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Original Article

Gastrointestinal symptoms in patients with diabetes mellitus and non-diabetic: A cross-sectional study in north of Iran

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ABSTRACT

Background and aim: Gastrointestinal (GI) symptoms are common in patients with diabetes mellitus (DM), which involved in high cost of health care and low quality of life. The aim of this study to investigate the prevalence of GI symptoms in diabetic patients referred to the Gastrointestinal and Liver Diseases Research Center (GLDRC), Guilan University of Medical Sciences (Rasht, Iran) using a validated questionnaire.
Methods: In this descriptive, cross-sectional study, 255 diabetic patients and 255 non-diabetic subjects were recruited. Participants were randomly selected. The questionnaire recorded GI symptoms among the study population.
Results: GI symptoms were reported in 91.4% of diabetic patients, and 42.1% of them were male. The common GI symptoms in diabetic patients were flatulence (33.0%), followed by retrosternal pain (14.9%), belching (13.7%), postprandial fullness (12.5%), and constipation (11.4%). Retrosternal pain, constipation, flatulence, loss of appetite, and abdominal distention were more prevalent in diabetic women than men.
Conclusions: DM is associated with high prevalence rate of upper and lower GI symptoms. This effect may be linked to gender and poor glycemic control in diabetic patients, but not to type and duration of diabetes.

1. Introduction

Diabetes mellitus (DM) is the most common metabolic disease. Global prevalence of DM has been increased considerably from 30 million in 1985 to 177 million people in 2000, and based on the accomplished researches, it will reached to 360 million in 2030 [1]. Chronic DM provokes several neuronal and vascular complications which are the main reasons of mortality and morality in diabetic patients [2,3]. Among diabetic complications, the gastrointestinal (GI) complications significantly become widespread as the prevalence of MD has increased [4,5].

Diabetic gastroparesis and enteropathy are the most prevalent GI complications, which is mostly a result of autonomic neuropathy [6–8]. About 75% of people patients suffering from DM may experience GI symptoms, involving in significant increase in health care costs and decrease in life quality of patients [9,10]. The GI tract symptoms of MD are belching, postprandial fullness, dysphagia with nausea, reflux episodes, heartburn, abdominal pain, diarrhea, and/or constipation [11].

The prevalence of diabetic GI symptoms varies based on type and duration of DM, glycemic control status, gender, obesity, metabolic syndrome, different racial groups, gene polymorphism and presence of other diabetic complications [12–18]. The GI symptoms are prevalent among women, type 2 diabetic patients

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and those patients with worst glycemic control [19–21]. Although some studies have shown an increase in the prevalence of GI symptoms in diabetic patients [11,22], it is mentioned in some other studies the prevalence of these symptoms were similar in diabetic and non-diabetic subjects [23].

According to available epidemiological studies, there is a controversy about the prevalence rate of diabetic GI symptoms and may be challenged on methodological reasons. Hence, the current study aimed to investigate the prevalence of GI symptoms in diabetic patients referred to the Gastrointestinal and Liver Diseases Research Center (GLDRC), Guilan University of Medical Sciences (Rasht, Iran).

2. Methods

2.1. Study population

This current study is a single-center, descriptive, cross-sectional study, contained of 510 participants who had been referred to GLDRC during 2017. All participants evaluated for the presence of DM, and classified as diabetic patients (diabetic group) and non-diabetic subjects (control group). DM was defined as fasting blood sugar (FBS) levels $\geq$ 126 mg/dL or Hemoglobin A1c (HbA1c) $\geq$ 6.5%, and previously diagnosed diabetes mellitus or currently use of oral antidiabetic agents. Patients with a history of malignancies, chronic inflammatory disease, acute and chronic infection, advanced renal or hepatic disease, thyroid diseases, GI organic disease and GI surgery were excluded from the study.

The study project was approved by the local ethics committee of the Guilan University of Medical Sciences, Rasht, Iran (Ethics committee No; p-3-132-2927), and informed consent was obtained from all of the enrolled participants.

2.2. Questionnaire

The GI symptoms of participants were assessed using "The GI symptom Questionnaire" designed by the GLDRC. The questionnaire consists of a total of 26 questions, and was categorized into three parts; upper, lower and general GI symptoms. The questionnaire was constructed with a five-point Likert-type scale (never, rarely, sometimes, often and always). This questionnaire were prepared according to the previous studies, and validated by experts. The reliability of this questionnaire assessed using cronbach's alpha (0.87).

2.3. Statistical analysis

Results were expressed as mean ± standard deviation (SD) or number (%). Comparisons between groups were conducted using the *t*-test and the chi-square test for continuous and categorical variables, respectively. $P < 0.05$ was considered as statistically significant.

3. Results

3.1. Characteristics of the study population

Study participants consisted of 255 patients with DM (diabetic group: 35.8% male, age 54.5 ± 11.7 years) and 255 non-diabetic subject (control group: 35.6% male, age 54.7 ± 11.1 years). Baseline characteristics of all 510 participants were presented in Table 1.

Diabetic patients were composed of 73 men and 182 women, and their age were 54.9 ± 10.4 and 54.3 ± 12.2 years for men and women, respectively. Type 2 diabetic patients were 80.0% (80.8 for men and 79.7 for women) of diabetic patients, and the average of duration of diabetes was 1.79 years. Other characteristics of diabetic patients were presented in Table 2.

3.2. Prevalence of GI symptoms

GI symptoms were reported in 91% of diabetic patients, and 42% of them were male.

3.3. Upper GI symptoms

According to the obtained results (Table 3) postprandial fullness, retrosternal pain, belching, and reflux episodes (12.5, 14.9, 13.7 and 12.2%, respectively) were the most prevalent upper GI symptoms in diabetic group. The prevalence of postprandial fullness, dysphagia, nausea, vomiting, retrosternal pain, early satiety, belching, and reflux episodes in diabetic patients were higher than control subjects, and these differences were statistically significant ($p < 0.001$).

Table 2
The characteristics of diabetic patients based on the gender.

Characteristics	Male (N = 73)	Female (N = 182)	*P*-value
Age, year	54.9 ± 10.4	54.3 ± 12.2	0.731
Current smoker	28 (38.4)	10 (5.5)	<0.001
Substance abuser	15 (20.5)	5 (2.7)	0.010
Type 2 diabetes	59 (80.8)	145 (79.7)	0.835
DD, year	1.7 ± 1.0	1.8 ± 0.9	0.196
FBS, mg/dl	231.4 ± 115.4	222.6 ± 97.7	0.568
HbA1c, %	8.2 ± 2.4	8.3 ± 2.1	0.679

Data were presented as number (%).
DD; duration of diabetes, FBS; Fasting blood glucose, HbA1c; Hemoglobin A1c, GI; gastrointestinal.
P values calculated by chi-squared test.

Table 1
The characteristics of the study population.

Characteristics	Total (N = 510)	Diabetic group (N = 255)	control group (N = 255)	*P*-value
Age, year	54.6 ± 11.4	54.5 ± 11.7	54.7 ± 11.1	0.796
Male	363 (71.2)	182 (71.4)	181 (71.0)	0.922
Married	435 (85.3)	215 (84.3)	220 (86.3)	0.532
Current smoker	46 (9.0)	38 (14.9)	8 (3.1)	<0.001
Substance abuser	27 (5.3)	20 (7.8)	7 (2.7)	0.010
FBS, mg/dl	153.9 ± 102.2	225.1 ± 102.9	82.4 ± 7.4	<0.001
HbA1c, %	6.69 ± 2.3	8.25 ± 2.20	5.13 ± 1.69	<0.001

Data were presented as mean ± SD or number (%).
Diabetic group consisted of diabetic patients and control group consisted of non-diabetic subject.
FBS; Fasting blood glucose, HbA1c; Hemoglobin A1c.
P values calculated by *t*-test or chi-squared test.

Table 3
The prevalence of upper gastrointestinal symptoms in the study population.

GI Symptoms	Total (N = 510)	Diabetic group (N = 255)	Control group (N = 255)	*P*-value
Postprandial fullness	34 (6.7)	32 (12.5)	2 (0.8)	<0.001
Dysphagia	26 (5.1)	26 (10.2)	0 (0.0)	<0.001
Nausea	22 (4.3)	22 (8.6)	0 (0.0)	<0.001
Vomiting	25 (4.9)	25 (9.8)	0 (0.0)	<0.001
Heartburn	20 (3.9)	20 (7.8)	0 (0.0)	<0.001
Retrosternal pain	38 (7.5)	38 (14.9)	0 (0.0)	<0.001
Early satiety	20 (3.9)	20 (7.8)	0 (0.0)	<0.001
Belching	35 (6.9)	35 (13.7)	0 (0.0)	<0.001
Reflux episodes	31 (6.1)	31 (12.2)	0 (0.0)	<0.001

Data were presented as number (%).
GI; gastrointestinal.
All symptoms rated "always".
Diabetic group consisted of diabetic patients and control group consisted of non-diabetic subject.
P values calculated by chi-squared test.

3.4. Lower GI symptoms

Constipation (11.4%), flatulence (33.0%), and borborygmus (10.6%) were assessed as the most prevalent lower GI symptoms in diabetic group. The prevalence of constipation, diarrhea, flatulence, inadequate evacuation, painful defecation, and borborygmus in diabetic patient were higher than control subjects. The prevalence of other lower GI symptoms were not statistically significant between diabetic and control groups (Table 4).

3.5. General GI symptoms

Tarry stool (6.7%) was the most prevalent general GI symptom in diabetic group. Moreover, the prevalence of loss of appetite, weight loss, and abdominal distention in diabetic patients were higher than control subjects, which were statistically significant ($P < 0.001$). Other general GI symptoms were not statistically significantly between groups (Table 5).

3.6. Prevalence of main GI symptoms based on gender

Heartburn and retrosternal pain were more prevalent in diabetic men than those of diabetic women. Other upper GI symptoms were not statistically significant between men and women. Among lower GI symptoms, constipation and flatulence were more prevalent in diabetic women. However, diabetic women showed higher prevalence of loss of appetite and weight loss, the prevalence of blood in stool was more in diabetic men. The prevalence of main GI symptoms were shown in Table 6.

4. Discussion

Diabetes mellitus (DM) is one of the most commonly diagnosed diseases worldwide, with over 200 million patients suffering from its complications. Diabetic GI complications are prevalent in diabetes patients, but the exact pathogenesis is still unknown [4,24]. Several studies have shown diabetic autonomic neuropathy has an underlying role in diabetic gastroparesis and enteropathy [7,25]. Disturbances in GI motility leads to most of the GI symptoms in diabetic patients, which increase costs of health care and decrease quality of patients' life [9,26]. There is a controversial information about the prevalence of diabetic GI symptoms in epidemiological studies based on methodological strategy, and this study aimed to investigate the prevalence of GI symptoms in diabetic patients.

The current study had a main methodological strengths. The survey was designed with significant power to show the differences in prevalence rates of 10% or more. Diabetic and control groups were matched in their age and gender distribution. The prevalence of GI symptoms were more in diabetic group (91.4%) than control group (26.2%). The prevalence of all upper GI symptoms are higher in the diabetic group compared to the control group. Among lower GI symptoms, constipation (11.4%), diarrhea (6.0%), flatulence (33.0%), painful defecation (2.7%), and Borborygmus (10.6%) were more prevalent in diabetic patients. Additionally, the prevalence of

Table 4
The prevalence of lower gastrointestinal symptoms in the study population.

GI Symptoms	Total (N = 510)	Diabetic group (N = 255)	Control group (N = 255)	*P*-value
Constipation				
<3 stools/week	15 (2.9)	15 (5.9)	0 (0.0)	<0.001
Pellet or hard stool	14 (2.7)	14 (5.5)	0 (0.0)	<0.001
Diarrhea				
≥3 stools/day	6 (1.2)	6 (2.5)	0 (0.0)	<0.001
Loose or watery stool	9 (1.8)	9 (3.5)	0 (0.0)	0.015
Both C or D	29 (5.7)	16 (6.3)	13 (5.1)	0.703
Flatulence	110 (21.5)	84 (33.0)	26 (10.2)	<0.001
Inadequate evacuation	10 (2.0)	10 (3.9)	0 (0.0)	0.003
Painful defecation	7 (1.4)	7 (2.7)	0 (0.0)	0.009
Relieved AP by defecation	23 (4.5)	10 (3.9)	13 (5.1)	0.516
Borborygmus	27 (5.6)	27 (10.6)	0 (0.0)	<0.001
Nocturnal urgency	21 (6.7)	21 (8.2)	13 (5.1)	0.214

Data were presented as number (%).
GI; gastrointestinal, C; constipation, D; diarrhea, AP; abdominal pain.
All symptoms rated "always".
Diabetic group consisted of diabetic patients and control group consisted of non-diabetic subject.
P values calculated by chi-squared test.

Table 5
The prevalence of general gastrointestinal symptoms in the study population.

GI Symptoms	Total (N = 510)	Diabetic patients (N = 255)	Control subjects (N = 255)	*P*-value
Loss of appetite	9 (1.8)	9 (3.5)	0 (0.0)	<0.001
Weight loss	11 (2.2)	9 (3.5)	2 (0.8)	<0.001
Abdominal distention	12 (2.4)	12 (4.7)	0 (0.0)	<0.001
Tarry stool	18 (3.5)	17 (6.7)	13 (0.4)	<0.001
Blood in stool	25 (4.9)	12 (4.8)	13 (5.1)	0.837
Mucus in stool	19 (3.7)	6 (2.4)	13 (5.1)	0.159

Data were presented as number (%).
GI; gastrointestinal.
All symptoms rated "always".
Diabetic group consisted of diabetic patients and control group consisted of non-diabetic subject.
P values calculated by chi-squared test.

Table 6
The prevalence of main gastrointestinal symptoms based on the gender.

GI symptoms	Male (N = 73)	Female (N = 182)	*P*-value
Heartburn	3 (4.1)	17 (9.3)	0.052
Retrosternal pain	3 (4.1)	35 (19.2)	<0.001
Early satiety	4 (8.2)	14 (7.7)	0.084
Constipation	7 (9.6)	22 (12.0)	<0.001
Diarrhea	5 (6.8)	10 (5.4)	0.042
Flatulence	18 (24.7)	66 (36.3)	0.020
Borborygmus	6 (8.2)	21 (11.5)	0.578
Loss of appetite	2 (2.7)	7 (3.8)	0.001
Abdominal distention	3 (4.1)	9 (4.9)	0.011
Blood in stool	7 (9.5)	5 (2.7)	0.011

Data were presented as number (%).
DD; duration of diabetes, FBS; Fasting blood glucose, HbA1c; Hemoglobin A1c, GI; gastrointestinal.
P values calculated by chi-squared test.

loss of appetite (3.5%), weight loss (3.5%), abdominal distention (4.7%), and tarry stool (6.7%) were also higher in diabetic group.

The analyses showed there was no significant correlation between GI symptoms and types and duration of diabetes. However, the prevalence of diabetic GI symptoms was associated with the age of patient and the glycemic control status evaluated by FBS and HbA1c levels.

The similar previous study has been reported the prevalence of most of upper and lower GI symptoms in the 190 patients with diabetes were 1.7 and 1.1 times more than the general population, respectively [27]. Another study has demonstrated that 42% of diabetic patients and 18% of non-diabetic subjects had at least one GI symptoms. Constipation, diarrhea, belching, and retrosternal pain were the most common GI symptoms in the diabetics [28]. It has also shown among GI symptoms, constipation, diarrhea, alternating bowel habit, abdominal pain, belching, and flatulence were significantly more prevalent in diabetic groups compared to control group [29], and these results were consistent with the result of present study. However, in one another study, there was no significant differences between the prevalence of almost all GI symptoms in diabetic and control. Only heartburn was more prevalent in diabetic patients [30].

In the present study, the GI symptoms were more prevalent among women, and this results were in consist with the results of previous studies reporting the prevalence rates of GI symptoms based on gender [31,32]. However, the frequencies of substance abuse like alcohol and smoking, which are the risk factor for GI diseases and symptoms, were higher in men. These could be explained by the fact that women show higher prevalence rates of GI symptoms totally, because of different reasons like high prevalence of functional GI disorders and high levels of psychosocial distress [4,33]. Among upper GI symptoms, heartburn (9.3%) and retrosternal pain (19.2%), and among lower GI symptoms, constipation (12.0%), diarrhea (5.4%) and flatulence (36.3%) as well as loss of appetite (3.8%) and abdominal distention (4.9%) were more prevalent in diabetic women than men.

5. Conclusion

DM is associated with high prevalence rate of upper and lower GI symptoms. This effect may be linked to gender and poor glycemic control of diabetic patients, but not to type and duration of diabetes.

5.1. Study limitation

The limitation of the current study is the investigation of the single-center population without assessment of treatment strategy in diabetic patients. Therefore, we suggest future multi-center studies with larger groups of diabetic patients and evaluation the adverse effects of antidiabetic medicines.

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Conflicts of interest

None declared.

Author contribution

Study design and supervision: M.A, F.J, A.P, R.M and F.M.
Analyzing and critical review: M.F, S.H and A.P, R.M and F.M.
Data gathering and writing: M.A, M.K and S.H.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2019.05.028.

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