Biomedical Research 2017; Special Issue: S507-S512 *ISSN 0970-938X*
www.biomedres.info

Frequency of gastroesophageal reflux disease in patients with type 2 diabetes mellitus.

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Abstract

The purpose of this study is to assess the severity and frequency of gastroesophageal reflux disease in patients with Type 2 Diabetes Mellitus and to evaluate some factors that are thought to be associated with Gastroesophageal Reflux Disease (GERD). The study was a cross-sectional study on individuals aged 18 years and over who applied to outpatient clinics in the Department of Family Medicine and Internal Medicine, Eskişehir Osmangazi University Medical Faculty Hospital between 1 January and 31 July 2016. In the study, information from 436 individuals using face-to-face interviews and laboratory values (fasting blood sugar and HbA1C) of individuals within the last three months was recorded on questionnaire forms. In the study, the National Institutes of Health Promis Gastroesophageal Reflux Disease Scale was used in the evaluation of GERD. The data were analyzed in the IBM SPSS (version 20.0) statistical package program. Chi-square test and logistic regression Backward: Wald method was used for variables. The statistical significance was accepted as $p \leq 0.05$. Among the patients with diabetes mellitus (DM), 134 patients (68.0%) had gastroesophageal reflux disease. 105 diabetic patients (53.3%) had obesity, 146 diabetic patients (74.1%) had high HbA1C levels and 84 diabetic patients (42.6%) had wider waist circumference. The most common treatment modalities for individuals with DM in the study group were oral antidiabetic treatment with a ratio of 65.5% (n=129). The most common gastroesophageal reflux disease severity in the DM group was the most symptomatic (67.2%). The purpose of this study is to investigate the incidence, frequency, and severity of gastroesophageal reflux disease in patients with Type 2 DM using the National Institutes of Health (NIH) Patient-Reported Outcomes Measurement Information System (PROMIS®) Gastroesophageal Reflux Disease (GERD) Scale. Thus helping early diagnosis and treatment of gastrointestinal complications that may occur in association with Type 2 DM.

Keywords: Gastroesophageal reflux disease, Type 2 diabetes mellitus, Epidemiology.

Accepted on March 17, 2017

Introduction

Diabetes mellitus is a metabolic disorder caused by insulin deficiency or resistance to insulin [1]. DM is a chronic disease that is very common both in our country and in the world. DM frequency in TURDEP-II study conducted in adults in Turkey in 2010 was found to be 13.7% [2]. Diabetes mellitus affects almost all organ systems and causes damage, malfunctions and defects in these organ systems depending on the duration and severity of the disease [3]. Complications of the gastrointestinal system are common in long-term diabetic patients [4].

The frequency of gastroesophageal reflux disease in Turkey was found 33.9% [5]. The frequency of GERD changes between 10.0% and 52.0% in various countries [6-9]. Gastroesophageal reflux disease has a high incidence in the general population [10].

For the development of gastrointestinal symptoms in diabetic patients; autonomic neuropathy [11,12], poor glycemic control [13], psychiatric disorders [14], and other metabolic disorders secondary to diabetes [15] can be effective. The incidence of GERD in diabetic patients can be as high as 41% [16]. Diabetic neuropathy has been found to be effective in gastroesophageal reflux disease in diabetic patients [17].

Clinical and laboratory diagnostic methods are used in the diagnosis of gastroesophageal reflux disease; One of the diagnostic tools used in community-based studies is the Gastroesophageal Reflux Disease Scale [18,19].

It is possible to control GERD, which is a common disease in diabetic patients, by lifestyle modification, diet and medical treatment in addition to early diagnosis of gastroesophageal reflux disease.

Materials and Methods

The study was a cross-sectional study on individuals aged 18 years and over who applied to outpatient clinics in the Department of Family Medicine and Internal Medicine,

Eskişehir Osmangazi University Medical Faculty Hospital between 1 January and 31 July 2016. In the study, the incidence of gastroesophageal reflux disease was accepted as 50%, the error margin was calculated as 5%, the confidence interval was 95% and the minimum number of people to be reached was 384.

For the purpose of the study, a questionnaire form was prepared by using the appropriate literature [20-23]. The prepared questionnaire contains some socio-demographic characteristics of the individuals, some factors thought to be related to gastroesophageal reflux disease, laboratory values within the last three months, the latest anthropometric measurements and questions about the PROMIS Gastroesophageal Reflux Disease scale which was developed by the National Institutes of Health. The study was approved by Eskisehir Osmangazi University Non-Interventional Clinical Investigation Ethics Board with the decision of 4 December 2015 and numbered 80558721/G-92. Required permission was obtained from Family Medicine and Internal Medicine Department for data collection.

During the study period, Informed Volunteer Consent Form was prepared for the individuals aged 18 years and above who were informed about the subject and the aim of the work which was applied to the outpatient clinics in Family Medicine and Internal Medicine Department and parents signed these forms. In the study, the information obtained using the face-to-face interview method and the laboratory values (HbA1C and fasting blood sugar) of the individuals within the last three months were recorded in pre-prepared questionnaire forms. This process took approximately 20-25 minutes.

The National Institutes of Health (NIH) PROMIS Gastroesophageal Reflux Disease (GERD) Scale was used to assess gastroesophageal reflux disease in the study. This scale was developed by the National Institutes of Health in 2014 and the validity and reliability study in Turkey was conducted by Özşeker et al. in 2016. This scale consists of 13 questions with 5 likert types. The answers for each question were scored from 0 to 4. Scores to be taken from this scale ranged from 0 to 52; 16 points and over was the most symptomatic, 8-15 points moderate symptomatic, 4-7 points mild symptomatic, 1-3 points were the least symptomatic and 0 points were considered as asymptomatic [20-24].

Patients with burning symptoms in the retrosternal region for at least 1 day in the last week were identified as having positive retrosternal burnings and those without food vomiting, or those with sickling or backflow symptoms were identified as regurgitation positive. Subjects with symptoms of retrosternal burning and regurgitation at least 1 day in one week in this study were accepted as GERD [23,25]. HbA1C was considered "normal" for individuals with <6.5%, "high" for individuals with ≥ 6.5% [26]. It is defined as "wide" when the waist circumference is greater than 88 cm in female and 102 cm in male [27]. According to the World Health Organization, those with body mass index (BMI) values ≥ 30 were defined as "obese" [28].

The data were evaluated in a computerized IBM SPSS (version 20) Statistical Package Program. Chi-square test and logistic regression Backward: Wald method was used for analysis. The statistical significance was accepted as $p \leq 0.05$.

Results

Among the patients in study group; 186 patients (42.7%) were male and 250 patients (57.3%) were female. Their ages ranged from 22 to 82 years with a mean of 50.43 ± 11.53 years. In the study, 243 (55.7%) of the individuals had GERD. The distribution of the socio-demographic characteristics of patients with and without gastroesophageal reflux disease in the study group is given in Table 1.

Table 1. *Distribution of patients with and without gastroesophageal reflux disease in the working group according to sociodemographic characteristics.*

Sociodemographic Features	Gastroesophageal Reflux Disease			Test value X2 ; p
	No n (%)*	Yes n (%)*	Total n (%)**	
Gender				
Male	97 (52.2)	89 (47.8)	186 (42.7)	8.174; 0.004
Female	96 (38.4)	154 (61.6)	250 (57.3)	
Age				
<45	70 (48.6)	74 (51.4)	144 (33.0)	2.734; 0.255
45-60	81 (40.1)	121 (59.9)	202 (46.4)	
>60	42 (46.7)	48 (53.3)	90 (20.6)	
Education status				
Under primary education	21 (26.2)	59 (73.8)	80 (18.4)	14.846;0.001
Primary school graduate	66 (44.0)	84 (56.0)	150 (34.4)	
High school and over	106 (51.5)	100 (48.5)	206 (47.2)	
Marital status				
Single	42 (52.5)	38 (47.5)	80 (18.3)	2.692: 0.101
Married	151 (42.4)	205 (57.6)	356 (81.7)	
Total	193 (44.3)	243 (55.7)	436(100.0)	

* Percentage was calculated according to row total.

** Percentage was calculated according to column total.

In our study, 146 (33.5%) patients had HbA1C elevation and 132 (30.3%) patients had increased waist circumference. Details are given in Table 2.

Table 2. *Distribution of patients with and without gastroesophageal reflux disease in study group according to factors associated with gastroesophageal reflux disease.*

Factors Associated with Gastroesophageal Reflux Disease	Gastroesophageal Reflux Disease			Test Value X^2; p
	No n (%)*	Yes n (%)*	Total n (%)**	
Smoking status				
Non-smoker	134 (43.9)	171 (56.1)	305 (70.0)	0.45; 0.832
Smoker	59 (45.0)	72 (55.0)	131 (30.0)	
Alcohol consumption status				
No	184 (44.2)	232 (55.8)	416 (95.4)	0.000; 1.000
Yes	9 (45.0)	11 (55.0)	20 (4.6)	
BMI (kg/m^2)				
<30	126 (46.5)	145 (53.5)	271 (62.2)	1.441; 0.230
≥ 30	67 (40.6)	98 (59.4)	165 (37.8)	
HbA1C				
Normal	135 (46.6)	155 (53.4)	290 (66.5)	1.834; 0.176
High	58 (39.7)	88 (60.3)	146 (33.5)	
Waist circumference				
Normal	151 (49.7)	153 (50.3)	304 (69.7)	11.890;0.001
Wide	42 (31.8)	90 (68.2)	132 (30.3)	
Gastroprotective agent use				
No	165 (59.6)	112 (40.4)	277 (63.5)	72.078;0.000
Yes	28 (17.6)	131 (82.4)	159 (36.5)	
Non-steroidal anti-inflammatory drug use				
No	126 (51.4)	119 (48.6)	245 (56.2)	11.629;0.001
Yes	67 (35.1)	124 (64.9)	191 (43.8)	
DM				
No	130 (54.4)	109 (45.6)	239 (54.8)	21.989;0.000
Yes	63 (32.0)	134 (68.0)	197 (45.2)	
Total	193(44.3)	243 (55.7)	436(100.0)	

*Percentage was calculated according to row total.

**Percentage was calculated according to column total.

Sixty (30.5%) of the individuals with DM in the study were male, while 137 (69.5%) were female. Their ages ranged from 22 to 80 years with a mean of 52.53 ± 11.95 years. Among the individuals who had DM in the study, 134 (68.0%) individuals had GERD.

In our study, logistic regression analysis was performed with variables such as age, HbA1C, waist circumference, gastroprotective agent usage, duration with DM presence, which were found to be related to gastroesophageal reflux disease in chi-square analysis of DM subjects. With this analysis; Gastroesophageal reflux disease in individuals with DM in study group was higher in patients aged between 45-60, patients with normal HbA1C, patients with wider waist circumference, patients using gastroprotective agents and patients whose DM was present ≥ 10 years when compared with patients <45 age group, patients with high HbA1C, patients with normal waist circumference, patients not using gastroprotective agents and patients whose DM was present <10 years, respectively (p=0.008), (p=0.000), (p=0.004), (p=0.000) and (p=0.019).

There was no significant difference between obese, smoking, sex, HbA1C value, waist circumference, education status, gastroprotective agent usage and NSAID use between patients with ≥ 10 years DM and <10 years with DM in our study, respectively (p=0.823), (p=0.735), (p=0.709), (p=0.567), (p=0.701), (p=0.078), (p=1.000) and (p=0.521).

The most common treatment modalities for individuals with DM in the study group were oral antidiabetic treatment with a ratio of 65.5% (n=129). No relationship was found between the DM treatment modality and gastroesophageal reflux disease severity (p=0.488).

There was no relationship between HbA1C level and gastroesophageal reflux disease severity in diabetic patients (p=0.728).

The most common gastroesophageal reflux disease severity in the DM group was the most symptomatic (67.2%) (Table 3).

Table 3. *Distribution of gastroesophageal reflux disease severity in DM individuals in the working group.*

GERD Severity	Number (Percent)
Mild symptomatic	2 (1.5%)
Moderate symptomatic	42 (31.3%)
The most symptomatic	90 (67.2%)
Total	134 (100.0%)

Discussion

GERD is a common disease of the gastrointestinal tract that affects the quality of life of people with various symptoms and complications [29,30]. GERD was found in 243 individuals (55.7%) of the study group. It has been reported that in some studies performed in various countries the frequency of GERD changes between 10.0% and 52.0% [6-9,23]. In Turkey, this frequency was found to be 19.3-33.9% in the general population [31,32].

Non-standard methods in GERD diagnosis, studies in different countries, cultural diversity, and food and drink habits varying with religious values can be shown among the reasons for different reported results.

In patients with diabetes, a delayed gastric content in gastric emptying, which is caused by diabetic neuropathy, is expected to result in a higher GERD frequency due to escape to the esophagus [33]. Among the individuals who had DM in the study, 134 (68.0%) individuals had GERD. Individuals with DM in the study had higher GERD than those without DM

(p=0.000). In some studies in various countries, the incidence of GERD was reported to be 41.0-43.5% in individuals with DM [16,34]. Similar results have been reported in various studies in the literature [35,36]. However, in a study conducted by Ha J. O. and colleagues in 442 individuals in Korea, it was reported that there was no difference in the incidence of GERD between those with DM and those without DM [37].

Individuals with DM between ages of 45-60 in our study were 3.665 times more likely to have gastroesophageal reflux disease than individuals younger than 45 years (p=0.008). There was no correlation between age and GERD in some studies done on individuals with DM in the literature [38,39]. While the results of some studies in the general population support our study [40-42], different results have been reported in some studies in the literature [43-46].

For those with DM in the study, frequency of GERD was found to be 9.540 times higher in patients with normal HbA1C when compared with patients who had high HbA1C (p=0.000). However, in some studies in the literature, it was reported that there is no relation between HbA1C level and GERD [16,47]. These results might because of the fact that treatment of GERD has already begun and therefore the symptoms decreased in these patients in whom GERD was a complication due to poor glycemic control in DM patients with high HbA1C levels. There was no relationship between HbA1C level and the use of the gastroprotective agent in our study (p=0.728).

The enlargement of the waist circumference, which means abdominal obesity, plays a role both in the etiology of type 2 DM and causes an increase in intraabdominal pressure, leading to the formation of reflux [48,49]. The large waist circumference in individuals with DM is an important risk factor for GERD (OR: 3.100; p=0.004). Similar results have been reported in various studies in the general population [50,51]. In a study by Sun H. and colleagues in individuals with DM in China, there was no relationship between waist circumference and GERD [38].

For those with DM in the study, frequency of GERD in those using gastroprotective agents were 6.585 times higher than those who did not use (p=0.000). This may have been the case in our study because patients with GERD were referred to our clinic and patients whose treatment had already begun.

Autonomic neuropathy, one of the chronic complications of diabetes mellitus, which is seen in late stages of DM, is thought to be involved in the pathogenesis of GERD [52].

In our study, the GERD frequency in patients with DM more than ten years was found to be 5.344 times higher than those who had DM less than ten years (p=0.019). The results of some studies in the literature also support my work [3,41]. In a study conducted by Sun H. and colleagues in China, there was no relationship between duration of diabetes exposure and GERD frequency [38]. In our study, there were no differences in terms of smoking and obesity between individuals with DM over ten years and those with DM less than ten years (p=0.735 and p=0.823).

Limitations

The questionnaire we used was designed to be structured by NIH for non-invasive and objective assessment of gastroesophageal reflux disease in primary health care centers.

In this study, only smoking and alcohol use have questioned. Use of chocolate, mint, etc was not questioned. There was no relationship found between smoking, alcohol use and gastroesophageal reflux disease.

Conclusions

In our study group; 186 (42.7%) individuals were male and 250 (57.3%) were female. Their ages ranged from 22 to 82 years with a mean of 50.43 ± 11.53 years. Among individuals with DM, 134 (68.0%) patients were detected to have gastroesophageal reflux disease. For individuals with DM in the study; 45-60 age group, normal HbA1C, wider waist circumference, gastroprotective agent use, and DM over a decade or more were found to be significant risk factors for gastroesophageal reflux disease. The most common gastroesophageal reflux disease severity in the DM group was most symptomatic with a ratio of 67.2%.

In our study, GERD was found to be a common complication in diabetic patients. From these results; diabetic patients should be screened for GERD.

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