

How is the gastroesophageal reflux disease prevalence, incidence, and frequency of complications (stricture/esophagitis/Barrett's esophagus/carcinoma) in Turkey compared to other geographical regions globally?

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THE EPIDEMIOLOGY OF GASTROESOPHAGEAL REFLUX DISEASE IN TURKEY AND AROUND THE WORLD

Although many studies are conducted on gastroesophageal reflux disease (GERD) and its complications, the questionnaires and reflux definitions used in the studies are different. Mayo, GERD-Q, DIGEST-Q, RDQ, and various other questionnaires that were created and have been used in the studies. The GERD definition that is mostly accepted around the world is the presence of the complaints of heartburn and/or regurgitation at least once a week. However, many different definitions, such as the presence of heartburn and/or regurgitation at least twice a week or at least once a year (if once a week, "frequent"; if once a year, "rare") and the presence of heartburn and/or regurgitation without considering the frequency and severity, were all used in the studies. Therefore, it is quite difficult to obtain a single datum by collecting these studies. However, studies including all questionnaires and reflux definitions were considered while collecting this data.

Another problem encountered while performing epidemiological scanning of GERD is that when the world was separated into two parts as the East and the West, some countries that were different from each other were included in the same group (such as Iran-China and Germany-Brazil). Even though continents are considered for this separation, countries that do not resemble each other from any perspective, such as Iran and China, were included in the same group. Therefore, groups must be formed according to the higher number of ethnic distributions. There are also regional epidemiological differences even in the same country. Moreover, there is no term equivalent to heartburn and regurgitation in some Eastern languages.

Turkey is geographically located in the middle of the Eastern and Western countries and the epidemiology of GERD and its complications is similar to both geographical groups (Figure 1). In the Eastern countries, the prevalence of GERD is lower and regurgitation is predominant. On the other hand, in the Western countries, the prevalence of GERD is higher and heartburn is predominant. Considering the complications, erosive esophagitis, Barrett's esophagus, and associated esophageal adenocarcinoma are seen in the Western countries more commonly.

In GERD epidemiological studies performed in Turkey, the Mayo questionnaire was mostly used (1, 2). The GERD-Q form was used in one study (3). The studies in which the Mayo questionnaire was used, found the prevalence of GERD as 20% (1), 19.3% (2), 12.5% (4), and 22.8% (5,6), respectively. In the study using the other question form, the prevalence of GERD was 24.7% (3). When 5 studies were evaluated cumulatively, the prevalence was calculated to be 23%. It was observed that regurgitation was predominant in all of the studies. In the cumulative evaluation, the rate of prevalence was 23% for regurgitation and 19% for heartburn.

While the date of the publications on the epidemiology of GERD goes back to the 2000s in the countries to the east of Turkey, the first articles on this subject were written in 1990s in the Western countries. The first extensive, randomized, and community-based study in the Eastern countries was performed in China using the Mayo questionnaire on phone interviewing. The prevalence of GERD was found to be 2.5% (7). However, in the following years, an increase

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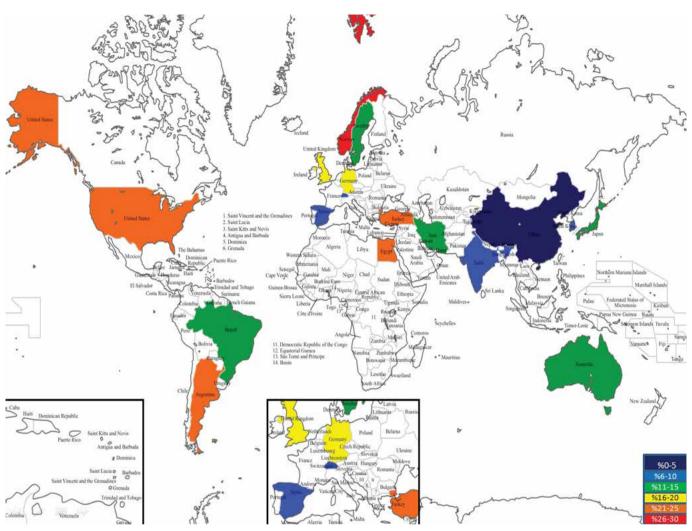


Figure 1. The distribution of GERD prevalence globally

up to 6.2% was observed in the values from China (8,9). In Japan, the prevalence of GERD was detected to be 16.5% with the QUEST questionnaire. This is one of the highest values from the Far East countries (10). On the other hand, in a study conducted on the Qashqai area of Iran, the rate of patients having reflux episode once a week during the last year was found to be 33%, and it was specified that this value increased with age (11). The authors explained that the reason for this higher value in nomads than in settled people was the fact that nomads had different socioeconomic features educational status, and lifestyles. Such a high prevalence of GERD was not reported from the other Middle Eastern countries (12,13). On the other hand, two studies from India were similar to each other (5.3% and 7.1%) but this study only included patients applying to hospitals for any reason (14,15).

Taking two studies from the South and East Mediterranean Region into consideration, the prevalence was found to be as high as 24.8% (because GERD was defined as heartburn and/or regurgitation once a year in the study) from Tunus (16), and as 12.5% in the Israel study where the Mayo questionnaire was used (17).

As a result of the cumulative evaluation of data from the abovementioned Eastern countries, the rate of prevalence was determined to be 8% for GERD, 4.2% for heartburn, and 5.3% for regurgitation.

According to data from the countries in the continents of Europe and America, the highest rates of GERD prevalence are in the northern countries. These high values were revealed in the epidemiologic studies from United States of America (USA) (18), Norway (19) and Sweden (20) were 26.2%, 26% and 25.9% respectively. In the study conducted in the USA, the prevalence values of GERD were divided into subgroups according to races, and some differences were found (38% in Hispanics; 14.7% in Asians; 29.9% in Caucasians; 22.1% in Africans) (18). In another study performed in the city of Olmsted (USA) where 90% of the population consisted of Caucasians, the prevalence of GERD was found to be 18.1% (21). According to the data from other Western countries, the prevalence rates vary between 8.5% and 18% (22-26). In the cumulative evaluation of Western data, the rate of prevalence was 16.1% for GERD, 23% for heartburn and 23% for regurgitation.

As a result, while Turkey is similar to Western countries, with a prevalence rate of 23%, it has a regurgitation-dominant GERD profile similar to the Eastern countries. When we divide the world as the East and the West, some dissimilar countries are included in the same group (such as Iran-China, Germany-Brazil, etc.). Therefore, further studies must be performed and groups must be formed based on ethnic distributions. There are regional epidemiological differences even in the same country. Moreover, there is no term equivalent to heartburn and regurgitation in some languages. Questionnaire forms and definitions of reflux used in the studies were different. For this reason, although it seems that there were many epidemiological studies in the literature, it is guite difficult to obtain a single datum by collecting all of these studies. Data on the incidence of GERD globally, particularly from the Western countries, is available; but no study has been performed on this subject yet in our country.

THE EPIDEMIOLOGY OF GERD COMPLICATIONS IN TURKEY AND AROUND THE WORLD

Erosive Esophagitis and Barrett's Esophagus

The most important GERD complications are erosive esophagitis (ERD), Barrett's esophagus (BE), and esophageal adenocarcinoma. The Los Angeles, and more rarely, the Savary Miller, classification systems were used for ERD. The diagnosis of BE was established histopathologically in many studies. On the other hand, in some studies from Eastern countries, BE was diagnosed using only endoscopic images. Histopathological diagnosis was made through the existence of intestinal metaplasia and columnar epithelial cells in the tissue samples collected from dark pink mucosa extending into the esophagus.

With the use of proton pump inhibitors in the last 30 years, the rates of stricture and bleeding associated with GERD have significantly decreased.

In the literature, the epidemiology of ERD, BE, and esophageal adenocarcinoma was evaluated in two groups: in patients with the complaint of GERD and in healthy individuals without GERD symptoms. However, the studies in Turkey were conducted either on patients having the complaints of GERD or on patients having undergone esophagogastroduodenoscopy due to any reason (such as dyspepsia).

The diagnosis of BE was established according to histopathological results in all studies performed in Turkey, and the prevalence rates of both endoscopic and pathological diagnoses of BE were published. In a study conducted in 2004, 395 endoscopies performed due to dyspeptic complaints were reviewed. The rate of BE was revealed to be 7.4%, which is a high rate. This is because the biopsy was taken from the Z-line in all patients although they seemed normal (27). Therefore, cardiac intestinal metaplasia was also included in the BE group. In the same study, the rate of ERD was found to be 17%. In another

study performed in 2006, the reports of endoscopy that were performed for any reason were retrospectively examined and the diagnosis of BE was verified through pathology reports. As a result, the prevalence of BE was detected to be 0.4% and the rate of ERD was 8% (28). On the other hand, in a study on patients having only GERD symptoms, the rate of ERD was found as 17% and the rate of BE was found as 2% histopathologically proven (29). In the GORHEN study, conducted on patients with GERD symptoms, the rate of BE was 1.05% and the rate of ERD was 34% (5). Odemis et al. (30) used the Savary Miller classification system for ERD. They found the rate of ERD as 11.9% and the rate of BE as 1.2%. In all studies, the rates of mild ERD were significantly higher (Los Angeles A-B, Savary Miller 1-2).

In the studies conducted on patients without GERD or any other gastrointestinal complaints in Eastern countries (China and South Korea), ERD was 15.7% and 7.9% and BE was histopathologically 0.06% and 0.84%, respectively (31,32). Four similar studies were performed in the USA, Sweden, and Italy (33-36). In the USA, the studies on BE and ERD were performed with patients that applied for colonoscopy for colorectal carcinoma screening. In a study by Gerson et al. (33) from the USA, it is striking that the rate of BE was histopathologically found to be 25% and the authors attributed this high value to the fact that the group that underwent colorectal carcinoma screening had features causing a risk for BE (being Caucasian, over-weight, old, and male). Ronkainen et al. (35) studied a more homogeneous group and they found the rate of ERD as 15.5% and the rate of BE as 1.2% in individuals not having GERD symptoms.

In the studies performed on patients with GERD or any gastrointestinal system complaint in the countries to the east of Turkey, the prevalence of ERD was between 3.4% and 66.5% (37,38) and the histopathological prevalence of BE was between 0.3% and 7.3% (39-43). On the other hand, in a study conducted in Japan, the rate of patients that were endoscopically diagnosed with BE was reported to be 37.6%. However, a problem in this study arises from the fact that the authors defined the esophagogastric junction as the area where the esophageal palisade vessels ended (44).

In the studies performed on patients with GERD or any gastrointestinal system complaint in the countries to the west of Turkey, the prevalence of ERD varied from 10.2% to 50% (45,46). Moreover, in a study on patients having only dyspepsia in Brazil, the rate of ERD was found to be as low as 8.6% (47). The study reporting the lowest rate of histopathological BE diagnosis was conducted in Spain (0.08%) (48). The highest prevalence of BE was detected in the USA (14.1%) (49).

In summary, the prevalence rates of ERD and BE were higher in the Western countries. Most of the ERD diagnoses were in the mild group, both globally and in Turkey (93% in Turkey, 91.2% in the Eastern countries, and 85% in the Western countries).

BARRETT-RELATED ESOPHAGEAL ADENOCARCINOMA

Epidemiological data on Barrett's esophagus-related dysplasia and esophageal adenocarcinoma generally come from longitudinal studies on incidence. In Turkey, the rates of Barrett's esophagus-related dysplasia were revealed through cross-sectional studies performed by reviewing endoscopic results of patients with GERD or any upper gastrointestinal complaint. However, there was no data on esophageal adenocarcinoma associated with Barrett's esophagus. The rate of distal and proximal gastric cancers was investigated and esophageal adenocarcinoma was included in the proximal cancers group. In this study, a relative increase was observed in the rates of proximal gastric cancer and indirectly in the rates of esophageal adenocarcinoma compared to distal gastric cancers (50).

Considering the countries to the east of Turkey, adenocarcinoma of the cardia was detected at the rate of 0.25% in the evaluation of the data obtained by reviewing the reports of endoscopic examinations performed for any reason in China. Because they were cross-sectional studies, it is unclear whether adenocarcinoma developed in association with Barrett's esophagus or not (42). In two cross-sectional studies conducted in Western countries, the prevalence of esophageal adenocarcinoma was 0%-0.1% (51,52). The symptoms of GERD were observed in approximately 1/10 of the individuals in the first study.

According to the studies on the incidence of esophageal adenocarcinoma, the risk rates can be summarized as 61/100,000 patientyear in patients undergoing endoscopy for any reason in China (meta-analysis); 26/100,000 and 6/100,000 patientyear in patients with and without ERD respectively, in Denmark; 3.9/100,000 patientyear according to patient databases in Holland; and 3.8/1000 patientyear in patients undergoing reflux surgery and 5.4/1000 patient year in patients receiving medical GERD treatment in the USA. The group under the highest risk seems to be in the USA (53-56).

AN INCREASE IN THE FREQUENCY OF GERD AND BARRETT'S ESOPHAGUS AROUND THE WORLD

When the Western studies defining GERD as the occurrence of heartburn and/or regurgitation at least once a week were evaluated in two groups, as the studies before and after 1995, a statistically significant increase was observed in the prevalence of GERD. However, when the data was evaluated at the intervals of 1995-1999, 2000-2004, and 2005-2009, this statistical difference disappears. Moreover, there were only 3 epidemiological studies conducted before 1995 (57). Based on the patient databases in England, the incidence of Barrett's esophagus has increased from 0.11 to 0.24/1000 in men and from 0.06 to 0.11/1000 in women (58). There were also other studies demonstrating an increase in the incidence of Barrett's esophagus (48,55,59-62).

RECOMMENDATIONS

- A standardization is needed in epidemiological definitions (gastroesophageal reflux disease, heartburn, regurgitation) and validated questionnaires must be used in research.
- The prevalence of GERD in Turkey is higher than that in the Eastern countries, but similar to that in Western countries.
- There is a predisposition towards an increase in the prevalence of GERD in the world and more studies are needed to be conducted on this subject in our country.
- In Turkey, the frequency of regurgitation is higher than that of heartburn similar with eastern countries.
- There is no data on the incidence of GERD in our country.
- The frequency of erosive esophagitis in Turkey is similar to that in other Western countries. In our country, mild esophagitis is apparently more common.
- The prevalence of Barrett's esophagus is higher in Western society and it is increasing. In the Eastern societies, it is apparently seen at lower rates.
- The frequency of Barrett's esophagus is lower than that in Western countries, but similar to that in Eastern countries in Turkey.
- The frequency of Barrett-related dysplasia and adenocarcinoma is unknown in Turkey.

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