

Dyspeptic Symptoms in Type 2 Diabetes Patients

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ABSTRACT

Background: Nearly half of the patients with diabetes experience diabetic gastroparesis. Some diabetic patients present with complaints of epigastric pain, vomiting, nausea, or postprandial fullness, however only a few have severe symptoms.

Objective: To determine the frequency of dyspepsia among T2DM patients.

Methods: This cross-sectional study was performed in Ziauddin Hospital Kemari Branch, Karachi, Pakistan after acquiring ethical approval from the hospital ethics committee. Short-Form Leeds Dyspepsia Questionnaire (SF-LDQ) was used to identify the presence of dyspepsia. Based on the sum of the frequency of symptoms, a cut-off value of 4 and above was used for the presence of dyspepsia.

Results: A total of 368 patients were included in the study with a median age of 68.6 ± 14.2 years. The majority were females (62.8%). The mean duration of diabetes was 15 ± 10.4 years. The frequency of indigestion, heartburn, regurgitation, and nausea was 35.3%, 30.7%, 31.5%, and 11.4% respectively. Out of 368, 168 (45.7%) patients were found to have dyspepsia. The risk of dyspepsia was significantly lower among younger age, male gender, and patients having controlled glycemic status, patients doing physical activity twice a week, taking all three meals on time, and always having their breakfast early. The odds of having dyspepsia were higher among those who are currently and formerly addicted to alcohol, current and former smokers, having comorbidity, consuming <8 glasses of water per day, and those who were always or sometimes sleeping within two hours of having dinner.

Conclusion: This study analyzed that dyspeptic symptoms including indigestion, heartburn, and regurgitation were common in T2DM patients, and about half of these patients had dyspepsia which was common among patients with poor glycemic control and those with unhealthy lifestyles.

Keywords: Type 2 diabetes, dyspepsia, dyspeptic symptoms, gastrointestinal symptoms, diabetes mellitus

INTRODUCTION

Diabetes mellitus (DM) is a disease of insufficient control of blood glucose levels [1]. It may occur because of any one of the reasons including inappropriate insulin secretion or resistance to peripheral insulin actions. In Type 2 diabetes mellitus (T2DM), the insulin response is impaired, and this state is considered insulin resistance. T2DM contributes to nearly 90% of all diabetic cases. T2DM is frequently diagnosed in individuals of age more than 45 years [2].

Nearly half of the patients either with or without insulin-dependent diabetes experience diabetic gastroparesis. Some diabetic patients present with complaints of epigastric pain, vomiting, nausea, or postprandial fullness, however only a few have severe symptoms [3]. The burden of dyspeptic symptoms is higher in diabetic patients than in non-diabetic individuals [4].

The dyspepsia origin in diabetes is controversial. The progression of dyspepsia in diabetic patients is multifactorial depending on gender, disease duration, occurrence of other diabetic complications, hyperglycemia management, and *Helicobacter pylori* infection [4]. However, the phenomenon leading

to digestive symptoms has not been completely understood yet [5].

Among diabetic patients, a link is suspected between diabetic complications GI symptoms, and poor glycemic control [6-8]. Globally dyspepsia is a public health issue with a gross burden of 25% prevalence [9]. Dyspeptic symptoms such as nausea, vomiting, and bloating, early satiety affect around 7-40% of the general population [10]. Because of the great burden of dyspeptic symptoms even in the general population, it becomes very critical to ascertain the burden of dyspepsia in a highly vulnerable population. The study will be beneficial for the medical community as it will make clinicians more vigilant in examining diabetic patients for dyspeptic symptoms with other diseases. The findings of the current study will improve the clinical guidelines for the treatment of diabetes and make clinical practices more improved and evidence-based. This is why the current study was planned to determine the frequency of dyspepsia among T2DM patients.

METHODOLOGY

This cross-sectional study was performed in outpatient clinics of family medicine and endocrinology in Ziauddin Hospital Kemari Branch, Karachi, Pakistan after acquiring ethical approval from the hospital ethics committee. Patients of age 18 years and above of any gender, willing to participate were included in this study. Patients diagnosed with any gastrointestinal disease before

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T2DM, type 1 diabetic patients, with any malignancy, with confirmed diagnosis of *H. pylori*, and those who recently received eradication therapy for *Helicobacter Pylori* infection were excluded from this study. Pregnant women and women in the lactation period were also excluded from this study. Non-probability consecutive sampling technique was used to enroll study participants. Patients were enrolled in the study with their written informed consent.

Online calculator Open-Epi was used to perform sample size computation by taking 60.3% frequency of dyspepsia

Table 1: Summary statistics for patients' profiles.

Study Variables	Frequency	Percentage
Age Groups		
≤50 years	34	9.2
>50 years	334	90.8
Gender		
Male	137	37.2
Female	231	62.8
Alcohol Use		
Current	91	24.7
Former	53	14.4
Never	224	60.9
Smoking Status		
Current	87	23.6
Former	71	19.3
Never	210	57.1
Comorbidity		
Yes	275	74.7
No	93	25.3
Glycemic Status		
Controlled	84	22.8
Uncontrolled	284	77.2
Physical Activity		
Daily	26	7.1
Twice a week	59	16.0
3-5 times per week	79	21.5
Never	204	55.4
Fizzy Drinks Consumption		
Daily	130	35.3
Occasional	133	36.1
Never	105	28.5
Water Intake Per Day		
<8 glasses	257	69.8
≥8 glasses	111	30.2
Daily Take all Three Meals on Time		
Always	102	27.7
Sometimes	266	72.3
Never		
Sleeping After 2 Hours of Dinner		
Always	240	65.2
Sometimes	73	19.8
Never	55	14.9
Breakfast Before 10:00 am		
Always	84	22.8
Sometimes	177	48.1
Never	107	29.1

among T2DM patients [11] at a 95% confidence interval and 5% margin of error, which yielded a sample size of 368 patients. Patients' demographic data including age and gender were recorded. Clinical history such as comorbidity, smoking status, and glycemic status was also noted. Glycemic status was considered as uncontrolled if HbA1c $\geq 7\%$ otherwise it was labeled as controlled diabetes. Alcohol consumption was defined as the intake of one alcoholic drink once a week as current. Former were those who were continuously taking alcohol previously and now quit it. Never was those who never consumed alcohol in their life or consumed one or two-pack ones in their life. Lifestyle factors such as daily water intake, physical activity, fizzy drinks consumption, and sleep after two hours of dinner and breakfast before 10:00 AM were also investigated during patient examination.

Short-Form Leeds Dyspepsia Questionnaire (SF-LDQ) was used to identify the presence of dyspepsia. SF-LDQ is a validated 8-item questionnaire that evaluates frequency and severity. This 4-item tool evaluates the frequency of upper gastrointestinal symptoms such as indigestion, heartburn, regurgitation, and nausea during the last two months, while severity is evaluated by rating the questionnaire from 0-32. The replies are evaluated on a scale of 0 (not at all) to 4 (once a day or more). The frequency and severity of all symptoms are then added together to determine the overall score. Based on the sum of the frequency of symptoms, Fraser *et al.* recommended a cut-off value of 4 and above for the presence of dyspepsia [12].

Data was entered and analyzed using SPSS version 26. Categorical variables were presented as frequency and percentage. Numerical variables were expressed as mean \pm standard deviation after confirming the normality assumption with the Shapiro-Wilk test. Patients' features were associated with those with and without dyspepsia using binary logistic regression. The odds ratio and their 95% confidence interval were computed. A p-value less than or equal to 0.05 was considered statistically significant.

RESULTS

The median age of patients was 68.6 ± 14.2 years with an age range of 38-99 years. The mean duration of diabetes was 15 ± 10.4 years. Table 1 displays the socio-demographic features of patients.

The median dyspepsia score based on the frequency of dyspeptic symptoms was 10 (IQR=8-12). Out of 368, 168 (45.7%) patients were found to have dyspepsia. **Fig. (1)** displays the frequency of dyspeptic symptoms among patients.

Table 2 shows a comparison of patients' profiles among those having and did not have dyspepsia and its univariate association with dyspepsia. The risk of dyspepsia was significantly lower among younger age ($p=0.004$), male

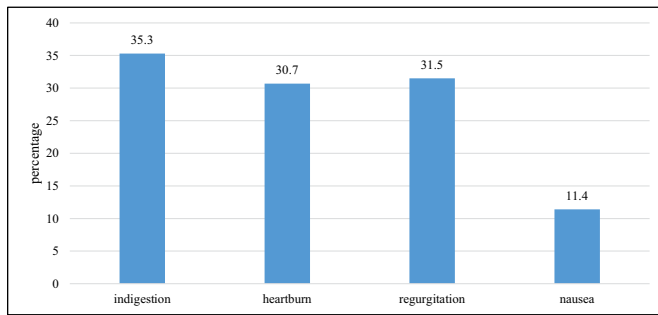


Fig. (1): Frequency of dyspeptic symptoms among patients.

Table 2: Association of patients' features with dyspepsia.

Variables	With dyspepsia n(%)	Without dyspepsia n(%)	OR (95% CI)	p-value
Age Groups				
≤50 years	7(20.6)	27(79.4)	0.28 (0.11-0.65)	**0.004
>50 years	161(48.2)	173(51.8)	Reference category	
Gender				
Male	43(31.4)	94(68.6)	0.38 (0.25-0.61)	**<0.001
Female	125(54.1)	106(45.9)	Reference category	
Alcohol Use				
Current	90(98.9)	1(1.1)	540 (72.6-4014.2)	**<0.001
Former	46(86.8)	7(13.2)	39.42 (16.3-94.9)	**<0.001
Never	32(14.3)	192(85.7)	Reference category	
Smoking Status				
Current	78(59.5)	53(40.5)	3.4 (2.1-5.5)	**<0.001
Former	40(56.3)	31(43.7)	3 (1.6-5.3)	**<0.001
Never	50(30.1)	116(69.9)	Reference category	
Comorbidity				
Yes	135(49.1)	140(50.9)	1.75 (1.07-2.85)	*0.024
No	33(35.5)	60(64.5)	Reference category	
Glycemic Status				
Controlled	29(34.5)	55(65.5)	0.55 (0.33-0.91)	*0.021
Uncontrolled	139(48.9)	145(51.1)	Reference category	
Physical Activity				
Daily	15(57.7)	11(42.3)	1.36 (0.59-3.11)	0.461
Twice a week	20(33.9)	39(66.1)	0.51 (0.28-0.94)	*0.030
3-5 times a week	31(39.2)	48(60.8)	0.65 (0.38-1.09)	0.105
Never	66(39.3)	102(60.7)	Reference category	
Fizzy Drink Consumption				
Daily	65(50)	65(50)	1.10 (0.65-1.84)	0.717
Occasional	53(39.8)	80(60.2)	0.73 (0.43-1.22)	0.230
Never	50(47.6)	55(52.4)	Reference category	
Water Intake Per Day				
<8 glasses	152(59.1)	105(40.9)	8.59 (4.78-15.43)	**<0.001
≥8 glasses	16(14.4)	95(85.6)	Reference category	
Daily Take All Three Meals on Time				
Always	34(33.3)	68(66.7)	0.49 (0.31-0.79)	**0.004
Sometimes	134(50.4)	132(49.6)	Reference category	
Sleeping After 2 Hours of Dinner				
Always	4(7.3)	51(92.7)	0.05 (0.02-0.13)	**<0.001
Sometimes	13(17.8)	60(82.2)	0.12 (0.07-0.13)	**<0.001
Never	151(62.9)	89(37.1)	Reference category	
Breakfast Before 10:00 am				
Always	8(9.5)	76(90.5)	0.02 (0.01-0.06)	**<0.001
Sometimes	74(41.8)	103(58.2)	0.17 (0.1-0.31)	**<0.001
Never	86(80.4)	21(91.6)	Reference category	

CI: Confidence interval, OR: Odds ratio, *Significant at p<0.01, **Significant at p<0.01

gender (p<0.001), patients having controlled glycemic status (p=0.021), patients doing physical activity twice a week (p=0.030), taking all three meals on time (p=0.004), always taking their breakfast early (p<0.001). The odds of having dyspepsia were higher among those who are currently (p<0.001) and formerly (p<0.001) addicted to alcohol, current (p<0.001) and former (p<0.001) smokers, having comorbidity (p=0.024), consuming <8 glasses of water per day (p<0.001) and those who were always (p<0.001) or sometimes (p<0.001) sleeping within two hours of having dinner.

DISCUSSION

About one-half of patients with insulin- or non-insulin-dependent diabetes have delayed gastric emptying (diabetic gastroparesis). Some of them complain of epigastric pain, nausea, vomiting, or postprandial fullness (diabetic dyspepsia), although only a minority are severely symptomatic [13]. As a consequence, Dyspeptic symptoms are a frequent finding in patients with diabetes and they are part of the so-called diabetic enteropathy (DE), which includes the GI manifestations of DM [14]. Despite the high incidence of dyspepsia in patients with diabetes, the current literature offers limited data about the clinical features of dyspepsia in this population. Therefore this study was conducted to determine the frequency of dyspepsia among T2DM patients.

This study analyzed that T2DM patients were experiencing dyspeptic symptoms with indigestion more frequent symptom followed by regurgitation, heartburn, and nausea. A similar Pakistani study reported that 38.3% of patients had a bloating complaint, and nausea, retching, and vomiting were present in 33.1%, 14.2%, and 4% respectively [15]. A recent study reported that about 25% of the patients with type II DM had heartburn, and acid regurgitation [16]. Another similar study reported GI symptoms were present in 30.3% of diabetic patients with a 17.5% prevalence of upper GI symptoms and a 17.7% prevalence of lower GI symptoms [17]. A similar study from Austria reported that among diabetic patients heartburn, epigastric pain, and regurgitation was found among 76.9%, 61.5%, and 47.7% of patients respectively [18]. An approach to diabetes management, self-care, and daily lifestyle could cause different findings among different regions and nations.

In this study, overall dyspepsia prevalence based on frequency of dyspeptic symptoms was 45.7%. A similar Russia-based study reported a dyspepsia frequency of 71% among T2DM [19]. A study from Italy demonstrated that 49.3% had dyspeptic symptoms among diabetic patients [20]. Another similar study from Turkey reported 60.3% dyspepsia prevalence among diabetic patients [21]. A study published in Saudi Arabia analyzed that 25.3% of patients had dyspepsia based on the cutoff for the summed frequency score of Leed's questionnaire [22]. A study from Nigeria found that dyspepsia was

present among 52% of diabetic patients [23]. The difference in dyspepsia prevalence among different studies likely reflects discrepancies in the methodology used and the patient populations studied.

The present study analyzed that patients older than 50 years were more likely to have dyspepsia than younger patients (<50 years). Kim *et al.* [24] reported that the elderly population are at higher risk of developing dyspepsia. Unfortunately, the data related to risk factors of dyspepsia in T2DM is lacking in the available literature. We assume that in older patients digestive health is not remarkable and a particular population is not physically active. Therefore adding the impact of all these factors in the presence of T2DM could have aggravated the condition and was the reason was higher frequency among the elderly population in our study.

The findings of this study suggested that females were more likely to have dyspepsia than males which is a consistently reported finding in existing literature [25-27]. In a recent meta-analysis, Ford *et al.* showed that women had a slightly higher pooled prevalence of dyspepsia than males (25.3 vs. 21.9%) when they looked at the prevalence of dyspepsia according to gender in 55 studies. In some nations, such as North America, northern Europe, southern Europe, the Middle East, and Southeast Asia, women were more likely than males to have dyspepsia, but not in Africa, South America, Australasia, or Central America [25].

There is evidence of a correlation between alcohol consumption and dyspeptic symptoms. Chronic alcoholics retain dyspeptic symptoms, pan-enteric, and functional alterations of gastric emptying, and oro-cecal transit tests, even after 12-month abstinence [28]. In this study, we also found a significant association between alcohol consumption with dyspepsia. Smoking is believed to be an important risk factor for dyspepsia. A study conducted in Olmsted County, Minnesota, evaluated the role of environmental factors, including smoking, in subjects with uninvestigated dyspepsia. The study found that smoking was associated with an increased risk of dyspepsia [29]. Another study conducted in Japan found that smoking was associated with an increased occurrence of overlapping gastroesophageal reflux disease (GERD), functional dyspepsia (FD), and irritable bowel syndrome (IBS) [26]. In line with the available literature, this study also found a higher risk of dyspepsia among patients who were current and former smokers than those who never smoked [30].

Diabetic patients with dyspepsia need to work with their healthcare provider to manage their symptoms and improve their glycemic control. This study analyzed that patients having controlled glycemic status were at less risk of dyspepsia than those who had uncontrolled glycemic status. A study conducted in the UK found that type 1 diabetes patient's gastrointestinal symptoms were

significantly associated with poorer glycemic control [31]. Another study conducted in Australia found that gastrointestinal symptoms, including dyspepsia, were associated with poor glycemic control among diabetic patients [32].

Lifestyle habits such as dietary intake, water consumption, and daily physical exercise impact gut health, and lifestyle changes are also recommended in addition to medication management among dyspeptic patients. This study also found that dyspepsia frequency was significantly higher among patients having poor lifestyles such as drinking inadequate water, consuming fizzy drinks, and not doing physical activity whereas the likelihood of dyspepsia was lower among patients sleeping after two hours of having dinner and having breakfast early. These findings are consistently reported in the literature [30, 33-35].

This study was based on the experiences of a single center in Karachi with a cross-sectional study nature and limited sample size. Moreover, in this study, we did not include the impact of diabetes complications. A future multi-center study should be planned with a larger sample size to address gaps in this study and validate the findings of the current study.

CONCLUSION

This study analyzed that dyspeptic symptoms including indigestion, heartburn, and regurgitation were common in T2DM patients, and about half of these patients had dyspepsia which was common among patients with poor glycemic control and those with unhealthy lifestyles.

ETHICAL APPROVAL

Ethical approval was obtained from the Ethical Review Committee of Ziauddin University, Karachi (Reference Code: 6680223ARMED). All procedures performed in studies involving human participants were by the ethical standards of the institutional and/ or national research committee and with the Helsinki Declaration

CONSENT FOR PUBLICATION

Written informed consent was taken from the participants.

AVAILABILITY OF DATA

The data set may be acquired from the corresponding author upon a reasonable request.

FUNDING

Declared none.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORS' CONTRIBUTION

AR & FZ conceptualized the study. FM & UJ designed the study protocol. MP and FZ were involved in data cleaning, analysis, result writing, and interpretation. FM and UJ prepared the initial draft of the manuscript. AR provided constructive criticism and updated the original copy. The manuscript was reviewed and approved by all authors.

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