

Evaluation of Gastroesophageal Reflux Disease and variables related with its severity in adults

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Summary. Gastroesophageal Reflux Disease is a chronic gastrointestinal disease that significantly reduces the quality of life and causes serious complications such as esophageal stricture, gastrointestinal bleeding or Barrett's esophagus in some patients. This study was undertaken to evaluate some factors that are considered to be related to Gastroesophageal Reflux Disease and severity among individuals who are 40 years of age and over. This study is a cross-sectional survey conducted with individuals who were at the ages of 40 years and over who applied to 6 Family Health Centers and Family Health Centers serving in the districts of Alpu and Mahmudiye located in 3 settlements with different socioeconomic levels in Eski ehir City Center between 01 November and 30 December 2016. During the study, Individuals with symptoms of retrosternal burning and regurgitation at least 1 day a week was accepted as Gastroesophageal reflux disease in the study and the severity of the disease was assessed with the National Institutes of Health Promis Gerd Scale. Stop Bang Scale was used in assessing the risk level of obstructive sleep apnea syndrome. Among the study sample; 920 individuals were (46.8%) male and 1046 (53.2%) were female. Their ages ranged from 40 to 80 years with a mean of 56.8 ± 10.6 years. Gastroesophageal Reflux Disease was found in 18.3% (n = 360) of the study group. In our study, female gender, moderate family income status, non-steroidal antiinflammatory drug use, family history of gastroesophageal reflux disease, previous gastroesophageal reflux disease, consumption of carbonated beverage, consumption of fatty food, consumption of fermented food, presence of chronic obstructive pulmonary disease story, asthma story presence and having high risk in terms of obstructive sleep apnea syndrome were found to be important risk factors for gastroesophageal reflux disease(each; $p \leq 0.05$). Drug therapy was the most common treatment method among individuals who previously had Gastroesophageal Reflux Disease diagnosis (76.6%). In the study group; the most common Gastroesophageal Reflux Disease severity was "most symptomatic" in individuals with high risk of Obstructive Sleep Apnea Syndrome (60.6%). In this study, it was determined that Gastroesophageal Reflux Disease is an important health problem in adults. In terms of preventing gastroesophageal reflux disease and risk factors; screening should be made and health education and information services should be provided to increase the level of awareness.

Key words: Gastroesophageal Reflux Disease, over 40 years of age, Eskişehir

Introduction

Gastroesophageal Reflux Disease (GERD) is defined as the escape of stomach contents to the esophagus, causing symptoms and/or complications that

disturb the person (1). Although the cause of GERD is not fully understood, genetic factors are thought to be more forward than environmental factors (2). Important risk factors for GERD include lifestyle factors such as smoking, chocolate, consumption of spicy

foods, consumption of cigarettes and alcohol, obesity, and the use of drugs such as aspirin and nonsteroidal antiinflammatory drugs (3-6).

In the physiopathology of GERD, a variety of theories such as transient lower esophageal sphincter loosening, reduced resting lower esophageal sphincter pressure, impaired esophageal acid clearance, delayed gastric emptying, and defects in esophageal epithelial preservation are suggested and the most important one among these is transient lower esophageal sphincter loosening (7, 8). Typical symptoms of GERD include pyrosis (retrosternal burning, heartburn) and regurgitation (9, 10). However, dysphagia, odynophagia, angina-like chest pain, globus sensation, belching and chronic cough can also be seen (4).

GERD diagnosis is based on anamnesis, and invasive techniques are used in the presence of atypical symptoms or for the assessment of complications (7). Clinical and laboratory methods or some scales are used to assess the severity of GERD, including the National Institutes of Health (NIH) PROMIS GERD scale (4, 11). It has been reported that the frequency of GERD is 6.2-31.3% in some studies among adults in various countries (12-14). In Turkey, this frequency ranges from 19.3% to 33.9% (15-17).

GERD and non-malignant complications such as esophageal erosion, ulcer, bleeding, perforation, stricture rarely cause death (18). Barrett's esophagus, a complication of GERD, causes adenocancer to cause death but this condition is not very often (19). GERD leads to significant economic losses as it affects health-related quality of life in a negative way, resulting in symptoms and inability to go to work, decreased productivity and reduced daily activities (20-23). In a study conducted by Zhao and colleagues in the USA, the total national hospital costs for hospitalization of individuals with GERD were reported to have risen from \$ 509 million in 1998 to \$ 622 million in 2005 (24).

One of the accompanying diseases of GERD is Obstructive Sleep Apnea Syndrome (OSAS); which is a disease characterized by intermittent partial or complete occlusion of the upper respiratory tract during sleep that causes decreased blood oxygen saturation (25, 26). It is suggested that in patients with OSAS, the increase in negative intrathoracic pressure during

the apneic episode caused GERD by creating a vacuum effect on the gastric content (27).

This study aimed to evaluate some factors that are considered to be related to GERD presence and severity among individuals who were 40 years of age and over.

Materials and Methods

This study is a cross-sectional survey conducted with individuals who were at the ages of 40 years and over who applied to 6 Family Health Centers and Family Health Centers serving in the districts of Alpu and Mahmudiye located in 3 settlements with different socioeconomic levels in Eskişehir City Center between 01 November and 30 December 2016.

Eskisehir province is in the 7th place in terms of socio-economic development order. Livelihood resources are based on industry in the province center and agriculture in the districts (28). According to the data of the Turkish Statistical Institute (TUIK) 2015; the total population of Eski ehir is 826,716 and the population over age 40 is 351,532 (29). Eski ehir Os-mangazi University Non-Interventional Clinical Research Ethics Board approved this study with decision numbered as 80558721 / G-268 and dated as 18 October 2016. In order to collect data, necessary permissions were obtained from Eski ehir Provincial Public Health Directorate and Family Health Centers.

There are 52 Family Health Centers (FHC) in the center of Eski ehir. A total of 8 FHC including 6 FHC in 3 settlements with different socioeconomic levels and 1 FHC in Alpu and 1 FHC in Mahmudiye were included in the study according to Eskisehir Provincial Public Health Directorate's opinion. The prevalence of gastroesophageal reflux disease was estimated to be 20%, the error margin was 5%, the confidence interval was 95%, the minimum number of people to be reached for each FHC was 245 and the total number of people was calculated as 1960 so that the reliability of the results could be accepted.

A questionnaire form was prepared using the appropriate literature in accordance with the purpose of the study, (30-34). The questionnaire contains some sociodemographic characteristics of the individuals,

some factors that are thought to be related to GERD, questions about the NIH PROMIS GERD Scale and STOP-BANG Scale.

After informing individuals aged 40 years and over who applied to FHC during the study period about the subject and the purpose of study; 1966 people who agreed to participate in the study formed the working group. Pre-prepared questionnaires were filled in by face-to-face interviewers. This process took approximately 20-25 minutes.

Patients with burning symptoms in the retrosternal region for at least 1 day in the last week were identified as retrosternal burning positive and patients with regurgitation of foods and drinks without vomiting were defined as regurgitation positive. Subjects with symptoms of retrosternal burning and regurgitation at least 1 week in the study were accepted as GERD (34, 35) and the NIH Promis Gerd Scale was used to assess severity. This scale was developed by the National Institutes of Health (NIH) in 2014 (30, 36) and the validity and reliability study in Turkey was conducted by Öz eker et al.. The scale consists of 13 questions with 5 likert types and the scores from each question range from 0-4. Scores to be taken from this scale ranged from 0 to 52, with 16 and over points were the most symptomatic, between 8-15 points were moderate symptomatic, between 4-7 points were mild symptomatic, between 1-3 points were the least symptomatic and 0 point was considered as asymptomatic (31).

Stop Bang scale was used to assess OSAS risk level. The Stop-bang scale was developed by Chung et al. in 2008 and the validity and reliability study in Turkey was conducted by Acar et al. in 2013. The scale consists of a total of eight questions whose answers were yes-no. Those who gave "yes" to three more questions were considered as high risky for OSAS and those who gave two or less "yes" responses were considered as low risky for OSAS (32, 37).

In this study, family income status was evaluated as "poor, moderate and good" according to their own perceptions.

The data were evaluated in the SPSS (version 15.0) Statistical Package Program. Chi-square test and Logistic Regression Analysis (Stepwise Backward Wald Regression) were used for the analyzes. Statistical significance was accepted as $p \leq 0.05$.

Results

Among the study sample; 920 individuals were (46.8%) male and 1046 (53.2%) were female. Their ages ranged from 40 to 80 years with a mean of 56.8 ± 10.6 years. Gastroesophageal Reflux Disease was found in 18.3% ($n=360$) of the study group. The distribution of the study group members according to some sociodemographic characteristics is given in Table 1.

Results of Logistic Regression Analysis; which were created with variables that were detected to be associated with GERD in Chi-Square analysis such as place of residence, gender, education status, family income status, regular exercise, non steroidal anti-inflammatory drug (NSAID) use, presence of a disease that requires continuous drug use, GERD diagnosis in

Table 1. Distribution of the study group according to socio-demographic characteristics

Sociodemographic characteristics	Number (n)	Percentage (%)
Place of residence		
Provincial center	1334	67.9
District	632	32.1
Age group		
40-49	559	28.4
50-64	904	46.0
Over 65 years	503	25.6
Gender		
Male	920	46.8
Female	1046	53.2
Education status		
Under primary education	1182	60.1
Primary school graduate	231	11.8
High school and above	553	28.1
Personality type		
A	950	48.3
B	1016	51.7
Family type		
Nuclear family	1548	78.7
Extended family	365	18.6
Fragmented family	53	2.7
Family income		
Poor	231	11.7
Moderate	1391	70.8
Good	344	17.5
Total	1966	100.0

family, previous GERD diagnosis, obesity, eating how many hours before bed time, spicy, fatty, salty, fermented food consumption, consumption of carbonated beverages, Diabetes Mellitus, Hypertension, Chronic Obstructive Pulmonary Disease (COPD), Asthma, OSAS risk status; were shown in Table 2.

Female gender, moderate family income status, NSAID use, family history of GERD, previous GERD, consuming carbonated beverages, consumption of fatty foods, consumption of fermented foods, presence of COPD history, presence of asthma, and having high risk in terms of OSAS; were all found as important risk

factors for GERD in our study according to Logistic Regression Analysis result (each; $p \leq 0.05$).

Of the study group, 474 (24.1%) individuals had previously diagnosed Gastroesophageal Reflux Disease and 417 (88%) of them had received any treatment due to Gastroesophageal Reflux Disease. Drug therapy was the most common treatment method among individuals who previously had Gastroesophageal Reflux Disease diagnosis (76.6%). The distribution of the individuals with GERD diagnosis in study group according to treatment methods was given in Table 3.

Table 2. Results of the Logistic Regression Model, which were formed by variables determined to be related to GERD in the study group (final step)

Variables	β	SE ^a	p	OR ^b	95% CI ^c
Gender (reference: Male)					
Female	0.463	0.144	0.001	1.589	1.199-2.105
Family income (reference: good)					
Moderate	0.450	0.195	0.021	1.568	1.071-2.295
Poor	0.291	0.258	0.260	1.338	0.806-2.221
Use of NSAID (reference: No)					
Yes	0.404	0.134	0.002	1.498	1.153-1.946
Family history of GERD (reference: No)					
Yes	0.489	0.137	0.000	1.631	1.246-2.135
Previous GERD diagnosis (reference: No)					
Yes	1.747	0.136	0.000	5.735	4.396-7.483
Consumption of carbonated beverages (reference: No)					
Yes	0.401	0.153	0.009	1.494	1.106-2.018
Consumption of fatty foods (reference: No)					
Yes	0.714	0.137	0.000	2.043	1.562-2.673
Consumption of fermented foods (reference: No)					
Yes	0.294	0.149	0.048	1.342	1.002-1.796
Diabetes Mellitus (reference: No)					
Yes	0.285	0.156	0.068	1.330	0.979-1.807
COPD (reference: No)					
Yes	0.707	0.329	0.032	2.028	1.064-3.865
Asthma (reference: No)					
Yes	0.589	0.211	0.005	1.802	1.191-2.724
OSAS risk status (reference: Low)					
High	0.545	0.173	0.002	1.725	1.228-2.422
Constant	-4.302	0.297	0.000	-	-

SE^a: Standard error, OR^b: Odd's ratio, CI^c: Confidence interval

Table 3. Treatment methods applied by individuals who already had GERD diagnosis in the study group

Treatment methods	Number (Percentage)
No treatment	57 (12.0)
Diet treatment	69 (14.6)
Medication	363 (76.6)
Other	4 (0.8)
Total	493 (100.0)

**Numbers were evaluated through treatment methods.*

Table 4. Distribution of GERD according to severity in individuals with high OSAS risk in the study group

GERD severity in individuals with high OSAS risk	Number (Percentage)
Mild symptomatic	14 (4.8)
Moderate symptomatic	101 (34.6)
Most symptomatic	177 (60.6)
Total	292 (100.0)

In the study group; OSAS was found to be high risky in 73% (n = 1440) and low risky in 27% (n = 526). Among the study group; the most common GERD severity was “most symptomatic” in individuals with high risk of OSAS (60.6%). Distribution of GERD according to severity in individuals with high OSAS risk in the study group was given in Table 4.

Discussion

GERD is a chronic gastrointestinal disease that significantly reduces the quality of life and causes serious complications such as esophageal stricture, gastrointestinal bleeding or Barrett’s esophagus in some patients (38). The prevalence of GERD in this study was detected as 18.3%. It has been reported in some studies among adults in various countries that the frequency of GERD varies between 6.2-31.3% (12-14). In Turkey, this frequency varies between 19.3% - 33.9% (15-17). The lack of standardization of the methods used to di-

agnose GERD in these studies can be shown among the reasons for the different results reported.

In our study, the frequency of GERD in women was 1.589 times higher than that of men. Similar results have been reported in a study conducted by Shaha and his colleagues in Bangladesh (39). Whereas Kay and his colleagues reported that the frequency of GERD in men was higher than in women (40) and on the other hand in Locke et al.’s study in Minnesota, there is no difference in the frequency of GERD between men and women (41).

In our study, the GERD frequency was higher in families with moderate income when compared with families that had good income (OR=1.568; $p \leq 0.05$). In a study conducted in Israel, it was reported that the frequency of GERD was high in families with low income (42). In a study conducted by Yöner and colleagues, it was reported that there was no relationship between family income status and GERD (15). Such an outcome may have occurred because individuals in the study assessed family income according to their own perceptions.

NSAID use is an important risk factor for GERD symptoms because it increases the duration of acid reflux (43). In our study, GERD frequency was found to be higher in people using NSAID (OR=1.498; $p \leq 0.05$). Similar results were reported in a study conducted by Martín-de-Argila et al. (44). However, in a study conducted by Bor et al. in Moscow, it was reported that there was no difference between GERD with use of NSAID (13).

It is known that genetic contribution is important in the etiology of GERD. The presence of upper gastrointestinal disease in the family is a risk factor for GERD (45). In the study group, GERD was found to be 1.631 times higher in those who had a diagnosis family history of GERD than those without family history of GERD. Similar results have been reported in a study by Rabieev et al., in Iran (46).

Several factors play a role in the pathogenesis of GERD. According to recent studies, genetic polymorphism in genes affecting the host’s inflammatory response, drug metabolism, cell cycle regulation, xenobiotic pathways, DNA repair, mutagenesis, esophageal sensory function and gene silencing are associated with GERD risk (47). In the logistic regression analysis; It

was found that the frequency of GERD was found to be 5,735 times higher in those who previously had GERD diagnosis history. In a multi-centered work by Kulig and his colleagues; duration of GERD was reported among the main factors related to the occurrence of GERD (48). The most important reason for the high rate in our study can be ineffective and insufficient treatment of GERD.

Carbonated drinks; increases gastric acid load and increases GERD probability (49). In this study, consumption of carbonated drinks was found to be a risk factor for GERD (OR=1.494; $p \leq 0.05$). Similar results have been reported in a study by Fass et al. (50). In a study conducted by Darvishmoghadam and his colleagues in Iran, it was reported that there was no difference in the frequency of GERD among those who consumed and did not consume carbonated beverages (51).

Fatty food consumption reduces the lower esophageal sphincter pressure, increases the frequency of GERD by delaying gastric emptying and extending esophageal acid exposure duration (52). Frequency of GERD in those who consume fatty foods were 2.043 times higher than those who did not consume. Similar results have been reported in the study of El-Serag et al. (53). In a study conducted by Mansour-Ghanaei et al., no relation was found between fatty food consumption and GERD prevalence (54).

Fermented foods (sour products) and drinks (alcohol) cause reflux by reducing the lower esophageal sphincter pressure, delaying gastric emptying, stimulating the sensory receptors in the esophagus and increasing gastric acid secretion (38). In the study group, consumption of fermented food was found to be an important risk factor for GERD (OR=1.342; $p \leq 0.05$). In a study conducted by Song and colleagues in Korea, it was reported that the frequency of GERD was higher in those who consume fermented food (breads) (55). However, Mansour-Ghanaei and colleagues reported that there was no difference in the frequency of GERD among those who consumed and did not consume fermented drink (drinking dough-yogurt with water) (54).

In patients with COPD, diaphragm flattening with increased respiratory distress, intra-abdominal pressure increase, and negative intrathoracic pressure may facilitate reflux of gastric contents (56). In our

study, the frequency of GERD in patients with COPD was found to be 2.028 times higher. A similar result was reported in a study by Mokhlesi et al. (57). In a study by Çil and colleagues, GERD was reported to be not a risk factor for patients with COPD in the acute exacerbation and respiratory insufficiency situation (58).

In asthmatic patients; the reduction of the diaphragm in pulmonary hyperinflation may cause the lower esophageal sphincter to hernify into the chest by increasing the pressure difference between the abdomen and chest. For this reason, it is expected that the frequency of GERD in asthmatic patients is higher (59). It was found that GERD frequency was higher in asthmatic patients in the study group (OR=1.802; $p \leq 0.05$). A similar result was reported in a study conducted by Yönm et al. (15). In a study conducted by Almadi and colleagues, it was reported that there was no difference in the frequency of GERD between those with asthma stories and those without asthma (60).

It is possible that the GERD frequency is higher due to the vacuum-like effect of the intrathoracic negative pressure increasing in the upper airway obstruction in OSAS and the tension of the phrenoesophageal ligament (61). We found that GERD frequency was higher in those who were at high OSAS risk status when compared with those who were not at high OSAS risk status (OR=1.725; $p \leq 0.05$). The results of some studies in the literature support our work (62, 63). However, a study by Kim and his colleagues found no relation between GERD symptoms and OSAS (64).

Conclusions

In this study, it was determined that Gastroesophageal Reflux Disease is an important health problem in adults. In terms of preventing gastroesophageal reflux disease and risk factors; screening should be made and health education and information services should be provided to increase the level of awareness. There is a need for more extensive work in order to establish the relationship between Gastroesophageal Reflux Disease and Obstructive Sleep Apnea Syndrome.

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