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Association between food consumption based on the degree of processing and dyslipidemia in Brazilian adults (CUME study)

Associação entre consumo de alimentos, baseados no grau de processamento, e dislipidemia em adultos Brasileiros (Estudo CUME)

Asociación entre el consumo de alimentos, según el grado de procesamiento, y la dislipidemia en adultos brasileños (Estudio CUME)

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Abstract *This study evaluated the association between food consumption, based on degree of processing, and the incidence of dyslipidemia in Brazilian adults. This prospective study was conducted with 2,771 Minas Gerais Universities Cohort (CUME Study) participants. They were free of dyslipidemia at baseline and had four years of follow-up. Generalized Equation Estimation was performed. The incidence of lipid profile alterations was 27.0 % for high-LDL-c, 20.6% for low-HDL-c, and 24.6% for hypertriglyceridemia. Although in the crude model, participants who consumed a greater proportion of energy from ultra-processed foods were at greater risk of elevated LDL-C and triglycerides and low HDL-C levels; and consuming a greater proportion of minimally processed foods was protective against dyslipidemia, this association did not persist in the adjusted model. This indicates that, in this study, food consumption, according to the NOVA classification, was not associated with changes in the lipid profile of CUME participants over the four-year follow-up period.*
Key words *Cohort Studies, Dyslipidemias, Noncommunicable Diseases, Incidence, Ultra-processed Food*

Resumo *Este estudo avaliou a associação entre o consumo alimentar, baseado no grau de processamento, e a incidência de dislipidemia em adultos brasileiros. Este estudo prospectivo foi conduzido com 2.771 participantes da Coorte de Universidades de Minas Gerais (Estudo CUME). Os participantes estavam livres de dislipidemia no início do estudo e tiveram quatro anos de acompanhamento. Foi realizada a Estimativa de Equação Generalizada. A incidência de alterações no perfil lipídico foi de 27,0% para LDL-c alto, 20,6% para HDL-c baixo e 24,6% para hipertrigliceridemia. Apesar de no modelo bruto, os participantes que consumiram uma maior proporção de energia de alimentos ultraprocessados apresentarem maior risco de níveis elevados de LDL-c e triglicerídeos e HDL-c baixo; e consumir maior proporção de alimentos minimamente processados ter sido protetivo contra a dislipidemia; esta associação não se manteve no modelo ajustado. Isso indica que, neste estudo, o consumo de alimentos, segundo classificação NOVA, não foi associado a alterações do perfil lipídico dos participantes da CUME ao longo de quatro anos de seguimento.*
Palavras-chave *Estudos de coorte, Dislipidemias, Doenças não transmissíveis, Incidência, Alimentos ultraprocessados*

Resumen *Este estudio evaluó la asociación entre el consumo de alimentos, según el grado de procesamiento, y la incidencia de dislipidemia en adultos brasileños. Este estudio prospectivo se realizó con 2.771 participantes de la cohorte de la Universidad de Minas Gerais (Estudio CUME). Los participantes no presentaban dislipidemia al inicio del estudio y tuvieron cuatro años de seguimiento. Se realizó una estimación de ecuaciones generalizadas. La incidencia de cambios en el perfil lipídico fue del 27,0 % para c-LDL alto, del 20,6 % para c-HDL bajo y del 24,6 % para hipertrigliceridemia. Si bien en el modelo crudo, los participantes que consumían una mayor proporción de energía proveniente de alimentos ultraprocesados presentaban un mayor riesgo de c-LDL y triglicéridos elevados y c-HDL bajo, y el consumo de una mayor proporción de alimentos mínimamente procesados protegía contra la dislipidemia, esta asociación no se mantuvo en el modelo ajustado. Esto indica que, en este estudio, el consumo de alimentos, según la clasificación NOVA, no se asoció con cambios en el perfil lipídico de los participantes del CUME durante el período de seguimiento de cuatro años.*
Palabras clave *Estudios de cohorte, Dislipidemias, Enfermedades no transmisibles, Incidencia, Alimentos ultraprocesados*

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Introduction

Dyslipidemia is any change in plasma lipid levels[1] and is an essential condition for the development of cardiovascular diseases (CVD)[1,2]. The most common form of dyslipidemia is hypercholesterolemia, which corresponds to elevated plasma LDL-cholesterol levels, being the 8th leading risk factor in the world for death in 2019[3]. The last Brazilian study evaluating the prevalence of dyslipidemia in the population was performed in 2016, VIGITEL, which identified a frequency of 22.6% of dyslipidemia, being higher among women (25.9%) than among men (18.8%)[4]. In this VIGITEL study, women over 55 years of age had a higher frequency of dyslipidemia, corroborating a study by Valença *et al.*[5]. No novel data about dyslipidemia are available in VIGITEL studies. However, Sousa *et al.*[6] carried out a study with data from Vigitel obtained from 2006 to 2016 and observed an increase in diagnoses from 16.9% (2006) to 22.6% (2016), with a growing rate of 0.33%, estimating a frequency of dyslipidemia of 28% in 2021.-

Based on the association of dyslipidemia and CVD, early identification of risk factors for prevention and treatment may be the way to control this problem and reduce mortality effectively. Although the determinants of dyslipidemia may vary considerably among individuals, some factors are crucial, such as diet, physical activity, and genetic inheritance[2]. Serum concentrations of total cholesterol and triglycerides may increase depending on the quality and quantity of food intake.

The modernization of life has modified people's daily routines and consequently impacted food consumption worldwide. According to this scenario, Brazil has adopted the NOVA classification as a theoretical reference for its recommendations regarding food consumption[7]. Based on this classification, foods are grouped into four categories: natural or minimally processed foods, culinary ingredients, processed foods, and ultra-processed foods[7].

Fresh or minimally processed foods (MPF) have not changed after leaving nature or have only been subjected to cleaning, grinding, drying, and other processes. Culinary Ingredients (CI) are products extracted from foods used to season, cook, and create culinary preparations. Processed foods (PF) are manufactured by the industry with processed culinary ingredients. In contrast, ultra-processed foods (UPF) are industrial formulations made mainly with substances derived from food, and many of the ingredients are for exclusive use by the industry[7,8]. According to the World Health Organization[9], this intake has increased, in relative and absolute terms, in high- and middle-income countries, especially in recent years[10,11].

Several studies have evaluated food consumption according to the NOVA classification with health outcomes, including dyslipidemia[12,13]. Some UPFs have been associated with lipid changes, childhood obesity, weight gain, CVD, and type 2 diabetes[14,15]. The trans fats present in UPF negatively affect cardiovascular health. Processed meats are associated with an increased risk of mortality from CVD and some types of cancer[16]. Fast foods are UPFs, and they have been linked to higher energy intake, weight gain, insulin resistance, and high triglyceride levels[17,18]. Studies conducted in different countries[19-21] have shown that high UPF consumption results in nutritionally unbalanced diets. This is due to these foods' high sugar content, total and saturated fat, high caloric density, and low fiber, minerals, vitamins, and protein content[22-24].

However, there are few cohort studies with Brazilian adults that have studied the relationship between food consumption, according to the NOVA classification, and the incidence of dyslipidemia. Considering this aspect, this study evaluated the impact of food consumption based on the degree of processing (NOVA classification) on the incidence of dyslipidemia in Brazilian adult participants of the Minas Gerais Universities Cohort (CUME Study).

Material and methods

Design and Study Population

The Cohort of Universities of Minas Gerais (CUME Study) is a prospective study performed with adults in Brazil. The objective is to evaluate the impact of Brazilian dietary patterns and food groups on the occurrence of NCD. The study began in 2016 and had a wave of follow-ups every two years. Graduates from seven Federal Universities located in Minas Gerais participate in this cohort. The study design, dissemination strategies, and profile of the first baseline participants were detailed in a previous publication[25]. Recruitment of participants is permanent, which allows for continuous growth in the sample size in each wave of follow-up, which occurs every two years. Thus, previously recruited participants receive new questionnaires (Q_2, Q_4,

Q_n), while new participants receive the baseline questionnaire (Q_0). Initially, 3,134 participants who did not report having dyslipidemia at the study baseline and completed follow-up questionnaires were included. Non-inclusion criteria were participants living abroad, from other nationalities, with total energy intake predefined as extreme (<600 or >6000 Kcal/day), and pregnant women. Then, the sample had 2,771 participants. From these, three separate databases were created, one excluding those who had LDL-c>129 (n=2,392), another excluding those with HDL-c<40 (n=2,094), and another excluding individual who had TG>150 (n=2,485) (Figure 1).

This study was conducted following the guidelines established in the Declaration of Helsinki, and all procedures involving study participants were approved by the Research Ethics Committee of the Federal University of Viçosa (UFV) (CAAE: 67808923.7.1001.5153) and endorsed by the Research Ethics Committee of the other institutions. Informed consent was obtained from all participants.

The study protocol and data collection

All alumni from universities participating in CUME were invited to participate in the study through electronic correspondence. Those who agreed to participate in the study received a link to access the questionnaires and were directed to the CUME virtual page (www.projetocume.com.br). Participants initially responded to the baseline questionnaire Q0 and, in subsequent years, responded to the Q2, Q4, and Q6 follow-up questionnaires. The baseline questionnaire consists of two blocks of questions; the first contains questions on sociodemographic and economic aspects, lifestyle, reported morbidity, medication use, personal history of clinical and biochemical tests over the last two years, and anthropometric data.

The second block is a consumption frequency questionnaire composed of 144 food items[26], separated into eight food groups (dairy products, meat and fish, cereals and legumes, oils and fats, fruits and vegetables, drinks and other foods, including food preparations, sugar, hon-

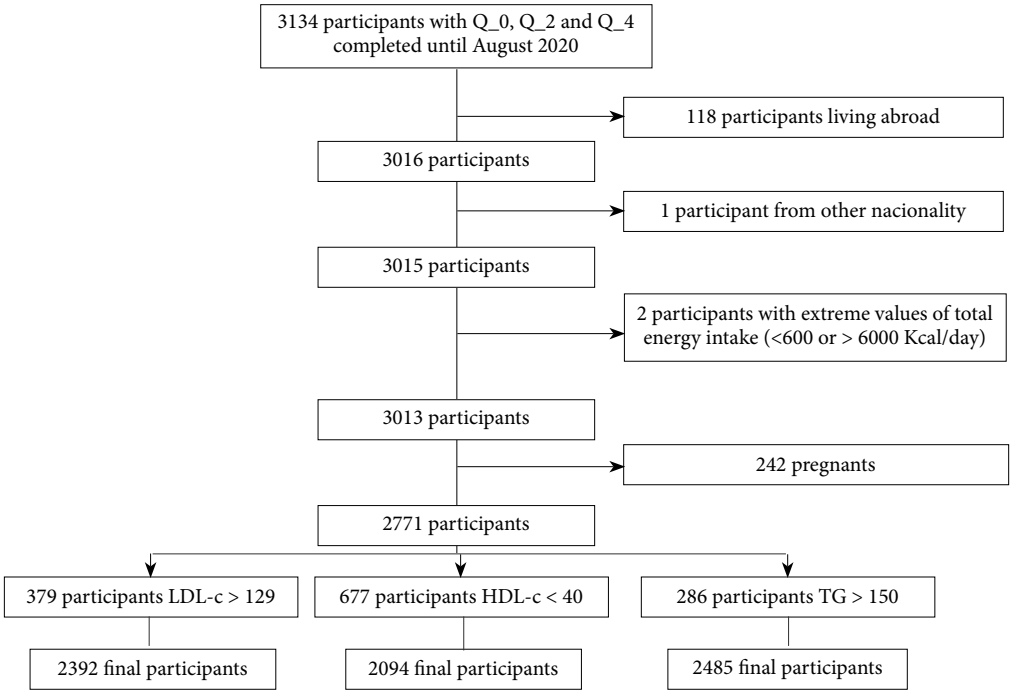

Figura 1. Flowchart demonstrating the inclusion of participants in the Minas Gerais Universities Cohort Study (CUME). Minas Gerais, Brazil, 2016-2020 (n=2771).

Source: Authors.

ey, sweets, among others). The follow-up questionnaires were answered by participants on the same platform and covered the same questions as Q0. These questionnaires aim to evaluate changes in the participants' lifestyle and incidence of diseases during follow-up.

Outcome variable: incidence of dyslipidemia

The criteria used to identify participants with dyslipidemia were having had a medical diagnosis of the disease, having the following tests: high LDL-c (above 129 mg/dL), hypertriglyceridemia (high-TG, above 150 mg/dL) and low-HDL-c (less than 40 mg/dL)[4,20] and use medication for dyslipidemia (simvastatin, fibrates). This information was extracted from the baseline and follow-up questionnaires. Thus, the incidence of dyslipidemia was defined when participants free of this disease at baseline were classified as having dyslipidemia at follow-up. The self-reported criteria of the metabolic syndrome[27] (Body Mass Index - BMI, blood pressure, blood glucose, total triglyceride cholesterol) in a sample of participants in this cohort were validated in a previous study[27] with moderate agreements (k=0.41 to 0.60).

Exposure variable: consumption of foods by degree of processing

The information on food consumption was extracted from a food consumption frequency questionnaire - FCFQ composed of 144 food items previously validated in Brazil with CUME participants[28]. Images of food items with different portion sizes and utensils were provided to participants to obtain a more reliable response to food consumption[29]. A list of items that constituted the food group was presented on each page, and the participant was instructed to select the foods consumed in the previous year. For each selected food, the participant indicated the portion size expressed in household measurements commonly used in Brazil (teaspoon, tablespoon, ladle, knife tip, pasta picker, saucer, cup, and glass) or in traditional portions of the food (unit, slices, and pieces) and the usual frequency of consumption (day/week/month/year). The intake frequencies of each food were transformed into daily consumption. Subsequently, the daily consumption of the food (grams or milliliters) was calculated by multiplying the portion size by the frequency of consumption. The Brazilian table of nutritional composition of foods was used to calculate caloric (kcal) and nutrient intake[30].

Subsequently, food items were characterized by degree of processing according to the NOVA classification as minimally processed foods and culinary ingredients (MPF&CI), processed foods (PF), and ultra-processed foods (UPF)[7,15]. The culinary ingredients group was included in the MPF&CI group since culinary preparations commonly combine unprocessed/minimally processed foods to make drinks, dishes, and meals[31]. The percentage contribution (%) of daily energy intake (calories/day in the diet) of each group, according to the degree of processing, was obtained by adding the energy of each food group and dividing the result by the total energy intake. Subsequently, the values were divided into tertiles for data analysis.

Evaluation of covariates

The covariates evaluated were obtained from the baseline and follow-up questionnaires. These include anthropometric characteristics (and BMI was calculated as weight divided by the square of the body height (in kg/m²). BMI was classified in 3 categories (<25; ≥25<30; and ≥30 kg/m²), sociodemographic (age classified in 3 categories ≤ 30; >30 ≤ 50; and >50; sex female and male) and lifestyle (physical activity classified in 3 categories 1x per week or less; 2 to 4x per week; and 5x per week or more; and smoking classified in 3 categories never; past; and current). The validation study[28] also indicated good accuracy in self-reporting excess weight among the participants.

It is noteworthy that, considering that menopause is a variable that can affect the level of lipid profile, in this study, when categorizing age, we placed a category equal to or above 50 years to try to identify whether women in this age range would have a higher incidence of this problem.

Analysis of results and statistics

According to a medical diagnosis of dyslipidemia, the participants were characterized through absolute and relative frequencies of sociodemographic and anthropometric variables, lifestyle habits, and food consumption using the NOVA classification by the qui-quadrate test.

The longitudinal analysis with Generalized Equation Estimation (GEE) with a binary logistic response model was used to analyze the association between food consumption assessed

by the NOVA classification and the incidence of dyslipidemia. Sex, age, BMI, smoker, and physical activity were used as adjustment variables and evaluated in two models (Model 1 - sex, age, BMI, smoker, physical activity; and Model 2 - Food consumption according to NOVA classification groups). The models were estimated using the Statistical Package for the Social Sciences (SPSS), version 18.0.

Results

Among the 2,771 participants, the majority are female (65.6%, n=1,818), between thirty and fifty years old (56.5%, n=1,567), with BMI less than 25 kg/m² (58, 7%, n=1,628), never smoked (79.6%, n=2,208) and practiced physical activity two to four times a week (64.7%, n=1,793). The incidence of changes in lipid profiles considering the two waves (Q2 and Q4) of CUME follow-up was 27.0% (645) for high-LDL-c, 20.6% (432) for low-HDL-c, and 24.6% (611) for high-TG.

The participants' characteristics, such as sex, age, BMI, physical activity, and smoking profile, regarding the incidence of changes in high-LDL-c, low-HDL-c, and high-triglyceride lipid concentrations, are presented in Table 1. There was a significant relationship ($p<0.05$) between the high LDL-c of participants and the sex, BMI, and smoking parameters, as well as for the consumption of MPF&CI and UPF.

Among the participants with high-LDL-c alterations, 61.7% (398) are female, 56.1% (362) have a BMI less than 25 kg/m², and 76.0% (490) never smoked. Regarding high-triglyceride, amongst 611 participants with alterations, 64.0% (391) are female, 53.5% (327) have BMI less than 25 kg/m², 75.9% (464) have never smoked, and 62.5% (382) practice physical activity from two to four days per week. Similarly, 59.9% (259) of participants with low-HDL-c are female, 56.2% (243) have a BMI between 25 and 30 kg/m², and 62.5% (270) practice physical activity from two to four days per week.

According to the qui-quadrate test, the consumption of MPF&CI and UPF products was significantly associated with the incidence of high-LDL-c and high-triglyceride in the cohort study participants. On the other hand, the consumption of PF affected the incidence of low-HDL-c in participants.

Although in the crude model, participants who consumed a greater proportion of energy from ultra-processed foods were at greater risk of elevated LDL-C and triglycerides and low HDL-C levels, and consuming a greater proportion of minimally processed foods was protective against dyslipidemia, this association did not persist in the adjusted model (Table 2). This indicates that, in this study, food consumption, according to the NOVA classification, was not associated with changes in the lipid profile of CUME participants over the four-year follow-up.

Table 1. Characteristics of participants according to the incidence of high-LDL-c, low-HDL-c and high-triglyceride, CUME Study (n=2,771; 2016-2020).

Variables	high-LDL-c		p-value⁺	low-HDL		p-value	high-triglyceride		p-value⁺
	Yes 27.0% (645)	No 73.0% (1,747)		Yes 20.6% (432)	No 79.4% (1,662)		Yes 24.6% (611)	No 75.4% (1,874)	
Sex			0.001			0.000			0.042
Female	61.7% (398)	68.8% (1,202)		59.9% (259)	71.8% (1,193)		64.0% (391)	68.4% (1,282)	
Male	38.3% (247)	31.2% (545)		40.1% (173)	28.2% (469)		36.0% (220)	31.6% (592)	
Age (years)			0.087			0.134			0.300
≤30	32.4% (209)	37.0% (647)		32.4% (140)	37.3% (620)		33.6% (205)	35.0% (655)	
>30≤50	59.2% (382)	56.0% (978)		57.2% (247)	54.0% (898)		58.4% (357)	55.3% (1,037)	
>50	8.4% (54)	7.0% (122)		10.4% (45)	8.7% (144)		8.0% (49)	9.7% (182)	

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Table 1. Characteristics of participants according to the incidence of high-LDL-c, low-HDL-c and high-triglyceride, CUME Study (n=2,771; 2016-2020).

Variables	high-LDL-c		p-value⁺	low-HDL		p-value	high-triglyceride		p-value⁺
	Yes 27.0% (645)	No 73.0% (1,747)		Yes 20.6% (432)	No 79.4% (1,662)		Yes 24.6% (611)	No 75.4% (1,874)	
BMI (kg/m²)			0.006			0.000			0.000
<25	56.1% (362)	63.2% (1,105)		56.2% (243)	63.5% (1,055)		53.5% (327)	64.2% (1,203)	
≥25<30	32.4% (209)	26.9% (469)		28.7% (124)	27.9% (464)		34.0% (208)	26.7% (500)	
≥30	11.5% (74)	9.9% (173)		15.1% (65)	8.6% (143)		12.4% (76)	9.1% (171)	
Smoking status			0.003			0.875			0.000
Never	76.0% (490)	82.0% (1,432)		78.7% (340)	79.6% (1,323)		75.9% (464)	81.7% (1,532)	
Past	13.2% (85)	10.2% (179)		12.5% (54)	11.6% (193)		11.8% (72)	11.4% (213)	
Current	10.8% (70)	7.8% (136)		8.8% (38)	8.8% (146)		12.3% (75)	6.9% (129)	
Physical activity			0.566			0.012			0.000
1x/week or less	28.5% (184)	22.1% (387)		29.2% (126)	23.9% (398)		28.6% (175)	21.6% (405)	
2 to 4x/ week	62.0% (400)	65.1% (1,137)		62.5% (270)	63.4% (1,053)		62.5% (382)	65.7% (1,231)	
5x/week or more	9.5% (61)	12.8% (223)		8.3% (36)	12.7% (211)		8.8% (54)	12.7% (238)	
MPF&CI*			0.007			0.097			0.006
Tertile1	38.8% (250)	31.9% (557)		37.7% (163)	33.3% (553)		38.0% (232)	31.3% (586)	
Tertile 2	30.4 % (196)	33.9% (592)		32.0% (138)	32.7% (544)		31.4% (192)	33.3% (624)	
Tertile 3	30.8 % (199)	34.2 % (598)		30.3% (131)	34.0% (565)		30.6% (187)	35.4% (664)	
PF**			0.230			0.012			0.261
Tertile 1	32.4% (209)	35.6% (621)		32.4% (140)	34.1% (566)		32.7% (200)	35.8% (671)	
Tertile 2	34.1% (220)	31.3% (547)		29.6% (128)	32.7% (544)		32.6% (199)	32.0% (599)	
Tertile 3	33.5% (216)	33.1% (579)		38.0% (164)	33.2% (552)		34.7% (212)	32.2% (604)	
UPF***			0.004			0.834			0.013
Tertile 1	30.1% (194)	35.1% (614)		33.3% (144)	34.1% (567)		32.7% (200)	35.9% (672)	
Tertile 2	31.6% (204)	33.4% (583)		32,2% (139)	32.6% (542)		30.3% (185)	33.1% (620)	
Tertile 3	38.3% (247)	31.5% (550)		34.5% (149)	33.3% (553)		37.0% (226)	31.0% (582)	

Notes: The percentages were expressed based on participants classified as YES and NO for each evaluated lipid (high-LDL-c, low-HDL-c, high-TG). ⁺p-values according to trend $\chi 2$ test. *Energy consumption of minimally processed foods and culinary ingredients (T1: ≤60.7%, T2: >60.7≤71.3%; T3: >71.3%). **Energy consumption of processed foods (T1: ≤7.2%; T2:>7.2≤11.7%; T3: >11.7%;). ***Energy consumption of ultra-processed foods (T1: ≤19.8%; T2: >19.8≤28.8%; T3: >28.8%). Difference was evaluated by the χ^2 test. BMI=Body mass index.

Source: Authors.

Table 2. Relative risk (RR) and 95% Confidence Interval (CI) for the incidence of alterations in lipid profile according to the degree of processing of foods (NOVA classification) over the six years (2016-2020), CUME Study (n=2,771).

Parameters	Energy consumption according to NOVA classification					
	Tertile 1	Tertile 2		Tertile 3		
	RR	RR	CI 95%	RR	CI 95%	P trend
High LDL-c						
MPF&CI						
Model 1	1(ref)	0.844	0.652-1.093	1.003	0.713-1.411	0.200
Model 2	1(ref)	0.837	0.646-1.084	0.980	0.697-1.376	0.216
PF						
Model 1	1(ref)	1.166	0.947-1.437	1.050	0.824-1.337	0.310
Model 2	1(ref)	1.217	0,987-1.500	1.157	0.914-1.465	0.180
UPF						
Model 1	1(ref)	1.225	0.964-1.557	1.463	1.056-2.026	0.700
Model 2	1(ref)	1.180	0.930-1.497	1.335	0.967-1.842	0.202
Low-HDL-c						
MPF&CI						
Model 1	1(ref)	0.901	0.659-1.231	0.833	0.542-1.280	0.696
Model 2	1(ref)	0.868	0.634-1.189	0.776	0.501-1.202	0.513
PF						
Model 1	1(ref)	0.789	0.606-1.026	0.942	0.698-1.272	0.168
Model 2	1(ref)	0.845	0.649-1.101	1.053	0.782-1.417	0.223
UPF						
Model 1	1(ref)	1.051	0.760-1.454	0.907	0.594-1.384	0.639
Model 2	1(ref)	1.058	0.765-1.463	0.845	0.554-1.290	0.365
High-Triglyceride						
MPF&CI						
Model 1	1(ref)	0.915	0.701-1.193	0.975	0.674-1.411	0.736
Model 2	1(ref)	0.855	0.656-1.113	0.884	0.613-1.275	0.500
PF						
Model 1	1(ref)	1.070	0.859-1.333	1.101	0.858-1.414	0.734
Model 2	1(ref)	1.111	0.892-1.383	1.188	0.930-1.518	0.378
UPF						
Model 1	1(ref)	1.024	0.791-1.325	1.201	0.855-1.688	0.463
Model 2	1(ref)	1.047	0.807-1.357	1.190	0.848-1.670	0.557

Model 1: adjusted by sex, age, BMI, smoking status and physical activity. Model 2: adjusted by food consumption according to NOVA classification groups. RR=Odds ration.

Source: Authors.

Discussion

In the present study, most participants are women, under 50 years of age, with a BMI below 25 kg/m², who practice physical activity between 2 and 4 times a week and have never smoked. According to the qui-quadrate test (crude analyses), sex and BMI were associated with altered levels of the three serum lipids evaluated; the practice of physical activity was associated with changes in HDL-c and triacylglycerols; the use of cigarettes and consumption of ultra-processed foods were associated with changes in LDL-c and triacylglycerols; while the consumption of natural foods was associated with changes in LDL-c.

The study by Sousa *et al.*[6], carried out with data from VIGITEL, shows that up to 44 years of age, the prevalence of dyslipidemia in the Brazilian population is very similar between men and women, and after this age, there is a difference in the prevalence of this problem. There is sufficient evidence in the literature to support the claim that excess weight, physical inactivity, and high consumption of UPF are risk factors for dyslipidemia[13,14,32-34] and that consumption of natural foods is a protective factor[35].

Also, in the crude analysis, greater intake of MPF&CI is associated with protection against changes in lipid metabolism. Natural foods provide high percentages of fiber and contain vitamins and minerals that have potential antioxidant and anti-inflammatory effects on the body, thus protecting against dyslipidemia and the emergence of NCDs[36]. Furthermore, the fibers present in MPF&CI contribute to the body's intestinal health. Several studies have indicated that alterations in microbiota diversity caused by an inadequate diet can modulate mechanisms that favor the emergence of cardiovascular diseases, including dyslipidemia[37,38]. The consumption of UPF showed a strong association with imbalances in serum parameters of high-LDL-c lipoproteins and high triglycerides.

These findings corroborate other research in which individuals with a poor diet, including high percentages of industrialized products, high energy intake, and high consumption of simple carbohydrates and trans and saturated fats, may be more susceptible to developing metabolic disorders[11,39,40]. UPFs are industrial formulations high in added sugars, fats (mainly trans and saturated fats), salt, and additives, but low in fiber and micronutrients[24]. Their impact on lipid metabolism involves several interrelated mechanisms such as hepatic de novo lipogenesis promoted by excess of calorie consumption, especially from refined sugars; atherogenic lipid profile (high LDL-c and lower HDL-c) due to high saturated and trans-fat content; increased inflammatory markers (e.g., CRP, IL-6, TNF-α), which inhibit insulin signaling and lipid metabolism regulation; promote gut dysbiosis by reducing microbial diversity and increasing pro-inflammatory species; and others[14,24]. On the other hand, a healthy gut microbiota helps maintain lipid balance through short-chain fatty acids (SCFAs) production**,** regulating lipogenesis, cholesterol synthesis, and fat oxidation in the liver; bile acids deconjugation, and increasing their excretion; promoting anti-inflammatory effects, and others[41].

Despite these results observed in the crude analysis, these associations were not maintained in the adjusted model. It was found that despite the high incidence of dyslipidemia over four years of follow-up of the CUME, energy consumption from ultra-processed, processed, and natural or minimally processed foods was not associated with this outcome.

Among the risk factors for dyslipidemia, there are modifiable factors, such as food consumption, cigarette use, physical activity, and BMI, and non-modifiable factors such as sex and age. And among these factors, lifestyle has been the most associated with this problem[2].

Dyslipidemia is considered when alterations in blood lipids are observed. LDL-c is a lipoprotein that carries cholesterol to cells; its excess can cause the accumulation of cholesterol in the arteries, forming plaques that can hinder or impede blood flow, increasing the risk for hypertension or cardiovascular events (stroke and heart attack). On the other hand, HDL-c is the lipoprotein responsible for reducing circulating cholesterol, which is deposited in blood vessels to be metabolized by the liver. Furthermore, there is evidence of this lipoprotein's antioxidant, anti-inflammatory, and antiplatelet properties[2,32]. Triglycerides are the energy reserve in the human body in the form of fat and are commonly found in the body. When foods rich in carbohydrates and fats are consumed in excess, the level of triglycerides may be elevated.

Despite the effects of UPF, PF, and MPF&CI on dyslipidemia[42-44], in this study, we did not identify a protective or risk effect of these foods for this outcome. In the study of Lima *et al.*[42], with adolescents, it was found that a higher UPF intake was negatively associated with HDL-c levels and positively associated with triglyceride levels and dyslipidemia. Therefore, UPF is associated with a worsening of the nutritional profile of the diet and contributes to negative changes in the lipid parameters of young individuals. A prospective study with older adults identified that those in the highest versus the lowest tertile of energy intake from UPFs had more than twice the odds of incident hypertriglyceridemia or low HDL cholesterol. However, UPF consumption was not associated with high LDL cholesterol plasma concentrations[43]. Another prospective study with Korean adults identified that higher UPF intakes assessed by the NOVA are associated with increased incidences of dyslipidemia and obesity[44].

Although energy intake from UPF, PF and MPF&CI was not associated with risk or protection for dyslipidemia in this study, it is important to highlight that studies about diets based on the degree of food processing according to NOVA classification have demonstrated that the current diet presents a reduced intake of fruits and vegetables, provides a greater amount of energy and saturated fat, has a high glycemic index, and reduced consumption of fiber, vitamins, and minerals[21,22]. This type of diet is directly associated with the risk of NCDs, such as obesity, diabetes, hypertension, dyslipidemia, cardio and

cerebrovascular diseases, and cancer in general[39,40]. Furthermore, the level of development of the countries and characteristics of populations, such as age, sex, culture, and others, may be associated with UPF consumption[13,33].

Despite the social inequality in Brazil, globalization, technology, and urbanization have led to a large-scale consumption of UPF due to the urgency of fast preparation. The insertion of women in the job market, who until now have been socially responsible for planning meals and preparing food, has drastically changed people's diets[32]. A decrease in the consumption of natural and healthy products and the potential consumption of quickly prepared foods, which are industrialized and ultra-processed, have been observed. Further, this is accompanied by a high consumption of animal protein diets rich in simple carbohydrates and a higher content of trans and saturated fats[45].

Some limitations must be considered when interpreting our results. The sample may only represent some alumni of the universities included in this study, as it is a Web Survey with a return rate of approximately 4%. However, this type of research offers an excellent opportunity to collect real-time data to monitor and understand different diseases in various settings, and it is low-cost research. Another limitation is that errors may occur in the non-differential classification of dyslipidemia, especially in underdiagnosed (false-negative) cases, as the study participants provided this information. However, blood lipid values and BMI were duly validated with a sample of participants in this cohort[27].

Furthermore, the difficulty in establishing a single criterion for characterizing dyslipidemia can be also a limitation of this study, since it is a disease with multiple factors such as the history and physical examination of the patient, the lipid profile including total cholesterol, LDL-c, HDL-c, non-HDL-c, triglycerides, glycated hemoglobin or fasting plasma glucose, and estimated glomerular filtration rate[34]. Moreover, it must be considered that food consumption was based on a self-report in an FCFQ of 144 food items and that, even having been previously validated[26-29], some information can be inaccurate.

In the unadjusted model, a higher proportion of energy intake from ultra-processed foods was associated with an increased risk of elevated LDL-C and triglyceride levels, as well as reduced HDL-C levels, whereas a higher proportion of minimally processed foods appeared to confer protection against dyslipidemia. However, these associations were no longer significant after adjustment for potential confounders. This finding suggests that, within the present study, dietary patterns classified according to the NOVA system were not independently associated with alterations in the lipid profile of CUME participants over the four-year follow-up period. It is possible that other, unmeasured factors may have influenced these results, underscoring the need for further research to clarify this relationship.

Collaborations

DJMM Nunes: conceptualization, investigation, methodology, data curation, formal analysis, visualization, and original draft writing. CL Ramos: conceptualization, project administration, methodology, writing, review, and validation. LN Nobre: conceptualization, methodology, writing, review, and validation. AM Pimenta: writing, review, and validation. HHM Hermsdorff: writing, review, and validation. J Bressan: writing, review, and validation. All authors have read and approved the final version of the manuscript.

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Data availability statement

All data described in the manuscript and analytic code will be made available upon request, pending reasonable solicitation and approval of the CUME team.

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