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Gastrointestinal manifestations in type 2 diabetes mellitus

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Abstract
Background: Gastrointestinal (GI) motor dysfunction in patients with diabetes affects esophagus, stomach and lower GI tract. Many diabetes patients have upper and lower GI symptoms. Reports have shown that GI tract related complications are now recognized as important cause of morbidity in patients with type 2 diabetes (T2DM).
Aims and objectives: To study GI manifestations with duration and severity of diabetes in T2DM patients.
Materials and Methods: Hundred T2DM patients were studied between November 2013 to August 2015 in the Department of Medicine, GR Medical College and JA Group of Hospitals, Gwalior, Madhya Pradesh. Details history, clinical profile and laboratory measurements, ECG, USG abdomen was performed in all the patients. Endoscopy was performed in patients who gave the written consent. Patients were asked about symptoms related to GI manifestation and diabetes, family and past history of disease.
Results: Mean age, height, weight and BMI were 54.24±12.64 years, 159.57±8.59 cm, 60.87±11.53 kg and 23.79±3.50 kg/m^2 respectively. Male (64%) outnumbered the female (36%). Most common HbA1c group was 7-9% (41%) and maximum have diabetes duration of <5 years. Maximum patients presented with GI symptoms (78%). Most common GI symptoms was constipation (22%) followed by acid peptic disease (15%). Fatty liver (21%) followed by hepatomegaly (20%) was the most common USG finding. In GI endoscopy, gastritis (13.63%) was the most common abnormality followed by esophagitis (9.09%).
Conclusion: Significant number of GI manifestations is observed in T2DM patients especially with increasing duration of diabetes and HbA1c.

Keywords: GI manifestation, diabetes mellitus, endoscopy, constipation, USG abdomen

Introduction
Gastrointestinal (GI) disorders are common in patients with type 2 diabetes mellitus (T2DM). Reports have shown that as many as 75% of the diabetes patients visiting to the clinic are presented with any kind of GI symptoms [1, 2].
Most of the patients go undiagnosed and undertreated. Patients with microvascular complications such as retinopathy, nephropathy, or neuropathy should be presumed to have one or more GI abnormalities until proven otherwise. In addition to pharmacologic therapy, glycemic control and dietary manipulation play an important role in managing GI disorders in people with T2DM [3].
Dysfunction of GI tract in patients with diabetes results because of diabetic autonomic neuropathy, impaired sensory innervations and because of a direct effect of chronic hyperglycemia [4].
Long standing diabetes mellitus, disturbed motility and delayed gastric emptying, this can be the result of diabetic neuropathy [5]. Because of that patients with diabetes endure abdominal distension, esophageal dysmotility and gastroparesis [6]. Hence, present study was performed to evaluate GI manifestation of patients with diabetes.

Materials and methods
A hospital based prospective study was done on 100 T2DM patients of either sex having age ≥30 years admitted in the Department of Medicine, GR Medical College and JA Group of Hospitals, Gwalior, Madhya Pradesh from November 2013 to August 2015.
Institutional Ethics Committee approval and a written informed consent were obtained from each patient before starting the study.
Patients included were diagnosed using American Diabetes Association (ADA) 2014 guidelines; fasting plasma glucose (FPG) ≥126 md/dL (fasting is defined as no calorie intake for at-least 8 hours) or post prandial blood glucose (PPBG) (2 hours after meals) ≥200 mg/dL or random plasma glucose (RPG) ≥200 mg/dL or HbA1c ≥6.5%, previously diagnosed and taking treatment for type 2 diabetes.
All T2DM patients of either sex who were of ≥30 years of age were included whereas patients with T1DM, HIV, HBsAg positive patients, absolute contraindications to endoscopy

include shock, acute MI, peritonitis, acute perforation, fulminant colitis, Relative contraindications include poor patients cooperation, coma (unless the patients is intubated) and acute arrhythmias or recent myocardial ischemia and pregnant women with T2DM were excluded from the present study.

A thorough patients history, clinical and appropriate laboratory data, ECG, USG abdomen and endoscopic findings were recorded for each patient. Patient's information regarding age, sex, residence, socioeconomic status were also collected. Patients were asked about symptoms related to GI manifestation and diabetes, family and past history of disease.

GI symptoms were defined as follows: dysphagia; medical term for the symptom of difficulty in swallowing, heart burn; water brash regurgitated into the chest causing a feeling of tightness or a burning or painful sensation one or moretimes weekly for the last year, Reflux; water brashor bitter water regurgitated into the mouth one or more times per week, epigastric pain; intermittent pain or burning localized to the epigastrium of at least moderate severity, at least once per week which is not relived by defecation or passing flatus, nausea and vomiting; nausea and vomiting one or more times a week, early satiety; stomach frequently feels full just after starting a meal, considering the amount of food consumed for at least 3 months, abdominal distension; the abdomen was tight for at least 3 months. Constipation was defined through the Rome III criteria, which are; (1) fewer than three bowel movements a week, (2) effort to evacuate,(3) presence of hard or lumpy stools, (4) sensation of incomplete evacuation, (5) sensation of obstruction or interruption of evacuation, and (6) manual maneuvers to facilitate defecation. Diarrhea: passage of abnormally liquid or unformed stool at an increased frequency more than 3 bowel movements per day. For adults on a typical western diet, stool weight>200 g/d can generally be considered as diarrhea.

Each patient subjected for USG abdomen to assess the sonological abnormality. Patients who were HBsAg and HIV negative and hemodynamically stable were subjected for Upper GI endoscopy with consent.

Data were analyzed using IBM SPSS Ver. 20 software. Descriptive statistical analysis has been carried out in the present study with student T test. Results on continuous measurements are presented on mean± SD. Significance is assessed at 5% level. P<0.05 was considered to be significant.

Results

Mean age (year), height (cm), weight (kg) and BMI (kg/m2) was 54.24±12.64, 159.57±8.59, 60.87±11.53 and 23.79±3.50 respectively. Most of the patients belong to age group of 50-59 years (32%) followed by 40-49 years (31%). Maximum patents were male (64%) followed by female (36%).

In present study most of the patients have HbA1c between 7-9% (41%) followed by 32% patients with HbA1c of more than 9%.Mean duration of diabetes was 7.55±5.75 years. Most of the patients belong to diabetes duration of <5 years (42%) followed by 33% patients in diabetes duration of >10 years.

Out of 100 patients, maximum presented with GI symptoms (78%).

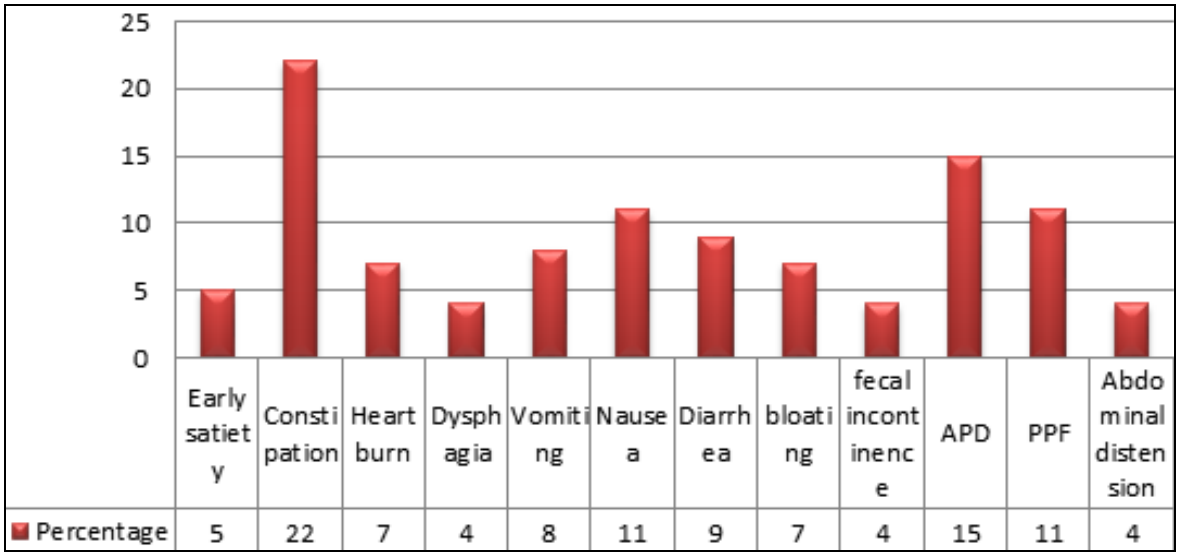

Fig 1: Distribution of patients according to presenting Gl symptoms

Mean TC, TG, LDL and HDL was 176.86±41.03 mg/dL, 148.85±64.97 mg/dL, 110.77±27.91 md/dL and 37.81±6.58 mg/dL respectively.

USG findings revealed that fatty liver was present in most of the patients (21%) followed by hepatomegaly in 20% patients, ascitis in 10% patients and cholelithiasis in 8% patients. GI endoscopy was done in 44% of the patients (gave consent for endoscopy) and findings revealed that 22 (50%) were within normal limit. Among abnormality gastritis was the most common [6 (13.63%)] followed by esophagitis in 4 (9.09%) and GERD in 3 (6.81%) patients.

Table 1: Distribution of GI manifestations according to duration of diabetes, HbA1c and BMI

Investigation	Parameters	DOD			HbA1c			BMI		
		<10 (n=63)	≥10 (n=37)	P	<7 (n=27)	≥7 (n=73)	p	<25 (n=67)	≥25 (n=37)	P
GI Symptoms (n=100)	Dysphasia	2 (3.17)	2 (5.40)	NS	3 11.11)	1 (1.36)	0.001	2 (2.98)	2 (5.40)	NS
	Heartburn	5 (7.93)	2 (5.40)	NS	2 (7.40)	5 (6.84)	NS	5 (7.46)	2 (5.40)	NS
	Early satiety	3 (4.76)	2 (5.40)	NS	0 (0)	5 (6.84)	0.009	4 (5.97)	1 (2.70)	0.001
	APD	9 (14.28)	6 (16.21)	NS	4 (14.81)	11 (15.06)	NS	9 (13.43)	6 (16.21)	NS
	PPF	6 (9.52)	5 (13.51)	NS	4 (14.81)	7 (9.58)	NS	7 (10.44)	4 (10.81)	NS
	Bloating	5 (7.93)	2 (5.40)	NS	2 (7.40)	5 (6.84)	NS	4 (5.97)	3 (8.10)	NS
	Nausea	5 (7.93)	6 (16.21)	0.012	5 (18.51)	6 (8.21)	0.006	3 (4.47)	8 (21.62)	0.001
	Vomiting	3 (4.76)	5 (13.51)	0.002	2 (7.40)	6 (8.21)	NS	6 (8.95)	2 (5.40)	NS
	Constipation	8 (12.69)	14 (37.83)	0.001	4 (14.81)	18 (24.65)	NS	18 (26.86)	4 (10.81)	0.001
	Diarrhea	5 (7.93)	4 (10.81)	NS	2 (7.40)	7 (9.58)	NS	6 (8.95)	3 (8.10)	0.037
	Fecal Incontinence	1 (1.59)	3 (8.10)	0.001	0 (0)	4 (5.47)	0.010	3 (4.47)	1 (2.70)	NS
	Abdominal distension	2 (3.17)	2 (5.40)	NS	3 (11.11)	1 (1.36)	0.001	4 (5.97)	0 (0)	0.001
USG abdomen (n=100)	Fatty liver	9 (14.28)	12 (32.43)	0.001	4 (14.81)	17 (23.28)	NS	7 (10.44)	14 (37.83)	0.001
	Hepatomegaly	14 (22.22)	6 (16.21)	NS	8 (29.62)	12 (16.43)	0.009	12 (17.91)	8 (21.62)	NS
	Cholelithiasis	2 (3.17)	6 (16.21)	0.001	2 (7.40)	6 (8.21)	NS	2 (2.98)	6 (16.21)	0.001
	Ascitis	6 (9.52)	4 (10.81)	NS	3 (11.11)	7 (9.58)	NS	8 (11.94)	2 (5.40)	0.016
	GB sludge	0 (0)	2 (5.40)	0.001	0 (0)	2 (2.73)	NS	1 (1.49)	1 (2.70)	NS
	Acalculous Cholecystitis	0 (0)	1 (2.70)	0.008	0 (0)	1 (1.36)	NS	1 (1.49)	0 (0)	NS
Upper GI endoscopy (n=44)	WNL	10 (15.87)	12 (32.43)	0.007	1 (3.70)	2 (2.73)	NS	3 (4.47)	0 (0)	NS
	GERD	3 (4.76)	0 (0)	0.006	5 (18.51)	17 (23.28)	NS	14 (20.89)	8 (21.62)	0.006
	Gastric mucosal erosion	1 (1.59)	0 (0)	NS	1 (3.70)	0 (0)	0.001	0 (0)	1 (2.70)	0.008
	Esophagitis	1 (1.59)	3 (8.10)	0.001	3 (11.11)	1 (1.36)	0.001	2 (2.98)	2 (5.40)	NS
	Gastritis	4 (6.34)	2 (5.40)	NS	0 (0)	6 (8.21)	0.001	5 (7.46)	1 (2.70)	0.030
	EVCG	1 (1.59)	1 (2.70)	NS	2 (7.40)	0 (0)	0.001	2 (2.98)	0 (0)	0.026
	Ulcer	1 (1.59)	1 (2.70)	NS	1 (3.70)	1 (1.36)	NS	1 (1.49)	1 (2.70)	NS

Data is expressed as no of patients (%). DOD; duration of diabetes, HbA1c; glycated hemoglobin, BMI; body mass index, APD, acid peptic disease, PPF, WNL; within normal limit, GERD; gastro esophageal reflex disease, EVCG, USG, ultra sonography, GI; gastro intestinal p value less than 0.05 is considered as significant.

Discussion

Since diabetes mellitus affects every organic system, it affects GIT as well. Chronic GI symptoms may represent a clinically important problem in a substantial number of patients with diabetes [7]. [7] Complications involving the GIT are an important cause of morbidity in patients with diabetes mellitus [7]. The prevalence of gastrointestinal symptoms amongst people with T2DM appears to be increased compared to the general population [8].

Bharucha *et al.* reported that the prevalence of selected GI symptoms such as constipation is greater in individuals with diabetes than in controls whereas for other symptoms, the prevalence is generally not different in persons with diabetes compared to those without [9]. In present study also constipation was the main presenting symptoms among T2DM patient; further constipation was significantly high among patients with diabetes duration of ≥10 years and patients with uncontrolled diabetes (HbA1c ≥7%).

An observational study from Bangladesh on 301 T2DM patients having duration of diabetes ≥10 years reported that maximum patients (90.7%) had GI symptoms with male predominance which is higher (78%) than the findings of the present study [10]. Most common GI symptom reported by Lona *et al.* was unspecified functional bowel disorder followed by cyclic vomiting syndrome and functional fecal incontinence, similar to that in present study vomiting and fecal incontinence was significantly higher in patients with diabetes duration of ≥10 year [10].

The prevalence of clinical symptoms of gastroparesis observed in the Saudi patients diagnosed with T2DM was 10.8% and was independently associated with poor controlled diabetes, hyperglycemia, and long duration of diabetes. The most common symptoms were bloating, stomach fullness and early satiety, similarly in present study also bloating and early satiety were not different among the patients with different diabetes duration, but significantly higher in patients with increased HbA1c and BMI [11]. [11]

Dedeli *et al.* studied the prevalence of GI symptoms and its effect on quality of life of 138 T2DM patients. Reported that the most commonly observed GI symptoms were abdominal distension, feeling of incomplete evacuation, reflux, and constipation. The results of this study indicated that patients with T2DM hold commonly complaint of GI symptoms and GI problems can impair well-being and quality of life in diabetes [12].

Kim *et al.* studied 190 diabetic patients and reported that 72% of the diabetic patients had GI symptoms which is in agreement with the present study findings. Most common GI symptoms were heartburn and dysmotility-like dyspepsia. They also reported that T2DM was associated with an increased prevalence of upper GI symptoms and these symptoms appeared to be independently linked to poor glycemic control, as measured by the HbA1clevels. Similar findings were revealed by the present study [7].

Cakir *et al.* compared the endoscopic parameters in 51 T2DM patients with and without gastroparesis and reported that erosive findings were more frequent in patients with than

without diabetic gastroparesis ($p<0.05$). They also reported ulcers in the antrum, ulcers in the bulbus, erosive gastritis and esophagitis in patients with T2DM [13]. Similar to that in present study GERD, esophagitis, gastric mucosal erosion and gastritis were higher in patients with longer duration of diabetes and with increased HbA1c.

The limitation of this study was that we investigated the single clinic population and no control group was recruited from the general non-diabetic population. A large randomized control group trial is required to strengthen the current findings.

Conclusion

Our findings suggest that duration of diabetes and gycaemia status plays an important role in the causing GI manifestations and there is a relationship between GI symptoms and DM. However, due to the world wide increase in incidence and prevalence of T2DM, special attention should be given to the presence of GI symptoms in the DM population, considering them as an indication of DM complications.

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