



Article Diets including Animal Food Are Associated with Gastroesophageal Reflux Disease

Luciana Baroni ^{1,*}, Chiara Bonetto ², Irene Solinas ³, Pierfrancesco Visaggi ³, Alexey V. Galchenko ¹, Lucia Mariani ³, Andrea Bottari ³, Mattia Orazzini ³, Giada Guidi ³, Christian Lambiase ³, Linda Ceccarelli ³, Massimo Bellini ³, Edoardo V. Savarino ⁴ and Nicola de Bortoli ^{3,5}

- ¹ Scientific Society for Vegetarian Nutrition, 30171 Venice, Italy; alexey.galchenko@scienzavegetariana.it
- ² Section of Psychiatry, Department of Neuroscience, Biomedicine and Movement Sciences,
- University of Verona, 37134 Verona, Italy; chiara.bonetto@univr.it
 ³ Division of Gastroenterology, Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, 56126 Pisa, Italy; i.solinas1@studenti.unipi.it (I.S.); pierfrancesco.visaggi@phd.unipi.it (P.V.); l.mariani10@studenti.unipi.it (L.M.); a.bottari@studenti.unipi.it (A.B.); m.orazzini4@studenti.unipi.it (M.O.); 27627122@studenti.unipi.it (G.G.); l.ceccarelli@ao-pisa.toscana.it (L.C.); massimo.bellini@unipi.it (M.B.); nicola.debortoli@unipi.it (N.d.B.)
- ⁴ Division of Gastroenterology, Department of Surgery, Oncology and Gastroenterology, University of Padua, 35124 Padua, Italy; edoardo.savarino@unipd.it
- ⁵ NUTRAFOOD, Interdepartmental Center for Nutraceutical Research and Nutrition for Health, University of Pisa, 56124 Pisa, Italy
- * Correspondence: luciana.baroni@scienzavegetariana.it

Abstract: Gastroesophageal reflux disease (GERD) is a clinical condition with a prevalence of up to 25% in Western countries. Typical GERD symptoms include heartburn and retrosternal regurgitation. Lifestyle modifications, including diet, are considered a first-line therapeutic approach. To evaluate the impact of life habits on GERD in this cross-sectional study, we used data collected through an online survey from 1146 participants. GERD was defined according to the Montreal Consensus. For all participants, clinical and lifestyle characteristics were recorded. Overall, 723 participants (63.1%) consumed a diet including animal food (non-vegans), and 423 participants (36.9%) were vegans. The prevalence of GERD was 11% (CI 95%, 9–14%) in non-vegans and 6% (CI 95%, 4–8%) in vegans. In the multivariate analysis, after adjusting for confounding factors, subjects on a non-vegan diet were associated with a two-fold increase in the prevalence of GERD compared to vegans (OR = 1.96, CI 95%, 1.22–3.17, *p* = 0.006). BMI and smoking habits were also significantly associated with GERD. This study shows that an animal food-based diet (meat, fish, poultry, dairy, and eggs) is associated with an increased risk of GERD compared to a vegan diet. These findings might inform the lifestyle management of patients with GERD-related symptoms.

Keywords: gastroesophageal reflux disease; GERD; animal-based diet; vegan diet; heartburn; regurgitation; lifestyle habits

1. Introduction

Heartburn and acid regurgitation are common in the general population and can cause varying levels of discomfort depending on the frequency and intensity of symptoms. While occasional mild reflux episodes are usually harmless and don't interfere with daily activities, more frequent and severe reflux symptoms can lead to health problems, including erosive esophagitis [1]. According to the Montreal consensus [2], gastroesophageal reflux disease (GERD) is diagnosed when the reflux of stomach contents causes troublesome symptoms and/or complications. In questionnaire-based studies, GERD is defined by the presence of heartburn and regurgitation, regardless of their severity, occurring at least two days per week [3–5]. Based on this definition, GERD prevalence ranges from approximately 10% to 25% in Western countries, with increasing disease burden in recent decades [5].



Citation: Baroni, L.; Bonetto, C.; Solinas, I.; Visaggi, P.; Galchenko, A.V.; Mariani, L.; Bottari, A.; Orazzini, M.; Guidi, G.; Lambiase, C.; et al. Diets including Animal Food Are Associated with Gastroesophageal Reflux Disease. *Eur. J. Investig. Health Psychol. Educ.* **2023**, *13*, 2736–2746. https://doi.org/10.3390/ ejihpe13120189

Academic Editors: María del Mar Molero Jurado and María del Carmen Pérez-Fuentes

Received: 14 September 2023 Revised: 12 October 2023 Accepted: 12 October 2023 Published: 22 November 2023



Copyright: © 2023 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). The increasing incidence of GERD has been linked to the Western lifestyle. Factors such as cigarette smoking, alcohol consumption, a high body mass index (BMI), the presence of a hiatus hernia, inadequate sleep, and lack of aerobic exercise have all been associated with reflux symptoms or GERD [6–8]. Additionally, certain foods and drinks can trigger symptomatic reflux, such as citrus, carbonated beverages, chocolate, and other food items [9]; reducing their consumption might decrease the prevalence and severity of reflux symptoms [10]. Recent observations also suggest that following a predominantly Mediterranean diet, which is a plant-based diet, is associated with a lower risk of reflux disease [11,12].

There is some evidence suggesting that vegetarian diets may offer protection against reflux disease [13–15]. However, there are currently no studies specifically assessing the prevalence of gastroesophageal reflux symptoms in subjects with a prevalent intake of animal food compared to those with an exclusive intake of plant food.

In this study, we performed a questionnaire-based online survey conducted among individuals from the general population. The primary aim was to compare the prevalence of GERD-related symptoms between consumers of animal food compared to subjects with an exclusive intake of plant food.

2. Materials and Methods

2.1. Study Design

The INVITA study (INVestigation on ITAlians' habits and health) is a cross-sectional study conducted using an online survey, which began on 26 July 2022, with the aim of collecting data on lifestyle habits, health conditions, and diet of the general Italian population. Participants were recruited online, on a voluntary basis, by the advertising of the survey access link through social media and newsletters. The exclusion criteria were being younger than 18 years, pregnancy or breastfeeding, and restrictive plant-based diets (macrobiotic, fruitarian, raw food, and hygienist). The survey ensured anonymity, and informed consent was obtained from all participants. The online questionnaires were hosted by the Scientific Society for Vegetarian Nutrition (a non-profit Italian organization) as a dedicated application on the domain studioinvita.it and could be accessed using computers, tablets, or smartphones. The collected data were downloaded and managed by responsible data management personnel who had no means of identifying study participants. This study was approved by the Bioethical Committee of the University of Pisa, Italy (Prot. N. 0116339/2021, approval date 29 September 2021).

2.2. Study Instruments

Sociodemographic characteristics were collected using an ad-hoc form, and included gender, age, marital status, living condition, education level, and occupation. Collected lifestyle habits included self-reported height and weight, diet (consumption of meat, fish, poultry, dairy, and eggs), alcohol consumption per month (1 alcohol unit, AU = 12 g of pure alcohol, which corresponds to an average 330 cc of beer, or 125 cc of wine, or 80 cc of vermouth, or 40 cc of liquor. 'At risk' consumption was defined as >60 AUs for males and >30 AUs for females [16,17] and currently a smoker (yes/no).

The dietary pattern (non-vegan or vegan) was defined by considering 'non-vegans' as those who consumed at least one food among meat, fish, poultry, dairy and eggs, and 'vegans' as those who did not consume meat, fish, poultry, dairy, and eggs. The BMI was calculated by dividing weight in kilograms by height in squared meters.

GERD was assessed by evaluating the presence of heartburn, regurgitation, and chest pain according to the Montreal consensus, and patients were categorized as having (GERD+) or not having (GERD-) GERD [2]. Symptoms were considered to be GERD-related when they occurred at least two or more times per week in the previous 30 days. An ad-hoc question regarding medications (antiacids, histamine 2 blockers, and/or proton pump inhibitors) was also asked. Participants taking such medications were classified as GERD+, regardless of GERD-related symptoms.

2.3. Statistical Analysis

Categorical variables were described as absolute numbers and percentages; continuous variables were summarized as means and standard deviations (SDs). Comparisons between groups were performed with the Chi-square test in the case of categorical variables, and with the *t*-test in the case of continuous variables. Subsequently, a series of univariate logistic regression models with having GERD+ as the dependent variable and each characteristic (gender, age, marital status, living condition, education, occupation, BMI, dietary pattern, alcohol consumption, and smoking) as the independent variable were estimated (unadjusted ORs). Those characteristics that resulted in an association (at p < 0.05) with GERD positivity entered the multivariate logistic regression model, thus giving adjusted ORs. All tests were bilateral, with a significance level of 0.05. Analyses were performed using Stata 17 for Windows.

3. Results

At the time the data were extracted (16 May 2023), 4352 subjects completed sociodemographics and life habits questionnaires. Out of them, 1146 (26.3%) completed the GERD survey, and they constituted the study sample. Participants in the GERD survey giving information about medications were 962 (184 missing). In this sub-sample, people taking antiacids, histamine 2 blockers, and/or proton pump inhibitors (PPI) were 19. Out of them, 6 were GERD+ and 13, who were GERD–, were classified as GERD+. Among the 19 subjects, 15 declared to take PPI. Out of them, 5 were GERD+ and 10, who were GERD–, were classified as GERD+.

By considering sociodemographic characteristics and life habits, completers, with respect to non-completers, were slightly older (37.1, SD 12.0 vs. 35.2 SD 11.8; *t* test, p < 0.001), less often living with friends/other relatives/others (6.7% vs. 9.8%; Chi-square test, p = 0.008), more often vegans (36.9% vs. 31.7%; Chi-square test, p = 0.001) and, finally, less often alcohol consumers belonging to the category 'at risk' (5.0% vs. 8.2%; Chi-square test, p < 0.001).

The description of the study sample is given in Table 1 (a and b). More than 90% were females; the mean age was 37 years (SD 12). The majority of the subjects had a degree or a post-degree (66.5%) and were employed (70.9%). More than 60% were married or co-habitants. By considering life habits, the mean BMI was 22.2 (SD 3.8), 37% were vegans, 5% belonged to the 'at risk' alcohol consumption per month, and 91% did not smoke.

The prevalence of gastroesophageal reflux and dyspepsia (GERD+) in the study sample was 9% (95%CI 8–11%), with a significant difference with dietary patterns [non-vegans 11% (95%CI 9–14%) vs. vegans 6% (95%CI 4–8%)]. By comparing all socio-demographic characteristics and life habits, only the BMI (GERD+ 24.1 SD 5.4 vs. GERD– 22.0 SD 3.5; p < 0.001 t test), the vegan dietary pattern (GERD+ 23.6% vs. GERD– 38.3%; p = 0.003 Chi-square test), and the smoking habit (GERD+ 16.2% vs. GERD– 8.5%; p = 0.009 Chi-square test) significantly differed between the two groups.

Table 2 shows the unadjusted OR for each sociodemographic characteristic and life habit for GERD+ participants.

BMI, dietary pattern, and smoking (p < 0.05) entered the multivariate logistic regression model by giving adjusted ORs (Table 3). A non-vegan dietary pattern (adj-OR = 1.96, p = 0.006), a higher BMI (adj-OR = 1.11, p < 0.001), and smoking (adj-OR = 2.09, p < 0.001) were significantly associated with having reflux and dyspepsia.

(a)	Sociodemographic Characteristics	Overall Sample n = 1146	GERD- n = 1040 (90.8%)	GERD+ n = 106 (9.2%)	<i>p</i> -Value
Geno	der, n (%)				0.509
Male		83 (7.2%)	77 (7.4%)	6 (6.7%)	Chi-square
Fem	ale	1063 (92.8%)	963 (92.6%)	100 (94.3%)	
Age,	mean (SD)	37.1 (12.0)	37.0 (11.9)	37.7 (12.9)	0.583 <i>t</i> test
BMI	mean (SD)	22.2 (3.8)	22.0 (3.5)	24.1 (5.4)	<0.001 <i>t</i> test
Mari	tal status, n (%)				0.888
Mar	ried/Cohabitant	702 (61.3%)	635 (61.1%)	67 (63.2%)	Chi-square
Sepa	rated/Divorced/Widowed	41 (3.6%)	37 (3.6%)	4 (3.8%)	oquare
Sing	le	403 (35.2%)	368 (35.4%)	35 (33.0%)	
Livir	ng condition, n (%)				0.315
Fam	ily of origin	208 (18.2%)	184 (17.7%)	24 (22.6%)	Chi-sauare
Part	her and/or children	707 (61.7%)	642 (61.7%)	65 (61.3%)	- 1
Alor		154 (13.4%)	145 (13.9%)	9 (8 5%)	
Frier relat	nds/Other ives/Others	77 (6.7%)	69 (6.6%)	8 (7.5%)	
Edua	ration n (%)				0 151
Prof	essional qualification	45 (3.9%)	40 (3.8%)	5 (4 7%)	Chi-square
Dinl	oma	339 (29.6%)	298 (28 7%)	41 (38 7%)	en square
Dom	200	599 (52 3%)	553 (53.2%)	46 (43.4%)	
Post	-degree	163 (14.2%)	149 (14.3%)	14 (13.2%)	
Occi	upation, n (%)	. ,	. ,		0.239
Emp	loved	812 (70.9%)	744 (71.5%)	68 (64.1%)	Chi-square
Hou	sewife/Student/Retired	271 (23.6%)	239 (23.0%)	32 (30.2%)	on square
Une	nployed	63 (5.5%)	57 (5.5%)	6 (5.7%)	
(b)	Life Habits	Overall Sample n = 1146	GERD- n = 1040 (90.8%)	GERD+ n = 106 (9.2%)	<i>p</i> -Value
Diet	arv pattern, n (%)				0.003
Non	-vegan	723 (63.1%)	642 (61 7%)	81 (76.4%)	Chi-square
Vega	n	423 (36.9%)	398 (38.3%)	25 (23.6%)	en square
Mon	thly alcohol consumption,	33 missing	31 missing	2 missing	0.870
Noc	onsumption	243 (21.8%)	222 (22.0%)	21 (20.2%)	Chi-square
Low	/Moderate ¹	814 (73.1%)	737 (73.0%)	77 (74 0%)	ern square
At ri	sk ²	56 (5.0%)	50 (5.0%)	6 (5.8%)	
Curr	ently smoking, n (%)	5 missing	4 missing	1 missing	0.009
No		1036 (90.8%)	948 (91.5%)	88 (83.8%)	Chi-square
Yes		105 (9.2%)	88 (8.5%)	17 (16.2%)	

Table 1. Sociodemographic characteristics (a) and life habits (b) of the overall sample and of GERD+ and GERD- participants (n = 1146).

 $^{1} \leq 60$ alcohol units for males; ≤ 30 alcohol units for females [17]; $^{2} > 60$ alcohol units for males; > 30 alcohol units for females [17].

17 (16.2%)

Independent Variable	OR (Unadjusted)	95% CI	<i>p</i> -Value
Gender			
Male	Ref.	-	-
Female	1.33	0.57–3.14	0.511
Age	1.00	0.99–1.02	0.582
BMI	1.12	1.07–1.17	< 0.001
Marital status			
Married/Cohabitant	Ref.	-	-
Separated/Divorced/Widowed	1.02	0.35-2.96	0.964
Single	0.90	0.59–1.38	0.635
Living condition			
Family of origin	Ref.	-	-
Partner and/or children	0.78	0.47 - 1.27	0.317
Alone	0.48	0.21-1.05	0.068
Friends/Other relatives/Others	0.89	0.38–2.07	0.785
Education			
Professional qualification	Ref.	-	-
Diploma	1.10	0.41-2.95	0.849
Degree	0.66	0.25 - 1.77	0.414
Post-degree	0.75	0.25-2.21	0.604
Occupation			
Employed	Ref.	-	-
Housewife/Student/Retired	1.46	0.94-2.28	0.092
Unemployed	1.15	0.48-2.77	0.752
Marital status			
Married/Cohabitant	Ref.	-	-
Separated/Divorced/Widowed	1.02	0.35-2.96	0.964
Single	0.90	0.59–1.38	0.635
Dietary pattern			
Vegan	Ref.	-	-
Non-vegan	2.01	1.26-3.20	0.003
Monthly alcohol			
consumption			
No consumption	Ref.	-	-
Low/Moderate ¹	1.10	0.67-1.83	0.700
At risk ²	1.27	0.49–3.31	0.626
Currently smoking			
No	Ref.	-	-
Yes	2.08	1.18-3.65	0.011

Table 2. Univariate logistic models for GERD+ participants: unadjusted ORs (n = 1146).

 $1 \le 60$ alcohol units for males; ≤ 30 alcohol units for females [17]. 2 > 60 alcohol units for males; >30 alcohol units for females [17].

The association between each item for detecting GERD and the dietary pattern is shown in Table 4. A significantly higher percentage of non-vegans experienced, in the previous month, a burning sensation in the center of the chest going up from the stomach to the neck at least two times per week (17.3% vs. 11.8%, p = 0.013), the sensation of liquid rising up in the throat or leaning forward at least two times per week (17.6% vs. 10.9%, p = 0.002), and a feeling of slow or difficult digestion with a sense of bloating after a meal more than two times per week (45.5% vs. 35.5%, p < 0.001).

Independent Variables	OR (Adjusted)	95% CI	<i>p</i> -Value
BMI	1.11	1.07-1.17	< 0.001
Dietary pattern			
Vegan	Ref.	-	-
Non-vegan	1.96	1.22–3.17	0.006
Currently smoking			
Ňo	Ref.	-	-
Yes	2.09	1.18–3.71	< 0.001
Number of observations		1141	
LR test, <i>p</i> -value		Chi2(3) = 37.74, <i>p</i> < 0.001	
Hosmer–Lemeshow goodness-of-fit (10 groups) Chi2(df), <i>p</i> -value	Chi2(8) = 14.97, <i>p</i> = 0.060		
Pearson goodness-of-fit			
Number of covariate patterns		1141	
Chi2(df), p-value		Chi2(804) = 875.91, p = 0.039	
Area under ROC curve		0.652	

Table 3. Multivariate logistic model for GERD+ participants: adjusted ORs (only independent variables significantly associated at p < 0.05 in univariate logistic regression models entered the multivariate logistic regression model).

Table 4. Association between dietary pattern and GERD status (total score and items) (n = 1146).

	Dietary Pattern		<i>p-</i> Value Chi-Square
GERD Status	Non-Vegan n (%)	Vegan n (%)	
GERD– GERD+	642 (88.8%) 81 (11.2%)	398 (94.1%) 25 (5.9%)	0.003
Q1 In the past 30 days, have you had a burning sensation in the center of your chest going up from your stomach to your neck at least 2 times a week or more?			
No Yes	598 (82.7%) 125 (17.3%)	373 (88.2%) 50 (11.8%)	0.013
Q2 In the past 30 days, have you had the sensation of liquid rising up in your throat or leaning forward at least 2 times a week or more?			
No Yes	596 (82.4%) 127 (17.6%)	377 (89.1%) 46 (10.9%)	0.002
Q3 In the past 30 days, have you felt the sensation of heaviness or pain in the center of your chest at least 2 times a week or more? No Yes	629 (87.0%) 94 (13.0%)	377 (89.1%) 46 (10 9%)	0.289
Q4 In the past 30 days, have you felt a feeling of slow or difficult digestion with a sense of bloating after a meal more than 2 times a week? No Yes	394 (54.5%) 329 (45.5%)	273 (64.5%) 150 (35.5%)	<0.001
Q5 In the past 30 days, did you feel pain in the 'pit of your stomach' (centrally just below the ribs) more than 2 times a week?	504 (82 2%)	250 (22 70/)	0.902
INO Yes	594 (82.2%) 129 (17.8%)	350 (82.7%) 73 (17.3%)	0.802

4. Discussion

In this study, we used anonymized data collected using an online survey to compare the prevalence of typical GERD-related symptoms between consumers of animal food and subjects with an exclusive intake of plant food. Animal food-based diets were associated with a two-fold increase in the prevalence of typical GERD-related symptoms, compared to vegan diets.

GERD has been identified as a major health concern, particularly in Western societies [18]. Patients with GERD report symptoms that have a significant impact on their quality of life, causing increased levels of anxiety, stress and visceral hypersensitivity [19]. Moreover, it has been established that symptomatic gastroesophageal reflux is the leading risk factor for esophageal adenocarcinoma, a cancer with a rapidly increasing incidence and a high mortality rate [20].

GERD therapy is based on acid suppression and mucosal protectant medical devices [21]. In the United States alone, GERD-related direct and indirect costs account for approximately \$15–20 billion [22], and 80% of this amount is due to drug treatments [23].

In line with the trend of proton pump inhibitor deprescription in GERD management [24], it is important to identify and reduce any modifiable risk factor of the disease. Several lifestyle factors have been associated with GERD [10]; however, beneficial effects have only been documented for weight loss and tobacco smoking cessation in obese patients and smokers, respectively, and for avoiding late evening meals and elevating the head of the bed for nocturnal GERD [8,21].

Previous data suggested that dietary changes can potentially reduce the risk of GERD. Despite conflicting evidence [25], it is widely accepted that certain foods may exacerbate typical GERD symptoms. In addition to components in food that are known to trigger GERD, certain dietary patterns and eating habits have also been linked to GERD [26,27]. For instance, a Western diet has been positively correlated with the risk of GERD, regardless of other factors [11]. In the last decades, population-based studies have shown that BMI and smoking may be considered important risk factors for GERD symptoms [19,28,29], as well as for the development of Barrett esophagus and esophageal adenocarcinoma [30]. It has also been suggested that certain foods (chocolate, peppermint, tomato, and tomato sauce) may be related to GERD symptoms, but evidence to support this information is still lacking [21]. Few studies have evaluated the effect of a diet including animal food in individuals with typical GERD-related symptoms.

Previous research regarding the impact of meat consumption on gastroesophageal reflux and its clinical implications have yielded inconsistent results. Using a food frequency questionnaire, O'Doherty et al. found that meat intake had no correlation with reflux symptoms, reflux esophagitis, or esophageal adenocarcinoma [31]. Furthermore, a large monozygotic co-twin study indicated no association between meat intake and the emergence of gastroesophageal reflux [32].

In contrast, an examination of Uygur and Han Chinese revealed that a diet high in meat increased the risk of GERD [33]. Additionally, a study performed on hospital employees showed that the number of meat servings consumed per day was associated with reflux esophagitis, although not always with reflux symptoms [34].

Our team in Pisa conducted a pathophysiologic study that evaluated the first postprandial hours after three meals. Impedance and pH analysis revealed that symptoms and acid reflux events were more prevalent following a meal with animal food compared to a meal with plant food [35]. A further possible explanation of our findings might be the increase of the proximal gastric acid secretion in the postprandial period due to the phenomenon of acid pockets present in all subjects, not only in those suffering from GERD [36]. Nevertheless, the increased amount of acid in the pocket and the increased acidity of the reflux events might be related to a greater amount of saturated fats in animal food compared to plant ones [37].

Accordingly, Van Boxel et al. demonstrated that GERD patients experienced a notable increase in heartburn and nausea during a lipid infusion, which can be attributed to

an increase in chylomicron production and secretion, which may trigger the release of cholecystokinin, a stimulant of vagal afferences [38]. Moreover, a study by Fox et al. showed that a high-fat diet, compared to a low-fat diet, had effects on esophageal acid exposure and, above all, was associated with the presence of typical reflux-related symptoms [39].

From a pathophysiological point of view, it appears clear that animal foods can represent a source of different compounds capable of increasing the reflux burden or even the perception of typical reflux-related symptoms.

On the other hand, there is strong evidence supporting a protective effect of an exclusive plant-based diet in reducing GERD symptoms. Bhatia et al., who conducted a survey of volunteers and patients in urban areas and slums of India, described a positive relationship between the consumption of non-vegetarian diets and reflux symptoms [13]. Similarly, Jung et al. reported a decreased risk of reflux esophagitis in vegetarian Buddhist priests, even when their BMI was elevated [14].

In line with this, vegetarian diets are known to be high in dietary fiber, which have been linked to a reduction in reflux symptoms [40–43]. Although the precise mechanism for this is still unclear, it has been suggested that dietary fiber may scavenge nitrites found in the stomach, thus decreasing the availability of nitric oxide synthesis [42]. This could potentially reduce nitric oxide concentration in the gastroesophageal junction and inhibit reflux [42].

The aim of our study was to compare the prevalence of typical GERD-related symptoms between consumers of animal food and subjects with an exclusive intake of plant food. Important risk factors such animal food-based diets, tobacco smoking, and higher BMI were associated with a higher prevalence of GERD-related symptoms (GERD+).

Our study showed that any typical GERD-related symptoms perceived more than two days per week occurred more frequently in non-vegan participants than in vegans. The protective effect of an exclusive plant-based diet on symptomatic reflux, as shown by multivariable analysis, was independent from confounding factors, such as BMI and smoking.

This study has several strengths. It involved a substantial number of participants (more than 1000). The use of an online survey facilitated data collection, making it convenient for participants to respond and reducing the chances of missing data. This study defined the prevalence of GERD-related symptoms according to the Montreal consensus [1] and when they occurred more than two times per week. Moreover, in our study, the number of vegans, although overrepresented with respect to their proportion in the Italian population, allowed us to have a dimension suitable for serving as a comparison sample (723 non-vegan vs. 423 vegans, 63.1% vs. 36.9%).

This study has also some limitations. The first limitation concerns the possibility of a selection bias. Despite the large sample size of participants to the INVITA study (n = 4352), the percentage of those who completed the GERD survey was low (26.3%). The comparison between those who completed GERD survey (n = 1146) and those who did not complete it (n = 3206) showed that completers were slightly older, less often living with friends/other relatives/others, more often vegans, and, finally, less often alcohol consumers belonging to the category 'at risk'. Moreover, the comparison between the whole INVITA sample (n = 4352) and the general Italian population (\geq 18 years) showed that there are differences in some characteristics like gender and overweight prevalence, age, education level, smoking habits, and 'at risk' alcohol consumption prevalence. The vegan dietary pattern, as mentioned above, is overrepresented [44,45]. The second limitation concerns the cross-sectional design, which does not permit the identification of causal relationships. The third limitation refers to data collection, which relies on self-reported data, which is conducive to a possible recall bias and a biased interpretation of the questions. In this study, GERD was defined based on the presence of typical symptoms. In this regard, both versions of the Lyon consensus [46,47] suggest that typical symptoms are associated with a high likelihood of having objective GERD, corroborating the use of a short treatment with PPIs in primary care. Finally, the study was conducted in Italy, which may limit the generalizability of the findings to other countries.

5. Conclusions

In summary, our results show that a diet including animal food (meat, fish, poultry, dairy, and eggs) is associated with troublesome reflux-related symptoms. The results of the multivariate analysis indicated a positive association between regular consumption of animal food and typical GERD-related symptoms. Our findings support that diets including animal food are associated, also after controlling for other risk factors, with a significant increase in the prevalence of gastroesophageal reflux (GERD).

These data, obtained through an observational study design, are further corroborated by the fact that the survey population featured a higher proportion of vegan subjects than found in the general population. Our findings indicated that it is quite important for general practitioners to advise patients with GERD-related symptoms to modify their dietary practices, beginning by decreasing the proportion of animal foods in their diet, in order to reduce the need for medication and improve symptom perception.

In fact, there may be various mechanisms influencing the potential triggering effects of a diet including animal food versus a plant-only diet, and this field of research requires further investigation.

Author Contributions: Conceptualization, L.B. and N.d.B.; methodology, C.B.; software, C.B.; validation, I.S., P.V. and A.V.G.; formal analysis, M.O., A.B. and C.B.; investigation, L.B. and A.V.G.; data curation, M.O., L.C. and M.B.; writing—original draft preparation, L.B., C.B. and N.d.B.; writing—review and editing, M.O., A.B. and L.C.; visualization, P.V., E.V.S., L.M., C.L. and G.G.; supervision, L.B. and G.G. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: This study was conducted in accordance with the Declaration of Helsinki and approved by the Bioethical Committee of the University of Pisa, (Prot. N. 0116339/2021, approval date 29 September 2021).

Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

Data Availability Statement: The data presented in this study are available on request from the corresponding author. The data are not publicly available due to privacy.

Acknowledgments: The authors wish to thank all the participants to the INVITA study and the Scientific Society for Vegetarian Nutrition of Italy for providing technical support to the survey.

Conflicts of Interest: The authors declare no conflict of interest.

References

- Visaggi, P.; Del Corso, G.; Gyawali, C.P.; Ghisa, M.; Baiano Svizzero, F.; Stefani Donati, D.; Venturini, A.; Savarino, V.; Penagini, R.; Zeki, S.; et al. Ambulatory pH-Impedance Findings Confirm That Grade B Esophagitis Provides Objective Diagnosis of Gastroesophageal Reflux Disease. Am. J. Gastroenterol. 2023, 118, 794–801. [CrossRef]
- Vakil, N.; van Zanten, S.V.; Kahrilas, P.; Dent, J.; Jones, R. Global Consensus Group The Montreal Definition and Classification of Gastroesophageal Reflux Disease: A Global Evidence-Based Consensus. *Am. J. Gastroenterol.* 2006, 101, 1900–1920; quiz 1943. [CrossRef] [PubMed]
- Ness-Jensen, E.; Lindam, A.; Lagergren, J.; Hveem, K. Changes in Prevalence, Incidence and Spontaneous Loss of Gastro-Oesophageal Reflux Symptoms: A Prospective Population-Based Cohort Study, the HUNT Study. *Gut* 2012, *61*, 1390–1397. [CrossRef] [PubMed]
- Dent, J.; El-Serag, H.B.; Wallander, M.-A.; Johansson, S. Epidemiology of Gastro-Oesophageal Reflux Disease: A Systematic Review. *Gut* 2005, 54, 710–717. [CrossRef] [PubMed]
- El-Serag, H.B.; Sweet, S.; Winchester, C.C.; Dent, J. Update on the Epidemiology of Gastro-Oesophageal Reflux Disease: A Systematic Review. *Gut* 2014, 63, 871–880. [CrossRef] [PubMed]
- Taraszewska, A. Risk Factors for Gastroesophageal Reflux Disease Symptoms Related to Lifestyle and Diet. *Rocz. Panstw. Zakl. Hig.* 2021, 72, 21–28. [CrossRef]
- Festi, D.; Scaioli, E.; Baldi, F.; Vestito, A.; Pasqui, F.; Di Biase, A.R.; Colecchia, A. Body Weight, Lifestyle, Dietary Habits and Gastroesophageal Reflux Disease. World J. Gastroenterol. 2009, 15, 1690–1701. [CrossRef]
- 8. Eherer, A. Management of Gastroesophageal Reflux Disease: Lifestyle Modification and Alternative Approaches. *Dig. Dis.* 2014, 32, 149–151. [CrossRef]

- Dağlı, Ü.; Kalkan, İ.H. The Role of Lifestyle Changes in Gastroesophageal Reflux Diseases Treatment. Turk J. Gastroenterol. 2017, 28, S33–S37. [CrossRef]
- Murao, T.; Sakurai, K.; Mihara, S.; Marubayashi, T.; Murakami, Y.; Sasaki, Y. Lifestyle Change Influences on GERD in Japan: A Study of Participants in a Health Examination Program. *Dig. Dis. Sci.* 2011, *56*, 2857–2864. [CrossRef]
- Mone, I.; Kraja, B.; Bregu, A.; Duraj, V.; Sadiku, E.; Hyska, J.; Burazeri, G. Adherence to a Predominantly Mediterranean Diet Decreases the Risk of Gastroesophageal Reflux Disease: A Cross-Sectional Study in a South Eastern European Population. *Dis Esophagus* 2016, 29, 794–800. [CrossRef] [PubMed]
- Surdea-Blaga, T.; Negrutiu, D.E.; Palage, M.; Dumitrascu, D.L. Food and Gastroesophageal Reflux Disease. *Curr. Med. Chem.* 2019, 26, 3497–3511. [CrossRef] [PubMed]
- 13. Bhatia, S.J.; Reddy, D.N.; Ghoshal, U.C.; Jayanthi, V.; Abraham, P.; Choudhuri, G.; Broor, S.L.; Ahuja, V.; Augustine, P.; Balakrishnan, V.; et al. Epidemiology and Symptom Profile of Gastroesophageal Reflux in the Indian Population: Report of the Indian Society of Gastroenterology Task Force. *Indian J. Gastroenterol.* **2011**, *30*, 118–127. [CrossRef]
- Jung, J.G.; Kang, H.W.; Hahn, S.J.; Kim, J.H.; Lee, J.K.; Lim, Y.J.; Koh, M.-S.; Lee, J.H. Vegetarianism as a Protective Factor for Reflux Esophagitis: A Retrospective, Cross-Sectional Study between Buddhist Priests and General Population. *Dig. Dis. Sci.* 2013, 58, 2244–2252. [CrossRef]
- 15. Mazzocchi, S.; Visaggi, P.; Baroni, L. Plant-Based Diets in Gastrointestinal Diseases: Which Evidence? *Best Pract. Res. Clin. Gastroenterol.* **2023**, *62–63*, 101829. [CrossRef]
- Ministero della Salute, Italia. Alcol, Zero o Il Meno Possibile. Available online: https://www.salute.gov.it/portale/alcol/ dettaglioContenutiAlcol.jsp?lingua=italiano&id=5526&area=alcol&menu=vuoto (accessed on 14 September 2023).
- Istituto Superiore di Sanità. Indicatori Passi: Consumo Di Bevande Alcoliche. Available online: https://www.epicentro.iss.it/ passi/indicatori/alcol (accessed on 14 September 2023).
- Nirwan, J.S.; Hasan, S.S.; Babar, Z.-U.-D.; Conway, B.R.; Ghori, M.U. Global Prevalence and Risk Factors of Gastro-Oesophageal Reflux Disease (GORD): Systematic Review with Meta-Analysis. *Sci. Rep.* 2020, 10, 5814. [CrossRef] [PubMed]
- Savarino, E.; de Bortoli, N.; De Cassan, C.; Della Coletta, M.; Bartolo, O.; Furnari, M.; Ottonello, A.; Marabotto, E.; Bodini, G.; Savarino, V. The Natural History of Gastro-Esophageal Reflux Disease: A Comprehensive Review. *Dis. Esophagus* 2017, 30, 1–9. [CrossRef]
- Visaggi, P.; Barberio, B.; Gregori, D.; Azzolina, D.; Martinato, M.; Hassan, C.; Sharma, P.; Savarino, E.; de Bortoli, N. Systematic Review with Meta-Analysis: Artificial Intelligence in the Diagnosis of Oesophageal Diseases. *Aliment. Pharmacol. Ther.* 2022, 55, 528–540. [CrossRef]
- Katz, P.O.; Dunbar, K.B.; Schnoll-Sussman, F.H.; Greer, K.B.; Yadlapati, R.; Spechler, S.J. ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease. Am. J. Gastroenterol. 2022, 117, 27–56. [CrossRef]
- 22. Shaheen, N.J.; Hansen, R.A.; Morgan, D.R.; Gangarosa, L.M.; Ringel, Y.; Thiny, M.T.; Russo, M.W.; Sandler, R.S. The Burden of Gastrointestinal and Liver Diseases, 2006. *Am. J. Gastroenterol.* 2006, 101, 2128–2138. [CrossRef]
- Francis, D.O.; Rymer, J.A.; Slaughter, J.C.; Choksi, Y.; Jiramongkolchai, P.; Ogbeide, E.; Tran, C.; Goutte, M.; Garrett, C.G.; Hagaman, D.; et al. High Economic Burden of Caring for Patients with Suspected Extraesophageal Reflux. *Am. J. Gastroenterol.* 2013, 108, 905–911. [CrossRef] [PubMed]
- 24. Turner, J.P.; Thompson, W.; Reeve, E.; Bell, J.S. Deprescribing Proton Pump Inhibitors. *Aust. J. Gen. Pract.* 2022, *51*, 845–848. [CrossRef] [PubMed]
- Sethi, S.; Richter, J.E. Diet and Gastroesophageal Reflux Disease: Role in Pathogenesis and Management. *Curr. Opin. Gastroenterol.* 2017, 33, 107–111. [CrossRef] [PubMed]
- Esmaillzadeh, A.; Keshteli, A.H.; Feizi, A.; Zaribaf, F.; Feinle-Bisset, C.; Adibi, P. Patterns of Diet-Related Practices and Prevalence of Gastro-Esophageal Reflux Disease. *Neurogastroenterol. Motil.* 2013, 25, 831-e638. [CrossRef] [PubMed]
- Yamamichi, N.; Mochizuki, S.; Asada-Hirayama, I.; Mikami-Matsuda, R.; Shimamoto, T.; Konno-Shimizu, M.; Takahashi, Y.; Takeuchi, C.; Niimi, K.; Ono, S.; et al. Lifestyle Factors Affecting Gastroesophageal Reflux Disease Symptoms: A Cross-Sectional Study of Healthy 19864 Adults Using FSSG Scores. *BMC Med.* 2012, 10, 45. [CrossRef]
- Ronkainen, J.; Aro, P.; Storskrubb, T.; Lind, T.; Bolling-Sternevald, E.; Junghard, O.; Talley, N.J.; Agreus, L. Gastro-Oesophageal Reflux Symptoms and Health-Related Quality of Life in the Adult General Population—The Kalixanda Study. *Aliment. Pharmacol. Ther.* 2006, 23, 1725–1733. [CrossRef] [PubMed]
- Ness-Jensen, E.; Hveem, K.; El-Serag, H.; Lagergren, J. Lifestyle Intervention in Gastroesophageal Reflux Disease. *Clin Gastroenterol Hepatol* 2016, 14, 175–182.e1-3. [CrossRef]
- Zhang, X.; Anandasabapathy, S.; Abrams, J.; Othman, M.; Badr, H.J. Lifestyle Risk Factors, Quality of Life, and Intervention Preferences of Barrett's Esophagus Patients: A Prospective Cohort Study. *Glob. Adv. Health Med.* 2021, 10, 21649561211001346. [CrossRef]
- O'Doherty, M.G.; Cantwell, M.M.; Murray, L.J.; Anderson, L.A.; Abnet, C.C.; FINBAR Study Group. Dietary Fat and Meat Intakes and Risk of Reflux Esophagitis, Barrett's Esophagus and Esophageal Adenocarcinoma. *Int. J. Cancer* 2011, 129, 1493–1502. [CrossRef]
- 32. Zheng, Z.; Nordenstedt, H.; Pedersen, N.L.; Lagergren, J.; Ye, W. Lifestyle Factors and Risk for Symptomatic Gastroesophageal Reflux in Monozygotic Twins. *Gastroenterology* **2007**, *132*, 87–95. [CrossRef]

- 33. Niu, C.-Y.; Zhou, Y.-L.; Yan, R.; Mu, N.-L.; Gao, B.-H.; Wu, F.-X.; Luo, J.-Y. Incidence of Gastroesophageal Reflux Disease in Uygur and Han Chinese Adults in Urumqi. *World J. Gastroenterol.* **2012**, *18*, 7333–7340. [CrossRef] [PubMed]
- El-Serag, H.B.; Satia, J.A.; Rabeneck, L. Dietary Intake and the Risk of Gastro-Oesophageal Reflux Disease: A Cross Sectional Study in Volunteers. *Gut* 2005, 54, 11–17. [CrossRef] [PubMed]
- Martinucci, I.; Guidi, G.; Savarino, E.V.; Frazzoni, M.; Tolone, S.; Frazzoni, L.; Fuccio, L.; Bertani, L.; Bodini, G.; Ceccarelli, L.; et al. Vegetal and Animal Food Proteins Have a Different Impact in the First Postprandial Hour of Impedance-pH Analysis in Patients with Heartburn. *Gastroenterol. Res. Pract.* 2018, 2018, 7572430. [CrossRef]
- 36. Boeckxstaens, G. The Relationship Between the Acid Pocket and GERD. Gastroenterol. Hepatol. N. Y. 2013, 9, 595–596. [PubMed]
- Becker, D.J.; Sinclair, J.; Castell, D.O.; Wu, W.C. A Comparison of High and Low Fat Meals on Postprandial Esophageal Acid Exposure. Am. J. Gastroenterol. 1989, 84, 782–786.
- van Boxel, O.S.; ter Linde, J.J.M.; Oors, J.; Otto, B.; Feinle-Bisset, C.; Smout, A.J.P.M.; Siersema, P.D. Duodenal Lipid-Induced Symptom Generation in Gastroesophageal Reflux Disease: Role of Apolipoprotein A-IV and Cholecystokinin. *Neurogastroenterol. Motil.* 2012, 24, 350-e168. [CrossRef]
- 39. Fox, M.; Barr, C.; Nolan, S.; Lomer, M.; Anggiansah, A.; Wong, T. The Effects of Dietary Fat and Calorie Density on Esophageal Acid Exposure and Reflux Symptoms. *Clin. Gastroenterol. Hepatol.* **2007**, *5*, 439–444. [CrossRef]
- Kaltenbach, T.; Crockett, S.; Gerson, L.B. Are Lifestyle Measures Effective in Patients with Gastroesophageal Reflux Disease? An Evidence-Based Approach. Arch. Intern. Med. 2006, 166, 965–971. [CrossRef]
- Nilsson, M.; Johnsen, R.; Ye, W.; Hveem, K.; Lagergren, J. Lifestyle Related Risk Factors in the Aetiology of Gastro-Oesophageal Reflux. *Gut* 2004, *53*, 1730–1735. [CrossRef]
- 42. Nocon, M.; Labenz, J.; Willich, S.N. Lifestyle Factors and Symptoms of Gastro-Oesophageal Reflux—A Population-Based Study. *Aliment. Pharmacol. Ther.* **2006**, 23, 169–174. [CrossRef]
- 43. Morozov, S.; Isakov, V.; Konovalova, M. Fiber-Enriched Diet Helps to Control Symptoms and Improves Esophageal Motility in Patients with Non-Erosive Gastroesophageal Reflux Disease. *World J. Gastroenterol.* **2018**, *24*, 2291–2299. [CrossRef] [PubMed]
- Istituto Superiore di Sanità. Sorveglianza PASSI 2021–2022. Available online: https://www.epicentro.iss.it/passi/dati/socio (accessed on 28 August 2023).
- 45. Eurispes. Rapporto Italia 2023. Available online: https://eurispes.eu/news/risultati-del-rapporto-italia-2023/ (accessed on 28 August 2023).
- 46. Gyawali, C.P.; Kahrilas, P.J.; Savarino, E.; Zerbib, F.; Mion, F.; Smout, A.J.P.M.; Vaezi, M.; Sifrim, D.; Fox, M.R.; Vela, M.F.; et al. Modern Diagnosis of GERD: The Lyon Consensus. *Gut* **2018**, *67*, 1351–1362. [CrossRef] [PubMed]
- 47. Gyawali, C.P.; Yadlapati, R.; Fass, R.; Katzka, D.; Pandolfino, J.; Savarino, E.; Sifrim, D.; Spechler, S.; Zerbib, F.; Fox, M.R.; et al. Updates to the Modern Diagnosis of GERD: Lyon Consensus 2.0. *Gut* **2023**, gutjnl-2023-330616. [CrossRef] [PubMed]

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.