REVIEW

Dietary and Lifestyle Factors Related to Gastroesophageal Reflux Disease: A Systematic Review

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Abstract: We performed this review to clarify which dietary and lifestyle factors are related to gastroesophageal reflux disease. Through a systematic search of the PubMed, EMBASE, China National Knowledge Infrastructure (CNKI), and Chinese BioMedical Literature (CBM) databases, we identified articles with clear definitions of GERD, including nonerosive gastroesophageal reflux disease (NERD), reflux esophagitis (RE) and Barrett's esophagus (BE), that included dietary and lifestyle factors as independent factors affecting the onset of GERD (expressed as odds ratios (ORs) or relative risks (RRs) and 95% confidence intervals (CIs)). Due to heterogeneity among the studies, we used descriptive statistical analyses to analyze and synthesize each outcome based on the disease type. In total, 72 articles were included, conducted in ten Western countries (26 articles in total) and nine Eastern countries (46 articles in total). We categorized dietary factors into 20 items and lifestyle factors into 11 items. GERD is related to many irregular dietary and lifestyle habits (such as a habit of midnight snacking: OR=5.08, 95% CI 4.03–6.4; skipping breakfast: OR=2.7, 95% CI 2.17–3.35; eating quickly: OR=4.06, 95% CI 3.11–5.29; eating very hot foods: OR=1.81, 95% CI 1.37–2.4; and eating beyond fullness: OR=2.85, 95% CI 2.18–3.73). Vegetarian diets (consumption of nonvegetarian food (no/yes); OR=0.34, 95% CI 0.211–0.545) and no intake of meat (OR=0.841, 95% CI 0.715–0.990) were negatively related to GERD, while meat (daily meat, fish, and egg intake: OR=1.088, 95% CI 1.042-1.135) and fat (high–fat diet: OR=7.568, 95% CI 4.557–8.908) consumption were positively related to GERD. An interval of less than three hours between dinner and bedtime (OR=7.45, 95% CI 3.38–16.4) was positively related to GERD, and proper physical exercise (physical exercise >30 minutes (>3 times/week): OR=0.7, 95% CI 0.6–0.9) was negatively correlated with GERD. Smoking (OR=1.19, 95% CI 1.12–1.264), alcohol consumption (OR=1.278, 95% CI 1.207–1.353) and mental state (poor mental state: OR=1.278, 95% CI 1.207–1.353) were positively correlated with GERD. RE (vitamin C: OR=0.46, 95% CI=0.24–0.90) and BE (vitamin C: OR=0.44,95% CI 0.2-0.98; vitamin E: OR=0.46, 95% CI 0.26–0.83) were generally negatively correlated with antioxidant intake. In conclusion, many dietary and lifestyle factors affect the onset of GERD, and these factors differ among regions and disease types. These findings need to be further confirmed in subsequent studies.

Keywords: gastroesophageal reflux disease, diet, lifestyle, systematic review

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Introduction

Gastroesophageal reflux disease (GERD) is a type of chronic gastrointestinal disease in which heartburn and regurgitation are the main clinical manifestations and esophageal and pulmonary symptoms may occur. According to endoscopic findings and esophageal pH monitoring, there may also be

asymptomatic manifestations.[1] The main pathological mechanism is the invasion of stomach contents and dysfunction of the esophageal antireflux barrier. The former is mainly caused by the formation of gastric acid pockets and delayed gastric emptying. The latter is mainly caused by dysfunction of the lower esophageal sphincter (LES). The frequency of transient lower esophageal sphincter relaxation (TLESR) increases, and esophageal acid removal dysfunction occurs, among other factors, but the specific causes of these factors are currently unclear.[2] The incidence rate is increasing annually, but there are substantial differences among regions. The highest incidence, which occurs in Europe and the United States, reaches 20%, and the lowest incidence, which occurs in Asia, is approximately 10%. Additionally, age, sex, race, genes, and factors related to diet and lifestyle (such as obesity and smoking) are related to GERD.[3,4] Effective treatments include lifestyle modification, proton pump inhibitors (PPIs) and surgery. With the recognition of the side effects of the long-term use of PPIs, as nondrug methods and first–line treatments, diet and lifestyle modifications are receiving increasing attention due to their importance in the prevention and treatment of GERD.[5–7]

Therefore, we reviewed and analyzed the current literature to elucidate which dietary and lifestyle factors are associated with GERD, provide specific and informative dietary and lifestyle recommendations for patients, and provide information for follow-up studies. We also attempt to elucidate the dietary and lifestyle differences associated with GERD between Western countries and Eastern countries.

Materials and Methods
Search Strategy
We conducted a comprehensive literature search in two English databases, ie, PubMed and EMBASE, and two Chinese databases, ie, the Chinese BioMedical Literature (CBM) and China National Knowledge Infrastructure (CNKI) databases, with appropriate search strategies. In PubMed, the search scope was limited to titles and abstracts, and we searched for articles related to diet and lifestyle using words such as diet, food, lifestyle, and nutrition. Free words and MeSH terms were used to perform the searches, and the search terms were connected by "and". Searches of English–language databases were limited to articles published in English articles that involved humans. We searched for articles published prior to 2020-03–01. The Chinese databases were searched by journal, and the search was limited to the core journals. We searched for articles published before 2020-03-14. The details of the search strategy for each database are shown in Appendix 1.

Data Selection
The inclusion criteria were as follows: ① clear definition of GERD, nonerosive gastroesophageal reflux disease (NERD), reflux esophagitis (RE) or Barrett's esophagus (BE) and ② articles involving diet and lifestyle as independent factors affecting the onset of GERD. Articles that met any of the following criteria were excluded: ① research subjects aged <18 years; ② no full text available; ③ reviews, systematic reviews, pooled analyses, and meta–analyses; ④ articles focusing on GERD symptom relief, recurrence, progression, and complications; ⑤ articles that did not provide the odds ratio (OR) or hazard ratio (HR) and 95% confidence interval (95% CI) values; and ⑥ articles in which the statistical methodology included only a univariate analysis that was not verified by a multivariate logistic regression.

Data Extraction and Management
Two researchers systematically screened the literature, extracted the data, ascertained the type of research, and submitted any objections to a third party for arbitration. The following data were extracted: title, author, year, country, standard of diagnosis, sample size, mean age (expressed as the mean ± standard deviation if available), sex ratio, and positive dietary and lifestyle risk factors (expressed as ORs or RRs and 95% CIs). For quantitative variables or grading variables, we only extracted the extreme values as comparators (such as maximum intake vs minimum intake or minimum intake vs maximum intake); for RE, we did not distinguish whether symptoms were present, and for BE, we did not distinguish whether dysplasia was present. The control group was asymptomatic or a population control. Because diet and lifestyle can be expressed in different ways, we classified these factors based on the original text and their intrinsic similarities.

Results

General Literature Characteristics

Finally, 72 articles were included. The specific reasons for exclusion and the numbers of articles excluded are shown in Figure 1. Among the included articles, ten studies were conducted in Western countries (26 articles in total), including Albania,[8,9] Ireland,[10–16] Australia,[17,18] Poland,[19,20] the Netherlands,[21] Canada,[22] the United States,[23–29] Norway,[30] Italy,[31,32] and the UK;[33] and nine studies were conducted in Eastern countries (46 articles in total), including Pakistan,[34] South Korea,[35–38] Malaysia,[39] Bangladesh,[40] Japan,[41–46] Saudi Arabia,[47] Iran,[48] India,[49–53] and China.[54–79] There were 4 cohort studies, 27 case-control studies, and 41 cross-sectional studies.

Regarding the classification of the related factors, we categorized 20 items related to diet and 11 items related to lifestyle. Then, according to the article, we classified the participants as having GERD, NERD, RE or BE. The details of each article are shown in Appendix 2, and the diet and lifestyle factors in different regions related to each disease type are shown in Table 1.

Dietary and Lifestyle Factors Related to GERD

In total, 42 articles described the relevant factors associated with GERD; of these studies, eight studies were conducted in Western countries, 34 studies were conducted in Eastern countries, 1 study was a cohort study, 9 studies were case-control studies, and 32 studies were cross-sectional studies. The sample size was 173,132, including 94,235 men and 78,897 women. The main findings related to GERD across the articles are shown in Table 2. The details of the factors are shown in Appendix 3.

Diet and GERD: A vegetarian diet was negatively correlated with GERD. Protein and fat were positively correlated with GERD, and tea was positively related to GERD, except for one article[62] that showed that greasy food and strong tea were negatively related to GERD. Coffee was negatively related to GERD; soft drinks and infrequent milk intake were positively related to GERD; fruits, citrus, and vitamin C were negatively related to GERD; and citrus intake between meals, sweet and spicy foods and poor eating habits were positively related to GERD. Sitting or walking after a meal instead of lying down was negatively correlated with GERD, and an interval of less than 3 hours between dinner and sleep was positively correlated with GERD.

The following lifestyle factors are associated with GERD: smoking, alcohol consumption, mental status, higher education, less sleep time, sedentary and physical occupational activities, night work, less exercise, and increased abdominal pressure are positively correlated
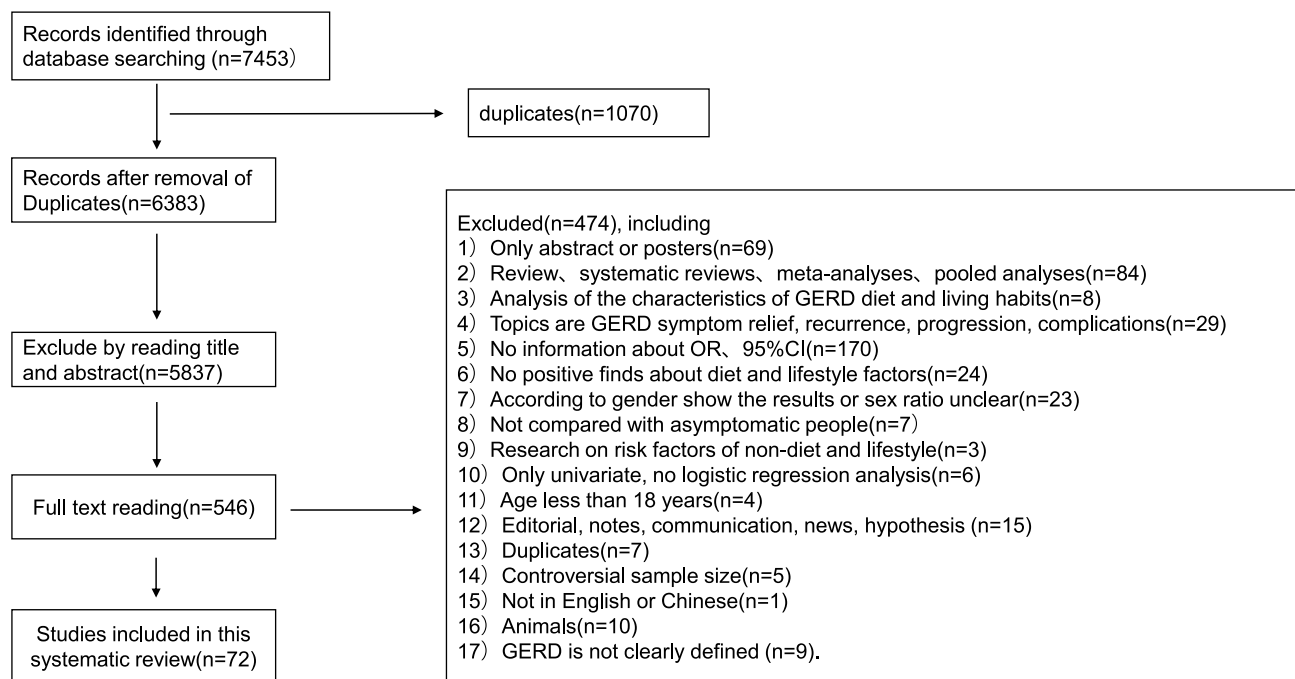

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┌─────────────────────────────┐
│ Records identified through   │
│ database searching (n=7453)  │
└─────────────────────────────┘
            │              ┌──────────────────────┐
            │──────────────▶│ duplicates(n=1070)   │
            ▼              └──────────────────────┘
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│ Records after removal of     │
│ Duplicates(n=6383)           │
└─────────────────────────────┘
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│ Exclude by reading title     │
│ and abstract(n=5837)         │
└─────────────────────────────┘
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┌─────────────────────────────┐
│ Full text reading(n=546)     │
└─────────────────────────────┘
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            ▼
┌─────────────────────────────┐
│ Studies included in this     │
│ systematic review(n=72)      │
└─────────────────────────────┘
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Excluded(n=474), including
1）Only abstract or posters(n=69)
2）Review、systematic reviews、meta-analyses、pooled analyses(n=84)
3）Analysis of the characteristics of GERD diet and living habits(n=8)
4）Topics are GERD symptom relief, recurrence, progression, complications(n=29)
5）No information about OR、95%CI(n=170)
6）No positive finds about diet and lifestyle factors(n=24)
7）According to gender show the results or sex ratio unclear(n=23)
8）Not compared with asymptomatic people(n=7)
9）Research on risk factors of non-diet and lifestyle(n=3)
10）Only univariate, no logistic regression analysis(n=6)
11）Age less than 18 years(n=4)
12）Editorial, notes, communication, news, hypothesis (n=15)
13）Duplicates(n=7)
14）Controversial sample size(n=5)
15）Not in English or Chinese(n=1)
16）Animals(n=10)
17）GERD is not clearly defined (n=9).

Figure 1 The flow diagram of the systematic review.

Table 1 Diet and Lifestyle Factors Related to Each Disease Type in Western and Eastern Country

Diet and Lifestyle Categories	Details About Each Category	GERD		NERD		RE		BE	
		W	E	W	E	W	E	W	E
Dietary pattern	Non-Mediterranean diet, consumption of non-vegetarian food, no intake of meat	+	+						
Dietary habits	Habit of midnight snacks, skipping breakfast, eating quickly, eating beyond fullness, eating very hot foods, frequent liquid food consumption		+		+		+		
Habits after a meal	Lying down soon after eating, Post dinner physical activity (walking), Post dinner physical activity (lying), Post dinner physical activity (sitting)		+						
Coffee	Coffee, former coffee drinkers	+					+	+	
Tea	Tea, peppermint tea, green tea, lower intake of salt tea, Tibetan sweet tea	+	+		+		+		+
Beverage	Soft drink	+							
Milk	Milk, infrequent milk intake		+		+				
Vegetables	Vegetable, dark green vegetable, bean, vegetable and fruit		+		+			+	
Fruit	Fruit, Citrus intake Between meals, citrus				+			+	
Vitamins	Vitamin-E, vitamin-C, folate, vitamin-B2, vitamin-B6, vitamin-B12, isoflavones, lutein, anthocyanidins	+					+	+	
Antioxidant correlation	Dietary inflammatory index							+	
Micronutrient	Magnesium, dietary iron intake						+	+	
Salt	Salt intake, extra salt on regular meals, Table salt use	+	+						
Taste and flavour of food	Raw or cold food, spicy, sweet		+		+				
Staple food	Bread high in dietary fibre content, starch	+					+		
Protein	Processed meat, Tibetan dried meat, egg, Daily meat, fish, and egg intake		+		+	+			
Fat	Fried food, greasy food, high fat diet, saturated fat, monounsaturated fat, total fat	+	+		+	+			+
Fiber	Total fiber							+	
Energy	Total energy				+		+		
Dinner to bedtime interval	Dinner within two hours before going to sleep, eat 2h before bed, dinner-to-bed time was less than 3 h		+						
Smoking related	Smoking, Current smoker, Former smoker	+	+	+	+		+	+	
Drinking related	Alcohol, liquor, wine, beer, alcohol-abusing, Tibetan barley wine	+	+	+	+	+	+	+	+
Psychological status	Depression, state anxiety, trait anxiety, anxiety, anxiety or depression, strong psychological stress, poor mental state		+		+		+		
Marriage state	Divorced/widowed, widowed/widowers, married		+		+		+		
Education	Education level only elementary, level of education, education level	+	+						
Occupation related traits	Sedentary lifestyle, standing occupations, physical labour, night shift		+					+	

(Continued)

Table I (Continued).

Diet and Lifestyle Categories	Details About Each Category	GERD		NERD		RE		BE	
		W	E	W	E	W	E	W	E
Abdominal pressure related	The belt too tight, wearing girdles or corsets, constipation		+		+				
Exercise	Never exercise, physical inactivity, Exercise time less than 30 minutes, exercise, exercise daily >30 minutes, Physical exercise of >30 minutes(>3times/week)	+	+						
Sleep	Insomnia, hours of sleep, staying up late		+						
Living environment	Altitude of residence, length of residence, rural, urban dwelling		+						
Others	Snore, Pan masala chewing		+		+				

Notes: +, stand as there are positive found in here.
Abbreviations: GERD, gastroesophageal reflux disease; NERD, nonerosive gastroesophageal reflux disease; RE, reflux esophagitis; BE, Barrett's esophagus; W, Western country; E, Eastern country.

with GERD. However, drinking beer is negatively correlated with GERD, while altitude, length of residence in the living environment, and urban or rural areas are positively correlated with GERD. Married, divorced, and widowed marital statuses are positively correlated with GERD.

Diet and Lifestyle Factors Related to NERD

Six articles discussed NERD-related dietary and lifestyle factors. All included studies were conducted in 6 non-European and American countries, 2 studies were case-control studies, and 4 studies were cross-sectional studies. The total sample size was 34,762, including 20,778 males and 13,984 females. There were 1398 confirmed NERD patients. The main findings related to the NERD across articles are shown in Table 3. The details of the factors are shown in Appendix 4.

Diet and NERD: Poor eating habits, including snacking at night and overeating, are positively associated with NERD. The consumption of vegetables, fruits, milk, and tea is negatively correlated with NERD, and the relationship between eggs and NERD is inconsistent. Raw, cold, or spicy food, fat, and high-calorie foods are positively related to NERD.

Lifestyle and NERD: Smoking, alcohol consumption, a poor mental state, insomnia, increased abdominal pressure, and snoring are positively correlated with NERD. Married status and NERD are negatively correlated.

Dietary and Lifestyle Factors Related to RE

Fifteen articles discussed the dietary and lifestyle risk factors for RE; 7 studies were conducted in European and American countries, 8 studies were conducted in non-European countries, 1 study was a cohort study, 7 studies were case-control studies, and 7 studies were cross-sectional studies. The total sample size was 60,718. There were 38,104 males, 22,614 females, and 1438 confirmed RE patients (with or without symptoms). The main findings related to RE across the articles are shown in Table 4. The details of the factors are shown in Appendix 5.

Diet and RE: Frequent consumption of liquids, coffee, and strong tea is positively correlated with RE; vitamins and micronutrients are negatively correlated with RE; and starch, protein, fat, and energy intake are positively correlated with RE.

Lifestyle and RE: Smoking, alcohol consumption, and a poor mental state are positively correlated with RE, but wine is negatively correlated with RE. Regarding marital status, both married and divorced statuses are positively correlated with RE.

Dietary and Lifestyle Factors Related to BE

Eighteen articles discussed the diet and lifestyle risk factors for BE; 15 studies were conducted in European and

Table 2 The Main Findings Related to GERD Across the Articles

First Author, Publication Year	Area (Country)	Clinical Study Design	Positive Related Factors	AOR (95% CI)	Negative Related Factors	AOR (95% CI)
I. Mone, 2016[8]	Western country (Albanian)	Cross-sectional study	Non-Mediterranean diet	2.3 (1.2–4.5)		
Lulzim Çela, 2013[9]	Western country (Albanian)	Cross–sectional study	Current smoker	29.3 (13.9–61.2)		
			Former smoker	9.79 (4.22–22.7)		
			Fried food	3.01 (1.52–6.20)		
			Physical inactivity	7.03 (2.68-18.4)		
Ai Kubo, 2014[23]	Western country (American)	Cross–sectional study	Soft drinks	1.86 (1.16–2.97)	Beer	0.54 (0.31–0.96)
			Tea	1.86 (1.02–3.4)	Citrus	0.62 (0.41–0.94)
			Total fat	1.77 (1.07–2.93)		
Frank K. Friedenberg, 2011[28]	Western country (American)	Cross–sectional study	Current smoker	1.74 (1.15–2.65)		
Gawon Ju, 2013[36]	Eastern country (Korea)	Cross-sectional study	Poor sleep quality	3.5 (1.3–9.3)		
			Depressed mood	2.8 (1.5–5.3)		
Yasuhiro Fujiwara, 2005[41]	Eastern country (Japan)	Case control study	Dinner–to–bed time was less than 3 h	7.45 (3.38–16.4)		
Tetsuya Murao, 2011[43]	Eastern country (Japan)	Cross–sectional study	Green tea drinker	1.44 (1.07–1.94)	Hours of sleep	0.90 (0.82–0.99)
					Exercise	0.74 (0.61–0.89)
Masaki Miyamoto, 2007[44]	Eastern country (Japan)	Cohort study	Constipation	7.259 (2.623–20.092)		
Maria Pina Dore, 2008[32]	Western country (Italy)	Case control study	Education level only elementary	3.2 (1.8–5.5)		
			Never exercise	1.9 (1.2–3.5)		
Mirosław Jarosz, 2014[20]	Western country (Australia)	Case control study	Peppermint tea	2.00 (1.08–3.70)		
Omid Eslami, 2017[48]	Eastern country (Iran)	Cross–sectional study	Citrus intake Between meals	2.22 (1.3–3.81)	≥ 12 years schooling	0.55 (0.33–0.91)
Haoxiang Zhang, 2019[54]	Eastern country (China)	Cross–sectional study	Education level (high school vs primary)	2.804 (2.090–3.761)		
			Altitude of residence	2.469 (1.714–3.556)		
			Length of residence	2.218 (1.836–2.679)		
			Tibetan sweet tea	2.158 (1.782 –2.613)		
			Tibetan barley wine	1.271 (1.060 –1.523)		
			Tibetan dried meat	1.278 (1.067 –1.532)		
			Staying up late	1.229 (1.026 –1.472)		
Jia He, 2010[56]	Eastern country (China)	Cross–sectional study	Rural	1.40 (1.13–1.72)		

(Continued)

Table 2 (Continued).

First Author, Publication Year	Area (Country)	Clinical Study Design	Positive Related Factors	AOR (95% CI)	Negative Related Factors	AOR (95% CI)
X.-Q. Ma, 2009[61]	Eastern country (China)	Cross-sectional study	Urban dwelling	3.6 (1.2–10.4)		
Yan Gong, 2019[57]	Eastern country (China)	Cross–sectional study	Smoking	1.19 (1.12–1.264)	Salt intake	0.903 (0.853–0.956)
			Alcohol consumption	1.278 (1.207–1.353)	Physical activity	0.846 (0.808–0.886)
			Daily meat, fish, and egg intake	1.088 (1.042-1.135)	Daily fruit intake	0.91 (0.856–0.967)
Ling-Zhi Yuan, 2019[58]	Eastern country (China)	Cross–sectional study	Eating quickly	4.06 (3.11–5.29)		
			Eating beyond fullness	2.85 (2.18–3.73)		
			Wearing girdles or corsets	2.19 (1.42–3.38)		
			Eating very hot foods	1.54 (1.16–2.05)		
			Lying down soon after eating	1.81 (1.37–2.4)		
			Smoking	1.52 (1.07–2.15)		
Juan Du, 2007[62]	Eastern country (China)	Cross–sectional study	Divorced/widowed	1.82 (1.27–2.60)	Greasy food	0.75 (0.60–0.95)
					Strong tea drinking	0.67 (0.50–0.89)
M Nilsson, 2004[30]	Western country (Norway)	Case Control study	Smoked daily for more than 20 years	1.7 (1.5–1.9)	Coffee	0.6 (0.4–0.7)
			Table salt use	1.5 (1.2–1.8)	Bread high in dietary fibre content	0.5 (0.4–0.7)
			Extra salt on regular meals	1.7 (1.4–2.0)	Physical exercise of >30 minutes (>3/week)	0.7 (0.6–0.9)
Sushil Kumar, 2011[49]	Eastern country (India)	Cross-sectional study	Sedentary lifestyle	2.786 (1.016–7.638)	Intake of fresh fruits ≥1/week	0.631 (0.409–0.973)
			Lower intake of salt tea	1.663 (1.014–2.726)	No intake of meat	0.841 (0.715–0.990)
Sudipta Dhar Chowdhury, 2019[50]	Eastern country (India)	Cross–sectional study	Living in urban area	2.3 (1.9 – 2.8)		
			Infrequent milk intake	1.6 (1.3–1.9)		
Hai-Yun Wang, 2016[51]	Eastern country (India)	Cross-sectional study	Urban	1.8 (1.3–2.5)		
			Pan masala chewing	2.0 (1.2-3.2)		
Praveen Kumar Sharma, 2010[52]	Eastern country (India)	Cross-sectional study	Current smoking	1.48 (1.19–1.83)		
Shobna J. Bhatia, 2011[53]	Eastern country (India)	Cross-sectional study			Consumption of non–vegetarian food	0.34 (0.211-0.545)

(*Continued*)

Table 2 (Continued).

First Author, Publication Year	Area (Country)	Clinical Study Design	Positive Related Factors	AOR (95% CI)	Negative Related Factors	AOR (95% CI)
Shahid Ahmed, 2020[34]	Eastern country (Pakistan)	Cross–sectional study	Exercise time less than 30 minutes	6.47 (4.91–8.53)	Post dinner physical activity (walking)	0.25 (0.13–0.47)
			Habit of midnight snacks	5.08 (4.03–6.4)	Post dinner physical activity (sitting)	0.45 (0.24–0.84)
			Feeling of inadequate sleep	3.22 (2.57–4.03)	Exercise daily >30 minutes	0.02 (0.01–0.03)
			Frequent skipping breakfast	7 (2.17–3.35)		
			Dinner within two hours before going to sleep	6.98 (5.36–9.08)		
			Habit of smoking	6.25 (4.4–8.91)		
			Post dinner physical activity (lying)	2.24 (1.19-4.2)		
Shaha M, 2012[40]	Eastern country (Bangladesh)	Cross–sectional study	Level of education (Primary)	3.095 (1.511–25.889)		
			Married	4.852 (2.23–10.553)		
			Widowed/widowers	14.6 (5.879–36.258)		
P. J. Veugelers, 2006[22]	Western country (Canada)	Case control study	Liquor	2.69 (1.05–6.92)	Vitamin C	0.4 (0.19-0.87)
Nabil Joseph Awadalla, 2019[47]	Eastern country (Saudi Arabia)	Cross-sectional study	Insomnia	1.65 (1.36–2.01)		
Modh Said Rosaida, 2004[39]	Eastern country (Malaysia)	Cross–sectional study	Alcohol	2.42 (1.11–5.23)		
			Education level	1.52 (1.02-2.26)		
ZHANG Min, 2018[63]	Eastern country (China)	Cross-sectional study	Greasy food	1.794 (1.237~2.731)		
			Smoking	2.071 (1.560~2.869)		
YAO XiaoJun, 2018[64]	Eastern country (China)	Cross–sectional study	Eating beyond fullness	3.2 (2.131–5.042)		
			High fat diet	7.568, (4.557–8.908)		
			Liquor	2.262 (1.871–4.322)		
			Mental stress	2.122 (1.551–4.072)		
			Constipation	2.329 (1.409–4.271)		
			Sweet	1.952 (1.121-3.122)		
JIANG Chenglin, 2016[66]	Eastern country (China)	Cross–sectional study	Strong tea	2. 145 (1.338–3. 438)		
			Greasy food	2. 016 (1.208–3.318)		
RONG Liang, 2013[68]	Eastern country (China)	Cross–sectional study	High fat diet	7.964 (6.146–10.319)		
			Alcohol	3.804 (2.982–4.852)		
			Strong tea	2.758 (2.17–3.504)		
			Eating beyond fullness	2.408 (1.896–3.06)		

(Continued)

Table 2 (Continued).

First Author, Publication Year	Area (Country)	Clinical Study Design	Positive Related Factors	AOR (95% CI)	Negative Related Factors	AOR (95% CI)
CHEN HuiXin, 2006[72]	Eastern country (China)	Case control study	Divorced, separated or widowed	4.61 (2.15–9.89)		
			Heavy working pressure	3.43 (1.72–6.84)		
JIANG Chu, 2010[69]	Eastern country (China)	Cross–sectional study	Rural	2.237 (1.422–3.517)		
			High educated	1.242 (1.001–1.542)		
			Work and life are stressful	1.277 (1.089–1.497)		
			Poor mental state	1.20 (1.046–1.665)		
SHEN Xu-De, 2010[70]	Eastern country (China)	Cross-sectional study	Eating beyond fullness	2.053 (1.293,–3.26)		
			Sweet	2.413 (1.252–3.679)		
			Constipation	1.65 (1.038–2.621)		
LIN XiaoDan, 2018[73]	Eastern country (China)	Case control study	Skipping breakfast	2. 879 (1.479 −5.605)		
			Eat 2h before bed	2. 402(1. 213 −4.756)		
			Tea	4.857 (2. 468–9. 559)		
			Alcohol	3.613 (1. 899 −6.874)		
			Shortage of sleep	2.832 (1. 501 −5.345)		
YUAN LinZHi, 2017[74]	Eastern country (China)	Case control study	Eating quickly	3.214 (2.171– 4.759)		
			Eating beyond fullness	2.936 (1.981–4.350)		
			The belt too tight	2.003 (1.013–3.961)		
			Eating very hot foods	1.570 (1.044~2.362)		
GAO HongLiang, 2012[75]	Eastern country (China)	Case control study	Spicy	5.469 (2.57–11.64)		
			Constipation	3.76 (1.592–8.884)		
YIN Yanwei, 2012[76]	Eastern country (China)	Cross–sectional study	Alcohol	2.65 (1.03–6.81)		
			Eating beyond fullness	2.81 (1.04–7.58)		
JIANG Xuan, 2011[77]	Eastern country (China)	Cross–sectional study	Alcohol	2.63 (1.17–5.92)		
			Physical work	1. 79 (1.13 −2.86)		
HU ShuiQing, 2009[78]	Eastern country (China)	Cross–sectional study	Eating beyond fullness	2.78 (1.76–4.18)		
			Greasy food	4.36 (2.61–9.08)		
			Constipation	2.06 (1.18–3.48)		
			Mental stress	2.11 (1.2–3.52.)		

(*Continued*)

Table 2 (Continued).

First Author, Publication Year	Area (Country)	Clinical Study Design	Positive Related Factors	AOR (95% CI)	Negative Related Factors	AOR (95% CI)
ZHANG Hong, 2007[79]	Eastern country (China)	Cross–sectional study	Night shift	1.381 (1.1113–1.713)		
			Physical labour	2.043 (1.554–2.687)		
			Eating beyond fullness	1.775 (1.506–2.091)		
			Greasy food	1.506 (1.269–1.788)		
			Strong tea	1.572 (1.314–1.88)		
			Sweet	1.273 (1.075–1.508)		
			Constipation	1.724 (1.438–2.068)		

Abbreviations: GERD, gastroesophageal reflux disease; AOR, adjusted odds ratio.

American countries, 3 studies were conducted in non-European countries, 2 studies were cohort studies, 13 studies were case-control studies, and 3 studies were cross-sectional studies. The sample size was 58,032, including 30,135 males and 27,897 females. Among the participants, 4185 participants were diagnosed with BE (with or without heterogeneous hyperplasia and symptoms). The main findings related to BE across the articles are shown in Table 5. The details of the factors are shown in Appendix 6.

Diet and BE: Coffee, tea and fruit are positively correlated with BE, and the intake of vegetables, vitamins, micronutrients, and fiber is negatively correlated with BE; however, vitamin B12 is positively correlated with BE.

Lifestyle and BE: Smoking and alcohol consumption are positively correlated with BE, but wine and beer are negatively correlated with BE. Standing occupational activity was negatively correlated with BE.

Discussion

In summary, protein and fat as dietary factors and smoking, alcohol consumption (except for beer and wine), and mental state as lifestyle factors were all observed to be positively correlated with GERD and other types of reflux. Vegetarian diets, fruits, vegetables, vitamins and fiber were negatively correlated with GERD and other types of reflux, while poor eating habits were positively correlated with GERD, GER, and NERD. This association was not found in the RE and BE types. We speculate that poor eating habits may aggravate the perception of symptoms of GERD. An interval of less than 3 hours between dinner and sleep or physical exercise was negatively correlated

with GERD. Many dietary and lifestyle factors affect the onset of GERD, and the factors influencing the different types vary.

We also found that eating citrus fruits with meals is positively correlated with GERD.[48] However, it has also been shown that citrus is negatively correlated with GERD, which may be related to the fact that GERD patients avoid eating such foods, which leads to biased results.[23] Studies have shown that acidic fruits, such as citrus fruits and tomatoes, can induce reflux–related symptoms. The possible reasons are increased acidic fluid intake and frequent swallowing.[80–82] Moreover, less volume to swallow and acidic beverages cause the pH of the esophagus to rapidly decrease to <4. In vitamin-related studies, vitamins have been shown to be negatively correlated with GERD, RE, and BE, but vitamin B12 was found to be positively correlated with BE. This finding may be explained by vitamin B12 being mainly derived from meat and milk, and vitamin B12 is almost absent from plant foods.[83]

The dietary factors related to fat in this article were fried foods, greasy foods, high-fat diets, saturated fatty acids, monounsaturated fatty acids, and total fats. Studies have shown that dietary fats are mainly used to enhance people's gastroesophageal reaction. The perception of fluid symptoms is thought to be involved rather than increasing the time of esophageal acid exposure and the frequency of TLESR.[84] Spicy food is positively correlated with GERD and NERD.[65,75] Capsaicin increases the pressure of the LES, esophageal contraction and transmission speed in healthy subjects, and as spiciness increases, the impact on the esophagus and stomach becomes more significant.[85,86]

Table 3 The Main Findings Related to NERD Across the Articles

First Author, Publication Year	Area (Country)	Clinical Study Design	Positive Related Factors	AOR (95% CI)	Negative Related Factors	AOR (95% CI)
Nobuyuki Matsuki, 2013[45]	Eastern country (Japan)	Cross–sectional study	Egg	1.89 (1.01–3.5)		
			Strong psychological stress	1.77 (1.18–2.62)		
			Sleep shortage	2.44 (1.54–3.88)		
Su Youn Nam, 2016[35]	Eastern country (Korea)	Cross–sectional study	Current smoker	1.54 (1.29–1.84)	Beans	0.78 (0.64–0.95)
			Total energy intake	1.07 (1.0–1.14)	Fruits	0.78 (0.64–0.95)
					Egg	0.78 (0.64–0.96)
					Milk	0.78 (0.65–0.94)
					Drink–tea	0.62 (0.5–0.76)
Ji Min Choi, 2018[37]	Eastern country (Korea)	Cross–sectional study	State anxiety	1.89 (1.53–2.33)	Marriage status	0.71 (0.58–0.87)
			Rait anxiety	1.78 (1.34–2.35)		
			Depression	2.21 (1.75–2.8)		
			Current smoking	1.37 (1.18–1.59).		
Juan Du, 2007[62]	Eastern country (China)	Cross–sectional study	Greasy food	1.65 (1.16–2.36)		
			Constipation	1.51 (1.01–2.25)		
CHEN LiPing, 2016[71]	Eastern country (China)	Case control study	Habit of midnight snacks	2.752 (1.449–5.228)		
			Snore	2.334 (1.361–4.004)		
			Alcohol	3.957 (1.067–14.673)		
			Anxiety or depression	2.723 (1.407–5.267)		
WANG Yi, 2018[65]	Eastern country (China)	Case control study	Raw or cold food	5.47 (1.21–24.71)		
			Spicy	3.36 (1.15–9.84)		
			Eating beyond fullness	9.98 (3.57–27.88)		
			Anxiety	4.09 (1.8–9.26)		
			Depression	2.21 (1.25–3.9)		

Abbreviations: NERD, nonerosive gastroesophageal reflux disease; AOR, adjusted odds ratio.

Regarding eating habits, eating snacks at night, frequently skipping breakfast, eating quickly, eating hot food, and overeating are positively correlated with GERD,[34,58,64,68,70,73,74,76,78,79] and snacking at night and overeating are positively correlated with NERD.[65,71] Frequent liquid consumption is positively correlated with RE.[55] We reasonably speculate that appropriate, moderate and regular eating habits are important factors for preventing GERD.

Regarding postmeal habits, sitting or walking after a meal instead of lying down is beneficial for patients with gastroesophageal reflux disease. It is inferred that a postprandial posture is a factor influencing GERD. However, studies have shown that body position does not impact the changes in gastric acidity that occur in healthy subjects after fasting or after meals.[87] In one study, 24-hour esophageal pH monitoring was used to compare subjects with esophagitis with bidirectional reflux and subjects with only upright reflux without esophagitis, and it was found that the subjects with bidirectional reflux and esophagitis experienced increased reflux in the supine

Table 4 The Main Findings Related to RE Across the Articles

First Author, Publication Year	Area (Country)	Clinical Study Design	Positive Related Factors	AOR (95% CI)	Negative Related Factors	AOR (95% CI)
Anna Boguradzka, 2011[19]	Western country (Australia)	Cross-sectional study	Alcohol–abusing	7.34 (2.27–23.7)		
Su Youn Nam, 2016[35]	Eastern country (Korea)	Cross–sectional study	Current smoker	1.7 (1.44–2.01)		
			Current drinker	1.26 (1.03–1.54)		
			Total energy.	1.08 (1.0–1.16)		
Ji Min Choi, 2018[37]	Eastern country (Korea)	Cross–sectional study	State anxiety,	2.2 (1.27–3.81)	Marriage status	0.45 (0.27–0.74)
			Depression	2.23 (1.18–4.22)		
			Current smoking.	2.28 (1.47–3.55)		
Hideyuki Chiba, 2012[42]	Eastern country (Japan)	Cross–sectional study	Alcohol	1.398 (1.040–1.880)		
			Smoking	1.884 (1.307–2.716)		
C. H. Park, 2012[38]	Eastern country (Korea)	Case control study	Smoking	2.827 (1.932–4.664)		
			Coffee	1.347 (1.131–1.428)		
Naomi Mochizuki, 2018[46]	Eastern country (Japan)	Cohort study	Current smoking	1.34 (1.12–1.61)		
			Alcohol consumption 20 g/day	1.57 (1.34–1.84)		
			High levels of stress	1.4 (1.17–1.68)		
Linda Sharp, 2013[10]	Western country (Ireland)	Case control study			Folate	0.34 (0.18–0.64)
					Vitamin B–6	0.30 (0.16–0.55)
					Vitamin B–2	0.35 (0.19–0.66).
LESLEY A. ANDERSON, 2009[11]	Western country (Ireland)	Case control study	Total alcohol consumption at age 21 years	2.24 (1.35–3.74)	Wine consumption at 5 Years Prior to Interview	0.45 (0.27–0.75)
Helen G. Mulholland, 2009[12]	Western country (Ireland)	Case control study	Starch	3.73 (1 1.2– 11.65)		
Mark G. O'Doherty, 2011[13]	Western country (Ireland)	Case control study	Total fat	3.54 (1.32–9.46)		
			Monounsaturated fat	2.63 (1.01–6.86)		
			Saturated fat	2.79 (1.11–7.04)		
			Processed meat	4.67 (1.71–12.74)		
Qi Dai, 2016[14]	Western country (Ireland)	Case control study			Magnesium	0.12 (0.02–0.73)
Seamus J. Murphy, 2010[16]	Western country (Ireland)	Case control study			Vitamin C	0.46 (0.24–0.90)
Kun Wang, 2019[55]	Eastern country (China)	Cross–sectional study	Ever smoking	1.416 (1.012–1.983)		
			Frequent liquid food consumption	1.502 (1.076–2.095)		

(*Continued*)

Table 4 (Continued).

First Author, Publication Year	Area (Country)	Clinical Study Design	Positive Related Factors	AOR (95% CI)	Negative Related Factors	AOR (95% CI)
S. Peng, 2009[60]	Eastern country (China)	Cross–sectional study	Alcohol	3.22 (1.92–5.39)		
Juan Du, 2007[62]	Eastern country (China)	Cross–sectional study	Strong tea drinking	1.62 (1.18–2.23)	Divorced/widowed	0.55 (0.36–0.85)

Abbreviations: RE, reflux esophagitis; AOR, adjusted odds ratio.

position, the patients with upright reflux without esophagitis experienced reduced reflux in the supine position, postprandial reflux was increased in the patients without esophagitis, and bidirectional reflux with esophagitis gradually decreased after meals; the differences between the two reflux diseases in different positions and 24 h postprandial esophageal pH monitoring indicated that the pathological mechanisms of different types of gastroesophageal reflux diseases may be different, but postprandial habits and posture indeed affect reflux.[88] Studies have shown that among patients with nocturnal acid reflux, changing the sleeping posture, ie, raising the head of the bed by 20 cm, can effectively reduce the acid reflux time, acid clearance time, and number of reflux events >5 min.[89] Another study showed that as a result of the use of a sleep-positioning device (SPD) among healthy subjects and the use of a left-side decubitus (SPD-L), the esophageal acid exposure time and reflux times were significantly lower than those associated with the right lateral position (SPD-R), any position with a standard wedge sleep aid device and the supine position.[90]

An interval of less than 2 hours between dinner and sleep, eating 2 hours before bed, and an interval of less than 3 hours between dinner and sleep were positively correlated with GERD.[34,41,73] Studies have shown that when the interval between dinner and sleep is less than 2 hours, the percentage of reflux time is significantly higher than when the interval between dinner and sleep is greater than 2 hours (22.6% vs 14.2%; P=0.012). There was no significant difference in the percentage of reflux time according to an interval between dinner and sleep less than 3 hours and an interval between dinner and sleep greater than 3 hours (16.3% vs 14.6%, P=0.798).[91] This finding suggests that GERD patients should stop eating 3 hours before bedtime.

Smoking and alcohol consumption are positively correlated with GERD. This finding is consistent with the conclusions of previous studies. A meta-analysis found that smoking is a risk factor for BE and that alcohol consumption is a risk factor for GERD.[92,93] However, wine is negatively correlated with RE 11 and BE,[25] and beer is negatively correlated with GERD 23 and BE.[17] Because the pathological changes associated with RE and BE are caused by the activation of inflammatory pathways by reflux substances, which leads to mucosal damage,[94] we suspect that this finding may be related to the antioxidant substances in beer and wine.[95,96]

Psychological factors were found to be positively correlated with GERD, NERD, and RE. However, it was found that the severity of anxiety was related to retrosternal pain and heartburn, while the levels of anxiety and depression were not associated with the number of reflux symptoms or the number of related reflux events reported by 24-hour pH impedance monitoring.[97]

Sleep time or quality is correlated with GERD. Previously, it was believed that a lack of sleep and GERD interact. Nocturnal acid reflux seriously affects the quality of sleep, and a lack of sleep can cause hyperalgesia of the esophageal mucosa to gastric acid.[98] A recent study found that night awakening can induce nocturnal acid reactions. However, acid reflux at night does not cause awakening.[99]

We conclude that exercise is beneficial for GERD, but relevant research concerning the type and degree of exercise that are most suitable for reducing GERD is lacking. A study involving 10 healthy athletes found that running could cause a significant increase in the percentage of time with PH<4 and that increasing the exercise intensity could lead to an increase in the frequency of reflux events and an extension of the duration of reflux.[100]

In our research, we found that lifestyle factors that increase abdominal pressure, such as belt tightness,[74] wearing girdles or corsets,[58] and constipation,[44,64,70,75,78,79] are positively correlated with GERD and NERD.[62] For example,

Table 5 The Main Findings Related to the BE Across the Articles

First Author, Publication Year	Area (Country)	Clinical Study Design	Positive Related Factors	AOR (95% CI)	Negative Related Factors	AOR (95% CI)
Olivia M Thompson, 2009[24]	Western country(American)	Case control study			Vegetables	0.33 (0.17–0.63)
					Vegetables and fruit	0.39 (0.21–0.75)
Ai Kubo, 2004[25]	Western country(American)	Case control study			Wine drinkers	0.44 (0.2–0.99)
Li Jiao, 2013[26]	Western country(American)	Case control study			Dark green vegetables	0.46 (0.26–0.81)
					Legumes	0.52 (0.30–0.90)
					Total fiber	0.50 (0.28–0.90)
					Isoflavones	0.45 (0.25–0.81)
					Total folate	0.52 (0.30–0.67)
					Vitamin E	0.46 (0.26–0.83)
					Lutein	0.45 (0.26–0.79)
Jessica L. Petrick, 2015[27]	Western country(American)	Case control study			Anthocyanidins	0.49 (0.30–0.80)
Douglas A. Corley, 2008[29]	Western country(American)	Case control study			Dietary iron intakes	0.37 (0.17–0.80).
Stephen Lam, 2017[33]	Western country(UK)	Cohort study			Standing occupation	0.51 (0.31–0.83)
Linda Sharp, 2013[10]	Western country (Ireland)	Case control study	Vitamin B-12	2.11 (1.12–3.98)	Folate	0.40 (0.21–0.75)
					Vitamin B–6	0.31 (0.16–0.58)
Helen G. Mulholland, 2009[12]	Western country (Ireland)	Case control study			Fiber	0.40 (0.22–0.73)
Qi Dai, 2016[14]	Western country (Ireland)	Case control study			Magnesium	0.24 (0.06–0.96)
Nitin Shivappa, 2017[15]	Western country (Ireland)	Case control study	Dietary inflammatory index	2.05 (1.22–3.47)		
RA Filiberti, 2017[31]	Western country (Italy)	Case control study	Former coffee drinkers higher with duration cup per day >1	3.79 (1.31–11.0)		
Aaron P. Thrift, 2011[17]	Western country (Australia)	Case control study			Beer	0.49 (0.25–0.96)
Torukiri I. Ibiebele, 2013[18]	Western country (Australia)	Case control study	Fruits	1.83 (1.02–3.29)	Total β-carotene	0.45 (0.20–1.00)

(*Continued*)

Table 5 (Continued).

First Author, Publication Year	Area (Country)	Clinical Study Design	Positive Related Factors	AOR (95% CI)	Negative Related Factors	AOR (95% CI)
Jessie Steevens, 2010[21]	Western country (Netherland)	Cohort study	Former cigarette smokers	1.33 (1.00–1.77)		
Yan-Hua Chen, 2019[59]	Eastern country(China)	Cross–sectional study	Tea	1.695 (1.043–2.754)		
S. Peng, 2009[60]	Eastern country(China)	Cross–sectional study	Alcohol consumption	2.67 (1.09–6.56)		
YIN CaiQiao, 2016[67]	Eastern country(China)	Cross–sectional study	High fat high	2.216 (1.06–2.695)		
P. J. Veugelers, 2006[22]	Western country (Canada)	Case-control study	Liquor	3.06 (1.23–7.62)	Vitamin C	0.44 (0.2-0.98)

Abbreviations: BE, Barrett's esophagus; AOR, adjusted odds ratio.

in obese people, the factors related to GERD include an increase in the diaphragm pressure gradient caused by an increase in abdominal pressure caused by central obesity rather than body mass index (BMI).[101]

We also noticed that some occupational characteristics are related to GERD. Standing occupational activity[33] was negatively correlated with BE. Sedentary labor,[49] physical labor,[77] and physical labor intensity[79] are positively correlated with GERD. Marital status, educational experience, and the living environment (urban or rural) are not associated with GERD, but it has been found that altitude and length of residence in the same area[54] are positively correlated with GERD, which may be the result of bias caused by the research design.

Studies[102] have shown that health-related behaviors do not occur simultaneously in individuals but rather in clusters. The investigation of four health-related behaviors, ie, smoking, drinking, diet and sports activities, showed that the aggregation of different behaviors has sex differences. In addition, these factors are related to age. Additionally, the behavioral risk factors for noncommunicable diseases[103] differ among groups with different socioeconomic statuses, and their dietary and lifestyle habits differ. In low-income and low-middle-income countries, groups with a low socioeconomic status more commonly smoke and consume alcohol than those with a high socioeconomic status. Compared with people with a high socioeconomic status, those with a low socioeconomic status consume less fruits, vegetables, fish and fiber; compared with people with a low socioeconomic status, people with

a high socioeconomic status exercise less and consume more fat, salt, and processed food. These findings further confirm that dietary structure[104] differs by age, gender, socioeconomic status, region (urban/rural) and residential area. In our research, we found that among all dietary and lifestyle risk factors, those associated with GERD in Eastern countries are eating habits, postprandial behaviors, milk, food taste, energy, time from dinner to sleep, psychological status, marital status, sleep, living environment, etc. The relevant influencing factors only identified in Western countries are staple food, fiber, vitamins, trace elements, dietary inflammatory factors, and soft drinks. However, whether differences exist in the incidence of GERD according to region, sex and age based on regional differences in diet and lifestyle habits requires further research and confirmation in follow-up studies.

Some studies have involved subgroup analyses based on symptoms, endoscopy, and pathological examinations. For example, two articles[35,37] simultaneously studied NERD and RE, four articles[10,12,14,60] conducted research concerning RE and BE, one article[22] conducted research concerning GERD and BE, and one article[62] conducted research concerning GERD, NERD, and RE simultaneously, further indicating that differences in diet and lifestyle exist among GERD, NERD, RE and BE. Since the risk factors for different types of gastroesophageal reflux differ, future research should focus on the different types of risk factors, targeted prevention and control to prevent the occurrence of these diseases.

There are some limitations in our study. We only searched two English databases and two Chinese databases, which may only reflect GERD-related factors associated with diet and lifestyle to a certain extent. Due to the heterogeneity among the studies and the different definitions and measurement methods used for each factor, we cannot make quantitative inferences regarding each variable or determine a dose effect. Additionally, the classification and division of various dietary factors cannot be absolutely accurate. For example, regarding sweets, the sweet taste is mainly due to the content of starch, and sweets might not be categorized as fat-related fried foods or greasy foods despite their fat content. Furthermore, we identified the independent factors influencing only GERD in the current literature. It is well known that a single influencing factor does not cause the disease. The disease is usually the result of multiple factors. What type of interaction exists among these factors? Further research is needed.

Conclusion

GERD is a chronic digestive system disease caused by multiple factors and multiple pathways. We found that various dietary and lifestyle factors affect the occurrence of GERD. Among GERD, RE, NERD, and BE, the associated diet and lifestyle factors are different. There were also differences in the diet- and lifestyle-related factors related to GERD according to region. Whether such differences are the cause of the differences in incidence requires further research. Whether the differences in diet and lifestyle structure associated with age and sex are also reasons for the difference in incidence needs further study.

Author Contributions

All authors made a significant contribution to the work reported, as related to the conception, study design, execution, acquisition of data, analysis and interpretation, or all of the above; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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