

# Diabetic Factors Associated with Gastrointestinal Symptoms in Adult Patients with Diabetes Mellitus in Dammam and Qatif, Eastern Province, Saudi Arabia

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**Abstract:** *Gastrointestinal autonomic neuropathy is reportedly common in diabetes mellitus. Increased the awareness among physicians toward gastrointestinal symptoms among diabetics is important for improving both diabetic care and quality of life of the affected patient. Objectives:* To estimate the prevalence of gastrointestinal symptoms, and to identify the most common gastrointestinal symptoms and its relationship with diabetic factors among adult diabetic patients in Eastern province, Saudi Arabia. *Methods:* This study was a cross-sectional study of diabetic patients who were being followed Primary health care centers and Hospitals, in Dammam and Qatif areas, Eastern province, Saudi Arabia. The diabetic patients were invited to participate in the questionnaire through interviewing them. Gastrointestinal symptoms were assessed using a validated structured questionnaire which was modified, it divided into two gastrointestinal categories (upper and lower gastrointestinal symptoms) and consisting of 22 individual symptoms. *Results:* Among the total of 356 diabetic patients (92.7% response rate), 310 (87%) had at least one gastrointestinal symptom, 298 (84%) had at least one upper gastrointestinal symptom, and 239 (67%) had at least one lower gastrointestinal symptom. Flatulence was the most common upper gastrointestinal symptoms; hard stool & constipation were the most common lower gastrointestinal symptoms. Female patients showed independently risk factor for prevalence of GI symptoms. Among the diabetic factors, the HbA1c >8%, and long duration of diabetes were significantly related to prevalence of GI symptoms. In addition, type 2 diabetes was a risk factor for lower GI symptoms. Prevalence of gastrointestinal symptoms was more common in patients with retinopathy and autonomic nervous dysfunction.

**Keywords:** diabetes mellitus, prevalence, digestive, diabetic complications

## I. Introduction

Autonomic innervation is essential for appropriate functioning of the gastrointestinal tract, including the synchronicity between the motility induced peristaltic movement and the sphincters as well as the secretory capacity of the GI glands. Therefore, several patients with diabetes mellitus (DM) of prolonged duration manifest chronic and recurrent clinical features related to the disordered motility of almost the whole GI tract including esophageal as well as epipharyngeal dysphagia, gastroparesis, constipation, diarrhea, and fecal incontinence (1)

Most studies suggest that there is an increased prevalence of gastrointestinal symptoms among diabetics and has substantial implications for glycemic control in both type 1 and type 2 DM (2), also gastrointestinal symptoms are associated with increased psychological stress, including anxiety and depression, as well as impaired quality of life (3). An ethnic and lifestyle predisposition may exist for experiencing GI symptoms, as shown in study done by Ko GT et al they found 70.5% Chinese patients with type 2 diabetes had GI symptoms, as opposed to 30.8% of controls (4), whereas Malekiet al(5) in Minnesota, United States found

that the prevalence of most GI symptoms seen in patients with diabetes is similar to the one in individuals without diabetes. And the data regarding the gastrointestinal symptoms among diabetic patient is deficient in Gulf area including Saudi Arabia which has ranked as the third most prevalent country with diabetes according to the International Diabetes Federation 2009 (6), that also has different lifestyles compared to other countries.

## II. Methodology

### A. Study setting and time

Ministry of health primary health care centers and hospitals in the Eastern province (Dammam and Qatif) Saudi Arabia, from October 2014 to April 2015.

### B. Study design

A cross sectional study through interview questionnaire with diabetic patients who being visited and followed diabetic clinics at primary health care centers and hospitals in Dammam and Qatif, in eastern province of Saudi Arabia. Interviews were done mainly by primary investigator (61.8%), in addition to trained doctor and nurses.

### C. Questionnaires

The questionnaire consists of five parts; the first part: the demographic portion of the questionnaire focused on age, sex, educational level, weight, and height of the patient “weight and height were taken from the file”.

The second part: the diabetic factors of the patient focused on type of diabetes, duration since diagnosis, type of therapy (oral, insulin, both, or only diet), and glycosylated hemoglobin during the last three months” HbA1c was taken from the file”.

The third part: microvascular complications include nephropathy, neuropathy, and retinopathy.

The fourth part: comorbidities (hypertension, dyslipidemia), and using of non-steroid anti-inflammatory drugs more than three days weekly.

The fifth part: the gastrointestinal symptoms which composed of twenty-two gastrointestinal symptoms. The first fifteen item are the symptoms of upper gastro-intestine, while the remaining seven items about lower gastro-intestine.

### D. Assessment of diabetic complications

Diabetic complications were adapted from validated questionnaire that has been design and used by researchers by Finckee et al(7), with adding of postural hypotension and sexual dysfunction “decrease libido and impaired erection of male patients”, complication were taken subjectively through the questions. Positive complication was recorded when there was yes answer to one of each complication questions.

### E. Assessment of gastrointestinal symptoms

The gastrointestinal questionnaire which was adapted from validated questionnaire that has been design and used by researchers by Oh JH et al (8), with modification by removing of non-functional symptoms that indicate organic gastrointestinal diseases e.g. melena, bloody stool, haematemesis and steatorrhea, also epigastric pain was omitted and suffice with abdominal pain.

### F. Sampling

A total of 384 participants are recruited to the study, which has distributed to the centers proportionally according to the number of patients recorded in each center per year.

### G. Validity and Reliability

A validated questionnaire was used and translated to Arabic. It approved by three consultant (Family, Endocrinologist, Gastroenterologist) and a clinical research expert.

Reliability of the two questionnaires (7, 8) were examined using Cronbach’s alpha statistic, which was 0.78, 0.75 respectively, that considered good reliability.

### H. Pilot study

A pilot study of 30 diabetic patients was done to assess the reliability of these questionnaires in our community. The internal consistency of the 30 responses was found to be good.

### I. Procedure of data collection

After granted the approval of the local research committee, the regional directorates of primary health care of (Dammam, Qatif), and regional directorates (Dammam Medical Complex, Qatif Central Hospital) have authenticate the start of our research. The questionnaires were distributed to diabetic patients to all centers according to number of Saudi diabetic patients they are following diabetic clinic in each center/year as shown in Table 1.

All of these centers under ministry of health, eastern province, Saudi Arabia. The information was obtaining by interviewing the patient through primary investigator or well-trained doctor and nurses (the interviewers were trained at meeting). The collection started October 2014 and ended on April 2015, total of 356 collected appropriately with response rate 92.7%, The primary investigator collected most of the data with frequency of 220 patients (61.8%). All the information taken from the patients directly except weight, height, and hemoglobin A1c were taken from the file.

**Table 1:** proportion of patients in health care centers

Health center	Number of patient/year	Percentage	number of patients
Dammam Medical Complex (DMC)	13'623	~43%	165
Qatif Primary Health Care (QPHC)	9'429	~30%	115
Qatif Central Hospital (QCH)	4'000	~14%	54
Dammam Primary Health Care (DPHC)	3'926	~13%	50
<b>Total</b>	<b>30'978</b>	<b>100%</b>	<b>384</b>

### J. Data processing

The Statistical Package of the Social and Sciences (SPSS) version 20.0 was used for the statistical analysis. All variables of the questionnaire were coded, checked for accuracy, and entered by the investigator before analysis was initiated.

Diabetic complications were taken subjectively through the questions. Positive complication was recorded when there was yes answer to one of each complication questions

The severity of Gastrointestinal symptom was rated on a 5-point Likert scale and coded as None, Mild, Moderate, Severe, and Very Severe. For the purposes of this analysis, a

positive GI symptom was recorded when the gastrointestinal symptom was reported to be mild or more.

According to severity prevalence of gastrointestinal symptom recorded when the troublesome symptom was reported to occur moderate, severe, or very severe.

Appropriate statistical analytical techniques were performed. Frequency distribution tables were constructed with the mean and standard deviation.

The chi-square ( $\chi^2$ ) and fisher exact tests were used to comparison categorical variables.  $P < 0.05$  was considered statistically significant. Multivariate analysis was performed using logistic regression for prevalence of GI symptoms and most common upper and lower GI symptoms

### K. Study strength and limitations

To our knowledge, this was the first study in Kingdom of Saudi Arabia, which focused on gastrointestinal autonomic dysfunction among diabetic patients. In addition, it is hoped that should help physicians to be aware about gastrointestinal manifestation among diabetics.

This study focused on gastrointestinal symptoms among diabetic patients.

to compare the prevalence, further study should be done on controlled patients (patients without diabetes). In addition, this study was cross-sectional, so it is limited in the evaluation of the time sequence and causal relationship observed.

### L. Ethical considerations

Approval was obtained from the local research committee of the Regional Directorate of primary care in the eastern province, Dammam Medical Complex, and Qatif Central hospital. Patients with diabetes were encouraged to participate in the study, but they were assured of their right to refuse the participation.

## III. Results

### A. Respondent's description

In total of 361 patients were interviewed, 5 were excluded because of incomplete data. A total of 356 patients were completed the interview questionnaire, yielding an overall response rate of 92.7% (sample size 384) as shown in figure 1

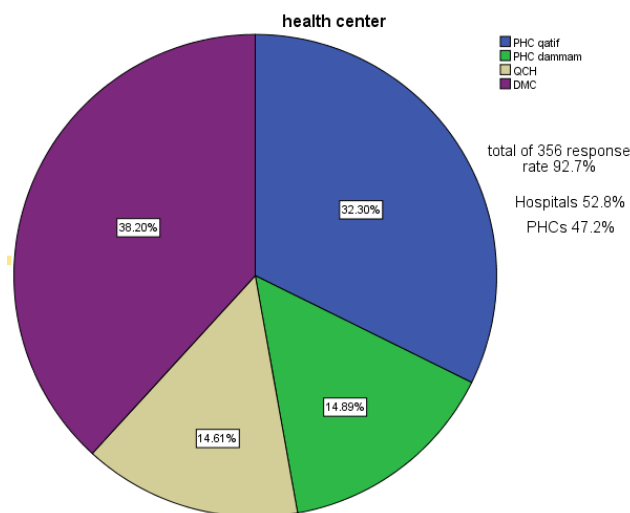


Figure 1: percentages of participants according to each center

QPHC; Qatif primary health, DPHC; Dammam primary health care, QCH; Qatif central hospital, DMC; Dammam medical complex.

### B. Diabetic factors

Eighty nine percent were type 2 diabetes and 11.0% were type 1 diabetes, and there was no sex variation in type of diabetes.

The mean duration of diabetes was  $10.4 \pm 8$  years (range, 0.1-40.0 years)

Hemoglobin A1c was done for 225 of patients within 3 months and the mean of HbA1c was  $8.3 \pm 2.1$  % (range, 4.3-15.7%)

### C. Diabetic complications

The frequency of nephropathy was 50(14.0%). there was more with type 1 diabetes compared to type 2 (30.8% vs 12.0%,  $P=0.005$ ).

The frequencies of retinopathy, and autonomic nervous dysfunction were 112(31.5%), 238(66.9%) respectively.

### D. Prevalence of gastrointestinal (GI) symptoms

Patients who had experienced at least one GI symptom for the last 4 weeks prior to interview accounted for 310 (87.1%) of the total.

Patients who had experienced at least one UGI symptom for the last 4 weeks prior to interview accounted for 298 (83.7%) of the total.

The most common UGI symptom was flatulence with frequency of 192 (53.9%), as shown in Table 2. The second common symptom was heartburn 161 (45.2%), the frequency of abdominal rumbling was 122 (34.3%), and postprandial fullness 121 (34.0%).

The prevalence of UGI symptoms according to the severity, it was found flatulence more common occurred in moderate to severe form than other UGI symptoms (27.8%), followed by heartburn (20.5%).

Patients who had experienced at least one LGI symptom for the last 4 weeks prior to interview accounted for 239 (67.1%) of the total.

The most common LGI symptom was hard stool with frequency of 146 (41.0%), as shown in Table 3. The second common symptom was constipation 135 (37.9%), the frequency of alternating diarrhea and constipation was 104 (34.3%), incomplete defecation 88 (24.7%), stool urgency 85 (23.9%), diarrhea 71 (19.9%), and pain during defecation 66 (18.5%).

The prevalence of LGI symptoms according to the severity, it was found hard stool more common occurred in moderate to severe form than other LGI symptoms (24.2%), followed by constipation (23.0%)

### E. The relationship of GI symptoms prevalence to demographic data

There was significant variation among health care centers between hospitals and primary health care centers with prevalence of GI symptoms (93.1%, 80.4% respectively,  $P < 0.001$ ).

Among them, 151(84.8%) men and 159(89.3%) women had GI symptoms, with no significant difference ( $P = 0.26$ ), the prevalence of GI symptoms was not associated with difference of weight, normal, overweight or obese (84.4%, 86.4%, and 88.0%) respectively ( $P = 0.76$ ).

The GI symptoms trend to be more with older and middle age group (89.7%, 86.4%, respectively) compared to younger patients (78.7%) ( $P = 0.19$ ).

After logistic regression analysis there was higher prevalence of gastrointestinal (GI) symptoms among female patients (O.R= 2.83, 95% CI= 1.15-6.98).

The female patients trend to had higher prevalence of most UGI symptoms than male with an insignificant value ( 87.1% vs 80.3%,  $P = 0.11$  ), but there were significantly associated with abdominal pain in common period and postprandial pain.

After logistic regression, patients with heartburn trend to be more with female patients (O.R.=1.91, 95% CI=1.08-3.40). There were no significant variation among the patients associated with UGI symptoms and difference of age group, except empty feeling, nausea, and loss of appetite were trend to be higher among young patients rather than middle and older group ( $P = 0.017$ ,  $P = 0.011$ , and  $P = 0.018$  respectively).

Although no significant association between UGI symptoms and body mass index, rumbling was significantly associated obese, and overweight patients rather than normal weight ( $P = 0.011$ ).

The prevalence of LGI composed of 120 (67.4%) male patients, and 119 (66.9%) female patients and there were no significant variation among the patients associated with LGI symptoms and difference of age group, except constipation, and hard stool were trend to be higher among older patients rather than middle and young age groups ( $P = 0.001$ , and  $P = 0.009$ ) respectively.

Although no significant association between LGI symptoms and body mass index, alternating diarrhea & constipation was significantly associated with obese patients rather than overweight or normal weight ( $P = 0.008$ ).

**Table 2:** the prevalence of UGI symptoms

UGI symptoms	Number/356	Percentage
Abdominal pain in common	109	30.6%
during fasting	68	19.1%
postprandial	69	19.4%
Heartburn	161	45.2%
Regurgitation	81	22.8%
Empty feeling	89	25.0%
Abdominal rumbling	122	34.3%
Nausea	80	22.5%
Vomiting	36	10.1%
Loss of appetite	85	23.9%
Postprandial fullness	121	34.0%
Belching	92	25.8%
Flatulence	192	53.9%
Dysphagia	55	15.4%
Solid	27	7.6%
Liquid		

**Table 3:** the prevalence of LGI symptoms

LGI symptom	Number/356	Percentage
Hard stool	146	41.0%
Diarrhea	71	19.9%
Constipation	135	37.9%
Alternating diarrhea & constipation	104	29.2%
Pain during defecation	66	18.5%
Stool urgency	85	23.9%
Incomplete defecation	88	24.7%

### F. The relationship of GI symptoms prevalence to diabetic factors:

There were no significant variation between the types of diabetes, type one and type two with the prevalence of GI symptoms (87.2%, 87.1%) respectively, while isolated LGI symptoms significantly associated with type 2 diabetes compared with type 1 (69.1% vs 51.3%,  $P = 0.031$ ).

We found no significant difference in prevalence of GI symptoms with different types of diabetic treatment ( $P = 0.27$ ) which include oral therapy, insulin, combined therapy, or diet only.

Although there were not significant association between uncontrolled HbA1c (>7%) and prevalence of GI symptoms, it was found significant relation between HbA1c > 8%



compared with HbA1c  $\leq 8\%$  and prevalence of GI symptoms (92.1% vs 83.1%,  $P=0.048$ ).

**Table 4:** relationship of GI symptoms prevalence to diabetic factors

	GI symptoms	UGI symptoms	LGI symptoms
<b>Types of DM</b>			
Type 1	34(87.2%)	34(87.2%)	20(51.3%)
Type 2	276(87.1%)	264(83.3%)	219(69.1%)
P value	1.00	0.65	0.031
<b>Duration of DM</b>			
$\leq 5$ years	109(82.6%)	103(78.0%)	85(64.4%)
6-10 years	73(84.9%)	72(83.7%)	53(61.6%)
$>10$ years	126(93.3%)	122(90.4%)	99(73.3%)
P value	0.023	0.022	0.13
<b>Treatment</b>			
Oral therapy only	192(84.6%)	183(80.6%)	148(65.2%)
Insulin only	62(91.2%)	60(88.2%)	44(64.7%)
Oral & insulin	50(90.9%)	49(89.1%)	43(78.2%)
Diet only	6(100%)	6(100%)	4(66.7%)
P value	0.27	0.17	0.30
<b>Hemoglobin A1c</b>			
$\leq 8\%$	103(83.1%)	97(78.2%)	68(54.8%)
$>8\%$	93(92.1%)	91(90.1%)	79(78.2%)
P value	0.048	0.019	$<0.001$

Most of UGI symptoms were not significantly related to types of diabetes except of pre-prandial pain and loss of appetite which trend to be more with type 1 than type 2 (35.9% vs 17.0%,  $P=0.007$ ) ( 43.6% vs 21.5,  $P=0.005$ ) respectively.

Although there were not significant association between uncontrolled HbA1c ( $>7\%$ ) and prevalence of UGI symptoms (83.7%), it was found significant relation between HbA1c  $> 8\%$  compared with HbA1c  $\leq 8\%$  and prevalence of UGI symptoms (90.1% vs 78.2,  $P=0.048$ ).

Empty feeling and vomiting were significantly associated with uncontrolled HbA1c ( $>7\%$ ) compared to controlled HbA1c ( $\leq 7\%$ ) with ( $P=0.004$ ,  $P=0.046$ ) respectively.

Although the prevalence of UGI symptoms were not significantly associated with different type of diabetic treatment, there were found significant relation between some of UGI symptoms include empty feeling ( $P=0.009$ ), postprandial fullness ( $P=0.020$ ), food dysphagia ( $P=0.001$ ), and liquid dysphagia ( $P=0.002$ ), which they were trend to be more with combined type of treatment "oral and insulin" rather than each one alone.

Most of LGI symptoms were not significantly related to duration of diabetes except of hard stool, constipation, and alternating diarrhea & constipation symptom which trend to be more with long duration of diabetes  $>10$  years (501.9%,  $P=0.004$ ), (48.9%,  $P=0.004$ ), and (37.8%,  $P=0.025$ ) respectively.

Although there were not significant association between uncontrolled HbA1c ( $>7\%$ ) and prevalence of LGI symptoms (67.1%), it was found significant relation between

HbA1c  $> 8\%$  compared with HbA1c  $\leq 8\%$  and prevalence of LGI symptoms (78.2% vs 54.8%,  $P=<0.001$ ).

Constipation was significantly associated with uncontrolled HbA1c ( $>7\%$ ) compared to controlled HbA1c ( $\leq 7\%$ ) with (42.6% vs 27.3%,  $P=0.029$ ).

Although the prevalence of LGI symptoms were not significantly associated with different type of diabetic treatment, there were significant relation between some of LGI symptoms including diarrhea ( $P=0.007$ ), stool urgency ( $P=0.002$ ), and incomplete defecation ( $P=0.031$ ), which they were trend to be more with combined type of treatment "oral and insulin" rather than one alone.

### G. The relationship of GI symptoms to diabetic complications:

There was no significant relation between nephropathy and prevalence of all GI symptoms ( $P=0.65$ ), as shown in Table 5 The presence of retinopathy significantly associated with prevalence of GI symptoms (93.8% vs 84.0%,  $P=0.011$ ), and higher prevalence associated with presence of autonomic nervous dysfunction (92.0% vs 77.1%,  $P=<0.001$ ), also it was found associated with symptoms of autonomic nervous dysfunction including leg numbness, postural hypotension and sexual dysfunction with  $P=0.001$ ,  $P=0.08$ ,  $P=0.001$  respectively.

All UGI symptoms trend to be more with patients with presence of nephropathy, and significant value associated with abdominal pain in common period and nausea ( $P=0.013$ , and  $P=0.003$  respectively).

All UGI symptoms were highly significant related to patients with postural hypotension. Empty feeling and rumbling were significantly related to patients with sexual dysfunction ( $P=0.013$ , and  $P=0.037$  respectively).

Although there were no significant relation between nephropathy& retinopathy and prevalence of LGI symptoms, as shown in Table 5, Alternating diarrhea & constipation symptom, and stool urgency significantly associated to patients with nephropathy ( $P=0.018$ ,  $P=0.047$ ) respectively, in addition, hard stool and constipation were highly significant to patients with retinopathy ( $P=<0.001$ ).

The presence of autonomic nervous dysfunction significantly associated with prevalence of LGI symptoms (76.5% vs 48.3%,  $P=<0.001$ ), also it was found associated with symptoms of autonomic nervous dysfunction including leg numbness, postural hypotension and sexual dysfunction with  $P=<0.001$ ,  $P=0.012$ ,  $P=<0.001$  respectively.

All LGI symptoms were highly significantly ( $P=<0.05$ ) related to patients with leg numbness except stool urgency which was trend to be more with patients with leg numbness with an insignificant value ( $P=0.13$ ).

All LGI symptoms significantly related to patients with postural hypotension ( $P=<0.05$ ). And Hard stool and constipation were significantly related to patients with sexual dysfunction ( $P=<0.001$ ).

**Table 5:** the relationship of GI symptoms to diabetic complication

	GI symptoms	UGI symptoms	LGI symptoms
<b>Nephropathy</b>			
Yes	45(90.0%)	45(90.0%)	35(70.0%)
No	265(86.6%)	253(82.7%)	204(66.7%)
P value	0.65	0.22	0.74
<b>Retinopathy</b>			
Yes	105(93.8%)	101(90.2%)	81(72.3%)
No	205(84.0%)	197(80.7%)	158(64.8%)
P value	0.011	0.030	0.18
<b>Autonomic neuropathy</b>			
Yes	219(92.0%)	213(89.5%)	182(76.5%)
No	91(77.1%)	85(72.0%)	57(48.3%)
P value	<0.001	<0.001	<0.001
<b>Leg numbness</b>			
Yes	152(93.3%)	148(90.8%)	131(80.4%)
No	158(81.9%)	150(77.7%)	108(56.0%)
P value	0.001	0.001	<0.001
<b>Postural Hypotension</b>			
Yes	144(90.6%)	143(89.9%)	118(74.2%)
No	166(84.3%)	155(78.7%)	121(61.4%)
P value	0.08	0.006	0.012
<b>Sexual Dysfunction</b>			
Yes	59(98.3%)	56(93.3%)	53(88.3%)
No	245(84.5%)	236(81.4%)	180(62.1%)
P value	0.001	0.022	<0.001

H. The relationship of GI symptoms prevalence to co-morbidities and using of non-steroidal anti-inflammatory drugs "NSAID":

There were no relations between prevalence of GI symptoms and hypertension, dyslipidemia, or using of NSAID.

Using of non-steroidal anti-inflammatory drugs associated with prevalence of UGI symptoms (P=0.013).

Regurgitation, belching, and food dysphagia occurred more commonly in patients with hypertension (P=0.042, P=0.020, P=0.026) respectively, while postprandial pain, nausea, vomiting, belching, and flatulence were significantly associated with using of NSAID (P=0.013, P=0.002, P=0.002, P=0.037, and P=0.049 respectively).

Among LGI symptoms, Hard stool, constipation, alternating diarrhea & constipation symptom occurred more commonly in patients with hypertension (P=0.002, P=0.001, P=0.019) respectively, while stool urgency was significantly associated with patients with dyslipidemia.

Using of NSAID showed significantly associated with constipation and pain during defecation with P=0.007, P=0.041 respectively.

#### IV. Discussion

This study investigated the prevalence of gastrointestinal (GI) symptoms in patients with diabetes for a short period of time at hospitals and primary health care centers in Dammam and Qatif area, eastern province, Saudi Arabia. In total, 356

patients were included and composed of 178 (50%) men and 178 (50%) women. Their mean age were  $52 \pm 14$  years, and the age distribution was similar to that of the national survey on prevalence of diabetes, which was done by Khalid A. Alqurashi, et al on 2009(9).

In this study, the patients' body mass index (BMI) were  $31.1 \pm 7.7$  (kg/m<sup>2</sup>), and around 75% of patients were obese or over weight (52.4%, 25.1%) respectively, and they did not differ from those of patients with diabetes in national survey, with a total of 6024 patients, the prevalence of (BMI) of  $\geq 25$  (kg/m<sup>2</sup>) was 72.5% , also total number of type 2 diabetes was 317 (89%) and type 1 diabetes 39 (11%), which corresponding to national survey, that found type 2 diabetes constitutes 90% to 95% of diabetic cases(9).

In this study, the prevalence of nephropathy, retinopathy, autonomic neuropathy among patients were taken subjectively which revealed 14%, 31.5%, 66.9% respectively, and the national study done by El-Asraret al showed the incidence of retinopathy among diabetic patients which was 31.3%(10), another study done in King Abdulaziz University hospital in Jeddah, Saudi Arabia, they studied neuropathy among diabetic patients (11), they found a symptomatic neuropathy was 56% of the patients with diabetes not including postural hypotension and sexual dysfunction which were included in this study.

Although this study was not a sample survey representing all patients with diabetes in Saudi Arabia, it's results are considered meaningful because we investigated patients visiting the primary care centers or secondary hospitals in two areas, sharing the same characteristic of diabetic patients in the kingdom of Saudi Arabia.

When the methods of this study were compared with those done in other countries, most of them they were compared the prevalence of GI symptoms in diabetic patients with those without diabetes which was not done in this study.

When the results of this study were compared with those were done in other countries, wide discrepancy related to prevalence of GI symptoms in diabetes could be due to different method, ethnicity, and lifestyle. A study done in Finland showed low prevalence of gastrointestinal symptoms in patients with diabetes mellitus (12). A Korean study of (13) 608 diabetic patients showed the prevalence of chronic GI symptoms accounted for 69.9% of the total, another study done by Feldman et al(14) in United States, the authors found that the prevalence of GI symptoms was 76% among type 2 diabetes mellitus. Also in United States Ricci et al(15) in North Carolina, United States, the authors found the prevalence of UGI symptoms among diabetic patients were 50%. A Chinese study done by KO GT et al in Honk Kong found that the prevalence of GI symptoms among type 2 diabetes was 70.5%, UGI symptoms was 44.3%, and LGI symptoms was 54.4% (4), while in another Korean study showed 43% of 190 patients with diabetes mellitus type 2 had UGI symptoms (16). Another study done in Tabriz, Iran showed gastrointestinal symptoms and signs were reported in 92% of patients with diabetes mellitus (17). In this study, the prevalence of GI symptoms was 87.1%, UGI symptoms was 83.7%, and LGI was 67.1% which consider high prevalence

could be due to methods of the study, which include diabetic patients experienced at least one GI symptom for the last 1 month from mild to severe form, or due to difference of lifestyle of Saudi population.

Also in this study, female had independently had more GI symptoms, and this result was the same as that in studies reporting that the prevalence rated of GI symptoms were higher in female than males (13, 15), the results that female had more GI symptoms could be explained by the fact that females show higher rate of GI symptoms in the general population (18). In this study, Although UGI and LGI symptoms were trend to be more with obese patients with no significant value ( $P>0.05$ ), it showed an UGI symptoms significantly associated with BMI in other studies (19, 20).

To evaluate the effects of diabetes morbidity duration on the prevalence of GI symptoms, patients were divided into greater than 10 year, 6 to 10 year, equal or less than 5 year, and prevalence of GI symptoms, specifically UGI symptoms were higher in greater than 10 year group, and these results compatible with Asian studies done in Korea and Taiwan (4, 13, 16), while Bytzer et al(21) in Australia found that the prevalence of GI symptoms not significantly associated with long duration of diabetes, and another study which was done in Iran by khoshbaten et al(17) found no significant relation to duration of diabetes although the prevalence of GI symptoms more common occurred with long duration of diabetes, also Ricci et al(15) in United States showed that the prevalence of UGI symptoms not significantly related to diabetes onset.

Multiple studies showed relation between poor glycemic control ( $HbA1c>7\%$ ) and experiencing of GI symptoms (21, 22). In contrast, Tsenget al in Taiwan found higher level of HbA1c were associated with lower prevalence of GI symptoms(23). In this study, although there were no significant relation between uncontrolled HbA1c ( $>7\%$ ) and prevalence of GI symptoms, we found highly significant relation between high HbA1c ( $>8\%$ ) and prevalence of upper and lower GI symptoms. And these results were similar to number of studies (13, 16).

Although the different type of diabetes were not related to prevalence of GI symptoms, we found prevalence of LGI symptoms significantly associated with type 2 diabetes compared to type 1. In contrast, Talley et al, in Australia found that LGI symptoms not generally related to type of diabetes (19).

The prevalence rates of diabetes complications were very different according definition among studies. According to the results of this study, the complications were taken subjectively through interviewing the patients. Among the complications, we found highly association between autonomic dysfunction and prevalence of upper and lower GI symptoms that could be due to that GI complication part of autonomic complications.

many studies have shown that diabetic neuropathy increase prevalence of GI symptoms (22, 24, 25), in contrast, one study reported no correlation between diabetic neuropathy and the occurrence of GI symptoms and neuropathy being

more related to mental factors (26). Among the patients with retinopathy, Abidet al(22) found that presence of diabetic retinopathy was significantly related to GI symptoms, which was similar to this study. In contrast to Talley et al(19) found that diabetic retinopathy not significantly related to the prevalence of GI symptoms. In the same study, they found also that diabetic nephropathy was not related to prevalence of GI symptoms, which was similar to this study.

Among the upper GI symptoms, the most common symptom was flatulence with prevalence of 53.9%. As recent study done by Hasler et al in United States, showed that the prevalence of abdominal flatulence (bloating) was 41-76% of the patients, while other studies done in U.S. (15) and Hong Kong (4) were reported flatulence of 21.0% and 21.5% respectively.

The rate of heartburn experienced mild to severe per month in this study was 45.2%. and the rate of heartburn in this study was considerably higher than that of Western patients with diabetes (25-31.7%) (12, 24), and much higher than that Asian patients (7.1-8.1%) (4, 13).

The nausea and vomiting prevalence rate were 22.5% and 10.1% respectively. Other studies have reported that prevalence rate of nausea and vomiting were 16.8-21% and 5.6-16.0% respectively, which were similar to this study. In contrast to Korean study showed that prevalence of nausea and vomiting were 6.7% and 1.6% respectively (13), and mentioned that the rational of variation between prevalence of nausea and vomiting Asian studies and Western caused by using of prokinetics drugs which had been used more with Asian patients rather than Western patients (13, 15), and this issue was not mentioned in this study.

Among lower GI symptoms, the prevalence of hard stool and constipation were 41.0% and 37.9% respectively. The prevalence rate for the U.S. sample survey was 10.1% (27), the European surveys were 13.1-22.1% (22.1% in a German survey (28), and 13.1% in a Swedish Survey (29)), and the Asian surveys were 15.0-27.5% ( 15.0% in Korean survey (13), and 27.5% in Hong Kong (4)). The higher prevalence of constipation in this study could be due to in addition to difference of methods and lifestyle, the using of laxative drugs that not studied in this study.

## V. Conclusion

This study explored the prevalence of gastrointestinal symptoms among patients with diabetes and its association with diabetic factors in hospitals and PHC centers, Eastern province, Saudi Arabia.

Overall, 87% of Saudi diabetic patients experience at least one GI symptom, 83% of them experience at least one LGI symptoms, and 67% of them experience at least one LGI symptoms. Around most of them following the hospitals. It revealed significant relation with female patients, the prevalence of GI symptoms was more common in patients who had long duration of diabetes, poor glycemic control ( $HbA1c>8\%$ ), retinopathy and autonomic neuropathy. In addition, type 2 diabetes significantly associated with experiencing of LGI symptoms.



The most common UGI symptom was flatulence, while hard stool and constipation were the most common among LGI symptoms.

## VI. Recommendations

Based on the finding of this study, the following could be made to administration of diabetic clinic in Ministry of Health;

- Implementing Screening tool for GI symptoms among diabetic patients
- Increase the awareness of physicians toward GI autonomic neuropathy among patients with diabetes mellitus, and appropriate treatment
- Providing a medication for most common GI symptoms among Saudi diabetic patients
- Further research on controlled group to compare the prevalence of GI symptoms between diabetic and non-diabetics

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