EXTRAESOPHAGEAL MANIFESTATIONS OF GASTROESOPHAGEAL REFLUX DISEASE WITH IMPLICATIONS FOR ORAL CAVITY

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ABSTRACT
Background: Gastroesophageal reflux disease (GERD) is one of the most common chronic disorders of modern humans. The manifestations of GERD are classically described as heartburn and reflux, but GERD may also present atypically. Common extraesophageal manifestations include reflux cough syndrome, reflux asthma syndrome and reflux laryngitis syndrome which leads to reduced quality of life. Aims: Our purpose was to study the prevalence of extraesophageal symptoms and oral manifestations associated with gastroesophageal reflux disease, to estimate the connection between them, certain risk factors and severity of the disease. Methods: A prospective study was performed in 154 hospitalized patients diagnosed with GERD by barium examination and in some cases by upper gastrointestinal endoscopy and 40 controls with extradigestive diseases. They were screened for oral changes including dental evaluation. Results. The prevalence of extraesophageal symptoms increases significant from 31.81% to 79.22% if oral manifestations are taken into account. We identified statistically significant increased prevalence of oral manifestations in GERD patients: dental erosion 42.2%, oral burning sensation, halitosis, impaired taste, hypersalivation, tooth sensitivity. However the prevalence of caries and other periodontal lesions was similar in reflux patients and controls. Oral symptoms in GERD are likely to be associated with smokers, alcohol intake, consumption of soft drinks and other extraesophageal manifestations. Hiatal hernia and esophagitis were found with a greater frequency in patients with oral symptoms reflecting a severity of the reflux disease more marked or a longer period of evolution. Conclusion: Oral manifestations, other than caries and periodontal lesions are a common finding in patients with GERD and should be considered an atypical manifestation of this disease. Collaborative medical and dental management is therefore required to establish early diagnosis and to prevent a lifetime of debilitating dentition and the need for complex restorative therapy.

Key words: gastroesophageal reflux disease, oral manifestations, extraesophageal symptoms

BACKGROUND
Gastroesophageal reflux disease (GERD) is one of the most common chronic disorders encountered in medical practice becoming a public health problem considering its possible severe complications (Barrett esophagus and esophageal cancer). The prevalence of the disease in the general population is differently reported in various studies ranging from 20-50% (1), due to the polymorphic clinical symptoms and to subsequent investigations
that are needed to confirm the diagnosis. The clinical spectrum combines digestive signs (esophageal) and extradigestive symptoms depending on the presence of esophagitis, the composition of the reflux, the period of contact with the esophageal mucosa and the tissue resistance. Classical symptoms of GERD considered as typical manifestations include heartburn, acid regurgitation, retrosternal pain, dysphagia, odynophagia (1). However some patients may experience atypical or extraesophageal manifestations (2) by direct injury of the larynx or pharynx caused by contact with gastric acid and by esophagobronchial reflex which is mediated by the vagus nerve. Most important expressions are chronic cough, asthma, aspiration pneumonia, laryngitis, posterior pharyngeal ulcers, angina-like chest pain, arrhythmias. A number of studies (3, 4) have shown the involvement of gastroesophageal reflux disease in the occurrence of dental erosion, sometimes severe, that need complex and expensive restorative treatment. In the present study we intended to identify oral changes in patients with gastroesophageal reflux disease and to evaluate possible correlations with risk factors, other extraesophageal manifestations or the severity of the disease.

OBJECTIVES
The aim of this study is to establish the prevalence of gastroesophageal reflux disease considering the patients presenting both esophageal and extraesophageal manifestations. We also analyzed the prevalence of extraesophageal symptoms in patients with gastroesophageal reflux disease and in particular to study the frequency of the oral manifestations. There have also been evaluated the potential risk factors for GERD, external lifestyle factors related to diet, alcohol, coffee, tobacco and some soft drinks along with the endogenous factors represented by hiatal hernia. The presence of general diseases such as diabetes, obesity, pulmonary chronic diseases, constipation was taken into account.

MATERIALS AND METHODS
To reach our goal we conducted a prospective study on patients hospitalized in the Vth Internal Medicine Clinic from Hospital CF Iasi who experienced digestive symptoms, more precisely heartburn, retrosternal pain, regurgitation, anorexia, dysphagia as well as patients with extradigestive manifestations, reported in the literature as possible events in gastroesophageal reflux disease. Barium X–Ray examination and in some cases upper gastrointestinal endoscopy were performed in all the patients. The patients who have been diagnosed with gastroesophageal reflux disease completed a questionnaire regarding demographic data, height and weight in order to determine nutritional status, symptoms, alcohol and coffee intake, soft drinks, tobacco, concomitant medication (nonsteroidal anti-inflammatory drugs, beta blockers, theophylline, benzodiazepines), comorbidities (chronic obstructive pulmonary disease, diabetes, chronic constipation). All patients with gastroesophageal reflux disease underwent a clinical examination of the oral cavity. According to the presence or the lack of oral manifestations they were divided into two groups which were compared in terms of risk factors, association with other symptoms of gastroesophageal reflux disease. The group with oral changes was also compared with a group of 40 patients hospitalized with extradigestive medical conditions such as angina, hypertension, kidney stones or rheumatic conditions. Patients treated with histamine receptor blockers or proton pump inhibitors and those diagnosed with duodenal ulcer, gastric cancer or gastrectomy were excluded. Recorded data were analyzed
statistically, a value of $p < 0.05$ being considered statistically significant.

RESULTS

Out of the 189 patients 154 (81.48%) were diagnosed with gastroesophageal reflux disease by X-ray or endoscopy. Patient’s age ranged between 38 and 78 years, with an average of 56.2 and 26% of patients were over 65 years old. Gender distribution was 93 men, 60.38% respectively and or 61 women (39.62%). Out of the 154 patients 111 (72.07%) had typical esophageal symptoms including heartburn (52.5%), 55.19% regurgitation, dysphagia 14.28%, 12.98% odynophagia, retrosternal pain 36, 36%. Out of the 154 recruited patients 111 (72,07%) were found to have typical esophageal symptoms including heartburn (52,5%), acid regurgitation (55,19%), dysphagia (14,28%), odynophagia (12,98%), retrosternal pain (36,36%). Out of the total of 111 patients only 32 (20.77% of all 154 patients with gastroesophageal reflux disease) were having only esophageal symptoms, the remaining 79 patients (51.29%) were associating other manifestations, including oral complains.

Taking into account oral changes, a total of 122 patients (79,22%) were found to have extragasotheageal manifestations associated (in 51,29%) or not (27,93%) to the typical esophageal symptoms. Note that of the 111 patients with tipical digestive complaints 22 (representing 14.28% of the total of 154 patients) had other than oral associated extradigestive complains, the rest of 89 patients (57.79%) showing exclusively digestive symptoms, with or without changes in the oral cavity. A total of 43 patients or 27.93% of the total patients experienced only esophageal symptoms.

If we considered as extraesophageal manifestations only the respiratory or othorhinolaryngological symptoms, excluding the oral involvement their prevalence were reduced to 31.81% of all patients, reaching 14.28% as manifestations associated with esophageal symptoms and 17 53% as exclusive extraesophageal events.

![Figure 1. Symptoms presented by patients with gastroesophageal reflux disease](image)

Patients diagnosed with gastroesophageal reflux disease were questioned on symptoms presented in the oral cavity as oral burning sensation, halitosis, impaired taste, sour or
acid taste, hypersalivation, tooth sensitivity, abrasive sensation. All patients with gastroesophageal reflux disease underwent a clinical examination of the oral cavity. Oral changes were recorded in 114 patients respectively 74.02% (figure 2), including dental erosion and aphthosis. Of the 111 patients with esophageal complaints, 75 (67.56%) were found to associate oral manifestations. Of the 89 patients with strictly digestive symptoms 57 or 64.04% showed changes in the oral cavity, while patients with digestive complaints associated to respiratory or otorhinolaryngological symptoms presented oral complaints in a significantly more important percentage (81, 81%) suggesting that the reflux disease was more severe. 36 patients with esophageal complaints had no changes in the oral cavity.

Among patients without esophageal complaints, 16 had only oral expression, representing 10.38% of all patients with gastroesophageal reflux disease. 23 (85.18%) of the 27 patients with respiratory symptoms (chronic cough, shortness of breath at night) or laryngeal symptoms had associated manifestations in the oral cavity. It resulted a number of 39 patients from 43 (90.69%) with extraesophageal manifestations that presented changes in the oral cavity.

![Figure 2. Prevalence of oral manifestations in different categories of patients with gastroesophageal reflux disease](image)

Patients with changes in the oral cavity were compared in terms of demographic characteristics and risk factors with those without changes at this level (Table 1). Among the first group we found a slightly higher percentage of males 62.28% versus 55%. High prevalence of oral manifestations seems not to correlate with age, the percentage of patients over 65 years being similar in both groups. Oral symptoms in GERD are likely to be associated with smokers, alcohol intake, consumption of soft drinks but obesity and diabetes showed no statistically differences. Drugs reported in the literature as favoring gastroesophageal reflux (theophylline, calcium blockers, bisphosphonates, antidepressants, beta blockers, benzodiazepines, nonsteroidal anti-inflammatory drugs) have been used more frequently in patients with oral symptoms.

Patients without oral changes were generally diagnosed on the basis of esophageal complains. A percentage of 65% of patients with changes in the oral cavity, especially those with dental erosions, also associated esophageal symptoms, especially
heartburn, acid regurgitation and retrosternal pain and even more serious complains, such as dysphagia (14.03%). Moreover, a large amount of them had other extraesophageal manifestations like cough (22.8%), dysphonia (13.15%), dyspnea (10.5%). We suggest that dental erosions are associated with more severe or prolonged reflux disease possibly due to the fact that presenting atypical manifestations or exclusively oral signs (14.03%) the patients request medical consultation after a longer period of time.

Barium X-ray identified the presence of hiatal hernia in 35 of the 114 patients (30.7%) with oral manifestations, while its prevalence in the control group was 15%. Upper endoscopy was performed on 29 patients with oral lesions, observing oesophagitis lesions in 16 of them (55.17%), and severe erosive esophagitis in 6 cases. In patients without oral changes endoscopy was practiced only in 8 patients and mild reflux esophagitis was identified in 2 patients.

### Table 1. Risk factors for gastroesophageal reflux disease in patients with and without oral manifestations

<table>
<thead>
<tr>
<th></th>
<th>Patients with oral manifestations n=114</th>
<th>Patients without oral manifestations n=40</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average age</td>
<td>65±10</td>
<td>52±4</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Patients over 65 years</td>
<td>29 (25,43%)</td>
<td>11 (27,5%)</td>
<td>0,03</td>
</tr>
<tr>
<td>Male</td>
<td>71 (62,28%)</td>
<td>22 (55%)</td>
<td>&lt;0,05</td>
</tr>
<tr>
<td>Smokers</td>
<td>45 (39,47%)</td>
<td>12 (30%)</td>
<td>&lt;0,05</td>
</tr>
<tr>
<td>Alcohol intake</td>
<td>25 (21,9%)</td>
<td>5(12,5%)</td>
<td>&lt;0,05</td>
</tr>
<tr>
<td>Soft drinks intake</td>
<td>27 (23,68%)</td>
<td>6 (15%)</td>
<td>&lt;0,05</td>
</tr>
<tr>
<td>Esophageal manifestations</td>
<td>75 (65,78%)</td>
<td>36 (90%)</td>
<td>0,03</td>
</tr>
<tr>
<td>Extraesophageal manifestation</td>
<td>45 (39,47%)</td>
<td>8 (20%)</td>
<td>0,04</td>
</tr>
<tr>
<td>Obesity</td>
<td>74 (64,9%)</td>
<td>24 (60%)</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>16(14,03%)</td>
<td>4 (10%)</td>
<td>NS</td>
</tr>
<tr>
<td>Drugs</td>
<td>36 (31,5%)</td>
<td>9 (22,5%)</td>
<td>&lt;0,05</td>
</tr>
<tr>
<td>Asthma, COPD</td>
<td>19 (16,66%)</td>
<td>5 (12,5%)</td>
<td>NS</td>
</tr>
<tr>
<td>Hiatal Hernia</td>
<td>35 (30,70%)</td>
<td>6 (15%)</td>
<td>&lt;0,04</td>
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</tbody>
</table>

The oral manifestations identified in the patients studied are shown in table ii compared with those recorded in a group of 52 controls without gastroesophageal reflux diagnosed with extradigestive conditions as angina, hypertension, kidney stones, rheumatic conditions. Patients were comparable in terms of age and sex without statistically significant differences in terms of chronic alcohol consumption or tobacco and similar proportion of obese patients.

### Table 2. The prevalence of oral manifestations in patients studied

<table>
<thead>
<tr>
<th></th>
<th>Lot studiu n= 154</th>
<th>Lot martor n=52</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average age</td>
<td>56,2</td>
<td>55,3</td>
<td>NS</td>
</tr>
<tr>
<td>Smokers</td>
<td>57 (37,01%)</td>
<td>18 (34,61%)</td>
<td>NS</td>
</tr>
<tr>
<td>Alcohol intake</td>
<td>30(19,48%)</td>
<td>7 (13,46%)</td>
<td>NS</td>
</tr>
</tbody>
</table>
Obesity | 95 (61.68%) | 30 (57.69%) | NS
Dental sensitivity | 79 (51.29%) | 9 (17.30%) | 0.005
Abrasive sensation | 26 (16.88%) | 1 (1.92%) | 0.04
Dental erosions | 65 (42.20%) | 8 (15.38%) | 0.03
Caries | 133 (86.36%) | 42 (82.28%) | NS
Burning sensation | 52 (33.76%) | 2 (3.8%) | 0.005
Impaired/sour or acidic taste | 81 (52.59%) | 3 (5.76%) | 0.001
Halitosis | 51 (33.11%) | 6 (11.53%) | 0.04
Periodontal disease | 37 (24.02%) | 11 (21.15%) | NS
Aphtosis | 27 (17.53%) | 3 (7.5%) | 0.04

It appears that the enamel erosions were more common (42.20% vs. 15.38%) and involved a higher number of teeth per person in patients with gastroesophageal reflux disease. Lingual and palatal surfaces were especially interested and dental erosions were generally accompanied by other oral manifestations such as an abrasive sensation, tooth sensitivity, burning sensation, aphtosis.

Surprisingly, the prevalence of dental caries showed no difference between groups, although theoretically acid environment could be a cause for their development. Perhaps other extrinsic factors (microorganisms from the board) and intrinsic host factors play a more important role or maybe the frequent association of bad breath and unpleasant taste has considerably increased oral hygiene measures. More abundant salivary flow with a buffer role may also be involved.

CONCLUSIONS
Gastroesophageal reflux disease is a common chronic disease in medical practice. Most patients have typical esophageal symptoms but frequently they associate extraesophageal complaints or those may be the only manifestation of the disease, their prevalence being greater when oral changes are included (79.22% versus 31.81%).

The results showed a strong correlation between oral manifestations and gastroesophageal reflux disease, being found in a rate of 74%, more common in men, smokers, alcohol and carbonated drinkers and patients consuming drugs that affect the lower esophageal sphincter tonus. Patients with changes in the oral cavity showed esophageal complaints with a rate of 65% but comparing to those without oral manifestations they associated more frequently extraesophageal symptoms (40%), hiatal hernia and sometimes severe oesophagitis lesions suggesting a more severe or prolonged reflux disease.

A percentage of 14.03% of patients with oral changes did not have any other complain so that the dentist may be the first to suspect the presence of gastroesophageal reflux disease requiring collaboration with the internist or the gastroenterologist. On the other hand, physicians should be informed on the important prevalence of oral manifestations in patients with reflux disease because some of them, as dental erosions, may develop silent till advanced stages. For this reason oral modifications should be considered as extraesophageal manifestations of gastroesophageal reflux disease and dental checkup should be mandatory for early detection and implementation of preventive or therapeutic measures.
REFERENCES