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 physiopathology 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.
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 factors 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).

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

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Country</th>
<th>Study design</th>
<th>Population size</th>
<th>Smoking assessment</th>
<th>Method of data collection</th>
<th>Association</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nilsson et al.</td>
<td>2004</td>
<td>Norway</td>
<td>Population-based, case-control</td>
<td>43363</td>
<td>- Daily tobacco smoking - Lifetime number of tobacco smoking</td>
<td>Questionnaire</td>
<td>Yes</td>
</tr>
<tr>
<td>Nandurkar et al.</td>
<td>2004</td>
<td>USA</td>
<td>Population-based, case-control</td>
<td>211</td>
<td>Ever smoked: No/yes</td>
<td>Validated questionnaire (interview or mail)</td>
<td>No</td>
</tr>
<tr>
<td>Bretagne et al.</td>
<td>2006</td>
<td>France</td>
<td>Population-based</td>
<td>5395</td>
<td>Smoking/nonsmoking</td>
<td>Mail Questionnaire</td>
<td>No</td>
</tr>
<tr>
<td>Nocon et al.</td>
<td>2006</td>
<td>Germany</td>
<td>Population-based</td>
<td>7124</td>
<td>Ex-smoker Smoker (number of cigarettes per day)</td>
<td>Symptoms and lifestyle questionnaire</td>
<td>Yes</td>
</tr>
<tr>
<td>Dore et al.</td>
<td>2008</td>
<td>Italy</td>
<td>Case-control</td>
<td>500</td>
<td>No/ex-smoker/yes</td>
<td>Questionnaire and upper endoscopy</td>
<td>No</td>
</tr>
<tr>
<td>Zagari et al.</td>
<td>2008</td>
<td>Italy</td>
<td>Population-based</td>
<td>1033</td>
<td>Never/former/current</td>
<td>Validated questionnaire and upper endoscopy</td>
<td>No</td>
</tr>
<tr>
<td>Eslick et al.</td>
<td>2009</td>
<td>Australia</td>
<td>Cross-sectional</td>
<td>1000</td>
<td>Current smoker</td>
<td>Self-reported validated questionnaire</td>
<td>Yes</td>
</tr>
<tr>
<td>Bhatia et al.</td>
<td>2011</td>
<td>India</td>
<td>Cross-sectional</td>
<td>3224</td>
<td>Smoking/chewing/smoking + chewing</td>
<td>Questionnaire</td>
<td>No</td>
</tr>
<tr>
<td>Yamamichi et al.</td>
<td>2012</td>
<td>Japan</td>
<td>Population-based</td>
<td>19864</td>
<td>Habit of smoking</td>
<td>Questionnaire and symptoms scale</td>
<td>Yes</td>
</tr>
<tr>
<td>Pandeya et al.</td>
<td>2012</td>
<td>Australia</td>
<td>Cross-sectional</td>
<td>1580</td>
<td>Never smoker/current smoker/ex-smoker</td>
<td>Questionnaire</td>
<td>No</td>
</tr>
<tr>
<td>Minatsuki et al.</td>
<td>2013</td>
<td>Japan</td>
<td>Hospital-based</td>
<td>10837</td>
<td>Current smoker/current nonsmoker</td>
<td>Upper endoscopy</td>
<td>Yes</td>
</tr>
<tr>
<td>Friedenberg et al.</td>
<td>2013</td>
<td>USA</td>
<td>Population-based survey</td>
<td>379 (weighted 22409)</td>
<td>Non-smoker Low/medium/high</td>
<td>Questionnaire</td>
<td>Yes</td>
</tr>
<tr>
<td>Pandeya et al.</td>
<td>2012</td>
<td>Australia</td>
<td>Cross-sectional</td>
<td>1580</td>
<td>Never smoker/current smoker/ex-smoker</td>
<td>Questionnaire</td>
<td>No</td>
</tr>
<tr>
<td>Minatsuki et al.</td>
<td>2013</td>
<td>Japan</td>
<td>Hospital-based</td>
<td>10837</td>
<td>Current smoker/current nonsmoker</td>
<td>Upper endoscopy</td>
<td>Yes</td>
</tr>
</tbody>
</table>
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 (7,16), 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 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). Furthermore, 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,

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

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

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

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

References


