

## Smoking, alcohol, physical activity and gastroesophageal reflux disease: A literature review and the Albanian experience

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### Abstract

The aim of this article was to review how the behavioral factors such as smoking, alcohol and physical activity are involved in gastroesophageal reflux diseases (GERD) pathogenesis. Different pathogenic mechanisms for the association between these behavioral factors and GERD development have been suggested. Smoking decreases the lower esophageal sphincter (LES) pressure, may reduce salivary bicarbonate secretion and affects the esophageal epithelium due to direct effect of smoke products. Alcohol consumption facilitates hydrogen ion penetration into esophageal mucosa, causes dysfunction of LES, abnormal esophagus peristalsis, motility disorder, and may increase the acid secretion through gastrin stimulation. Physical exercise reduces gastrointestinal blood flow, alters the motor function of the esophagus and increases inspiratory thoraco-abdominal pressure gradient leading to reflux of gastric content into the esophagus. On the other hand, physical exercise may increase the inspiratory striated muscle tone, a key component of the antireflux barrier. However, there is sufficient evidence to show that modulation of these agents is either effective or ineffective in GERD symptoms. Further prospective studies are warranted to investigate the impact of these modifiable behavioral factors which, with prevention mechanisms, can help to reduce the burden of GERD in the general population.

**Keywords:** alcohol, gastroesophageal reflux disease (GERD), physical activity, smoking.

## Introduction

Gastroesophageal reflux disease (GERD) is one of the most common gastrointestinal disorders in the Western world (1). It was compared as an “iceberg”, in which only a small part is visible and this visible part has been growing steadily in the developed countries (2).

GERD is defined as an increased frequency or duration of exposure of the distal esophagus to gastric contents (3). GERD is a chronic disease, with a large clinical spectrum of signs and symptoms, usually interesting many other regions of the body, including the mouth, lungs, ear, nose and throat, and it is associated with frequent relapses. The classic symptoms of GERD are heartburn and acid regurgitation. The presence of these symptoms is used to diagnosis this condition and are sufficient to start empiric therapy (3).

GERD is a multi-factorial process and its pathophysiology is complex. Many different aggressive and defensive factors are involved promoting or retarding the reflux of gastric content into the esophagus: reduced lower esophageal sphincter (LES) pressure, hiatal hernia, acid pocket, impaired esophageal clearance, increased abdominal pressure, visceral hypersensitivity, impaired mucosal integrity, central sensitization, and psychological factors (4). Also, these mechanisms can interplay with epidemiological risk factors for GERD at many different levels. Furthermore, GERD different environmental and lifestyle factors may contribute to its pathophysiology (5). Dietary habits such as fatty foods, spicy foods, carbonated beverages and coffee, body weight, smoking alcohol consumption and physical activity have been implicated in increasing the risk for GERD (2). However, the exact role of these factors in the pathophysiology of GERD is still under debate and the effectiveness of recommended changes in lifestyle habits is also controversial (6).

In this article, our aim was to explore how behavioral factors such as smoking, alcohol consumption and physical activity are involved in gastroesophageal reflux pathogenesis.

## Smoking and gastro-esophageal reflux disease

It is common believe that smoking and its intensity is a risk factor for GERD. Different studies have analyzed the relationship between smoking and GERD but conflicting results have been obtained. Multiple studies have shown that smoking increase the risk for developing GERD (7-16), whereas some studies did not show any significant association or reported a negative association (17-24). However, these studies have utilized different definition of GERD (symptom questionnaire, self-administrated questionnaire, upper endoscopy) as well as different assessment of tobacco smoking (smoking/nonsmoking, number of tobacco smoking, smoking habit, type of tobacco smoking) (Table 1). Furthermore, another explanation for these heterogeneous results may be related with the synergistic and multiplicative effect of the combination of alcohol and tobacco use (25). Also, it has been shown that more than 75% of chronically alcoholic consumers are smokers (25). Hence, in the epidemiological studies is difficult to evaluate the different and separate effects of these factors.

Despite these conflicting results, different pathophysiologic mechanisms for the relationship between smoking and development of GERD have been suggested. First, smoking chronically diminished the LES pressure and then promotes the reflux of gastric content into the esophagus and heartburn (26). Second, it may reduce salivary bicarbonate secretion and thus prolonged acid esophageal clearance time (27). Third, tobacco use affects the esophageal epithelium due to direct effect of smoke products. Moreover, nicotine concentration in saliva was 10 times more than in blood resulting in reduction of mucosal barrier functions (26). Fourth, it has been shown that increase rate of reflux episodes among smokers probably was related with the respiratory complications and the majority of reflux episodes occurred during coughing or deep inspiration (28). However, no data show that cessation of tobacco smoking leads to reduction of GERD symptoms.

**Table 1. Association between smoking and GERD**

Author	Year	Country	Study design	Population size	Smoking assessment	Method of data collection	Association
Nilsson et al. (7)	2004	Norway	Population-based, case-control	43363	- Daily tobacco smoking - Lifetime number of tobacco smoking	Questionnaire	Yes
Nandurkar et al. (20)	2004	USA	Population-based nested case-control	211	Ever smoked: No/yes	Validated questionnaire (interview or mail)	No
Bretagne et al. (17)	2006	France	Population based	5395	Smoking/nonsmoking	Mail Questionnaire	No
Nocon et al. (8)	2006	German	Population-based	7124	Ex-smoker Smoker (number of cigarettes per day)	Symptoms and lifestyle questionnaire	Yes
Dore et al. (23)	2008	Italy	Case-control	500	No/ex-smoker/yes	Questionnaire and upper endoscopy	No
Zagari et al. (22)	2008	Italy	Population-based	1033	Never/former/current	Validated questionnaire and upper endoscopy	No
Eslick et al. (14)	2009	Australia	Cross-sectional	1000	Current smoker	Self-reported validated questionnaire	Yes
Bhatia et al. (21)	2011	India	Cross-sectional	3224	Smoking/chewing/ smoking + chewing	Questionnaire	No
Yamamichi et al. (9)	2012	Japan	Population-based	19864	Habit of smoking	Questionnaire and symptoms scale	Yes
Pandeya et al. (24)	2012	Australia	Cross-sectional	1580	Never smoker/current smoker/ex-smoker	Questionnaire	No
Minatsuki et al. (10)	2013	Japan	Hospital based	10837	Current smoker /current nonsmoker	Upper endoscopy	Yes
Friedenberg et al. (11)	2013	USA	Population based survey	379 (weighted-22409)	Non-smoker Low/medium/high	Questionnaire	Yes
Pandeya et al. (24)	2012	Australia	Cross-sectional	1580	Never smoker/current smoker/ex-smoker	Questionnaire	No
Minatsuki et al. (10)	2013	Japan	Hospital based	10837	Current smoker /current nonsmoker	Upper endoscopy	Yes

Meta-analyses of three case-control studies did not demonstrate any improvement in GERD symptoms after cessation of tobacco smoking (6). Recently, a prospective study of the population of Nord-Trøndelag County, Norway did not find any association between cessation of tobacco use and improvement of GERD symptoms in individuals not using regular anti-reflux medication (29).

### **Alcohol consumption and gastro-esophageal reflux disease**

Alcohol consumption is a huge international problem and one of the major risk factor for morbidity and mortality worldwide. Several studies showed the alcohol consumption to be associated with many adverse health problems, including GERD (1). Most

researchers and physiologic studies have concluded that drinking alcohol worsens esophageal acid exposure and is frequently associated with GERD symptoms (19,25,30-32). There are several possible factors that may contribute to the development of GERD in the chronic and long-term consumption of drinking alcohol. Alcohol consumption facilitates hydrogen ion penetration into the esophageal mucosa and may cause direct mucosal injury (31). It has been shown that alcohol consumption was associated with the development of GERD through dysfunction of lower esophageal sphincter, abnormal esophagus peristalsis and motility disorder (33). Acetaldehyde is the first product of ethanol metabolism which has been shown to be a highly toxic substance and could affect the function of the esophagus (34). Likewise, alcohol

may impair the gastric emptying and increase the acid secretion through gastrin stimulation (32,35). Despite this, some surveys have demonstrated that alcohol consumption has been inversely associated with GERD symptoms or did not affect the risk of reflux (7,8,16,18,21-24). Furthermore, a recent systematic review reported that there is insufficient evidence to support the benefit of stopping alcohol use on esophageal pH levels or GERD symptoms (6). These contradictory results between studies may relate with the different effects of beers, wines and liquors, and the effects of non-alcoholic compounds in those alcoholic beverages on the risk of GERD (Table 2) (25,36-39).

### Physical activity and gastro-esophageal reflux disease

It has been argued that physical activity represents another risk factor for developing GERD but its role is complex and intriguing. Previous investigations have demonstrated that frequent leisure physical activity is inversely associated with GERD symptoms (7,8,16), while strenuous exercise and physical activity at work exacerbated symptoms of GERD (16,40,41). On the other hand, other studies have been unable to show any association between physical activity and reflux episodes or LES parameters (42-44). The discrepancy between studies may be related with the fact that

**Table 2. Association between alcoholic beverages and GERD**

Author	Country	Study design	Population size	Method of data collection	Alcoholic beverages	OR (95%CI)	P value
Pehl et al., 1998 (37)	Germany	Crossover	20 healthy volunteers	1-h postprandial esophageal manometry pH measurement	White wine	13.2 (0.3-58.1)	< 0.01
					Red wine	2.3 (0.7-24.4)	< 0.05
Veugelers et al., 2006 (38)	Canada	Hospital based case-control	431	Upper endoscopy	Beer	1.21 (0.54-2.71)	Ns
					Wine	0.71(0.23-2.20)	Ns
					Liquor	2.69 (1.05-6.92)	<0.05
Anderson et al., 2009 (36)	Ireland	Population based case-control	941	Interview	Beer	0.94 (0.57-1.54)	NS
					Wine	0.45 (0.27-0.75)	<0.05
					Liquor	1.22 (0.77-1.93)	NS
Seidl et al., 2011 (39)	Germany	Case- control	21	Upper endoscopy 24-h pH measurement	White wine (wine vs water)	23.4 (1.5-46.4)	< 0.001
					Rose wine (white wine vs rose wine)	9.3 (0.2-42.7)	< 0.05
					Beer	9.5 (0.8-24.1)	< 0.05
					(white wine vs beer)		< 0.01

intensity, length, type and specific physical activity undertaken play a different pathogenic role on occurrence of GERD symptoms (45).

However, experimental studies suggest that intense exercise may increased reflux symptoms because of different path-physiological mechanisms (45). Intense exercises reduced gastrointestinal blood flow as a result of sympathetic stimulation, secretion of substance such as vasoactive intestinal peptide, secretin and peptide-histidine-methionine, as well as dehydration. High-intensity exercise alters the motor function of the esophagus and the ventricle and may worsen the symptoms of the upper gastrointestinal tract (45). Also, exercise may alter the secretion of neuroendocrine factors which may increases or decreases the gastrointestinal motility (45). Further-

more, during exercise the inspiratory thoraco-abdominal pressure gradient is increased, leading to reflux of gastric content into the esophagus (46).

Despite these convincing evidences from experimental studies, in a case control study, Dore et al. found that having physically heavy jobs did not increase the risk of GERD and regular exercise had a protective effect (23). Also, participants who never exercise had almost three times greater risk of having GERD than those who exercised two or more hours per week (OR = 2.7; 95% CI = 1.6-4.6) (P = 0.001) (23). Similar results have been obtained by a cross-sectional study in Australia. Pandeya et al. have reported that regular physical activity was associated with lower prevalence of frequent GERD symptoms (moderate physical activity: Prevalence Ratio=0.68,

95%CI= 0.49–0.94; high physical activity: Prevalence Ratio= 0.46; 95%CI=0.32–0.66) (24).

Recently, a population-based study by Friedenberget al. found that moderate and high physical activity were inversely associated with heartburn, OR=0.32; 95% CI = 0.28"0.36 and OR=0.40; 95%CI= 0.35"0.45 respectively (11). A proposed mechanism is that strength and tone of inspiratory striated muscle, a key component of the antireflux barrier may modify and increases during training and exercises (7,16,47). Similarly, a prospective randomized controlled study have shown that actively training of diaphragmatic muscle using breathing training exercises can facilitating reflux symptoms (48). Therefore, the authors recommended that lifestyle intervention could help to improve the GERD symptoms. However, it is unclear whether the protective effect resulted from increased physical activity or from benefits of physical activity on weight. For example, in a population-based study Djärv et al. reported that intermediate physical activity in obese individuals was associated with decreases risk of GERD, while no effect of physical activity was found in normal or overweight individuals (44).

### **Lifestyle characteristics and gastro-esophageal reflux disease: the Albanian experience**

Population-based data on the prevalence and the contribution of lifestyle factors to GERD in transitional countries of Southeast Europe including Albania are scarce. Traditionally, Albania population consuming

the Mediterranean type diet rich in olive oil, fruits and vegetables and relatively low in meat and dairy products. Since the 1990s, after the end of the communist regime the Albanian diet is become more diversified and has include an emerge “western” behaviors consisting of high in saturated fats, trans-fatty acids, free sugars and salted foods.

Therefore, we conducted two studies to assess the prevalence and lifestyle correlates of GERD in the adult population of Albania (49,50). The first, a case-control study, was conducted in Tirana in 2005-2007. The 378 participants who consisted in the hospital patients underwent a structure questionnaire and upper endoscopy. Assessment of GERD was based on the Los Angeles criteria (49). The second, a cross-sectional study, was conducted in Tirana during 2012. A total of 845 individuals

(≥18 years), a representative sample of Albania, were interviewed. Assessment of GERD was based on Montreal definition (50).

We obtained important evidence on the prevalence and lifestyle factors associated with GERD in a Western Balkans’ country. One hundred and one (11.9%) of 845 individuals had GERD symptoms. There were no significant sex-differences and individuals with GERD were older. We found that smoking and physical inactivity was risk factor for GERD in Albanian population while alcohol consumption did not affect the risk of GERD (Table3). However, findings from our studies should be replicated in future longitudinal studies in Albania.

**Table 3. Association of smoking, alcohol consumption, physical activity with GERD in the Albanian population**

Author	Study design	Population size	Method of data collection	Exposure	OR (95%CI)	P value	Adjustment
Kraja et al., 2008 (49)	Case-control	126 cases 252 controls	Questionnaire Upper endoscopy	Smoking (no/yes)	1.64 (1.04–2.59)	0.03	Age
				Alcohol (drinks/day)	1.01 (0.84–1.22)	Ns	
				Physical activity (little vs. moderate)	0.54 (0.32-0.91)	0.02	
Cela et al., 2013 (50)	Cross-sectional	845	Questionnaire	Smoking (never vs. current)	29.3 (13.9-61.2)	<0.001	Age, sex, socioeconomic variable and behavioral factors
				Alcohol (moderate/heavy vs. no/occasional)	1.83(1.10-3.06)	Ns	
				Physical activity (low vs. high)	5.47 (2.32-12.9)	<0.001	

## Conclusions

This review has emphasized our understanding on the role of factors such as smoking, alcohol and physical activity on GORD symptoms over the last years. Although researchers have published wide-ranging results, their overall influence on the development of GERD is relatively weak. Also, there is sufficient evidence to show that modulation of these agents is

either ineffective or effective in GERD symptoms. Further prospective studies are warranted to investigate the impact of these modifiable behavioral factors which with prevention mechanism can help to reduce the burden of GERD in the population.

**Author's contribution:** The authors have contributed equally.

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