Original Article

Comparison of gastric motility in patients of type 2 diabetes mellitus with various degrees of glycemic control

ABSTRACT

The aim of this study was to evaluate the effect of glycemic control as estimated by glycated hemoglobin A1c (HbA1c) on gastric emptying in patients with type 2 diabetes mellitus (DM) using gastric emptying scintigraphy (GES). This was a cross-sectional study conducted at a tertiary health care center in Northern India. The study included 44 patients who underwent GES using a radiolabeled solid *Idli* meal containing 1 mCi of Tc-99 m Sulfur Colloid. Patients were divided into three groups based on glycemic control as Group A, B, and C with HbA1c <7%, 7%–9%, and >9%. Statistical analysis was performed using the IBM® SPSS® Statistics Version 23.0 The comparison of proportions was done using the Chi-square test and Fisher's exact test. Means were compared using the independent *t*-test and one-way analysis of variance. $P < 0.05$ was considered statistically significant. No statistically significant correlation was found between delayed gastric emptying and glycemic control ($P = 0.09$), gender ($P = 0.228$), dietary patterns ($P = 0.91$), symptoms of gastroparesis ($P = 0.06$), body mass index (BMI) ($P = 0.267$), and duration of type 2 DM ($P = 0.565$). No statistically significant association was also found between glycemic control and time taken for half gastric emptying (t1/2) ($P = 0.225$). Scintigraphy using Tc-99m Sulfur Colloid radiolabeled *Idli* meal can be effectively used for the assessment of gastric emptying. There is no significant correlation of delayed gastric emptying with glycemic control, gender, BMI, type of diet, and duration of diabetes mellitus.

Keywords: Diabetic gastroparesis, gastric emptying scintigraphy, hemoglobin A1c

INTRODUCTION

Gastric emptying scintigraphy (GES) is the investigation of choice for evaluating the disorders of gastric emptying because it is a simple, physiological, and sensitive investigation to objectively assess gastric emptying. Diabetes mellitus (DM) is the most common identifiable cause of gastroparesis, which is defined as delayed gastric emptying in the absence of gastric outlet obstruction. Cardinal symptoms of gastroparesis include nausea, vomiting, postprandial fullness, early satiety, and bloating. The aim of this study was to evaluate the effect of glycemic control as estimated by hemoglobin A1c (HbA1c) on gastric emptying in patients with type 2 DM (T2DM) using GES.[1,2]

SUBJECTS AND METHODS

This cross-sectional study was conducted over a period of 18 months from March 2018 to September 2019. The present study was conducted after getting clearance from the Institutional Ethics Committee letter with reference number AIIMS/IEC/18/115 dated 04/01/2018. Informed consent was obtained from all participants regarding participation in the study and publication of the data obtained from the study.

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Adult patients of T2DM aged between 18 and 65 years of both sexes with a disease duration of at least 5 years were included in the study. Drugs that may affect gastric emptying (e.g., Glucagon-like peptide 1 analogs, Dipeptidyl peptidase 4 inhibitors, Prokinetic drugs, etc.) were withdrawn for at least 1 week before GES in consultation with the treating physician, and the patients were excluded from the study if these drugs could not be withheld in these patients for any reason. Pregnant and lactating women, patients who were severely ill and hospitalized, with a prior history of surgery on stomach or gastrointestinal tract, active peptic ulcer disease, connective tissue disorders, with fasting blood glucose levels of >275 mg/dL on the day of GES were also excluded.[3,4]

Fasting blood glucose levels were checked on the day of GES using capillary blood using Glucometer (Glucocare Sense™ by RMD Mediaids limited, Gurugram, India). Nearest HbA1c levels (within 3 months of the study) of all the participants were also recorded. Participants who smoked cigarettes were asked to refrain from smoking on the day of study until the completion of the study.

Sixty-two eligible patients were interviewed to participate in the study, subsequently 47 patients underwent GES. Of these, 44 participants completed the study satisfactorily.

GES was performed using a previously standardized radiolabeled *Idli* meal containing 1 mCi of Tc-99 m Sulfur colloid to evaluate gastric emptying for solids. *Idli* consists of savory cake made by steamed batter composed of rice and black gram (lentils). Several premixed formulations are available, packaged premixed rice *idli* formula (MTR foods, Bengaluru, India) was used in this study. 50 mL of water was added to 50 g of the *Idli* mix and mixed thoroughly to produce smooth and uniform batter. Tc-99 m Sulfur colloid was prepared using the cold kits obtained from the board of radioisotope technology, India. 1 mCi of Tc-99 m Sulfur colloid in 1 mL volume was mixed with the batter and then spooned into the mold of a pan. The pan was then steamed for 10–15 min inside a cooking vessel. The *Idli* was then dislodged from the mold and served with 1 *Chapati* (Indian flatbread), and 50 ml of thick curry of *Arhar dal* (pigeon pea) within 10 min with 100 ml of water, and instructed not to consume any other meal or beverage until completion of imaging (4 h). The total energy of the meal was approximately 350 kcal.[4,5]

The present study was carried out for a total duration of 4 h with image acquisition done for 1 min-anterior and posterior views. The images were acquired: immediately after ingestion of meal, 30 min, 1 h, 2 h, and 4 h after meal using GE NMCT 670 (integrated SPECT/CT-single photon emission computed tomography by GE Healthcare, Chicago, USA) dual-headed gamma camera with 140 keV Tc-99 m photopeak with 20% window (140keV ± 10%). Computerized digital images were acquired in 128 × 128 word mode matrix. The images were acquired with patient standing upright in front of the camera[1] [Figures 1-4].

Images were processed on GE Xeleris workstation version 4.0 (GE Healthcare, Chicago, USA). Manual regions of interests (ROI) were drawn on the anterior and posterior images on all acquisition times using an ROI tool to outline the stomach. The geometric mean of anterior and posterior gastric counts of each time point was calculated. Decay correction was performed automatically by gastric emptying analysis software on the Xeleris workstation. The results were expressed as percentage remaining in the stomach at each time point with the total gastric counts normalized to 100% at $t = 0$ (immediate post meal image) [Figures 1-4].

Patients were divided into three groups based on glycemic control as Group A, HbA1c <7% (Good glycemic control), Group B, HbA1c 7%–9% (Fair glycemic control), Group C, HbA1c >9% (Poor glycemic control).[6-8]

Interpretation

In accordance with the consensus recommendations for GES: A joint report of the American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine, the studies in which gastric retention of the radiolabeled solid meal of >10% was observed at 4 h were considered positive for delayed gastric emptying.[1]

Statistical analysis

Statistical analysis was performed using the IBM® SPSS® Statistics Version 23.0 (Armonk, New York, USA). Comparison of proportions was done using the Chi-square test and Fisher's exact test. Means were compared using the independent *t*-test and one-way analysis of variance. $P < 0.05$ was considered statistically significant.

RESULTS

The patient characteristics and results are summarized in Tables 1 and 2. Out of the 44 patients who satisfactorily completed GES, 11 patients had good (Group A, HbA1c <7%), 18 patients had fair (Group B, HbA1c 7%–9%), and 15 patients had poor (Group C, HbA1c >9%) glycemic control. Fasting blood glucose (mean ± standard deviation [SD]) in Groups A, B, and C was 133.8 ± 27.0 mg/dL, 156 ± 33.0 mg/dL, and 175.8 ± 39.9 mg/dL, respectively.

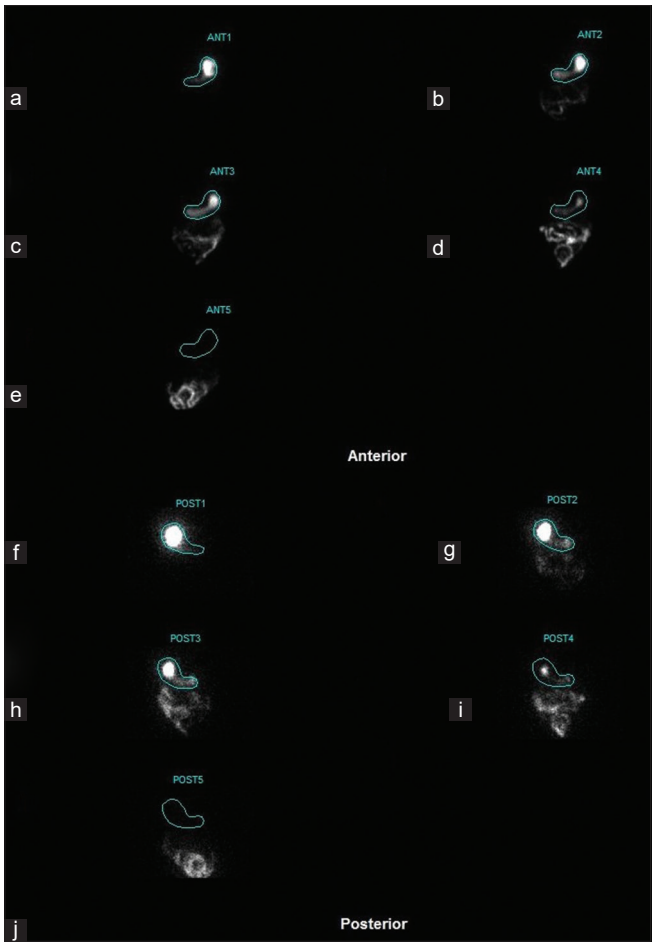

Figure 1: Gastric emptying scintigraphy performed in a 48-year-old female patient of type 2 diabetes mellitus of 7 years' duration. Images were acquired in anterior (a-e) and posterior (f-j) projections after administration of radiolabeled Idli meal immediately, at 30 min, 1 h, 2 h, and 4 h. Entire tracer is seen in the stomach in the first images acquired immediately post meal (a and f) and is gradually noted in the intestines in the images acquired subsequently. Images at 4 h (e and j) correspond to near complete gastric emptying of tracer

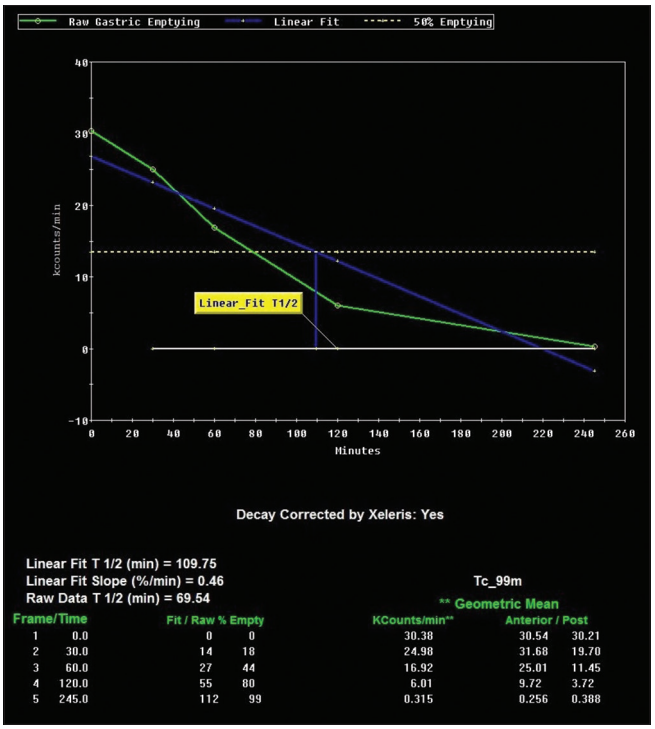

Figure 2: Time activity curve and quantitative parameters of gastric emptying scintigraphy of patient in Figure 1 correspond to normal gastric emptying (retention at 4 h is approximately 1%)

Mean gastric emptying at 4 h in Group A, B, and C was 10.8, 6.8, and 11.4%, respectively, with a SD of 8.8, 5.4, and 7.1%, respectively. No significant difference in gastric emptying was found between the three groups ($P = 0.143$). It was observed that 36.3%, 16.6%, and 53.3% of the patients in Groups A, B, and C had delayed gastric emptying at 4 h respectively. None of the patients were found to have rapid gastric emptying. No statistically significant relation between degree of glycemic control and gastric emptying ($P = 0.09$). Mean T1/2 in Group A, B, and C was 97.8, 72.8, and 84.3 min, respectively, with a SD of 48.9, 18.2, and 32.02 min, respectively, indicating no significant difference between groups ($P = 0.225$). Furthermore, no statistically significant correlation was found between delayed gastric emptying and gender ($P = 0.228$), type of diet (P 0.91), BMI ($P = 0.1$), and duration of T2DM ($P = 0.565$). Of the patients who had the classical symptoms of gastroparesis ($n = 27$), majority had the symptoms related to postprandial fullness and bloating ($n = 22/27$). None of the patients had complaints of nausea, vomiting, and abdominal pain. Hence, individual symptoms were not analyzed, and analysis was done on basis of the presence or absence of symptoms only. No statistically significant difference ($P = 0.06$) was found between the symptoms of gastroparesis and gastric emptying.

DISCUSSION

Diabetic Gastroparesis results in significant morbidity and adversely affects the quality of life. Importance of early diagnosis and management of diabetic gastroparesis is being increasingly emphasized to improve the patient outcomes. Objective assessment of gastric emptying for diagnosis and follow-up after intervention is imperative. Conflicting findings in the literature prompts to evaluate the parameters that may affect gastric emptying in patients of type 2 diabetes mellitus.

In our study, no statistically significant correlation was found between delayed gastric emptying and glycemic control, gender, BMI, duration of type 2 diabetes mellitus, or type of diet. Izzy *et al*. found that poor glycemic control is associated with delayed gastric emptying ($P = 0.03$). Their cross-sectional study included 299 patients of type 1 and type 2 diabetes mellitus, and the patients were subdivided into three groups

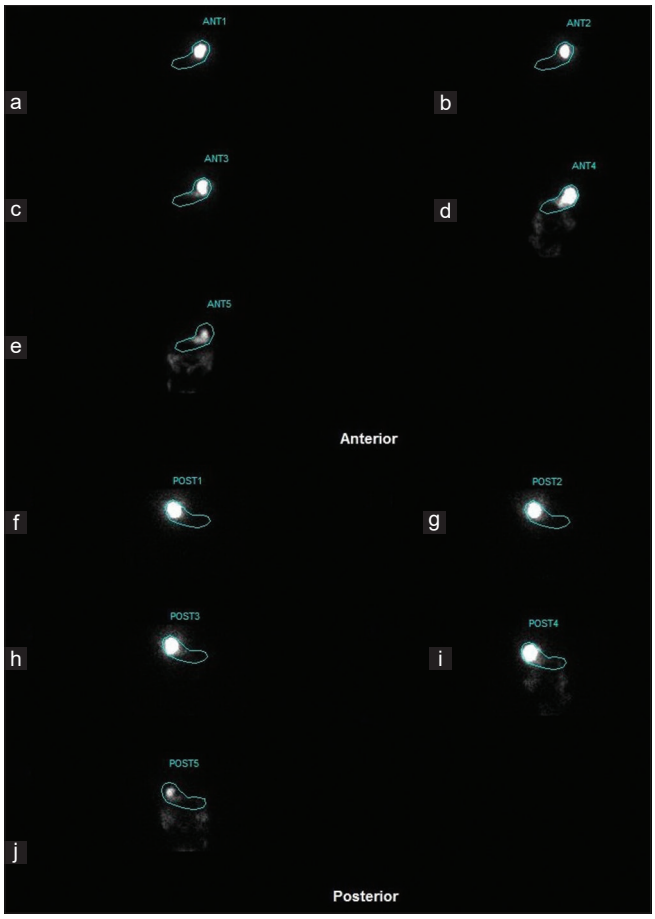

Figure 3: Gastric emptying scintigraphy performed in a 47-year-old male patient of type 2 diabetes mellitus of 10 years' duration. Images were acquired in anterior (a-e) and posterior (f-j) projections after the administration of radiolabeled *Idli* meal immediately, at 30 min, 1 h, 2 h, and 4 h. Entire tracer is seen in the stomach in the first images acquired immediately post meal (a and f) and is gradually noted in the intestines in the images acquired subsequently. Images at 4 h (e and j) correspond to significant tracer retention in the stomach

Table 1: Patient characteristics

Characteristics	Value
Total	44
Male	26
Female	18
Age (years), mean±SD	51±9.02
Duration of Type 2 diabetes mellitus (years), mean±SD	10.0±5.24
BMI (kg/m^2), mean±SD	25.49±4.11

SD: Standard deviation, BMI: Body mass index

as good, fair, and poor glycemic control similar to our study.[6] However, Reddy *et al*. found no significant correlation between gastric emptying time estimated using GES and HbA1c, although they had comparable sample size (n = 250) with the study conducted by Izzy *et al*.[9] Community-based data regarding gastroparesis are scarce, and results of a notable study from Olmsted county in Minnesota, USA revealed that age adjusted prevalence of gastroparesis was

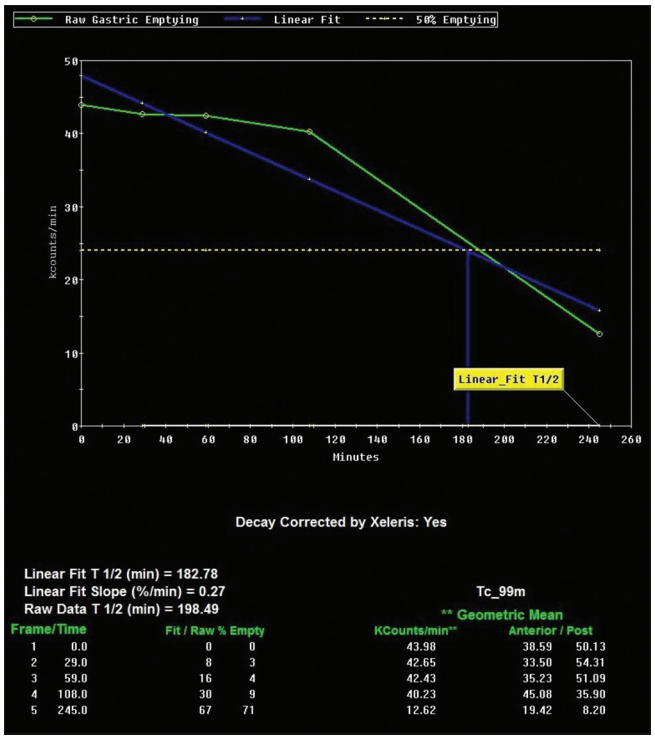

Figure 4: Time activity curve and quantitative parameters of gastric emptying scintigraphy of patient in Figure 3 correspond to delayed gastric emptying (retention at 4 h is approximately 29%)

higher in females (37.8/100,000 persons for women versus 9.6/100,000 for men). However, the study was not confined to diabetic patients.[10]

The results of cross-sectional study conducted by Anudeep *et al*. which included 140 patients of long-standing T2DM revealed no statistically significant correlation of gender, symptoms of gastroparesis with delayed gastric emptying in patients of T2DM. However, they found that BMI and glycemic control (HbA1c) were the significant predictors of delayed gastric emptying.[4] Desai *et al.* conducted their study on 60 patients of which 21 were diabetics. The results of this study did not demonstrate statistically significant difference in gender among patients with normal, delayed, or rapid gastric emptying.[11] Javadi *et al*. in their study on 19 patients with T2DM concluded that gender and duration of T2DM were not correlated with gastric emptying time, however HbA1c had significant effect on gastric emptying time.[12] Kojecky *et al*. studied 147 patients of type 2 diabetes and found no correlation of gastric emptying with body weight, duration of diabetes, neuropathy, current glycemia, or total upper gastrointestinal symptoms score.[13] Bharucha *et al.* in their study on 74 patients of type 1 DM found that duration of diabetes was found to be an independent risk factor for delayed gastric emptying.[3]

Different types and compositions of meal have been used for GES in different parts of the world. Classic meal used in

Table 2: Summary of results comparing various patient characteristics in terms of the results obtained by gastric emptying scintigraphy

Variable	Delayed gastric emptying	Normal gastric emptying	*P*
Group			
A (HbA1c <7%)	4 (36.3)	7 (63.6)	0.09
B (HbA1c 7-9%)	3 (16.6)	15 (83.3)	
C (HbA1c >9%)	8 (53.3)	7 (46.6)	
Gender			
Female	8 (44.4)	10 (55.6)	0.228
Male	7 (26.9)	19 (73.1)	
Diet			
Vegetarian	8 (34.8)	15 (65.2)	0.91
Nonvegetarian	7 (33.3)	14 (66.7)	
Symptoms of gastroparesis			
Present	12 (44.4)	15 (55.6)	0.06
Absent	3 (17.6)	14 (82.4)	
BMI* (kg/m^2)			
18.5-24.9	8 (38.1)	14 (61.9)	0.267
25.0-29.9	6 (33.3)	12 (66.7)	
>30	1 (25)	3 (75)	
Duration of Type 2 diabetes mellitus (years)			
5-9	9 (39.1)	14 (60.9)	0.565
10-15	5 (33.3)	10 (66.7)	
>15	1 (16.7)	5 (83.3)	

*None of the participants had BMI <18.5 kg/m^2. BMI: Body mass index, HbA1c: Glycated hemoglobin

Western countries is egg white sandwich, while different regional meals have been used and standardized in India. In our study, radiolabeled *Idli* meal was used, which has the advantages of simplicity of preparation, low fat content, and is prepared by steaming, and is acceptable to most Asian patients. Somasundaram *et al.* conducted their study with aim to elaborate the procedure of preparation of radiolabeled *Idli* meal with Tc-99 m Sulfur colloid. They used packaged mix to make the batter for preparation of *Idli*. They also found that more than 96% of the sulfur colloid was bound to the meal at 4 h of suspension in simulated gastric fluid and concluded that radiolabeled *Idli* meal is a good alternative to egg white sandwich.[5] Indian Round breads (*Chapati*) has also been standardized in the study by Awasthi *et al.*, results of which showed ~90% of the radiolabel remained bound to the solid phase at 3 h at all pH levels.[14] Both *Idli* and *Chapati* are widely acceptable meals in India. We used radiolabeled *Idli* meal because of simplicity of the preparation of meal using a packaged mix, which has widespread availability globally. Anudeep *et al.* used radiolabeled *Idli* meal for GES in their study on 140 patients of type 2DM using a marketed premixed formula for Rice *Idli* conducted at a tertiary care center in Southern India.[4] Ora *et al.* used radiolabeled *Chapati* meal for GES in their study on 50 patients of functional dyspepsia.[15] As per the consensus recommendations for GES, low fat meal is preferred for initial screening; however, these guidelines also suggest that meal composition may be changed depending on patients symptoms. Approximate energy of the meal used in our study was ~350 kcal with low fat content of ~2.3% and 67% carbohydrate which aligns with the consensus recommendations.[1]

The data from the Northern India for diabetic gastroparesis and its predictors are scarce. Hence, this study was designed for a better insight into this area. However, both community-based and hospital-based studies are needed in the region for greater understanding of the prevalence and predictors of gastroparesis in diabetic patients.

The limitations of our study were relatively smaller sample size, and inclusion of only T2DM patients. Furthermore, this was a hospital-based study, and follow-up study of the patients was not done.

CONCLUSION

Radionuclide gastric emptying with Tc-99 m Sulfur Colloid radiolabeled *Idli* meal can be used as an effective objective noninvasive outpatient tool for functional assessment of gastric motility. Glycemic control, gender, BMI, type of diet, classic symptoms of gastroparesis, and duration of diabetes show no statistically significant correlation with gastric emptying in our study. Further studies with a larger cohort may provide more information on significance of factors affecting to gastric motility in T2DM.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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