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Exploring the link between dietary patterns and gastric adenocarcinoma in Brazil: a mediation analysis

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Abstract

Background The causal pathway between different dietary patterns (DPs) and gastric adenocarcinoma (GA) remains largely unexplored. The study aimed to identify DPs and evaluate how selected nutrients mediate the relationship between DPs and GA.

Methods This multicenter case–control study in Brazil involved 1751 participants (600 cases, 377 endoscopic controls, and 774 hospital controls). DPs were identified through exploratory factor analysis. A counterfactual-based mediation analysis was performed to decompose the total effect of DPs on GA into direct and indirect effects mediated by saturated fatty acids, added sugars, total fiber, and sodium intakes. Effects were expressed as ORs and 95% CIs.

Results Two DPs were identified—“unhealthy dietary pattern” (UDP) and “healthy dietary pattern” (HDP), which were associated with an increased and decreased risk of GA, respectively. Added sugars partly mediated the association between UDP and GA (percentage mediated between 7.3 and 21.7%), while sodium intake mediated most of the association between HDP and GA (percentage mediated between 52.4 and 100%). No significant mediating effects were detected for saturated fatty acids and total fiber.

Conclusions This study contributes innovative insights into the DPs-GA relationships, highlighting the significant mediating roles of sodium and added sugars, offering valuable information for preventive strategies and public health interventions targeting GA.

Keywords Gastric cancer, Cancer prevention, Nutrients, Added sugars, Sodium, Mediation analysis, Risk factors, Dietary patterns, Case–control study

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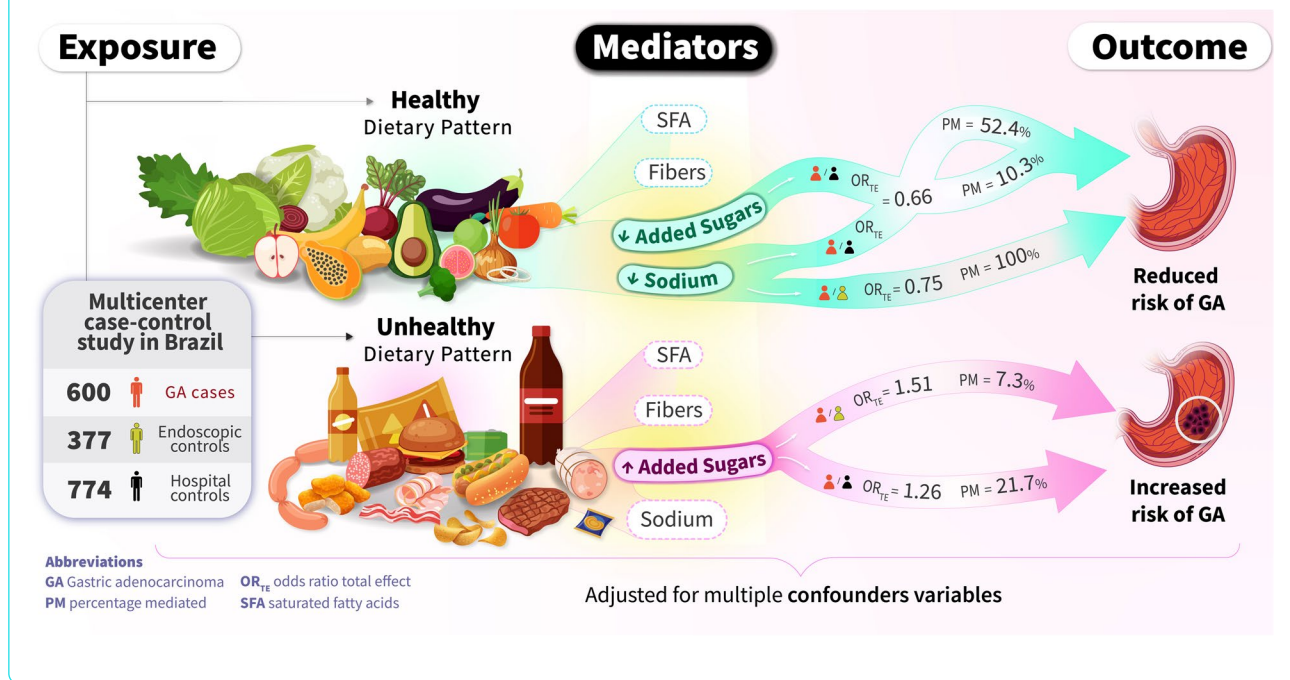
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Graphical Abstract



Background

The incidence and mortality of gastric cancer (GC) have decreased in recent decades, but it is still the fifth most incident and the fifth in cancer mortality worldwide [1, 2]. Notably, in the Americas, there is a rising trend in GC incidence attributed to aging and growing of high-risk populations [3]. In Brazil, an estimated 21,480 new cases are expected from 2023 to 2025, positioning GC as the fifth most frequently diagnosed cancer in the country [4].

Gastric adenocarcinoma (GA) is the predominant histological type, accounting for 90% of all GC cases. The primary risk factor for non-cardia GA is *Helicobacter pylori* (*H. pylori*) infection, implicated in 90% of cases [5, 6]. GA is also associated with modifiable risk factors, notably the diet. Diet factors include alcohol consumption, excessive salt, nitrites, nitrates, red and processed meats, preserved foods, high-fat diets rich in saturated fatty acids (SFA), sucrose, cholesterol, and animal proteins. Conversely, protective factors for GA are related to consumption of diets rich in polyunsaturated fatty acids, vegetable fats (from olive oils, nuts), fruits, vegetables, fibers, and whole grains [7–9].

The conventional approach to studying the relationship between diet and cancer has typically focused on individual foods or nutrients, disregarding the broader perspective of dietary patterns. The complexity arises from the interrelationship of various dietary

factors [10, 11]. The United States 2020–2025, Dietary Guidelines, advocate shifting emphasis towards understanding overall dietary patterns, instead of looking exclusively at a single dietary component [12]. Dietary pattern analysis is preferred to the single food/nutrient approach because it considers how people typically combine different foods and drinks in their diet. This allows to capture the complex interplay between various dietary components, providing a more complete picture than focusing on individual foods or nutrients [10, 11]. A more recent review on dietary patterns and GC identified that “Western/Unhealthy” diets, rich in starchy, meat, fats, and alcohol, associated with an increased GA risk, while “Prudent/Healthy” diets, abundant in fruits and vegetables, were associated with reduced risk [13, 14]. Others subsequent original research have been conducted [10, 15–18]. The only study on dietary patterns and GA in Brazil, conducted in a single center in Goiânia (Goiás state), identified three dietary patterns but they did not analyze the association between these patterns and GA risk [19]. Moreover, little is known regarding the role of varying levels of nutrient intakes, which characterize the identified dietary patterns, on the evaluate potential mechanisms of action these patterns to GA risk.

Therefore, our study aims to identify dietary patterns within the Brazilian population and explore the

causal pathway linking the identified patterns to the associated risk of GA.

Methods

Study population and design

GE4GAC-Brazil is a large, hospital-based, multicenter case–control study carried out in five capitals of different Brazilian regions [20]. Briefly, all cases were diagnosed with GA, confirmed by histology, and coded according to the International Classification of Diseases in Oncology (C16). Two control groups were used. The control I included participants with gastric complaints who underwent endoscopy, with a negative diagnosis for GC or a premalignant lesion. Control II was composed of hospital individuals, without gastric disorders or gastric cancer, recruited from ophthalmology, traumatology, physiotherapy, and nutrition clinics and from cancer prevention programs organized by hospitals. The exclusion criteria for participants were previous malignancy, except for non-melanoma skin cancer; participants with impaired mobility due to illness or mental and cognitive conditions that prevented them from understanding the questions asked by the interviewers; and cases that had been diagnosed with GA more than 2 years prior to the interview or those with advanced cancer (i.e., terminal stage with no feasible chance of survival). The study was approved by the Committee on Ethics in Human Research of Antônio Prudente Foundation—A.C.Camargo Cancer Center, as well as the local ethics committees of the study centers, under registration on the Brazil platform linked to the National Health Council of Brazil (grant no. 4708881–February 2016, registration CAAE: 53,166,915.9.1001.5432). All participants provided written informed consent for data collection and storage.

This study used a database from four Brazilian capitals with complete data collection, São Paulo (São Paulo state; southeastern region/metropolitan), Belém (Pará state; northern region/Amazon Rainforest), Goiânia (Goiás state; central-western region/agrobusiness), and Fortaleza (Ceará state; northeast region/coastal). Recruitment was conducted from April 2016 to November 2023. In the central-western and northeast regions, pairing was not performed. All participants provided written informed consent for data collection and storage.

Participants with no dietary data information and implausible energy intake (< 500 or > 5000 kcal per day) [21] were excluded. A total of 1751 participants: 600 cases, 377 control I, and 774 control II, were included in the study (Fig. 1).

Data collection

Face-to-face interviews were conducted at baseline by trained personnel using an online structured epidemiological questionnaire on the REDCap® platform. Anonymized data were recorded on the platform at participating centers. We collected data on sex (female or male), age (years), education (≤ 8 years = illiterate to elementary school, 9 to 12 years = high school, and ≥ 13 years = higher education), and lifestyle habits (i.e., alcohol consumption and tobacco smoking). To calculate alcohol consumption (g/day), we used a previously reported method [22] and we classify as no consumption, low consumption (≤ 12 g/day), or moderate/higher (> 12 g/day alcohol) consumptions [23], while tobacco smoking was calculated in packs/year [24] and we classify as no consumption, low consumption (≤ 10 packs/year), or intermediate/higher (> 10 packs/year) consumptions [23].

Information was collected on the presence peptic ulcer (yes or no) and clinical data/family history of cancer in first-degree relatives (yes or no). Additionally, in accordance with the guidelines of the World Health Organization (WHO), we measured weight (kg) and height (m) for the calculation of body mass index (BMI, kg/m^2) and BMI category (< 18.5 , 18.5 – 24.9 , 25 – 29.9 , ≥ 30 kg/m^2) [25]. For cases, clinical information on anatomical location (cardia or non-cardia), tumor histological subtype (diffuse, intestinal, or mixed) [26], and status of *H. pylori* infection (positive or negative) were collected from medical records, the latter also having been collected for control I individuals based on gastric endoscopy reports.

Assessment of dietary patterns

To assess food and nutrient intakes of study participants, we used a validated food frequency questionnaire (FFQ) containing 130 food items [27]. The FFQ asked about their usual food consumption over the past year. Each item was collected based on the frequency and portion size: (1) frequency of food consumption—ranging from 1 to 10 times daily, weekly, monthly, or yearly and (2) size of the portion ingested—small, medium, or large (each food had its portion in grams and its equivalent in slices, spoons, and/or cups/glasses). Consumption of each item was calculated in grams per day.

Nutrient intake was determined using the Nutrition Data System for Research software—NDSR® version 2021 (Minneapolis, MN, USA). Nutrients were energy adjusted using the density method per 1000 kcal [28].

The 130 food items listed in the FFQ were grouped into 31 food groups based on similarities of nutrient profiles and culinary usage (Table S1).

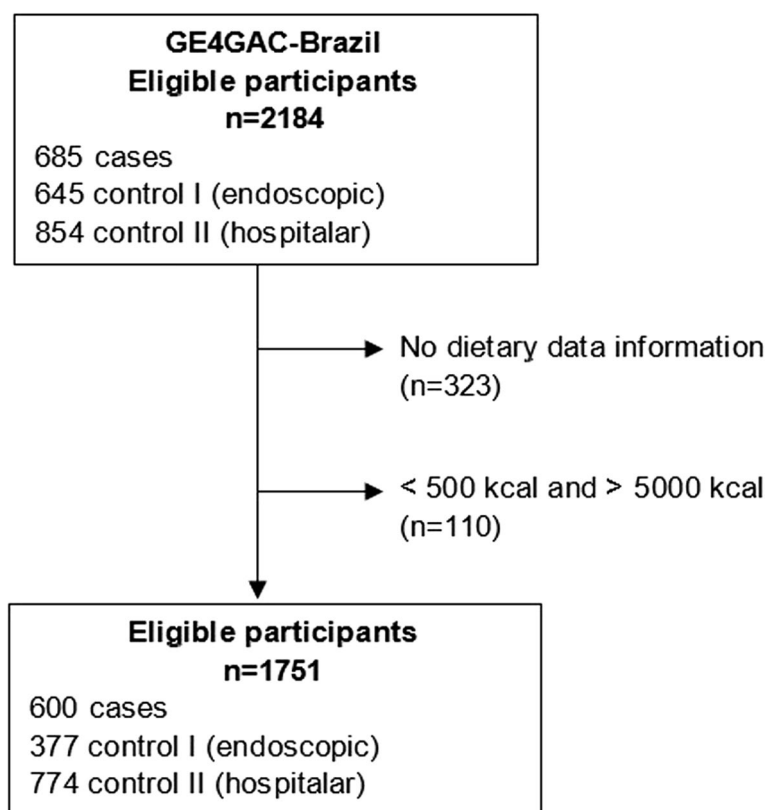


Fig. 1 Flow chart of study population selection

We conducted an exploratory factor analysis to extract dietary patterns potentially linked to GC from the 31 food groups. Initially, these food consumption data were recorded in grams per day, but they exhibited a right-skewed distribution and zero-inflation. To address this, we categorized the data into ordinal variables with four categories based on tertiles computed among consumers: (1) no consumption, (2) < 1 tertile, (3) ≥ 1 and < 2 tertile, and (4) ≥ 2 tertile. We then conducted an exploratory factor analysis using a polychoric correlation matrix calculated from the 31 food groups. We opted for the polychoric correlation matrix over the Pearson correlation matrix because the latter assumes continuous variables following a multivariate normal distribution. We assessed the adequacy of the polychoric correlation matrix using Bartlett's test of sphericity, where a significant result indicates that the matrix is suitable for factor analysis. Additionally, we considered the overall Kaiser–Meyer–Olkin (KMO) measure of sampling adequacy, with a value greater than 0.80 indicating suitability for factor analysis. The principal factor solution was used as factoring method. To determine the number of factors to retain, we considered the scree plot, the eigenvalue > 1 criterion, and the interpretability of the retained factors.

Factor loadings were obtained through varimax rotation, and food groups were assigned to factors based on their highest contribution. The names of the rotated factors were derived from the variables with the strongest correlations. The factor analysis was performed using the “fa” function of the R package “psych.”

Association between dietary patterns and gastric cancer risk

To assess the association between the dietary patterns and the risk of GA, participants were categorized into four groups based on quartiles of factor scores within the control population. We then estimated the odds ratios (OR) and their corresponding 95% confidence intervals (95% CI) for each group using multivariable logistic regression models. The group with the lowest factor score served as the reference category. The models were adjusted for the following covariates: sex, age (continuous), education, family history of cancer, BMI category, tobacco smoking, alcohol consumption, study region, and energy intake (continuous). Additionally, for control I, we adjust for peptic ulcer and *H. pylori* status. We also conducted tests for linear trend by regressing the OR on the midpoint of the limits defining the factor score groups.

All tests were two-sided, and the significance level (α) was 5%. Analyses were performed using the software STATA® 17.0 (College Station, TX, USA).

Mediation analysis

To further explore the role of specific nutrients within the dietary pattern, we conducted a mediation analysis to decompose the total effect of the dietary pattern into direct and indirect effect mediated by a priori defined set of nutrients. This set included SFA (% of kcal), added sugars (% of kcal), total fiber (g/1000 kcal), and sodium (g/1000 kcal) intakes. These nutrients are relevant sources of concern in the diet of many Brazilians who tend to have a high intake of SFA, added sugars, and sodium and low intake of fiber [29–31]. The exposure variables in this analysis were the factor scores (in continuous) related to the two dietary patterns identified in the factor analysis.

The mediation analysis employed the technique described by Yu and Li [32], implemented in the R package “mma.” This technique allows for the simultaneous consideration of multiple mediators of different types, enabling the separation of individual mediators’ indirect effects from the total effect.

The *mma* package includes a function to identify mediators, i.e., variables significantly associated to both the predictor and the outcome. Variables that did not meet both conditions were considered as covariates. To identify mediators, we set the alpha values for association at 0.1. The directed acyclic graph (DAG) which depicts the hypothesized causal model is shown in Fig. 2. General

linear models were used to fit the variable relationships and to estimate the mediation effects, which were presented as OR (95% CI). The OR for the indirect effects indicates the effect of the dietary patterns on GA risk conveyed by the mediator.

The percentage mediated (PM) was calculated as the ratio of the indirect effect to the total effect, both on the log scale, and then multiplied by 100. Inferences on the mediation effects were made using the bootstrap method with 500 resamples.

We conducted separate mediation analyses using control group I or II. For control I, we employed regression models with a complete set of covariates, including also adjustments for peptic ulcer and *H. pylori* infection.

Results

The cases were predominantly males (59.0%), with a median age of 58 years, and education levels ≤ 8 years (52.7%). Approximately 62.8% of the cases had a family history of cancer in first-degree relatives, 41.1% exhibited intermediate/high tobacco smoking, and 47.5% reported intermediate/high alcohol consumption. Additionally, 11.0% had peptic ulcer disease, and 41.6% were obese, with a median energy intake of 2265 kcal, which was higher than that observed in the control groups ($p < 0.001$). Most cases (78.3%) had GA located in the non-cardia region, and 48.7% were classified as diffuse type (Table 1).

The Bartlett test of sphericity ($p < 0.001$) and the KMO (0.85) indicated the adequacy of the correlation matrix for factor extraction. Consequently, we proceeded with

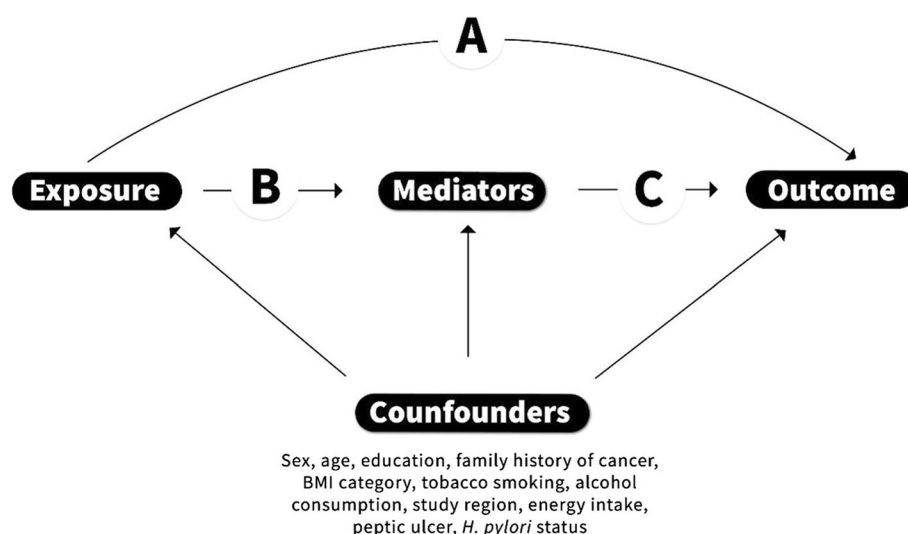


Fig. 2 Directed acyclic graph dietary patterns’ relation to gastric adenocarcinoma risk and effect decomposition. Arrow A displays the direct effect (DE) of dietary patterns on gastric adenocarcinoma risk, while path B + C displays the indirect effect (IE) mediated by the sodium, added sugars, fibers, and saturated fatty acids. The sum of DE and IE gives the total effect

Table 1 Characteristics of the cases and controls enrolled in the study, GE4GAC-Brazil (2016–2023)

Variables	GE4GAC-Brazil <i>n</i> = 1751			<i>p</i> -value ¹
	Cases <i>n</i> = 600	Control I <i>n</i> = 377	Control II <i>n</i> = 774	
	Median (P ₂₅ , P ₇₅) or <i>n</i> (%)			
Sex				0.001
Female	246 (41.0)	195 (51.7)	378 (48.8)	
Male	354 (59.0)	182 (48.3)	396 (51.2)	
Age (years)	58 (49, 66) ^a	57 (44, 64) ^b	55 (44, 64) ^b	< 0.001
Education (years) †				< 0.001
≤ 8	316 (52.7)	96 (25.5)	172 (22.2)	
9 – 12	55 (9.2)	46 (12.2)	89 (11.5)	
≥ 13	229 (38.1)	235 (62.3)	513 (66.3)	
Family history of cancer in first-degree relatives				< 0.001
No	374 (62.8)	217 (57.7)	382 (49.5)	
Yes	222 (37.2)	159 (42.3)	390 (50.5)	
Tobacco smoking §				< 0.001
No	100 (16.8)	66 (17.6)	107 (13.9)	
Low	250 (42.1)	82 (21.9)	171 (22.2)	
Intermediate/High	244 (41.1)	277 (60.5)	492 (63.9)	
Alcohol consumption ¥				< 0.001
No	102 (17.4)	90 (24.2)	106 (13.9)	
Low	206 (35.1)	102 (27.4)	148 (19.5)	
Moderate/High	279 (47.5)	180 (48.4)	507 (66.6)	
Peptic ulcer				0.001
No	504 (89.0)	358 (95.0)		
Yes	62 (11.0)	19 (5.0)		
<i>H. pylori</i> status*				0.262
Negative	148 (74.0)	232 (69.5)		
Positive	52 (26.0)	102 (30.5)		
BMI (kg/m ²)				< 0.001
< 18.5	173 (29.8)	24 (6.4)	82 (10.7)	
18.5 – 24.9	91 (15.7)	118 (31.5)	222 (29.0)	
25.0 – 29.9	75 (12.9)	86 (22.9)	140 (18.3)	
≥ 30	241 (41.6)	147 (39.2)	321 (42.0)	
Energy intake (kcal/day)	2265 (1686, 2885) ^a	2080 (1518, 2675) ^b	1780 (1337, 2375) ^c	< 0.001
Anatomical location				
Cardia	108 (21.7)			
Non-cardia	390 (78.3)			
Histological subtype				
Diffuse	213 (48.7)			
Intestinal	198 (45.3)			
Mixed	26 (6.0)			

Numbers may differ because of missing values. Control I individuals (endoscopic controls); Control II individuals (hospital controls). † ≤ 8 years = Illiterate to elementary school, 9 to 12 years = High school and ≥ 13 years = Higher education. § Low smoking: ≤ 10 packs/year and Intermediate/High smoking: > 10 packs/year. ¥ Low: ≤ 12 g/day and Moderate/High: > 12 g/day alcohol. * 400 cases and 43 control I individuals were not tested. ¹ Pearson χ^2 test for categorical variables. Kruskal–Wallis test with a Dunn–Bonferroni post hoc test for continuous variables. Different letters on the same line mean statistical difference between groups. Significance *p*-value < 0.05

a factor analysis involving two latent factors. Figure 3 shows the factor loading matrix for the two latent factors. Collectively, these two factors explained 25.8%

of the variance. Factor 1 explained 13.1% of the total variance and was characterized by high factor loadings (≥ 0.6) for the food groups “preserved, processed and

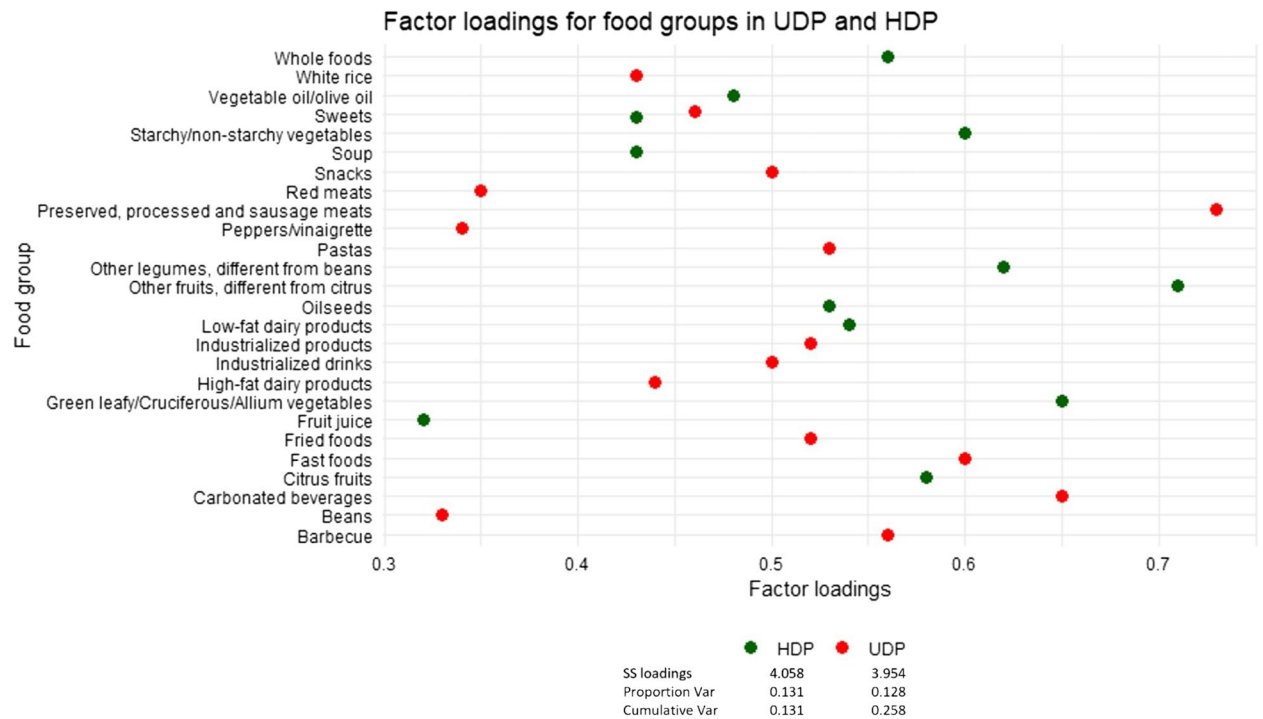


Fig. 3 Factor loading matrix for food groups in two dietary patterns from factor analysis extraction. Abbreviations: HDP, healthy dietary pattern; UDP, unhealthy dietary pattern. Only factor loadings with absolute value > 0.30 are shown

sausage meats,” “carbonated beverages,” and “fast food.” We named factor 1 “unhealthy dietary pattern” (UDP). Factor 2 explained 12.7% of the total variance and exhibited high factor loadings (> 0.6) for the food groups “other fruits, different from citrus,” “green leafy/cruciferous/allium vegetables,” “starchy/non-starchy vegetables,” and “other legumes, different from beans.” We named factor 2 “healthy dietary pattern” (HDP).

Figure 4 shows the OR and the corresponding 95% CI for the association between the dietary patterns and GC. The estimates were obtained using different types of controls and adjustments. In the analysis using control I, we found a significant increased risk associated with the UDP, and no significant association with the HDP. The OR for participants with the highest factor score (G4) for UDP compared to those with the lowest score (G1) was 1.70 (95% CI: 1.01–2.05) in the partially adjusted model and 3.96 (95% CI: 1.75–8.96) in the fully adjusted model. In the analysis using control II, we found a positive association with the UDP (OR_{G1vsG4}: 2.17, 95% CI: 1.39–3.39) and a negative association with the HDP (OR_{G1vsG4}: 0.50, 95% CI: 0.32–0.78). The test for trend indicated a significant linear trend in the associations mentioned above.

Individuals with elevated scores in the UDP showed higher consumption of animal protein, added sugars, total fat, SFA, monounsaturated fatty acids (MUFA),

and sodium and lower intake of total fiber and total carbohydrates. On the other hand, those with higher scores in the HDP had increased consumption of vegetable protein, total carbohydrates, added sugars, MUFA, and total fiber, while reducing their intake of total protein, animal protein, and sodium (Table S2).

Table 2 presents the mediation analysis results. The estimates of the effects of each dietary pattern are presented as OR for GC associated with 1-point increase in the dietary factor score. Added sugars was a significant mediator in the association between UDP and GA, as indicated in both analyses involving control I (PM: 7.3%, $p=0.04$) and control II (PM: 21.7%, $p<0.01$).

Regarding HDP, the total effect of HDP was an OR of 0.75. Given that the OR for the indirect effect of sodium was 0.64 (an effect greater than the total effect), it indicates that sodium intake fully mediated the association with GA in control I (100%, $p<0.01$). In the control II analysis, sodium intake partially mediated the association between HDP and GA (PM: 52.4%, $p<0.01$). Added sugars mediated 10.3% of the association between HDP and GA ($p<0.01$) in the control II analysis. Neither fiber nor SFA intakes showed significant mediation effects in the association between dietary patterns and GA (Table 2).

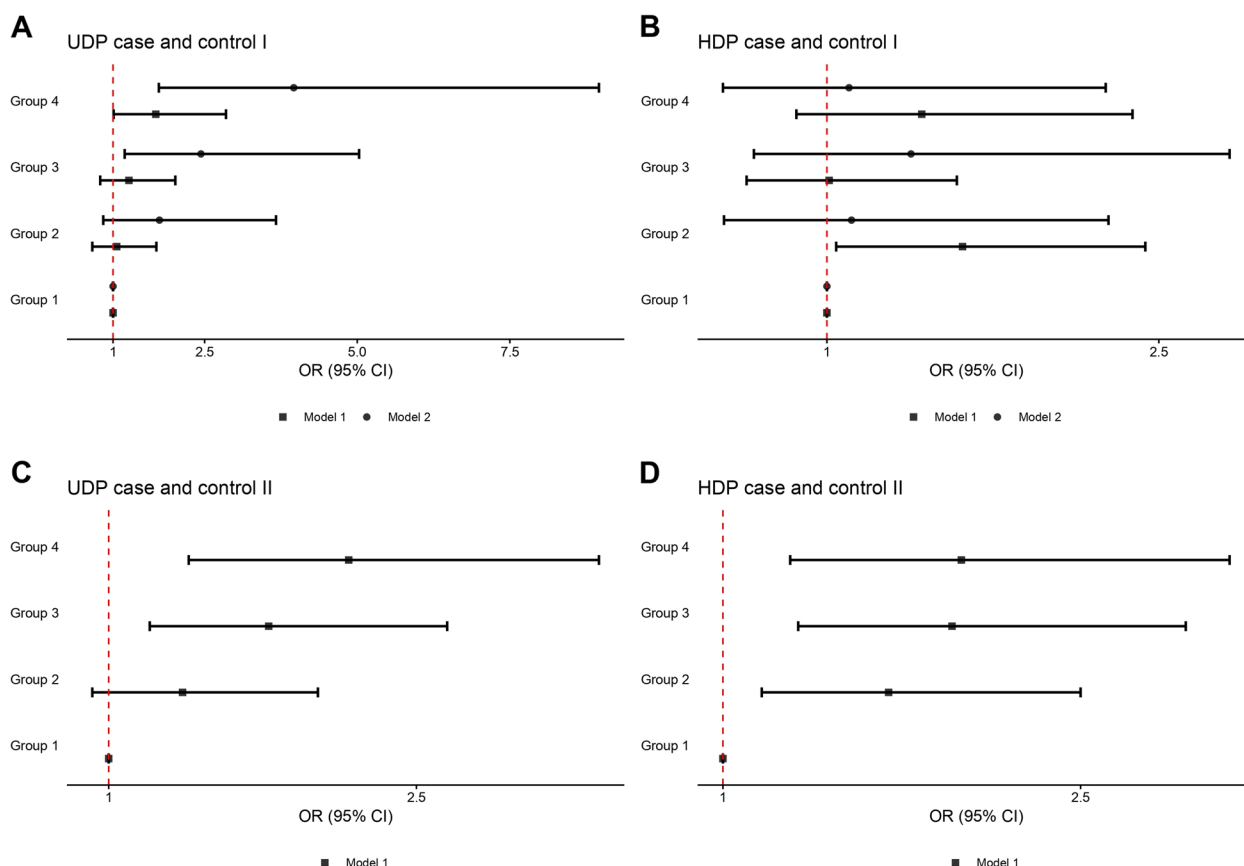


Fig. 4 Odds ratios for gastric adenocarcinoma based on dietary patterns, controls, and adjustments. Abbreviations: HDP, healthy dietary pattern; UDP, unhealthy dietary pattern. Control I individuals (endoscopic controls); control II individuals (hospital controls). Model 1: adjusted for sex, age, education, family history of cancer in first-degree relatives, study region, total energy intake, BMI categories, tobacco smoking, and alcohol consumption. Model 2: further adjusted for peptic ulcer and *H. pylori* status

Discussion

We evaluated the relationship between different dietary patterns and GA risk in a large population of GA cases and controls in Brazil, integrating a counterfactual-based mediation analysis to identify the main nutrients implicated in these associations. This novel approach provides unique insights into how selected nutrients mediate the relationship between dietary patterns and GA.

Several studies have examined the association between dietary patterns and the risk of GA in populations from China, Iran, Jordan, Korea, Mexico, Uruguay, and Canada. They generally concluded that patterns labeled as Healthy/Prudent/Mediterranean reduce the risk of GA, while Unhealthy/Western patterns increase the risk of GA [10, 15–17, 33–36].

While these studies focused only on food or nutrient groups as risk factors for GA, our study not only assessed food patterns as exposure factors but also estimated the mediated effect of multiple nutrients related to healthy or unhealthy dietary patterns, and potentially implicated in the risk of GA. Previous studies employing mediation

analysis to explore the relationship between diet and cancer risk have mainly focused on individual nutrients rather than dietary patterns, thus limiting direct comparisons with our findings due to the absence of similar methodologies in previous literature [37–43].

Our study highlights sodium as a strong mediator in the association between a HDP and GA risk. Sodium demonstrates a complete mediated effect in cases versus control I analysis and a partially mediated effect in cases versus control II. A recent national dietary survey estimated that approximately 60% of the Brazilian adult population exceed the recommended limits for sodium intake, primarily through white bread, toast, beans, white rice, beef, and poultry meat [31]. However, products labeled as “whole grain” such as breakfast cereals, bread, and cookies, for instance, may contain high sodium content [44]. Therefore, strategies involving the reading of food labels, for example, may have the potential to decrease sodium intake through these products. In 2022, Brazil implemented new food labeling legislation to enhance the comprehension of nutritional information

Table 2 Mediation effects of the nutrients on the relationship between dietary patterns and gastric adenocarcinoma

Dietary pattern, type of control	Effects ^a	OR (95% CI) ^b	p-value	PM (%) ^c
UDP, I	Total	1.51 (1.07–2.59)	0.04	–
	Direct	1.39 (1.04–2.46)	0.04	–
	Indirect—total	1.03 (1.00–1.07)	0.04	7.3
	Indirect—added sugars	1.03 (1.00–1.07)	0.04	7.3
HDP, I	Total	0.75 (0.49–1.07)	0.12	–
	Direct	1.15 (0.88–1.67)	0.32	–
	Indirect—total	0.64 (0.47–0.87)	< 0.01	100
	Indirect—SFA	1.02 (1.00–1.04)	0.12	–
	Indirect—sodium	0.64 (0.47–0.85)	< 0.01	100
UDP, II	Total	1.26 (1.07–1.52)	< 0.01	–
	Direct	1.20 (1.01–1.45)	0.04	–
	Indirect—total	1.05 (1.02–1.08)	< 0.01	21.7
	Indirect—added sugars	1.05 (1.02–1.08)	< 0.01	21.7
HDP, II	Total	0.66 (0.54–0.76)	< 0.01	–
	Direct	0.75 (0.61–0.89)	< 0.01	–
	Indirect—total	0.88 (0.74–0.99)	0.02	31.0
	Indirect—sodium	0.80 (0.70–0.86)	< 0.01	52.4
	Indirect—added sugars	1.03 (1.01–1.06)	< 0.01	10.3
	Indirect—total fiber	1.06 (0.97–1.17)	0.22	–

Control I individuals (endoscopic controls); control II individuals (hospital controls)

Abbreviations: HDP healthy dietary pattern, UDP unhealthy dietary pattern, SFA saturated fatty acids, PM percentage mediated

^a The following variables were tested as potential mediators: saturated fatty acid (% of kcal), added sugars (% of kcal), total fiber (g/1000 kcal), and sodium (g/1000 kcal) intakes. For a variable to be considered as a mediator, it had to be significantly associated to both the predictor and the outcome. Variables that did not meet both conditions were considered as covariates, and no indirect effect was estimated

^b The ORs were estimated for 1-unit increase in the dietary factor score

^c When the estimate of the indirect effect exceeds the total effect, it indicates that the variable fully mediates the association between the dietary pattern and GA

on product labels. The goal is to aid consumers in making informed and conscientious food choices, with an emphasis on highlighting elevated nutrient levels on packaging [45].

Sodium is a well-established and significant risk factor that directly influences gastric carcinogenesis. Excessive sodium intake has detrimental effects on the gastric mucosal membrane, resulting in inflammation and synergistic interactions with *H. pylori* colonization. The disruption of the mucosal barrier can further enhance the penetration of recognized carcinogens, such as N-methyl-N-nitro-nitrosoguanidine from the diet. Moreover, increased sodium intake can independently induce atrophic gastritis and metaplasia, stemming from the chronic irritation of the gastric mucosa, thereby accelerating the progression of intestinal metaplasia leading to GA [7, 46, 47].

The association between the UDP and GA is partly mediated by added sugars, with higher scores in this dietary pattern linked to an increased GA risk. Existing studies on the link between added sugars and GA are limited. Li et al. [48] found no direct association between sugars intake and the incidence and mortality related to

GA. Nevertheless, excessive sugar consumption is a recognized factor for adiposity, obesity, diabetes, and cardiometabolic disturbances—established risk factors for various cancer sites, including cardia GA [8, 9, 49]. It has also been suggested that sugars are associated with other mechanisms for cancer, including oxidative stress, inflammation, or activation of the insulin pathway leading to insulin resistance, even in the absence of weight gain [49]. To our knowledge, there are no established mechanisms directly linking excessive consumption of added sugars to gastric carcinogenesis.

Added sugars are introduced during food processing and can be found in sweeteners such as table sugar, syrups, honey, industrialized fruit or vegetable juices, soft drinks, and energy beverages. Importantly, natural sugars of milk, fruits, and vegetables are not considered added sugars [50]. In Brazil, 9.2% of adults regularly consume soft drinks, with higher prevalence among men and the younger population. Recent estimates show a 14% frequency of soft drink consumption on five or more days per week, with a higher prevalence among men compared to women in Brazilian capitals [51]. Overall, our findings suggest that the

implementation of additional initiatives and strategies for healthier food options, with a focus on reducing sodium and added sugars intake, is crucial to decreasing the risk of GA.

The strengths of this study include (1) it represents the first robust multicenter case–control study employing exploratory factor analysis to determine dietary patterns and assess GA risk in the Brazilian population; (2) its relatively large sample size with individuals from four capitals located in four different regions of Brazil; (3) the innovative approach used to identify the mediators involved in the link between dietary patterns and GC risk. To our knowledge, it is also the first in the literature to use nutrients related to gastric carcinogenesis as mediators; and (4) the completeness and accuracy of dietary intake data collected thorough a comprehensive and validated FFQ.

Despite its strengths, this study has some limitations: (1) the derivation of dietary patterns from the exploratory factor analysis method involved subjective decisions when selecting and grouping the food items, when extracting the number of factors, and even when labeling the patterns. Additionally, dietary patterns are closely related to country-specific properties (e.g., food availability and cultural habits). Therefore, patterns may lack robustness and reproducibility, especially when assessed in different populations or with different numbers of diet components; (2) two dietary patterns derived from the analysis accounted for approximately 25% of the total variation in food intake, which is a small proportion of the variation in diet. Although it is a common trend in other studies that have conducted dietary pattern analyses, the identified patterns may not thoroughly capture the interindividual variation in dietary habits [52]; (3) the recall and selection biases that are frequent in case–control studies; (4) the reverse causation bias (in case–control study), as a diet may be affected by the diagnosis of GA; and (5) the use of the NDSR[®] software for dietary nutritional analysis of the participants. As it is a US food database, it may not reliably reflect the nutritional composition of Brazilian foods; however, it is considered a robust and complete nutrient database, widely used in epidemiological studies both in Brazil and in other countries. Because there is no Brazilian nutritional composition table with these characteristics, its use was adopted with the inclusion of typically national foods. Finally, we only tested the mediation effect of a limited set of nutrients using a theoretical model that cannot capture the complexity of the additive or synergistic effects of various nutrients and phytochemicals introduced through the diet.

Conclusions

This study provides new insights into the link between diet and GC, highlighting the mediating role of added sugars and sodium in the association between dietary patterns and GC risk. Our results show a protective association between a HDP characterized by high vegetable and fruit consumption and GA risk. Conversely, an UDP marked by high consumption of preserved and processed meats, carbonated beverages, and fast food was associated with an increased GA risk. Sodium emerged a pivotal mediator in both the HDP-GA risk association. The research contributes to elucidating the mechanisms involved in gastric carcinogenesis from an epidemiological perspective, with implications for public health.

Abbreviations

BMI	Body mass index
CG	Gastric cancer
CI	Confidence interval
DAG	Directed acyclic graph
DP	Dietary pattern
FFQ	Food frequency questionnaire
GA	Gastric adenocarcinoma
HDP	Healthy dietary pattern
<i>H. pylori</i>	<i>Helicobacter pylori</i>
KMO	Kaiser–Meyer–Olkin test
MUFA	Monounsaturated fatty acids
NDSR	Nutrition Data System for Research
OR	Odds ratio
PM	Percentage mediated
SFA	Saturated fatty acids
UDP	Unhealthy dietary pattern
WHO	World Health Organization

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12916-024-03785-2>.

Additional file 1: Tables S1–S2. Tables S1– Food groups. Tables S2– Nutrients distribution across dietary patterns categories.

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Authors' contributions

Conceptualization: ARCS, MPC; Methodology: ARCS, MPC, GA, VRG, PPFG; Data collection: PPA, MSB, ROS, FJFC; Formal analysis and investigation: ARCS, MPC, GA, PPFG; Writing—original draft preparation: ARCS, MPC, GA, VRG; Writing—review and editing: All authors; Funding acquisition: MPC; Resources: MPC; Supervision: MPC. All authors reviewed the manuscript.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The study was conducted in accordance with the Declaration of Helsinki after obtaining the approval of the Committee on Ethics in Human Research of Antônio Prudente Foundation—A.C. Camargo Cancer Center under registration on the Brazil platform linked to the National Health Council of Brazil (grant no. 4708881—February 2016, registration CAAE: 53166915.9.1001.5432), as well as the local ethics committees of the study centers. All participants provided written informed consent for data collection and storage.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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