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Prevalence of Gastrointestinal Symptoms among Individuals with and without Diabetes: A Cross-Sectional Study from the PERSIAN Guilan Cohort Study

ABSTRACT

Objective: Gastrointestinal (GI) symptoms are the most common complaint among individuals with diabetes. This study investigated the prevalence of upper, lower, and general GI symptoms in individuals with and without diabetes among the Prospective Epidemiological Research Studies in Iran (PERSIAN) Guilan Cohort study (PGCS) population.

Materials and methods: This cross-sectional study of PGCS was conducted on 2669 participants, 1364 with diabetes and 1305 without diabetes. The first part of the questionnaire collected demographical and clinical data, and the second part collected GI symptoms. A 4-point Likert Scale was used for each question. Data were analyzed using SPSS software version 16, and the significance level was considered < 0.05.

Results: The mean age of the participants was 52.24 ± ± 8.75 years, and 55.5% were female. Patients with diabetes have an increased incidence of upper GI symptoms (adjusted odds ratio [aOR] = 1.19, 95% confidence interval [CI]: 1.00–1.42, p = 0.045) compared to individuals without diabetes. The most common upper GI symptom in patients with diabetes compared to those without diabetes was eructation (18.6% vs. 14.9%, p = 0.009).

Conclusions: The prevalence of GI symptoms was high in patients both with and without diabetes, and the chance of developing GI upper symptoms was higher in patients with diabetes. (Clin Diabetol 2023; 12; 6: 370–376)

Keywords: diabetes mellitus, gastrointestinal symptoms, type 2 diabetes

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Introduction

The prevalence of diabetes has reached alarming levels, making it one of the most severe and common chronic diseases. This condition poses life-threatening risks and leads to disabling complications, reducing life expectancy [1]. Globally, the number of adults living with diabetes has increased to 537 million, with projections estimating a further increase to 643 million by 2030 and 783 million by 2045 [2]. Diabetes is associ-

ated with many complications, including macrovascular conditions such as coronary heart disease, stroke, and peripheral arterial disease, and microvascular conditions such as patients with diabetic kidney disease, retinopathy, and peripheral neuropathy [3].

While the complications of diabetes have received significant attention, the impact of gastrointestinal (GI) symptoms on individuals with diabetes has often been overlooked. GI symptoms represent a significant cause of morbidity and have the potential to significantly affect the quality of life and overall disease management for individuals with diabetes [4]. Gastrointestinal symptoms observed in patients with diabetes can manifest in various ways that encompass a range of symptoms affecting the upper and lower GI tracts, including heartburn, dyspepsia, dysphagia, gastroparesis, constipation, diarrhea, and fecal incontinence [5].

Epidemiological studies on the prevalence of GI symptoms in patients with diabetes have yielded conflicting results [6]. Some suggest that GI symptoms are more common in patients with diabetes [4], while other studies have found no significant difference in symptom prevalence between individuals with and without diabetes [6, 7]. These discrepancies may arise due to methodological challenges and inconsistencies in the available epidemiological data, challenging the current understanding of GI symptoms in diabetes [8]. Given the conflicting evidence surrounding the prevalence of GI symptoms, the high prevalence of diabetes, and the adverse impact of these symptoms on the quality of life in patients with diabetes, this study aims to investigate the prevalence of GI symptoms individuals in both with and without diabetes in Prospective Epidemiological Research Studies in Iran (PERSIAN) Guilan Cohort study (PGCS).

Methods and materials

Study population

This cross-sectional study was a part of the PGCS [9, 10] conducted on 2669 participants in 2019. The study was approved by the ethical committee of the Guilan University of Medical Sciences, Rasht, Iran (IR.GUMS.REC.1398.482), and all participants provided informed consent upon entering the study. Males and females aged 35 to 70 from Sowm'e Sara, Guilan province, Iran, who met the study's inclusion criteria were included. Those with a fasting blood glucose (FBS) of 126 and higher, a history of insulin injection, oral hypoglycemic medication, or self-declaration of the disease were considered patients with diabetes. About 1364 patients with diabetes and 1305 without diabetes were evaluated. Afterward, every participant received an 11-digit code based on the previous data and information provided by the host.

Questionnaires

The data were obtained through a questionnaire consisting of two sections. The first section included demographic factors (gender, age, marital status, education, body mass index [BMI]) along with a history of smoking, alcohol consumption, FBS, and comorbidities. The second section consisted of 32 questions regarding GI symptoms. The 4-point Likert scale for every question was used to record the frequency of GI symptoms in the last three months. The GI symptoms were divided into three categories: upper GI symptoms including postprandial fullness, odynophagia, dysphagia, difficulty starting to swallow, epigastric pain, bloating, nausea, vomiting, heartburn, retrosternal pain, early satiety, eructation, GI reflux, night cough, and morning hoarseness; lower GI symptoms including constipation, diarrhea, sometimes diarrhea or sometimes constipation, inadequate evacuation, painful defecation, relieved abdominal pain by defecation, borborygmus, pellet or hard stool, loose or watery stools, nocturnal urgency, and flatulence; and general symptoms including loss of appetite, weight loss, abdominal distension, tarry stool, blood in stool, and mucus in stool.

Statistical analysis

The qualitative variables were reported by frequency (percentage and number). The chi-square test was used to compare the variables of individuals with and without diabetes. Furthermore, for evaluating individual factors related to GI symptoms, single-variable analyses (simple logistic regression model) and multivariable analyses (multiple logistic regression model) were used. The results of these two analyses were presented as odds ratios (OR) in both crude and adjusted forms, with a 95% confidence interval (CI). The data were analyzed using SPSS software version 16, and a significance level of 0.05.

Results

Characteristics of the study population

A total of 2669 participants were included in the study, in which about 994 individuals (37.2%) were 56 years and older, 1480 (55.5%) were female, 2448 (91.7%) were married, and 1841 (69.00%) were rural residents. About 626 individuals (23.5%) were smokers, 349 (13.1%) consumed alcohol, and 1653 (61.9%) had a history of underlying disease (Tab. 1).

Table 2 and Figure 1 illustrate the frequency of GI symptoms among participants. Among the upper

Table 1. Demographic and Clinical Characteristics of the Participants with and without Diabetes

	Total (n = 2669)	Diabetic individuals (n = 1364)	Non-diabetic individuals (n = 1305)
Age [years]			
36–55	1675 (62.8)	995 (72.9)	680 (52.1)
> 55	994 (37.2)	369 (27.1)	625 (47.9)
Mean±SD	52.24 ± 8.75	50.14 ± 8.37	54.42 ± 8.62
Gender			
Male	1189 (44.5)	649 (47.6)	540 (41.4)
Female	1480 (55.5)	715 (52.4)	765 (58.6)
Marital status			
Married	2448 (91.7)	1277 (93.6)	1171 (89.7)
Single	60 (2.2)	34 (2.5)	26 (2.0)
Widowed	136 (5.1)	36 (2.6)	100 (7.7)
Divorced	25 (0.9)	17 (1.2)	8 (0.6)
Education level			
Illiterate	404 (15.1)	126 (9.2)	278 (21.3)
Primary	758 (28.4)	349 (25.6)	409 (31.3)
Secondary	537 (20.1)	291 (21.3)	246 (18.9)
Diploma	784 (29.4)	476 (34.9)	308 (23.6)
University	186 (7.0)	122 (8.9)	64 (4.9)
Habitat			
Urban	828 (31.0)	226 (16.6)	602 (46.1)
Rural	1841 (69.0)	1138 (83.4)	703 (53.9)
BMI [kg/m^2]			
Underweight	34 (1.3)	20 (1.5)	14 (1.1)
Normal	646 (24.2)	382 (28.0)	264 (20.2)
Overweight	1071 (40.1)	537 (39.4)	534 (40.9)
Obese	918 (34.3)	425 (31.2)	493 (37.8)
Mean ± SD	28.36 ± 5.20	27.69 ± 4.85	29.05 ± 5.46
Smoking			
No	2043 (76.5)	1020 (74.8)	1023 (78.4)
Yes	626 (23.5)	344 (25.2)	282 (21.6)
Alcohol			
No	2320 (86.9)	1161 (85.1)	1159 (88.8)
Yes	349 (13.1)	203 (14.9)	146 (11.2)
Underlying disease			
No	1016 (38.1)	631 (46.3)	385 (29.5)
Yes	1653 (61.9)	733 (53.7)	920 (70.5)
Diabetes			
No	1305 (48.9)	–	–
Yes	1364 (51.1)		

BMI — body mass index

GI symptoms, the frequency of eructation (18.6%), retrosternal pain (6.4%), early satiety (5.1%), and night cough (4.2%) in patients with diabetes were higher than those without diabetes ($p < 0.05$) (Tab. 2 and Fig. 1A). Among the lower GI symptoms, the frequency of constipation, painful defecation, and nocturnal urgency in patients with diabetes (15.0%, 3.2%, and 1.2%) was lower than in individuals without diabetes, ($p < 0.05$) (Tab. 2 and Fig. 1B). Among the general GI symptoms, the frequency of tarry stools (2.7%) was significantly lower in patients with diabetes compared to those without diabetes ($p < 0.05$), (Tab. 2 and Fig. 1C).

The prevalence of GI symptoms in patients with diabetes was higher than in individuals without diabe-

Table 2. Comparison of the Frequency of GI Symptoms between Participants with and without Diabetes

	Patients with diabetes (n =1364), n (%)	Patients without diabetes (n =1305), n (%)	P
GI symptoms			
Postprandial fullness	133 (9.8)	123 (9.4)	0.775
Odynophagia	30 (2.2)	27 (2.1)	0.816
Dysphagia	48 (3.5)	50 (3.8)	0.668
Difficulty starting to swallow	35 (2.6)	27 (2.1)	0.394
Epigastric pain	137 (10.0)	139 (10.7)	0.606
Bloating	377 (27.6)	348 (26.7)	0.572
Upper			
Nausea	82 (6.0)	80 (6.1)	0.898
Vomiting	29 (2.1)	34 (2.6)	0.415
Heartburn	209 (15.3)	209 (16.0)	0.623
Retrosternal pain	87 (6.4)	58 (4.4)	0.028
Early satiety	70 (5.1)	45 (3.4)	0.032
Eructation	254 (18.6)	194 (14.9)	0.009
GI reflux	301 (22.1)	312 (23.9)	0.258
Night cough	57 (4.2)	31 (2.4)	0.009
Morning hoarseness	53 (3.9)	36 (2.8)	0.105
Lower			
Constipation	204 (15.0)	246 (18.9)	0.007
Diarrhea	64 (4.7)	63 (4.8)	0.869
Sometimes diarrhea or sometimes constipation	56 (4.1)	46 (3.5)	0.434
Inadequate evacuation	44 (3.2)	59 (4.5)	0.082
Painful defecation	43 (3.2)	69 (5.3)	0.006
Relieved abdominal pain by defecation	66 (4.8)	81 (6.2)	0.121
Borborygmus	173 (12.7)	148 (11.3)	0.287
Pellet or hard stool	190 (13.9)	215 (16.5)	0.067
Loose or watery stools	72 (5.3)	63 (4.8)	0.595
Nocturnal urgency	17 (1.2)	33 (2.5)	0.015
Flatulence	271 (19.9)	229 (17.5)	0.125
Loss of appetite	33 (2.4)	47 (3.6)	0.073
Weight loss	65 (4.8)	69 (5.3)	0.537
General			
Abdominal distention	35 (2.6)	36 (2.8)	0.757
Tarry stool	37 (2.7)	60 (4.6)	0.009
Blood in stool	20 (1.5)	15 (1.1)	0.472
Mucus in stool	1 (0.1)	0 (0.0)	0.999†

Values are shown as "frequency (percent)", †Fisher exact test

tes (57.8% vs. 54.8%) but this difference was not statistically significant ($p > 0.05$) (Tab. 3). The prevalence of GI symptoms was higher in patients with diabetes compared to participants without diabetes, but it was not statistically significant ($p > 0.05$) (Tab. 3 and Fig. 1D). According to the logistic regression analysis (Tab. 3), patients with diabetes were 1.19 times more likely to develop upper GI symptoms (aOR = 1.19, 95% CI: 1.00–1.42, $p = 0.045$). The risk of developing GI symptoms was higher in patients with diabetes, but no statistically significant relationship was observed $p < 0.05$).

Discussion

The current study illustrated that the prevalence of GI symptoms was high in both patients with diabetes and individuals without diabetes. In addition, the chance of developing upper GI symptoms was higher

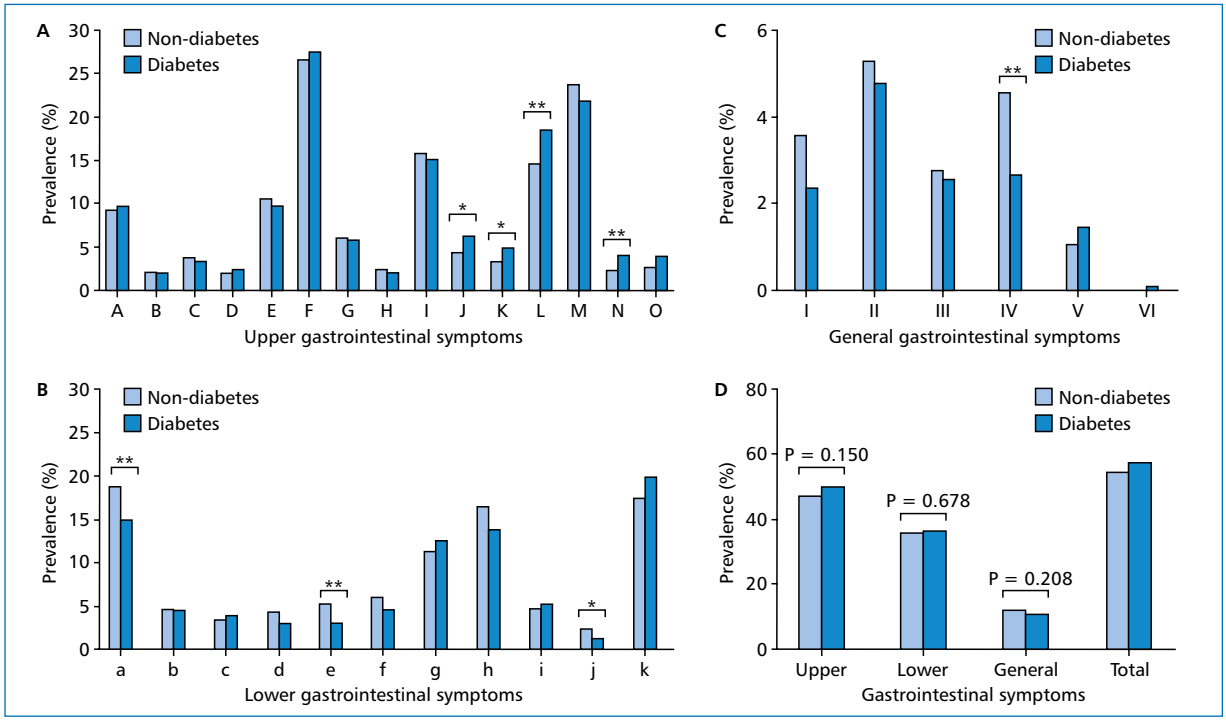

Figure 1. Comparison of the Frequency of Gastrointestinal Symptoms between Individuals with and without Diabetes; **(A.)** Frequency of upper GI symptoms: A. Postprandial fullness; B. Odynophagia; C. Dysphagia; D. Difficulty starting to swallow; E. Epigastric pain; F. Bloating; G. Nausea; H. Vomiting; I. Heartburn; J. Retrosternal pain; K. Early satiety; L. eructation; M. Gastrointestinal reflux; N. Night cough; O. Morning hoarseness; **(B.)** Frequency of lower GI symptoms: a. Constipation; b. Diarrhea; c. Sometimes diarrhea or sometimes constipation; d. Inadequate evacuation; e. Painful defecation; f. Relieved abdominal pain by defecation; g. Borborygmus; h. Pellet or hard stool; i. Loose or watery stools; j. Nocturnal urgency; k. Flatulence; **(C.)** Frequency of general GI symptoms: I. Loss of appetite; II. Weight loss; III. Abdominal distension; IV. Tarry stool; V. Blood in stool; VI. Mucus in the stool; **(D).** Upper, lower, general, and total GI symptoms are frequent among individuals with and without diabetes
*< 0.05; **< 0.001

in patients with diabetes than in individuals without diabetes. Different studies indicated that individuals with diabetes experienced higher upper and lower GI symptoms than healthy controls [4, 7, 11, 12]. On the other hand, a study using the Bowel Disease Questionnaire (BDQ) demonstrated that the frequency of GI symptoms was similar in individuals with and without diabetes [6]. In another study, patients with diabetes represented a similar prevalence of at least one GI symptom, notably lower GI symptoms. In contrast, Sang et al. reported that the frequency of upper GI symptoms was higher compared to those without diabetes [13].

Additionally, it was indicated that among GI symptoms, patients with diabetes had significantly higher rates of constipation, diarrhea, alternating bowel habits, abdominal pain, eructation, and flatulence than control groups [13–15]. Consistently, in the present study, among upper GI symptoms, patients with diabetes had a higher proportion of eructation, retrosternal pain, early satiety, and night cough than those without diabetes.

Gastric emptying significantly impacts postprandial blood glucose in healthy individuals and those with type 2 diabetes. Disruptions in gastric emptying are common in diabetes, including delayed and accelerated emptying. Delayed gastric emptying, known as diabetic gastroparesis, can cause upper gastrointestinal symptoms, but treatment effectiveness is limited. In insulin-treated patients, disordered gastric emptying can lead to suboptimal glycemic control. Conversely, interventions that slow gastric emptying, like certain medications, can reduce postprandial blood glucose in type 2 diabetes. Accurate measurement of gastric emptying is crucial for evaluating therapies in clinical trials [16]. Halland et al. reported that although acute severe and chronic hyperglycemia has the potential to delay gastric emptying, the available evidence suggests that there is limited support for delayed gastric emptying

Table 3. Factors Associated with GI Symptoms among Total Participants (with and without Diabetes)

Variables	Diabetes	Prevalence	Simple logistic regression		Multiple logistic regression	
		n (%)	OR (95% CI)	P	aOR (95% CI)	P
Upper GI symptoms	No	619 (47.4)	1		1	
	Yes	685 (50.2)	1.12 (0.96–1.30)	0.150	1.19 (1.00–1.42)	0.045
Lower GI symptoms	No	474 (36.3)	1		1	
	Yes	506 (37.1)	1.03 (0.88–1.21)	0.678	1.02 (0.85–1.21)	0.856
General GI symptoms	No	164 (12.6)	1		1	
	Yes	150 (11.0)	0.86 (0.68 10.09 [1.09???])	0.209	0.95 (0.73–1.23)	0.695
Total GI symptoms	No	715 (54.8)	1		1	
	Yes	788 (57.8)	1.13 (0.97–1.32)	0.121	1.18 (0.99–1.40)	0.061

aOR — adjusted odds ratio; BMI — body mass index; CI — confidence interval; OR — odds ratio

being an independent risk factor for impaired glycemic control or hypoglycemia in individuals with diabetes [17]. In contrast, some studies reported that among patients with diabetes, no marked changes in gastric emptying or upper GI symptoms were observed [18, 19].

Moreover, it has been shown that diabetic patients frequently describe lower GI tract symptoms. In a study by Reszczyńska et al., patients with diabetes exhibit enhanced dyssynergia defecation features, impaired visceral sensation, and impaired external anal sphincter function. Both anal sphincters in people with long-standing diabetes and enteropathy symptoms have severely reduced function [12]. A study by Leeds et al. showed that gastrointestinal symptoms are more prevalent in individuals with type 1 diabetes and are linked to lower quality of life and glycemic control. The investigation of diarrhea in people with type 1 diabetes has proven beneficial, as it often reveals treatable conditions and leads to a change in management for approximately three-quarters of the cases [14].

Managing GI symptoms in patients with diabetes involves a multifaceted approach. Strategies include dietary modifications such as increasing fiber intake or following a low-fiber diet, medications like laxatives or antidiarrheals, maintaining stable blood glucose levels through proper treatment adherence, stress reduction techniques, regular physical activity, adequate hydration, probiotics for gut health, and addressing underlying conditions [20]. Consulting with healthcare professionals is essential to develop an individualized management plan for effectively alleviating these symptoms and improving overall well-being in patients with diabetes [21]. Specific lifestyle changes can help enhance bowel function in individuals with diabetes and enteropathy symptoms. These include dietary modifications such as gradually increasing fiber intake, staying adequately hydrated, and consuming smaller, more frequent meals [22].

The study emphasized the risk factors affecting GI symptoms among individuals with and without diabetes to represent the prevention and better clinical management, while it should be considered that the cross-sectional nature of the study and the lack of follow-up might limit the precise observation of the exact effect of diabetes on the chance of developing GI symptoms.

Conclusions

Consequently, we have demonstrated that GI is common in the PGCS population with and without diabetes, and the risk of developing upper GI symptoms was significantly higher in patients with diabetes. These observations could help clinicians for better clinical management to reduce GI symptoms in individuals with and without diabetes.

Article information

Availability of data and materials

The study protocol and the datasets analyzed are available from the corresponding author upon request.

Ethics approval and consent to participate

This study was approved by the ethics committees of the Guilan University of Medical Sciences (IR.GUMS.REC.1398.482). Informed consent was obtained from all individual participants.

Author contributions

FJ, MSM, and FMGH participated in the research design. SY, EA, ZAR, and MSA participated in writing the first draft. SH, ZAR, and SM participated in the performance of the research and analytic tools. SH, FJ, and MN participated in data analysis. All authors reviewed and confirmed the final manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

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