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ORIGINAL ARTICLE

Observational Study

Prevalence of gastroesophageal reflux disease in a country with a high occurrence of *Helicobacter pylori*

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Abstract

AIM

To evaluate the prevalence of gastroesophageal reflux disease (GERD) with additional symptoms, relationship with *Helicobacter pylori* (*H. pylori*) of this country-wide study.

METHODS

Data from 3214 adults were obtained with validated questionnaire. Eight hundred and forty-one subjects were randomized to be tested for *H. pylori via* the urea breath test. "Frequent symptoms" were defined heartburn and/or regurgitation occurring at least weekly.

RESULTS

The prevalence of GERD was 22.8%, frequent and occasional heartburn were 9.3%-12.7%, regurgitation were 16.6%-18.7%, respectively. Body mass index (BMI) $\leqslant$ 18.5 showed a prevalence of 15%, BMI > 30 was 28.5%. The GERD prevalence was higher in women (26.2%) than men (18.9%) (P < 0001). Overall prevalence of *H. pylori* was 75.7%. The prevalence was 77.1% in subjects without symptoms *vs* 71.4% in subjects with GERD (χ^2 = 2.6, P = 0.27). Underprivileged with the lowest income people exhibit a higher risk.

CONCLUSION
GERD is common in Turkey which reflects both Western and Eastern lifestyles with high rate of *H. pylori*. The presence of *H. pylori* had no effect on either the prevalence or the symptom profile of GERD. Subjects showing classical symptoms occasionally exhibit more additional symptoms compared with those without classical symptoms.

Key words: Heartburn; Regurgitation; Gastroesophageal reflux disease; Epidemiology; Prevalence

Core tip: Using a validated gastroesophageal reflux disease (GERD) questionnaire and the urea breath test for *Helicobacter pylori* (*H. pylori*), we found a relatively high prevalence of GERD and more frequent regurgitation than heartburn. We also determined that the prevalence of GERD increases with increased body mass index and with female gender and decreases with increased education and income, whereas there was no relationship with age, alcohol use, or smoking. Additionally, we found that *H. pylori* did not affect the prevalence or symptom profile of GERD and that Turkish individual with classical symptoms were more prone to additional symptoms. This unique disease profile may be attributable to Turkey's combination of Western and Eastern lifestyles.

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INTRODUCTION

Gastroesophageal reflux disease (GERD) is a common clinical disorder that can cause significant morbidity, impact the patient's quality of life, and result in high costs to health care systems worldwide[1,2]. This disease is recognized as a common health problem of Western countries but is uncommon in Eastern countries, among Asians, and possibly among Africans in developing and under-developed countries[3,4]. However, different factors might have an impact on the prevalence and presentation of the disease spectrum, either separately or in combination[5], such as the following: a high prevalence of *Helicobacter pylori* (*H. pylori*); genetic factors (low maximal acid output and small parietal cell mass in the stomach); a lower body mass index (BMI) and obesity; lower consumption of carbonated drinks, alcohol, tea, and coffee; smoking; the use of fewer medicines; and dietary factors such as low fat consumption. *H. pylori* needs to be considered in countries where it shows a high prevalence because it may affect GERD. There is an ongoing debate regarding whether *H. pylori* protects by the increase in the prevalence or severity of GERD or vice versa. The studies addressing this topic have generally been performed in Western countries where there is a low prevalence of *H. pylori* and a high prevalence of GERD and Barrett's esophagus. However, in Turkey, a country characterized by both Western and Eastern lifestyles, there is a high rate of *H. pylori* infection but a very low prevalence of Barrett's esophagus. Furthermore, the majority of the studies addressing the prevalence of GERD have been performed using different methodologies and questionnaires, which makes comparing their results difficult. Using one of the widely studied questionnaire might provide an opportunity to compare results between different countries[6-8]. We used a reflux questionnaire[9] derived from Locke *et al*[6], previously validated in an English-speaking Western culture. Turkey exhibits a different profile than Western counterparts for GERD, *H. pylori* is very common, the prevalence of Barrett's esophagus is very low, social, geographicraphical and economic status are different. Wide-scale studies from non-Western, Caucasian studies are lacking. We aimed to evaluate the prevalence of GERD and its relationship with *H. pylori* in a Caucasian country with low prevalence of Barrett's esophagus and high rate of *H. pylori*.

MATERIALS AND METHODS

Data from 3214 representatively selected subjects aged 20 years or older were obtained from a representation list produced by the Governmental Statistics Institute. Those subjects were selecte according to the age and gender distribution of the country and provided by the Institute. The study was performed in 17 cities in Turkey, and we included one district and village from each city. The cities were selected according to the representative characteristics of the area in which they were located, and all major cities with a population over 1 million people were included. The total population of Turkey was 67803927 on the date of the study, and the citizens living in these cities represented 72% of the country's population. Trained interviewers (medical doctors) were employed for data collection. Randomization was performed with the assistance of the Turkish Prime Ministry.

Statistical institute

Sampling method: Three-stage stratified cluster sampling (cases from households on streets of urban and rural areas of seven geographicraphical regions) with deterministic components (household-based age and gender quotas).

At the first step, cities were selected from seven geographicraphical regions. We included the three major cities of the country and selected two cities form each of the seven geographicraphical regions. The cities were selected *via* lottery by the Institute with chances to be drawn proportional with the ratio

of population of the city over population of the region, they are located.

At the second step, two counties, one from urban and the other from rural areas, were selected *via* lottery with chances to be drawn proportional with the ratio of population of the district over population of the area, they are located. Therefore, overall 34 districts were included in the sample. The numbers of cases to be included in the sample in each districts were determined proportionally based on the ratio of population of region they are located, over population of country. Accordingly, more individuals were included from cities selected from crowded geographic regions, than from uncrowded geographic regions.

At the third step, streets from each districts, were selected randomly from official lists of streets. The number of streets changed among districts due to different sample sizes in each district.

Representatively selected street numbers were provided by the Turkish Statistical Institute, and interviewers counted every fifth house on their right side. A quota was determined for each house based on age and gender, and only one adult was included from each house. The questionnaire was administered during face-to-face interviews at each subject's home. The urea breath test was performed on 854 subjects who were randomly selected from the study population. The test was conducted while fasting (> 4 h after their last meal). A 150 mL test meal of orange juice or apple juice was first given to the subjects, after which 75 mg of ^{13}C-labeled urea dissolved in 20 mL of juice was administered, followed by another 30 mL of juice to rinse the tracer from the mouth. Mass spectrometry analysis was performed blindly on expired air samples collected before urea was administered and 30 min after its ingestion. All tubes were collected and tested at the same center (INFAI GmbH, Cologne, Germany). If a subject was taking an antibiotic and/or a proton pump inhibitor (PPI), the interviewers set another visit to perform the test. The exclusion criteria were as follows: gastric or esophageal surgery, refusal to participate in the test, pregnancy, and current malignancy other than non-melanoma skin cancers. Subjects were excluded if they died or moved from the city before the interview, possessed any mental or psychiatric disease, were unable to communicate due to dementia, refused to attend the survey, or had an incorrect address or name within the registration system. The results of a previous study that we performed in a small city led us to assume a maximum GERD prevalence of 20% in this population[10], and the interviewers therefore stopped enrollment when a sample size of 3214 was reached (95%CI, and the worst acceptable was ± 3%).

Questionnaire

The total questionnaire contained 49 questions. We used a reflux questionnaire derived from Locke *et al*[6] that was previously validated in an English-speaking, Western culture, and the instrument was translated into Turkish, linguistically validated, and adapted to the cultural profile of Turkey[9]. The translation process included an independent translation, a back translation, and a pilot test using 15 subjects, and a review and approval by the original questionnaire developers. The test-retest reliability was analyzed for each respondent using Cohen's kappa coefficient, and the obtained Cronbach's alpha values were all higher than 70% for all major symptoms (heartburn, regurgitation). Questions related to the presence of the following characteristics were employed: (1) major (heartburn, regurgitation) and related (dyspepsia, dysphagia, odynophagia, chest pain) symptoms and triggering factors for these symptoms; (2) associated medical conditions; (3) the past medical history of upper (dyspepsia, nausea, vomiting, belching) and lower gastrointestinal symptoms (abdominal pain or discomfort) and respiratory, throat and cardiac problems (cough, dyspnea, hoarseness, hiccups, globus, asthma), the number of physician visits and diagnostic procedures related to upper gastrointestinal symptoms, medication use [non-steroidal anti-inflammatory drugs (NSAIDs), aspirin and all related drugs associated with upper gastrointestinal complaints, and those for treating other health problems], smoking and alcohol, coffee or tea consumption; (4) demographic and socioeconomic data, including the number of households and children, total monthly income, age, weight, height, employment, level of education, and marital status; and (5) additional conditions which might have an effect on symptoms such as stress; similar with the original questionnaire the question was asking whether the subject has stress and if yes whether there is an effect on symptoms.

"Frequent symptoms" were defined as a major symptom (heartburn and/or regurgitation) occurring at least once a week, and common and "occasional symptoms" were an episode of one of the major symptoms less than once a week within the past year, as previously defined by our group and others[10]. Frequent heartburn and/or regurgitation were defined as GERD. The period considered for the prevalence of symptoms was the previous 12 mo. Each symptom (heartburn, regurgitation, dysphagia and chest pain) was scored for frequency and severity by the subject. Symptom frequency was measured on the following five-point scale: less than once a month, once a month, once a week, several times a week, and daily.

The analyses were conducted with the Statistical Package for Social Sciences, 9.0 for Windows. Statistical significance was assigned to *P* values of less than 0.05, except for post-hoc multiple pairwise comparisons. All analyses comparing the study groups were performed twice: first to compare the two groups "GERD present" *vs* "GERD absent"; and then to compare the three groups "Never", "Occasional" and "Frequent". Comparisons of data between two or three groups were performed with the chi-square test, unless any expected cell value was lower than 2

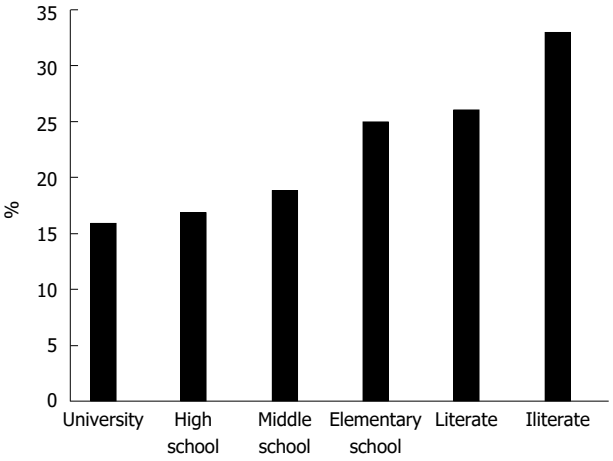

Figure 1 Prevalence of gastroesophageal reflux disease according to education.

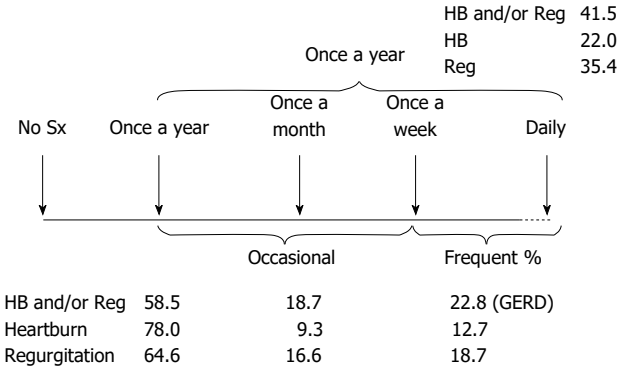

Figure 2 Prevalence of gastroesophageal reflux disease symptoms. GERD: Gastroesophageal reflux disease.

or more than half of the cell values were lower than 5. When any expected cell value was lower than 2 or more than half the cell values were lower than 5, Fisher's exact test was employed instead of the χ^2 test for 2 × 2 contingency tables. Comparisons of ordinal data or non-normally distributed numeric data between two groups were performed with the Mann-Whitney *U* (MWU) test. When three groups were to be compared with regard to an ordinal variable, Kruskal-Wallis nonparametric analysis of variance (ANOVA) was used for global comparisons, after which pairwise group comparisons were performed with the MWU test. Comparisons of normally distributed numeric data between two groups were conducted with Student's *t* test for independent groups. When three groups were to be compared, one-way ANOVA was used for global comparisons, and pairwise group comparisons were then performed with the Tukey Honestly Significance Difference test.

RESULTS

Demographics

The questionnaire was administered to 3214 total subjects, which included 1516 (47.2%) males. In terms of educational status, 61% of subjects had graduated from or left primary school, and 8.2% had graduated from university (Figure 1). The percentages concerning the marital status of the participants were 74.1% married, 16.8% single and 9.1% divorced. The percentages of different occupations among the participants were 42.1% housewife, 13.4% self-employed, 13% retired, and 9.7% blue-collar workers.

Prevalence of GERD

The prevalence of symptoms is shown in Figure 2. The prevalence of GERD (once a week or common heartburn and/or regurgitation) was 22.8%; that of heartburn was 12.7%; and that of regurgitation was 18.7%. A similar pattern was observed in the frequency of occasional heartburn and regurgitation, which showed prevalences of 9.3% and 16.6%, respectively. GERD was detected in 18.9% of the male subjects *vs* 26.2% of the females (P < 000.1, χ^2 = 38.003). The prevalence of GERD according to marital status was as follows: 23.4% of GERD patients were married; 15.6% were single; and 22.8% were divorced, with the single group exhibiting significantly less GERD (χ^2 = 25.749, P < 0.0001). The prevalence of GERD was also evaluated according to geographical areas (Figure 3).

The northern part of the country showed a significantly higher prevalence rate (27.3%) than the southern part (19.3%) (P < 0.0001). However, no difference was observed between the areas in the east and the west according to the prevalence of GERD or major symptoms. This finding is interesting because the eastern part of the country presents a different life profile than the west, which is closer to the Western lifestyle.

Medications

Among the patients in the study population, 71.2% had not taken any gastric medication. 28.8% of subjects were taking different medications daily: 17.7% used antacids; 11.0% used H2 blockers; and 6.9% used PPIs (some subjects were taking more than one type of medication). NSAID consumption was 27.7% overall, and 9.7% of the patients took NSAIDs daily.

Antacids/alginates, acid inhibitors, and aspirin/NSAIDs all were taken significantly more often by participants with frequent or occasional symptoms compared with those with no major symptoms. There was a difference according to the frequency of symptoms and medications, with values of 4.3% for antacids/alginates and 6.7% for acid inhibitors being recorded for frequent *vs* occasional symptoms, respectively; however, this difference was not significant (Table 1).

Lifestyle

Among the subjects, 44.7% smoked, and 9.7% consumed alcoholic beverages more than once a week, but no difference was found according to smoking and alcohol habits between subjects with or without

Table 1 Consumption of medications

	Major symptoms		No major symptoms
	Frequent	Occasional	
Antacids/alginate	31.2%	26.9%	9.2%
Acid inhibitors	28.2%	21.5%	7.2%
Aspirin	40.0%	40.9%	45.1%
NSAIDs	29.0%	30.1%	22.2%

NSAID: Non-steroidal anti-inflammatory drug.

Table 2 Body mass index and gastroesophageal reflux disease prevalence

	Total	GERD
	n	*n* (%)
BMI (kg/m^2)		
≤ 18.5	107	16 (15.0)
18.6 - 24.9	1272	254 (20.0)
25.0 - 29.9	1110	257 (23.2)
30+	492	140 (28.5)
Mantel-Haenszel χ^2 test		$P < 0.0001$

BMI: Body mass index; GERD: Gastroesophageal reflux disease.

GERD. The percentages of participants who exhibited increased symptoms of GERD based on lifestyle factors were as follows: 41.6% with tea/coffee; 15% with alcohol; and 53.8% with stress. Additionally, 12.7% of subjects within the GERD group had been woken up because of heartburn, and there was a linear association between BMI and GERD (Table 2). Monthly income was inversely associated with the prevalence of the disease, with the richest group exhibiting a rate of 17%, compared with 26% for the lowest income group ($P = 0.003$). Furthermore, 3.8% of the general population and 35.4% of the GERD population reported GERD symptoms in their first-degree relatives and/or spouse.

H. pylori

A similar randomization was performed within the 3214 subjects, and 854 eligible participants were evaluated for *H. pylori* status with the urea breath test. This subgroup exhibited a demographic pattern that was similar to that of the overall population (data not shown). In this population, 23% of individuals had GERD, which was similar to the whole group (22.8%, $P > 0.05$). The prevalence of *H. pylori* was 75.8% overall. The geographicraphical distribution of *H. pylori* prevalence is shown in Figure 3; a significant difference between geographicraphical areas was observed. The northern and western areas exhibited lower prevalences compared with the middle, eastern and southern areas ($P < 0.001$). The mean age of the *H. pylori*-negative group was 45.6 ± 17.1 *vs* 41.9 ± 15.7 for the *H. pylori*-positive group ($P = 0.004$), and the income level was slightly lower in the *H. pylori*-positive group (199.4 TL *vs* 171.6 TL, $P = 0.072$). No differences were found in relation to alcohol consumption, smoking, BMI, stress, coffee or tea consumption, and antacid, H2 blocker, proton pump inhibitor, or NSAID usage.

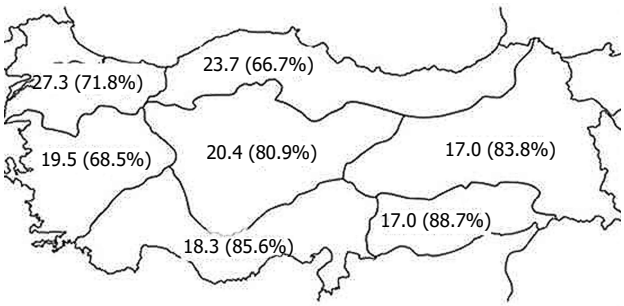

Figure 3 Prevalence of gastroesophageal reflux disease and *Helicobacter pylori* positivity (between parenthesis) according to geographicraphical areas.

No relationship was observed between *H. pylori* status and the prevalence of GERD. The only variable relating *H. pylori* positivity and heartburn was the time frame of heartburn, for which a negative linear association was found a drop in the prevalence of *H. pylori*. When the history of heartburn was shorter than 5 years, *H. pylori* prevalence was 73.9%; when the history heartburn was longer than this time frame, *H. pylori* prevalence was 65.7% ($P = 0.05$).

DISCUSSION

In this country-wide study involving 3214 participants, we showed that the prevalence of GERD was 22.8% and that heartburn was less common (12.7%) than regurgitation (18.7%). Although GERD was related to increasing age, female gender, a single marital status, BMI, and high stress levels, there was an inverse relationship between income and educational levels. No relationship between GERD and *H. pylori* positivity was found. The pivotal study results from Olmsted county showed that the prevalence of GERD was 19.8%[1], but the population exhibited a different symptom profile consisting of a lower prevalence of regurgitation (6.3%) and a higher prevalence of heartburn (17.8%), similar to other studies from Western countries.

Many useful studies have been published since the epidemiology of GERD has gained increased attention. As a consequence, one might assume that sufficient data accumulation has been achieved. However, the following are reasons that additional research is needed in this area. (1) more than ten different questionnaires are employed in the literature (*e.g.,* Mayo, GERD-Q, Montreal, Digest Q, RDQ, Romes), and each questionnaire employs different validation techniques, symptom interpretations and frequencies for definition; (2) there are large language and cultural differences in symptom perception and interpretation. It is difficult to understand the word "reflux" in many languages including English-speaking countries. This situation was demonstrated in a multiethnic study in Boston in which this term was understood by only 35% of Caucasian patients, 54% of African American patients and 13% of Asian patients[11]; and (3) there

Table 3 Prevalence of additional symptoms according to symptom frequency

(χ^2)	Frequent	Occasional	None
NCCP (179)	35.9%[a,c]	30.2%[a]	13.7%
Dysphagia (230)	24.5%[a]	18.6%[a]	4.6%
Belching (221)	36.8%[a]	28.3%	11.9%
Nausea (601)	29.7%[a]	10.6%	3.4%
Vomiting (417)	15.7%[a]	3.4%	0.9%
Hematemesis (33)	2.6%[a]	1.4%	0.2%
Hiccup (68)	6.4%[a]	7.0%[a]	1.2%
Cough (70)	16.3%[a]	11.7%	5.9%
Asthma (24)	8.2%[a]	3.8%	3.7%
Hoarseness (48)	6.2%[a]	4.0%	1.3%
Chronic pharyngitis (32)	8.4%[a]	7.2%[a]	3.3%

[a]$P < 0.05$ *vs* subjects without symptoms; [c]$P < 0.05$ *vs* subjects with occasional symptoms. NCCP: Noncardiac chest pain.

Table 4 Prevalence of additional symptoms in studies using the Mayo questionnaire

	Olmsted (United States)[1]	Turkey	Moscow (Russia)[17]	Argentina[18]	North West China[8]
NCCP	23.1	35.9	15.5	37.6	34.7
Dysphagia	13.5	24.5	25.5	26.8	6.5
Odynophagia	-	-	34.4	-	10.7
Globus	7.0	23.8	25.5	26.3	15.2
Dyspepsia	10.6	-	60.2	38.7	29.3
Belching	-	36.8	43.0	-	-
Nausea	-	29.7	53.8	-	-
Vomiting	-	15.7	29.1	-	-
Hiccup	-	6.4	6.8	-	-
Cough	-	16.3	36.7	-	8.9
Asthma	9.3	8.2	-	6.7	4.2
Pharyngeal symptoms and Hoarseness	14.3	7.3	10.4	21.8	9.4

NCCP: Noncardiac chest pain.

are differences related to the development rates of countries in indices such as income, access to health care facilities, the consumption and accessibility of aggregating or therapeutic medications (especially proton pump inhibitors), genetic factors, obesity, dietary factors, alcohol consumption, smoking, the prevalence of *H. pylori* in particular, and increases in basal and stimulated gastric acid secretion irrespective of *H. pylori*[4,12]. Major variations based on geographicraphical areas and cultures have been demonstrated. Estimates of GERD prevalence range from 18.1%-27.8% in North America, 8.8%-25.9% in Europe, 2.5%-7.8% in East Asia, 8.7%-33.1% in the Middle East, 11.6% in Australia and 23.0% in South America[13]. For the reasons summarized above, the current study addressed a number of different features to allow comparisons with the Western literature on the subject. The population of Turkey, a predominantly Caucasian country characterized by both Eastern and Western lifestyles, shows a high rate of *H. pylori* infections (75.8%), relatively low income and low alcohol consumption (9.7%) but exhibits smoking (44.7%) as a common habit.One very interesting interesting difference is that the prevalence of Barrett's esophagus is very low (0.8% short segment and 0.2% long segment in patients with GERD), and severe erosive esophagitis is also less common compared with studies from Western countries[14-16]. The prevalence of GERD observed in this study was 22.8%, which is one of the highest rates in the literature. Additionally, a symptom pattern of a high prevalence of regurgitation and low prevalence of heartburn was detected, which differs from Western countries. It is also clear that this pattern is consistent with Eastern countries starting from Turkey and extending to Far East Asia, with the exception of Russia and Argentina, which show an equal prevalence of symptoms[17-19]. *H. pylori* infections in general, and especially those involving *Cag*A-positive strains, have been found to be negatively associated with erosive gastroesophageal reflux disease, Barrett' s esophagus, and particularly distal esophageal adenocarcinoma[20,21]. It is debatable whether the difference in the symptom profile is related to the high *H. pylori* prevalence in our country and in studies from other Eastern countries. Turkey, similar to other regurgitation-dominant countries, exhibits a very high rate of *H. pylori* and *Cag*A positivity (38.8%)[22]. *H. pylori* decreases gastric acidity if it predominantly induces corpus gastritis as a result of *Cag*A positivity. Patients who regurgitate less acidic gastric contents predominantly exhibit regurgitation with less heartburn sensation, which in addition to *Cag*A-positive *H. pylori* infections, might be a reason for the low prevalence of Barrett's esophagus in Turkey.

This is one of the largest series in the literature comparing such a high prevalence of *H. pylori* positivity and its effect on GERD, as studies from Western countries show a low rate of *H. pylori* infection. However, we did not find any difference between the *H. pylori* -positive and *H. pylori*-negative groups in terms of GERD prevalence (23% *vs* 22.8%, respectively) or in major symptoms (*i.e.,* regurgitation and heartburn). One possible reason for this result is that we did not evaluate the *Cag*A status of the participants.

It was shown that all additional symptoms were significantly more common in subjects with frequent symptoms compared with subjects without symptoms. Extraesophageal findings from our study (Table 3) and other studies performed using the Mayo questionnaire (Table 4) are summarized. An interesting finding is that additional symptoms were also significantly more common in subjects with occasional symptoms compared with those with no symptoms. This means that subjects with uncommon classic GERD symptoms (less than a week to once a year) exhibited more additional symptoms.

We showed that obesity was a significant risk factor for GERD in the current study. Five out of seven studies using the same questionnaire applied in this work have shown a significant correlation between obesity and

GERD. Regarding the two studies that found no such correlation, one was performed by our group[10], and the other was from Moscow[17] and reported a numerical difference, but without reaching statistical significance.

Our study has limitations; first of all, not all the subjectes were tested for *H. pylori*. We could not perform *Cag*A measurements. Number of subjects from Eastern part of the study was lower than Western part because of the population density.

In conclusion, this study involved an *H. pylori*-prevalent population that exhibited a low prevalence of Barrett's esophagus and was mostly Caucasian. The prevalence of GERD recorded in the study is among the highest found in studies performed using the Mayo questionnaire irrespective from low prevalence of Barrett's esophagus or *H. pylori.*

In addition, a different symptom profile was observed in which regurgitation was more common than heartburn. This profile especially regurgitation predominance can be seen in limited number of studies from other non-western countries and because of the lower response rate to PPIs to regurgitation, it might be clinically meaningful. The reasons for the differences in symptom profiles between countries should be evaluated. *H. pylori* did not show any effect on prevalence but more studies performed with *Cag*A status are needed. We also found that subjects showing classic GERD symptoms for less than a week to once a year exhibit more additional symptoms compared with those without symptoms implicate that extraesophageal symptoms can be observed frequently without typical symptoms.

COMMENTS

Background

To summarize concisely and accurately the relevant background information so that readers may gain some basic knowledge about your study's relevance and understand its significance for the field as a whole.

Research frontiers

To introduce briefly the current hotspots or important areas in the research field as related to your study.

Innovations and breakthroughs

To summarize and emphasize the differences, particularly the advances, achievements, innovations and breakthroughs, as compared to other related or similar studies in the literature, which will allow the readers to assimilate the major points of your article.

Applications

To summarize the practical applications of your research findings, so that readers may understand the perspectives by which this study will affect the field and future research.

Terminology

To describe concisely and accurately any terms that may not be familiar to the majority of the readers, but which are essential for understanding your article.

Peer-review

The authors report an analysis in Turkey of the prevalence of esophageal reflux and associated symptoms where there is also a high prevalence of *Helicobacter pylori* infection. The contribution is unique and interesting and casts light on variant presentation of symptoms of reflux disease in a country with mixed Western and Eastern influences. The work is ambition and thought provoking.

REFERENCES

1 **Locke GR**, Talley NJ, Fett SL, Zinsmeister AR, Melton LJ. Prevalence and clinical spectrum of gastroesophageal reflux: a population-based study in Olmsted County, Minnesota. *Gastroenterology* 1997; **112**: 1448-1456 [PMID: 9136821 DOI: 10.1016/S0016-5085(97)70025-8]

2 **Nguyen NQ**, Holloway RH. Gastroesophageal reflux disease. *Curr Opin Gastroenterol* 2003; **19**: 373-378 [PMID: 15703580 DOI: 10.1097/00001574-200307000-00009]

3 **Goh KL**. Changing epidemiology of gastroesophageal reflux disease in the Asian-Pacific region: an overview. *J Gastroenterol Hepatol* 2004; **19** Suppl 3: S22-S25 [PMID: 15324378 DOI: 10.1111/j.1440-1746.2004.03591.x]

4 **Wong BC**, Kinoshita Y. Systematic review on epidemiology of gastroesophageal reflux disease in Asia. *Clin Gastroenterol Hepatol* 2006; **4**: 398-407 [PMID: 16616342 DOI: 10.1016/j.cgh.2005.10.011]

5 **Goh KL**, Chang CS, Fock KM, Ke M, Park HJ, Lam SK. Gastro-oesophageal reflux disease in Asia. *J Gastroenterol Hepatol* 2000; **15**: 230-238 [PMID: 10764021 DOI: 10.1046/j.1440-1746.2000.02148.x]

6 **Locke GR**, Talley NJ, Weaver AL, Zinsmeister AR. A new questionnaire for gastroesophageal reflux disease. *Mayo Clin Proc* 1994; **69**: 539-547 [PMID: 8189759 DOI: 10.1016/S0025-6196(12)62245-9]

7 **Diaz-Rubio M**, Moreno-Elola-Olaso C, Rey E, Locke GR, Rodriguez-Artalejo F. Symptoms of gastro-oesophageal reflux: prevalence, severity, duration and associated factors in a Spanish population. *Aliment Pharmacol Ther* 2004; **19**: 95-105 [PMID: 14687171]

8 **Wong WM**, Lai KC, Lam KF, Hui WM, Hu WH, Lam CL, Xia HH, Huang JQ, Chan CK, Lam SK, Wong BC. Prevalence, clinical spectrum and health care utilization of gastro-oesophageal reflux disease in a Chinese population: a population-based study. *Aliment Pharmacol Ther* 2003; **18**: 595-604 [PMID: 12969086 DOI: 10.1046/j.1365-2036.2003.01737.x]

9 **Kitapcioglu G**, Mandiracioglu A, Bor S. Psychometric and methodological characteristics of a culturally adjusted gastroesophageal reflux disease questionnaire. *Dis Esophagus* 2004; **17**: 228-234 [PMID: 15361096 DOI: 10.1111/j.1442-2050.2004.00413.x]

10 **Bor S**, Mandiracioglu A, Kitapcioglu G, Caymaz-Bor C, Gilbert RJ. Gastroesophageal reflux disease in a low-income region in Turkey. *Am J Gastroenterol* 2005; **100**: 759-765 [PMID: 15784016 DOI: 10.1111/j.1572-0241.2005.41065.x]

11 **Spechler SJ**, Jain SK, Tendler DA, Parker RA. Racial differences in the frequency of symptoms and complications of gastro-oesophageal reflux disease. *Aliment Pharmacol Ther* 2002; **16**: 1795-1800 [PMID: 12269973 DOI: 10.1046/j.1365-2036.2002.01351.x]

12 **Kinoshita Y**, Kawanami C, Kishi K, Nakata H, Seino Y, Chiba T. Helicobacter pylori independent chronological change in gastric acid secretion in the Japanese. *Gut* 1997; **41**: 452-458 [PMID: 9391241 DOI: 10.1136/gut.41.4.452]

13 **El-Serag HB**, Sweet S, Winchester CC, Dent J. Update on the epidemiology of gastro-oesophageal reflux disease: a systematic review. *Gut* 2014; **63**: 871-880 [PMID: 23853213 DOI: 10.1136/gutjnl-2012-304269]

14 **Bor S**, Vardar R, Vardar E, Takamz S, Mungan ZA. Endoscopic findings of gastroesophageal refluxdisease in Turkey: multicenter prospective study (GORHEN). *Gastroenterology* 2008; **134** (Suppl): T2014, A-600 [DOI: 10.1016/S0016-5085(08)62804-8]

15 **Bayrakçi B**, Kasap E, Kitapçioğlu G, Bor S. Low prevalence of erosive esophagitis and Barrett esophagus in a tertiary referral center in Turkey. *Turk J Gastroenterol* 2008; **19**: 145-151 [PMID: 19115148]

16 **Yilmaz N**, Tuncer K, Tunçyürek M, Ozütemiz O, Bor S. The

prevalence of Barrett's esophagus and erosive esophagitis in a tertiary referral center in Turkey. *Turk J Gastroenterol* 2006; **17**: 79-83 [PMID: 16830286]

17 **Bor S**, Lazebnik LB, Kitapcioglu G, Manannikof I, Vasiliev Y. Prevalence of gastroesophageal reflux disease in Moscow. *Dis Esophagus* 2016; **29**: 159-165 [PMID: 25604401 DOI: 10.1111/dote.12310]

18 **Chiocca JC**, Olmos JA, Salis GB, Soifer LO, Higa R, Marcolongo M. Prevalence, clinical spectrum and atypical symptoms of gastro-oesophageal reflux in Argentina: a nationwide population-based study. *Aliment Pharmacol Ther* 2005; **22**: 331-342 [PMID: 16098000 DOI: 10.1111/j.1365-2036.2005.02565.x]

19 **Bor S.** Worldwide Epidemiology of Gastroesophageal Disease. WGO Handbook on Heartburn: A Global Perspective. World Dig Health Day, 2015: 12-14

20 **Malfertheiner P**, Megraud F, O'Morain CA, Atherton J, Axon AT, Bazzoli F, Gensini GF, Gisbert JP, Graham DY, Rokkas T, El-Omar EM, Kuipers EJ. Management of Helicobacter pylori infection--the Maastricht IV/Florence Consensus Report. *Gut* 2012; **61**: 646-664 [PMID: 22491499 DOI: 10.1136/gutjnl-2012-302084]

21 **Rubenstein JH**, Inadomi JM, Scheiman J, Schoenfeld P, Appelman H, Zhang M, Metko V, Kao JY. Association between Helicobacter pylori and Barrett's esophagus, erosive esophagitis, and gastroesophageal reflux symptoms. *Clin Gastroenterol Hepatol* 2014; **12**: 239-245 [PMID: 23988686 DOI: 10.1016/j.cgh.2013.08.029]

22 **Yakut M**, Örmeci N, Erdal H, Keskin O, Karayel Z, Tutkak H, Soykan I. The association between precancerous gastric lesions and serum pepsinogens, serum gastrin, vascular endothelial growth factor, serum interleukin-1 Beta, serum toll-like receptor-4 levels and Helicobacter pylori Cag A status. *Clin Res Hepatol Gastroenterol* 2013; **37**: 302-311 [PMID: 23137754 DOI: 10.1016/j.clinre.2012.09.013]

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