	17.70
Skin color	97.00		
White		37	16.40
Non-white		188	83.60
Education	97.40		
Yes		88	38.90
No		138	61.10
Marital status	100.00		
With a partner		127	54.70
Without a partner		105	45.30
Income	93.50		
> 1 minimum wage		29	13.40
≤ 1 minimum wage		188	86.60
Alcohol consumption	100.00		
No		183	78.90
Yes		49	21.10
Tobacco use	100.00		
No		209	90.10
Yes		23	9.90
C. of eggs, beans, lentils, or soy	100.00		
Yes		219	94.40
No		13	5.60
C. of meat, chicken, or fish	99.10		
Yes		226	98.30
No		04	1.70
C. of fruits and/or vegetables	100.00		
Yes		170	73.30
No		62	26.70
Level of physical activity	100.00		
Sufficient		107	46.10
Insufficient		125	53.90
Sedentary behavior	100.00		
Low		174	75.00
High		58	25.00
Abdominal obesity	90.50		
No		115	54.80
Yes		95	45.20
Hypertension	100.00		

(Continues)

TABLE 1 (Continued)

Variables	% response	N	%
No		95	40.90
Yes		137	59.10
Diabetes mellitus	100.00		
No		194	83.60
Yes		38	16.40
Hypercholesterolemia	100.00		
No		152	65.50
Yes		80	34.50
Occurrence of falls	97.40		
No		193	85.40
Yes		33	14.60
Suspicion of CMD	100.00		
No		155	66.80
Yes		77	33.20
Self-perceived health	98.30		
Positive		118	51.80
Negative		110	48.20

Abbreviations: %, percentage; C, consumption; CMD, common mental disorders; N, absolute frequency.

In parallel, SB, characterized by activities that result in low energy expenditure (≤ 1.5 metabolic equivalents), performed during waking hours in a sitting, lying, or reclining position,³¹ has been shown to be prevalent at all ages but is of particular concern in older populations due to its association with various chronic conditions.³² This behavioral pattern can lead to a significant decrease in energy expenditure, which promotes excessive fat accumulation in adipose tissue,³³ making this endocrine organ more active and resulting in disturbances in lipid metabolism. This can culminate in dyslipidemias, such as increased LDL, decreased HDL, and hypercholesterolemia.^{34,35}

Evidence demonstrates a strong association between SB and elevated levels of inflammatory markers, such as C-reactive protein.^{32,33} Chronic systemic inflammation can exacerbate hypercholesterolemia, facilitating the formation of atherosclerotic plaques in arteries and increasing the risk of cardiovascular diseases. Moreover, the decrease in muscle mass, common in older adults with high exposure to SB,^{34,35} tends to result in a reduced basal metabolic rate, which can hinder cholesterol regulation.³⁵

Therefore, it is crucial to emphasize the need to interrupt prolonged periods of SB to mitigate its health impacts.³² The simple act of standing up results in muscle contractions necessary to maintain an upright posture, which increases basal metabolic expenditure and can attenuate the harmful effects of hypokinesia.³³ Additionally, the Brazilian Ministry of Health (BMH)³⁶ and the World Health Organization (WHO)²² recommend replacing sedentary time with PA to minimize the harmful effects of SB. Decreasing sedentary time and replacing it with regular PA for older adults is essential for preventing hypercholesterolemia and its associated complications. In this sense, the BMH and WHO recommend 150–300 min

TABLE 2 Prevalence of hypercholesterolemia according to independent variables in the study population.

Variables	Hypercholesterolemia		p-value
	Prevalence (%)	Gross PR (95% CI)	
Sex			
Male	21.90	1	0.002
Female	43.40	1.98 (1.29–3.03)	
Age group			
60–69 years	33.70	1	0.842
70–79 years	36.90	1.08 (0.73–1.59)	
≥80 years	31.70	0.94 (0.55–1.59)	
Skin color			
White	35.10	1	0.948
Non-white	34.60	0.98 (0.60–1.59)	
Education			
Yes	43.20	1	0.037
No	29.70	0.68 (0.48–0.97)	
Marital status			
With a partner	31.50	1	0.292
Without a partner	38.10	1.21 (0.84–1.72)	
Income			
> 1 minimum wage	36.20	1	0.607
≤ 1 minimum wage	31.00	1.16 (0.65–2.07)	
Alcohol consumption			
No	36.60	1	0.200
Yes	26.50	0.72 (0.43–1.19)	
Tobacco use			
No	34.40	1	0.975
Yes	34.80	1.01 (0.56–1.82)	
C. of eggs, beans, lentils or soy			
Yes	33.30	1	0.080
No	53.80	1.61 (0.94–2.76)	
C. of meat, chicken, or fish			
Yes	34.50	1	0.466
No	50.00	1.45 (0.53–3.92)	
C. of fruits and/or vegetables			
Yes	35.30	1	0.670
No	32.30	0.91 (0.60–1.38)	
Level of physical activity			
Sufficient	34.40	1	0.969
Insufficient	34.40	1.00 (0.70–1.48)	
Sedentary behavior			
Low	30.50	1	0.019
High	46.60	1.53 (1.07–2.18)	
Abdominal obesity			
No	23,50	1	<0.001
Yes	49,50	2.10 (1.43–3.10)	

TABLE 2 (Continued)

Variables	Hypercholesterolemia		p-value
	Prevalence (%)	Gross PR (95% CI)	
Diabetes mellitus			
No	29.90	1	<0.001
Yes	57.90	1.93 (1.37–2.73)	
Hypertension			
No	26.30	1	0.036
Yes	40.10	1.52 (1.03–2.62)	
Occurrence of falls			
No	33.20	1	0.278
Yes	42.40	1.28 (0.82–1.99)	
Suspicion of CMD			
No	32.30	1	0.305
Yes	39.00	1.21 (0.84–1.73)	
Self-perceived health			
Positive	27.10	1	0.010
Negative	43.60	1.61 (1.11–2.31)	

Values in bold indicate $p \leq 0.20$. Abbreviations: %, percentage; C, consumption; CI, confidence interval; CMD, common mental disorders; PR, prevalence ratio.

TABLE 3 Hierarchical model of the association between independent variables and hypercholesterolemia in the study population.

Level	Variables	Adjusted PR (95% CI)	p-value
1	Sex		
	Male	1	0.002
	Female	1.94 (1.27–2.97)	
	Education		
	Yes	1	0.069
	No	0.73 (0.51–1.02)	
	C. of eggs, beans, lentils or soy		
2	Yes	1	0.200
	No	1.53 (0.79–2.93)	
	Sedentary behavior		
	Low	1	0.031
	High	1.47 (1.03–2.09)	
	Abdominal obesity		
	No	1	0.026
3	Yes	1.65 (1.06–2.57)	
	Diabetes mellitus		
	No	1	0.031
	Yes	1.54 (1.04–2.29)	
	Self-perceived health		
	Positive	1	0.151
	Negative	1.30 (0.90–1.87)	

Values in bold indicate $p < 0.05$. Abbreviations: C, consumption; CI, confidence interval; PR, prevalence ratio.

per week of moderate-intensity PA, or 75–150min per week of vigorous-intensity PA.^{22,36}

Regarding the association between abdominal obesity and hypercholesterolemia, Araújo et al.³⁷ conducted a cross-sectional population-based epidemiological study in Lafaiete Coutinho, Bahia, Brazil, with 296 older adults. The results indicated that participants with elevated waist circumference had a 2.82 times higher chance of presenting hypercholesterolemia (OR: 2.82; 95% CI: 1.68–4.74). Therefore, abdominal obesity has been identified as a central factor in the pathogenesis of various morbidities, including coronary heart disease, insulin resistance, and atherosclerosis.² Adipose tissue is considered a complex secretory organ that performs various metabolic functions, influencing energy expenditure, appetite, insulin sensitivity, bone metabolism, reproductive and endocrine functions, inflammation, and immunity.^{9,38} Thus, visceral fat appears to pose a high risk for cardiometabolic diseases.^{38–40}

Diabetes mellitus is a metabolic disease characterized by elevated and sustained blood glucose levels due to insulin resistance or insufficient insulin production.⁴¹ When not adequately controlled, diabetes mellitus can affect lipid metabolism, resulting in dyslipidemia. Both insulin resistance and relative insulin deficiency can lead to mixed hyperlipidemia, characterized by low HDL levels and, occasionally, high LDL levels.⁴² In addition, there is a greater stimulus for fat deposition in adipocytes, which consequently generates inflammation, immune system dysregulation, and development of atheromas in blood vessels.⁴² The common pattern of dyslipidemia in patients with diabetes mellitus shows elevated triglycerides and low HDL. Furthermore, since LDL has smaller and denser particles, they are more susceptible to oxidative processes, increasing the risk of cardiovascular events.⁴³

Evidence shows that strict glycemic control in patients with diabetes mellitus reduces cardiovascular morbidity and mortality. It is also observed that both hyperglycemia and diabetic dyslipidemia accelerate atherogenic processes. Individuals with diabetes mellitus who achieve adequate glycemic control demonstrate LDL, total cholesterol, triglycerides, and HDL levels closer to normal. On the other hand, those who maintain unsatisfactory glycemic control have an atherogenic profile, with elevated LDL and total cholesterol and low HDL.³⁹

Therefore, the associations of abdominal obesity and diabetes mellitus with hypercholesterolemia, in the present study, evidence a concerning situation. They reveal a possible high burden of comorbidities in the older population of Aiquara, Bahia, Brazil, composed of diseases that constitute the metabolic syndrome. This syndrome is characterized by insulin resistance, sustained high blood pressure, obesity, and dyslipidemia, which increases the risk of mortality.⁴⁴ Thus, it is essential to implement prevention and control strategies for these conditions to improve the health and quality of life of this population.

This epidemiological investigation has some limitations, including the self-reported diagnosis of conditions such as diabetes mellitus, hypertension, and hypercholesterolemia, which may not motivate seeking care in health services due to their initial manifestations being silent. Additionally, the indirect quantification of time spent in physical activity and sedentary behavior may result in inaccuracies in estimating the time spent in such behaviors. However, the use of the MMSE to exclude older adults with cognitive impairment is a strength of the study, as it was adopted to attenuate the memory bias in obtaining this information.

Another strength of this research is its census approach, which allowed for the assessment of the older population of a small municipality in northeastern Brazil, a region with low socioeconomic indicators and difficulties in providing health services.^{12,17,18} Thus, it is hoped that the evidence presented can provide subsidies for the actions of health professionals in the context of primary care, aiming at the prevention of hypercholesterolemia and the implementation of interventions that improve the prognosis of older people with this condition. This is relevant not only for Aiquara, Bahia, Brazil, but also for other localities with similar characteristics.

Establishing protocols for the regular monitoring of cholesterol levels, especially for high-risk groups, can help to detect and treat hypercholesterolemia early. The integration of health services that address hypercholesterolemia along with other chronic conditions, such as diabetes mellitus and obesity, can improve care coordination and health outcomes.⁴⁵ Finally, in the context of primary care, it is suggested to implement health education actions to reduce sedentary time and, at the same time, strengthen health promotion programs, which increase the time spent in PA, such as community walks, exercise groups, and individual counseling, to encourage the adoption of these practices by the older population.

5 | CONCLUSION

The results of this study corroborate the hypothesis, since female sex, high exposure to sedentary behavior, abdominal obesity and diabetes mellitus were the multiple factors (socioeconomic, behavioral and health) that showed a positive association with hypercholesterolemia in the study population. Thus, the findings of the study provide valuable information for clinical practice in PHC, allowing the development of targeted interventions that can reduce the prevalence of hypercholesterolemia and its complications, through education, counseling, monitoring and health surveillance strategies, based on the factors associated with the outcome.

AUTHOR CONTRIBUTIONS

Maria Clara Alves de Oliveira, Júlia Perfeito Andrade, Ana Carolina Souza Porto, Gizelly Maria Torres Martins, Nurielly Monteiro Campos, Paulo da Fonseca Valença Neto, Claudio Bispo De Almeida, Saulo Sacramento Meira, Beatriz Cardoso Roriz, Débora Jesus da Silva, Victor Giovannino Accetta, Cezar Augusto Casotti, and Lucas dos Santos participated in the project conception, study design, writing and critical review of the manuscript. In addition, Lucas dos Santos and Maria Clara Alves de Oliveira carried out the data analysis and interpretation. All the authors declare no conflict of interest and have approved the final version of the manuscript. They are also responsible for all aspects of the work, including ensuring its accuracy and integrity.

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CONFLICT OF INTEREST STATEMENT

The authors declare that there is no conflict of interest.

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