Original Research Article

Prevalence and determinants of gastroparesis symptoms among type 2 diabetic patients in Tabuk City

Abstract

Background: The gastrointestinal complications` development and progression in type 2 diabetic patients is one of the main contributors in the clinical course of the disease. Therefore, early recognition of gastroparesis is an important issue, despite this is not an easily task.

Objectives: to estimate the prevalence and identify determinants of gastroparesis symptoms among type 2 diabetic patients.

Patients and methods: A cross sectional study was conducted at Tabuk city, Saudi Arabia among all patients diagnosed with type II diabetes and attended the chronic illness clinics of King Khalid Armed Forces hospital throughout the period April-May, 2022. An interview questionnaire was utilized including 5 main parts: Demographic data of patients, medical history, weight and height measurements, the most recent glycated hemoglobin(HbA1c), and the Gastroparesis Cardinal Symptoms Index (GCSI) to estimate the prevalence of gastroparesis.

Results: The study included 348 type 2 diabetic patients. More than half of them (57.8%) were females. Their age ranged between 23 and 75 years with an

arithmetic mean±standard deviation of 54±11.3 years. The commonest reported gastroparesis symptoms were stomach fullness (45.1%), nausea (42%), loss of appetite (42%) and feeling excessively full after meals (41.1%). Overall, the prevalence of gastroparesis symptoms among type 2 diabetic patients was 11.8%. Multivariate logistic regression analysis revealed that females were at higher significant risk for developing gastroparesis symptoms compared to males (Adjusted odds ratio "AOR"==2.49, 95% confidence interval "CI": 1.18-5.27), p=0.016. Participants` glycated hemoglobin level was not significantly associated with gastroparesis symptoms after controlling for confounding effect.

Conclusion: Prevalence of gastroparesis symptoms among type 2 diabetic patients was not high. Symptoms were more likely to affect female than male patients. However, they were not independently associated with glycemic control or use of metformin.

Keywords: Diabetes type II, Gastroparesis, Prevalence, Determinants, Saudi Arabia

Introduction

The International Diabetes Federation (IDF) has described diabetes mellitus (DM) as one of the highest global health emergencies of the 21st century[1]. Currently, it has affected approximately 415 million adults aged between 20 and 79 worldwide[2].

The Kingdom of Saudi Arabia (KSA) has one of the highest prevalence rates of type 2 diabetes mellitus all over the world.[1]The Arabian Gulf wealth, including KSA has led to better living conditions resulting in an increase in urbanization, major changes in nutrition, decreased physical activity, and further dependency on migrant workers[3]. In KSA, the prevalence of DM in adults was 25%[4]. Recent research in Saudi Arabia suggested that more than 44% of individuals aged 55 or older had severe to uncontrolled diabetes with long-term complications[5].

The gastrointestinal complications` development and progression in type 2 diabetic patients is one of the main contributors in the clinical course of the disease. Therefore, early recognition of gastroparesis is an important issue, despite this is not an easily task. Moreover, the impairment of gastric motor-evacuation function in diabetic patients is associated with in ability to work as well as it impacts the quality of life in patients, increasing the risk of the progression of other microvascular and macrovascular diabetic complications [6-8].

It has been documented that the prevalence of gastroparesis symptoms was

higher in Type 1 diabetes (T1DM) than type 2 diabetes (T2DM)[9].However, literature suggested that upper GI symptoms are common in T2DM,but with inconsistent evidence[10].

Most internists and gastroenterologists still think that early diabetic gastroparesis `s manifestations are the symptoms of different gastrointestinal diseases and often diagnose the problem too late[11].

Up to our knowledge, there is no accurate estimation of the prevalence of gastroparesis symptoms in patients with type 2 diabetes mellitus in KSA, therefore, this study aimed to explore the magnitude and determinants of gastroparesis symptoms among type 2 diabetic patients.

Patients and methods

A cross sectional study design was conducted at Tabuk city, which is located 2200 feet above sea level and has moderate climate in comparison with other Saudi cities. It has a population of nearly 700,000 (2019 estimated census) [12]. All patients diagnosed with type II diabetes and attended the chronic illness clinics of King Khalid Armed Forces hospital in Tabuk throughout the period April-May, 2022 were eligible for inclusion in the study, provided that they aged 18 years or more and less than or equal 75 years. Patients with gestational diabetes, Type 1 diabetes, acute diabetic complications, severe cardiac, lung or mental problems,

gastrointestinal diseases and those with previous gastric surgery were excluded from the study.

The researcher fulfilled all the required official approvals, particularly the approval of the regional Research and Ethics committee (Institutional Review Board) and those of the hospital medical director.

An interview questionnaire was utilized in the present study. It includes 5 main parts: Demographic data of the patients (age, gender, marital status, and body mass index), medical history (duration of diabetes, presence of other comorbid chronic diseases, treatment of diabetes, and fasting blood glucose), which were collected from the patient`s medical record, weight and height measurements (weight and height were measured by the researcher and filled in the questionnaire). Weight was measured by electronic valid machine in kg. It was measured as the subject wears the ordinary clothes. Extra clothes were removed before measurements. Height was measured by valid machine in meter. Footwear was removed before measurement. Body mass index (BMI) assessed the body weight relative to height. It was calculated as weight in kilograms divided by height in meters squared, rounded to one decimal place. Obesity in adults was defined according to National Institute of Health categorization as BMI greater than or equal to 30 kg/m², while BMI from 25-29.9 kg/m² was considered overweight, BMI from 18.5- 24.9 was considered normal while BMI < 18.5 was considered

underweight [13]. In addition, the most recent glycated hemoglobin (HbA1c), taken within the last three months, were recorded from the patients` charts. The Gastroparesis Cardinal Symptoms Index (GCSI) to estimate the prevalence of gastroparesis among type 2 diabetic patients. The GCSI composed of three subscales of symptom, chosen to measure important symptoms related to gastroparesis, that is nausea/vomiting (nausea, retching, and vomiting), postprandial symptoms/early satiety (stomach fullness, inability to finish a normal-sized meal, feeling excessively full after meals, and loss of appetite, and bloating (bloating, and visibly larger stomach or belly after meals [14].The GCSI includes 9 questions and each question is scored according to symptoms` severity from 0 (no symptoms to 5 (Severe symptoms). Total scores ≥ 1.90 was selected as a cutoff to diagnose gastroparesis [15, 16]. Data were collected by the investigator and trained medical students.

The data were collected and verified by hand then coded before computerized data entry. The statistical Package for Social Sciences (SPSS) software version 26.0 was used for data entry and analysis. Descriptive statistics (e.g. number, percentage, mean, range, standard deviation) and analytic statistics using chi-square, Fischer exact and independent samples t-tests were applied. Multivariate logistic regression analysis was performed to control for the confounding effect and p-values ≤0.05 were considered as statistically significant.

Results

The study included 348 type 2 diabetic patients. More than half of them (57.8%) were females. Their age ranged between 23 and 75 years with an arithmetic mean±standard deviation of 54±11.3 years. Majority (80.2%) were married. Table 1

More than half (52%) of them were obese as illustrated from Figure 1. History of other chronic diseases was observed among 70.4% type 2 diabetic patients; particularly hypertension (50.6%) and dyslipidemia (47.1%). Figure 2

Duration of diabetes ranged between 6 and 10 years among 31.7% of patients whereas it exceeded 15 years among 22.1% of them. Fasting blood glucose was 126 mg/dL or more among 66.4% of patients while HbA1c% exceeded 7% in 57.4% of patients. Metformin was the commonest reported medication (90.4%). Table 2

Table 3 and Figure 3 show that the commonest reported gastroparesis symptoms were stomach fullness (45.1%), nausea (42%), loss of appetite (42%) and feeling excessively full after meals (41.1%).

Overall, the prevalence of gastroparesis symptoms among type 2 diabetic patients was 11.8% as seen in Figure 4. Female type 2 diabetic patients were more likely than males to develop gastroparesis symptoms (15.4% vs. 6.8%), 0.014. there was significant association between level of glycated hemoglobin and the

development of gastroparesis symptoms as 23.5% of patients whose HbA1c% ranged between >- and 10% compared to none of those whose HbA1c% was less than 5% had gastroparesis symptoms, p=0.049. However, 26.7% of patients whose HbA1c% ranged between 5 and 6% had gastroparesis symptoms. Other studied factors (age, marital status, body mass index, history of other chronic diseases, duration of diabetes, level of fasting blood glucose and Metformin treatment) were not significantly associated with gastroparesis symptoms. Table 4

Multivariate logistic regression analysis revealed that females were at higher significant risk for developing gastroparesis symptoms compared to males (Adjusted odds ratio "AOR"==2.49, 95% confidence interval "CI": 1.18-5.27), p=0.016. Participants` glycated hemoglobin level was not significantly associated with gastroparesis symptoms after controlling for confounding effect. Table 5

Discussion

As the research in the area of the magnitude and determinants of gastroparesis among type 2 diabetic patients is still relatively deficient, the present study was conducted in trying to fill this gap of knowledge. In the present study, the prevalence of gastroparesis symptoms among type 2 diabetic patients was 11.8%. This rate coincides with the lower limit of the figures reported from specialized centers as the rate ranged between 10% and 30% [17–19]. Also, it is very

close to the rate reported by Almogbel RA, et al in their study carried out in Qassim (10.8%)[20]. However, it is higher that the rates reported recently in Jeddah (7.9%)[21] and Riyadh (6.3%)[22]. In Ukraine, the prevalence of diabetic gastroparesis symptoms was very high compared to our figure (45.5%) [11]. In India (2016), prevalence of delayed gastric emptying was 28.6%[23]. Difference in the rates of gastroparesis symptoms among type 2 diabetic patients between studies could be explained by variations in the demographic characteritics of patients, level of glycemic control as well as the study settings.

In the present study, the commonest reported symptoms of gastroparesis were stomach fullness (45.1%), nausea (42%), loss of appetite (42%) and feeling excessively full after meals (41.1%). In a recent Saudi study carried out in Jeddah, the commonest reported symptoms were bloating (34.8%), and stomach fullness (26.6%) and the lowest common was vomiting (4.1%)[21]. In Qassim, bloating (63.9%), stomach fullness (55.1%) and early satiety (48.3%) were the commonest reported symptoms[20]. In Israel, The commonest reported symptoms were stomach or belly visibly larger after a meal (53%), bloating (48.8%), post-prandial fullness (44.6%) and nausea (24.8%) [24].

In the current study and in agreement with others [20, 22, 24, 25], female patients were more likely than males to develop gastroparesis symptoms, even after controlling for the confounding effect in multivariate logistic regression analysis.

This finding could be attributed to the influence of female sex hormones on the gastrointestinal motility [26-28], as females have a longer delay in gastric emptying time than males [29].

Metformin use has been observed as a risk factor for gastroparesis symptoms among type 2 diabetic patients in some studies, [22, 24, 30, 31] who attributed this association to the synergistic effect of metformin with gastroparesis to induce gastrointestinal symptoms, or the likelihood of the association of post-prandial distress syndrome with existence of gastrointestinal symptoms, rather than delay in gastric emptying. Alam et al (2010) attributed the association between metformin ause and gastroparesis symptoms to delayed gastric emptying induced by Dipeptidyl peptidase (DPP)-IV inhibition [32]. However, in these studies, symptoms of diarrhea, nausea, abdominal pain and heartburn, which are commonly reported with metformin use ere not frequently observed, this could eliminate the possibility of association of metformin use with gastroparesis symptoms. The current study revealed no association between metformin use and gastroparesis symptoms among type 2 diabetic patients.

The present study showed that in univariate analysis, there was an association between glycemic control and gastroparesis symptoms. However, after controlling for the confounding effect in multivariate analysis, this effect disappeared. On the

other hand, literature showed conflicting results regarding the association between glycemic control and gastroparesis symptoms [12, 22, 24, 25, 33, 34].

Some important limitations of the present study should be addressed. Being a single-center study could impact the ability to generalize the findings over other centers, despite the fact that this center is the main one caring for type 2 diabetic patients in Tabuk city. Using a cross-sectional design could affect the establishment of the causal relationship between dependent and independent variables. Absence of normal non-diabetic control to compare with diabetic subjects could be a limitation of the study. Finally, the possibility of false positive cases was not ruled out through performing gastroduodenoscopy in patients with positive gastroparesis symptoms, to exclude mechanical causes of symptoms.

Conclusion

Prevalence of gastroparesis symptoms among type 2 diabetic patients was not high and coincides with most of the rates reported from Saudi Arabia. Symptoms were more likely to affect female than male patients. However, they were not independently associated with glycemic control or use of metformin. Based on study results, we recommend screening for type 2 diabetic patients regarding gastroparesis symptoms and performing gastroduodenoscopy for positive cases to exclude mechanical reasons. Conduction further multicenteric longitudinal

prospective study including patients from different disciplines to achieve a clearer image of the situation.

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Table 1: Demographics of type 2 diabetic patients, King Khalid Armed Forces hospital, Tabuk, Saudi Arabia

	Frequency	**Percentage**
Gender		
Male	147	42.2
Female	201	57.8
Age in years		
Range	23-75	
Mean±SD	54.0±11.3	
Marital status		
Single	19	5.5
Married	279	80.2
Divorced	13	3.7
Widowed	37	10.6

SD: Standard deviation

Table 2: Type 2 diabetic related history among patients, King Khalid Armed Forces hospital, Tabuk, Saudi Arabia

	Frequency	Percentage
Duration of diabetes in years		
≤5	100	28.7
6-10	110	31.7
11-15	61	17.5
>15	77	22.1
Fasting blood glucose (n=342)		
≤99 mg/dL	34	9.9
100-125 mg/dL	81	23.7
≥126 mg/dL	227	66.4
Glycated hemoglobin %		
<5	11	3.8
5-6	30	10.5
>6-7	81	28.3
>7-8	77	26.8
>8-9	39	13.6
>9-10	17	5.9
>10	32	11.1
Treatment (n=332)*		
Metformin	300	90.4
Other oral hypoglycemic	208	62.7
Insulin	132	39.8

*Not mutually exclusive

Table 3: Prevalence and severity of gastroparesis symptoms among type 2 diabetic patients, King Khalid Armed Forces hospital, Tabuk, Saudi Arabia

Symptoms	None N (%)	Very mild N (%)	Mild N (%)	Moderate N (%)	Severe N %)	Very severe N (%)
Nausea	202 (58.0)	48 (13.8)	56 (16.1)	24 (6.9)	15 (4.3)	3 (0.9)
Retching	256 (73.6)	28 (8.0)	32 (9.2)	15 (4.3)	15 (4.3)	2 (0.6)
Vomiting	297 (85.3)	13 (3.7)	19 (5.5)	15 (4.3)	2 (0.6)	2 (0.6)
Stomach fullness	191 (54.9)	38 (10.9)	59 (17.0)	44 (12.6)	13 (3.7)	3 (0.9)
Not able to finish a meal	215 (61.8)	41 (11.8)	48 (13.8)	29 (8.3)	13 (3.7)	2 (0.6)
Feeling excessively full after meals	205 (58.9)	41 (11.8)	58 (16.7)	30 (8.6)	12 (3.4)	2 (0.6)
Loss of appetite	202 (58.0)	61 (17.6)	46 (13.2)	25 (7.2)	14 (4.0)	0 (0.0)
Bloating	212 (61.0)	30 (8.6)	51 (14.7)	37 (10.6)	12 (3.4)	6 (1.7)
Stomach or belly visibly larger	215 (61.8)	38 (10.9)	43 (12.4)	39 (11.2)	9 (2.6)	4 (1.1)

Table 4: Factors associated with gastroparesis symptoms among type 2 diabetic patients

	Gastroparesis		p-value
	No N=307 N (%)	Yes N=41 N (%)	
Gender			
Male (n=147)	137 (93.2)	10 (6.8)	
Female (n=201)	170 (84.6)	31 (15.4)	0.014*
Age in years			
Mean±SD	54.0±11.3	54.1±11.1	0.986˚
Marital status			
Single (n=19)	18 (94.7)	1 (5.3)	
Married (n=279)	248 (88.9)	31 (11.1)	
Divorced (n=13)	10 (76.9)	3 (23.1)	
Widowed (n=37)	31 (83.8)	6 (16.2)	0363
Body mass index			
Underweight (n=2)	2 (100)	0 (0.0)	
Normal (n=42)	34 (81.0)	8 (19.0)	
Overweight (n=123)	112 (91.1)	11 (8.9)	
Obesity (n=181)	159 (87.8)	22 (12.2)	0.337*
History of other chronic diseases			
No (n=103)	93 (90.3)	10 (9.7)	
Yes (n=245)	214 (87.3)	31 (12.7)	0.437*
Duration of diabetes in years			
≤5 (n=100)	90 (90.0)	10 (10.0)	
6-10 (n=110)	98 (89.1)	12 (10.9)	
11-15 (n=61)	53 (86.9)	8(13.1)	
>15 (n=77)	66 (85.7)	11 (14.3)	0.812*
Fasting blood glucose (n=342)			
≤99 mg/dL (n=34)	26 (76.5)	8 (23.5)	
100-125 mg/dL (n=81)	74 (91.4)	7 (8.6)	
≥126 mg/dL (n=227)	202 (89.0)	25 (11.0)	0.066*
Glycated hemoglobin %			
<5 (n=11)	11 (100)	0 (0.0)	
5-6 (n=30)	22 (73.3)	8 (26.7)	

>6-7 (n=81)	75 (92.6)	6 (7.4)	
>7-8 (n=77)	68 (88.3)	9 (11.7)	
>8-9 (n=39)	36 (92.3)	3 (7.7)	
>9-10 (n=17)	13 (76.5)	4 (23.5)	
>10 (n=32)	29 (90.6)	3 (9.4)	0.049*
Metformin treatmen (n=332)			
No (n=32)	28 (87.5)	4 (12.5)	
Yes (n=300)	265 (88.3)	35 (11.7)	0.535**

*Chi-square test **Fischer Exact test

˚ Independent samples t-test

Table 5: Predictors of gastroparesis among type 2 diabetic patients: Multivariate logistic regression analysis

	B	SE	AOR	95% CI	p-value
Gender					
Male[a]			1.0	---	
Female	0.916	0.381	2.49	1.18-5.27	0.016

[a]: Reference category B: Slope SE: standard error

AOR: Adjusted odds ratio CI: Confidence interval

Term of glycated hemoglobin was not significant and removed from the final regression model

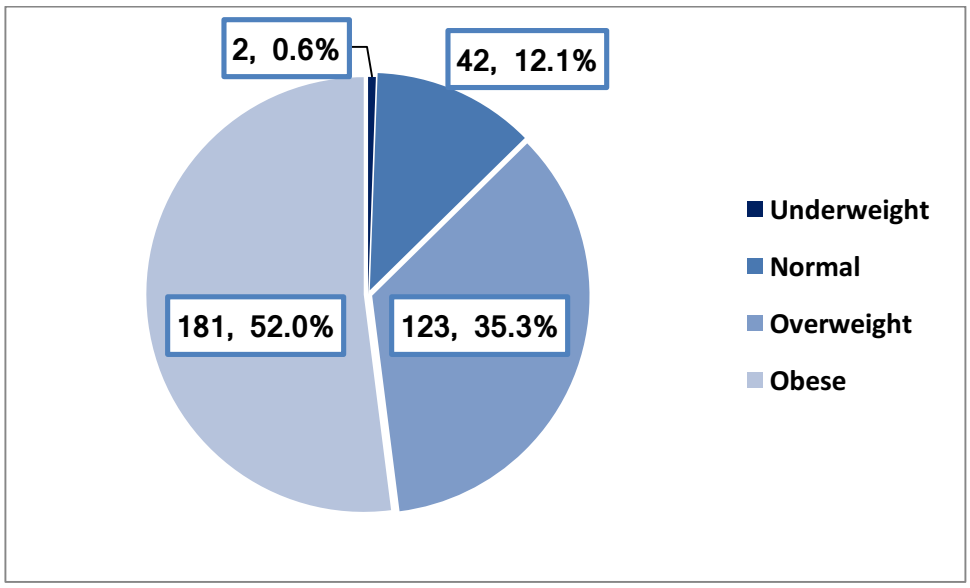

Figure 1: Body mass index of the type 2 diabetic patients, King Khalid Armed Forces hospital, Tabuk city

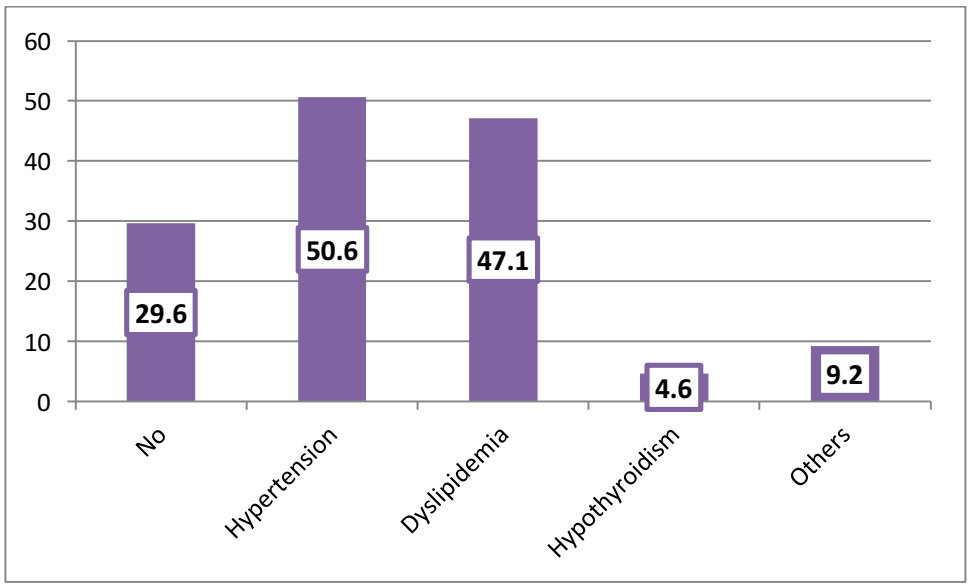

Figure 2: History of other chronic diseases among type 2 diabetic patients, King Khalid Armed Forces hospital, Tabuk city

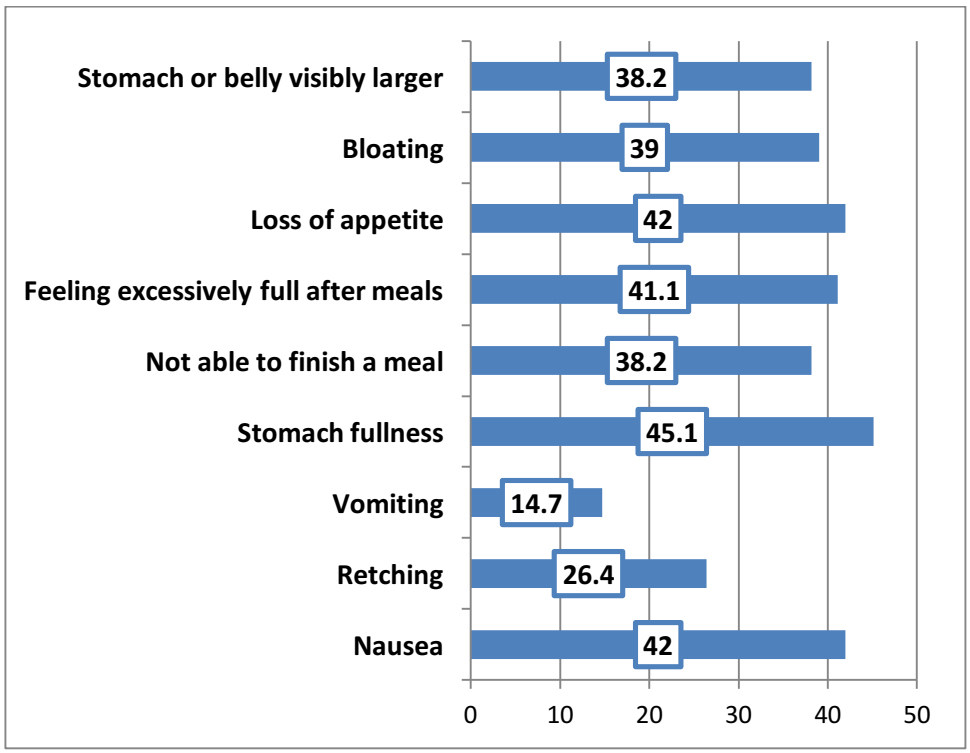

Figure 3: Frequency distribution of gastroparesis symptoms among type 2 diabetic patients, King Khalid Armed Forces hospital, Tabuk

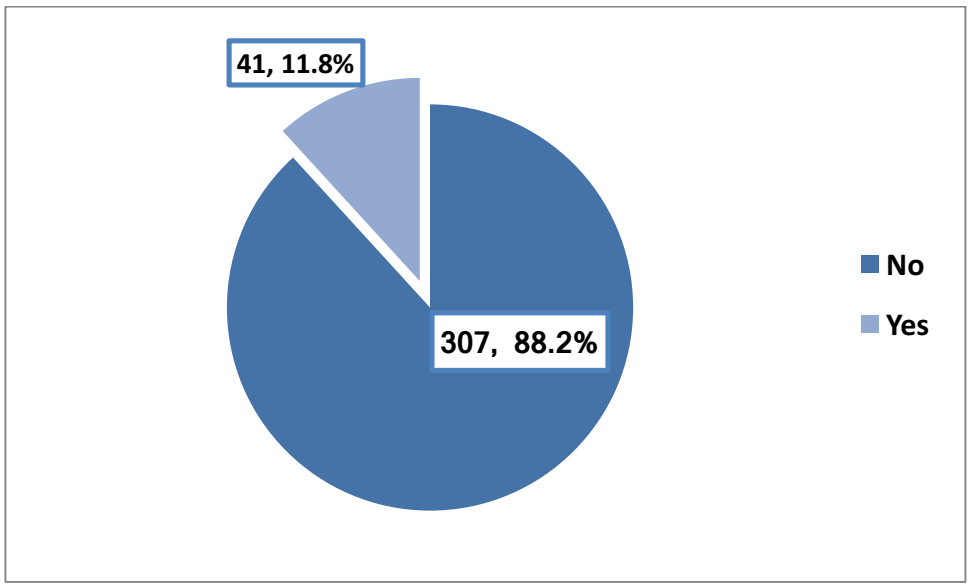

Figure 4: Prevalence of gastroparesis symptoms among type 2 diabetic patients, King Khalid Military hospital, Tabuk, Saudi Arabia