

Assessment of Gastric Dysmotility Using Standardized Tc-99m Sulfur Colloid-Labeled Rice Cakes in Diabetic Patients

Abstract

Background: Diabetes mellitus is a common lifestyle disease where patients suffer from gastric dysmotility, which is usually underdiagnosed. The aim of this study was to evaluate the utility of Tc-99m sulfur colloid-labeled meal gastric emptying scintigraphy in Type 2 diabetic patients. **Methods:** A total of 43 patients and 30 controls, satisfying the inclusion criteria from March 2019 to August 2020, were included. Serial planar images were acquired in both anterior and posterior projections for an iso-time of 1 min at 1 min, 60 min (1 h), 120 min (2 h), and 240 min (4 h) after consumption of Tc-99m SC-labeled idly (rice cakes). The gastric emptying was considered delayed if there was <10% emptying at 1 h, <70% emptying at 2 h, and <94% emptying at 4 h. **Results:** The mean T1/2 was similar among cases (44.11 ± 10.52 min) and controls (49.56 ± 13.44 min, $P = 0.056$) while the mean gastric emptying at 1 h was slower in cases compared to controls, $P = < 0.01$. Two cases (4.6%) had delayed gastric emptying while none of the controls had delayed gastric emptying. T1/2 showed no association with duration of diabetes or HbA1c levels ($P = 0.76, 0.45$) and a weak correlation with fasting blood sugar (FBS) on the day of scan (R value = 0.18). **Conclusion:** In comparison to controls, diabetic patients had faster gastric emptying with no association with duration of diabetes or HbA1c levels and a weak correlation with FBS on the day of scan.

Keywords: Gastric dysmotility, gastric emptying study, Type 2 diabetes mellitus

Introduction

Globally, diabetes mellitus (DM) is one of the most common metabolic disorders and its incidence is increasing in developing countries.^[1,2] The complications due to diabetes increase with increasing duration of the disease.^[3]

Autonomic neuropathy is one of the complications of diabetes, but its clinical significance is undermined. As with other complications, incidence of diabetic autonomic neuropathy (DAN) increases with increased duration of diabetes and increased glycemic level.^[4] Although the exact mechanism of gastric dysfunction in DAN is unknown, a number of contributing factors have been proposed. DAN can involve both sympathetic and parasympathetic systems, and symptoms are seen accordingly. Any section of the gastrointestinal (GI) tract may be affected resulting in esophageal enteropathy, gastroparesis, constipation, diarrhea, and fecal incontinence.^[5]

A wide array of investigations such as ultrasound abdomen, endoscopy, colonoscopy, magnetic resonance imaging are used to detect the structural abnormalities associated with GI tract disorders. Clinical examination and few other tests are used to evaluate the GI tract physiology. Fluoroscopic study with barium swallow is useful in assessing GI tract morphology and to some extent its motility function.^[6,7] pH manometry is used in evaluation of reflux disorders. However, manometry is an invasive technique and has poor patient acceptance and compliance. Recently, some new diagnostic techniques such as gastric emptying breath test, electrogastrography, and electronic capsule tests have been developed and appearing to be promising for early detection of GI tract physiology-related disorders.^[8]

In nuclear medicine, various radiotracer-based tests are available to evaluate the GI tract motility disorders affecting esophagus, stomach, small intestine, large intestine, gall bladder, etc., Tc-99m sulfur colloid-labeled test meal

Nimmagadda Ajit,
Alok Sachan¹,
Ranadheer
Gupta Manthri,
Krishna Mohan VS,
RamyaPriyaRallapeta,
Tekchand Kalawat

Departments of Nuclear
Medicine and Endocrinology
and Metabolism, Sri
Venkateswara Institute of
Medical Sciences, Tirupati,
Andhra Pradesh, India

Address for correspondence:

Dr. Tekchand Kalawat,
Department of Nuclear
Medicine, Sri Venkateswara
Institute of Medical Sciences,
Tirupati, Andhra Pradesh, India.
E-mail: kalawat.svims@gmail.
com

Received: 11-03-2022

Revised: 07-05-2022

Accepted: 17-05-2022

Published: 02-12-2022

Access this article online

Website: www.ijnm.in

DOI: 10.4103/ijnm.ijnm_48_22

Quick Response Code:



How to cite this article: Ajit N, Sachan A, Manthri RG, Mohan VS, Rallapeta RP, Kalawat T. Assessment of gastric dysmotility using standardized Tc-99m sulfur colloid-labeled rice cakes in diabetic patients. Indian J Nucl Med 2022;37:359-66.

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

studies are used for evaluation of gastric emptying time which provide semi-quantitative and qualitative assessment of the gastric motility. However, heterogeneous food habits may cause variable results; therefore, guidelines recommend to perform these studies using standardized radiolabeled test meals that match with the local food habits.^[9]

Hence, the current study is designed to study the gastric dysmotility among Type 2 DM patients with Tc-99m sulfur colloid-labeled rice cakes (idlis), which is a common food item in the local study population in the southern part of India.

Methods

It is a prospective analytical study conducted in known diabetic patients and controls. A total of 43 patients and 30 controls, from March 2019 to August 2020, were recruited for the study.

Study population

Type 2 DM patients between the ages of 35 and 60 years and willing to participate in the study were included. Patients on glucagon-like peptide-1 drugs such as exenatide, prokinetics such as metoclopramide, domperidone, and erythromycin, and proton-pump inhibitors were excluded from the study. Pregnant and lactating females were also excluded from the study. Controls between the age group of 35 and 60 years and controls who were nondiabetic with HbA1c levels <5.8% and willing to participate in the study were included.

All the patients were explained about the procedure, purpose, benefits, and side effects of the study. Fasting blood sugar (FBS) and HbA1c levels among cases and controls were recorded. The scintigraphic study was performed after at least 6 h of fasting. Complete history was taken and complete general examination was conducted for all the recruited patients. Patients were instructed to remove all metal objects and articles to avoid any artifacts.

Meal preparation

Batter was prepared using 50 g of commercially available packaged idly mix according to the guidelines given by the vendor. Tc-99m SC was prepared using cold kits provided by the Board of Radiation and Isotope Technology, India. 1 mCi (37 MBq) of the prepared radiopharmaceutical in 1 ml volume was then mixed with the batter. Quantitatively, the batter was then spooned into the molds of a nonstick idli pan that had previously been brushed with oil to allow easy dislodgement after cooking. The pan was steamed for 12–15 min in a food steamer. A patient was advised to chew it well and consume the food within 10 min along with groundnut chutney.

Image acquisition and analysis

All studies were performed on a dual-head gamma camera obtained from M/s SIEMENS, Germany, equipped with low-energy high-resolution collimator. During the data acquisition, energy window for image collection was centered 10% above and below 140 keV photopeak of Tc-99m. Serial static images were acquired soon after the ingestion of radiolabeled test meal, using a 64 × 64 matrix for a duration of 1 min using both detectors. Electronic magnification was used to optimize the pixel size.

Serial planar images were acquired in both anterior and posterior projections for an iso-time of 1 min at 1 min, 60 min (1 h), 120 min (2 h), and 240 min (4 h) after consumption of standard meal. Manual region of interest was drawn for stomach in both anterior and posterior images. Decay correction factor was applied. The geometric mean of counts was obtained from anterior and posterior images for each point of time. The percentage of gastric emptying was calculated at each point of time. The gastric emptying was considered delayed if there was <10% emptying at 1 h, <70% emptying at 2 h, or <94% emptying at 4 h. Appearance of radiotracer within 2 h of the study was considered gastric hurrying (32). Cases with HbA1c levels >8% were considered to have poor glycemic control. Patients with body mass index (BMI) >30 kg/m² were considered obese as per the WHO criteria.^[11]

Statistics

Demographic data, parameters of T_{1/2}, and serially assessed clearance values obtained from Tc-99m SC gastric emptying study were recorded on a predesigned pro forma and managed using Microsoft Excel worksheet. All the entries were double-checked to detect any possible error. Statistical analysis was done Statistical Package of Social Sciences (SPSS) software versions 21.0 M/s International Business Machines (IBM), Armonk, New York, United States of America. Student *t*-test was used to compare the means of gastric emptying between cases and controls. Chi-square test was used for categorical variables and Pearson test to assess the correlation between continuous variables.

Regulatory approvals

The study was performed after obtaining approval from the Institutional Thesis Protocol Approval Committee and Institutional Ethics Committee (Roc No. AS/11/IEC/SVIMS/2017 IEC No. 176). Written informed consent was obtained from all the patients and controls.

Results

A total, *n* = 73 subjects underwent a Tc-99m SC-labeled meal gastric emptying study between March 2019 and August 2020. Of these, 43 were cases and 30 were controls. Neither of them had any adverse events. For all the cases and controls, demographic data were analyzed. Of the

43 patients, 26/43 (60.4%) were men and 17/43 (39.6%) were women.

Demographic data of cases and controls

The mean age for cases was 51.6 ± 6.0 (35–60) years, with the mean age for men being 52.8 ± 4.85 years and women being 51.46 ± 7.48 years with no significant difference among the two ($P = 0.44$). However, there was a significant difference in the means of BMI ($P = 0.01$) between men and women with the mean BMI in men being 25.01 ± 4.28 (19.1–33.2) kg/m^2 and in women being 28.86 ± 5.72 (21.6–36.9) kg/m^2 . The mean BMI of the cases was 26.53 ± 5.13 (19.1–36.9) kg/m^2 and 9/43 cases were found to be obese (20.9%). Of these, obese cases 6 were females and 3 were males (female-to-male ratio of 2:1). The demographic parameters and clinical findings of controls did not vary between males and females [Table 1].

Comparing the age of the cases and controls, significant difference ($P = < 0.01$) was observed. The mean age of cases was 51.60 ± 6.0 (35–60) years and the mean age of controls was 44.86 ± 6.55 (35–60) years, respectively. BMI comparison between cases and controls showed no significant difference ($P = 0.26$). The mean BMI of cases was 26.53 ± 5.13 (19.1–36.9) kg/m^2 vs. 25.29 ± 3.88 (20.9–32.5) kg/m^2 for controls [Table 2].

Treatment history of cases

The mean duration of Type 2 DM in the cases was 10.38 ± 5.21 (0.5–20) years [Figure 1]. Among males, it was 9.9 ± 4.49 (0.5–19) years and in females 11.1 ± 6.23 (2–20) years ($P = -0.46$). 18/43 (42%) patients maintained their glycemic control on oral hypoglycemic drugs such as metformin, pioglitazone, and glibenclamide, 18/43 (42%) maintained on both Oral Hypoglycemic drugs (OHD) plus insulin, and the remaining 7/43 (16%) maintained on insulin treatment alone. Seven cases (1 man and 6 women) presented with clinical symptoms such as bloating, early satiety, abdominal pain, and increased frequency of defecation.

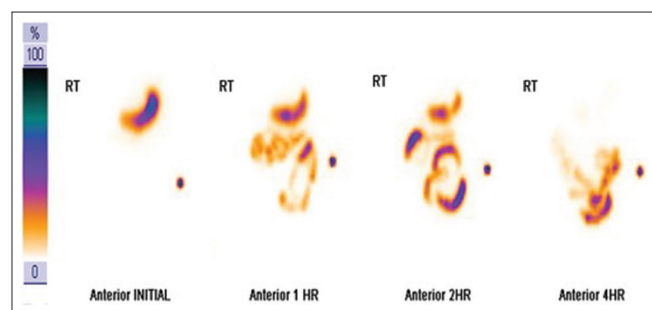


Figure 1: A case of Type 2 diabetes mellitus for 5 years with bloating and dyspepsia, with Tc-99m SC-labeled meal gastric emptying study scintigraphic findings showing delayed gastric emptying with immediate visualization of stomach at 0 min image, 41% emptying at 1 h, 68% emptying at 2 h, and 89% emptying by 4 h. The T1/2 in the study was 75 min

Glycemic control of cases

Glycemic control of the cases was checked using the available biochemical parameters. The mean FBS on the day of scan was 157.74 ± 71.0 (76–384) mg/dl. There was no significant difference between the mean FBS of males, 158.73 ± 77.46 (76–384) mg/dl, and females, 156.23 ± 62.09 (83–284) mg/dl, with the $P = 0.91$. Similarly, the mean HbA1c level of cases was $8.88 \pm 2.02\%$ (5.7–12.8), with no significant difference between males and females ($P = 0.78$). The mean HbA1c level in males was $8.81 \pm 2.06\%$ (5.7–12.5) and the mean HbA1c level in females was $8.98 \pm 2.01\%$ (6.2–12.8). With a cutoff of 8% of HbA1c, poor glycemic control was seen in 16/26 (61.5%) males and 10/17 (59%) females.

Scan findings of cases

Of all the cases, 2 women had delayed gastric emptying, with the calculated prevalence of gastroparesis among Type 2 DM patients in our study being 4.6%. The mean T1/2 for cases was 44.11 ± 10.52 (27–75) min. The percentage of gastric emptying at 1 h ranged from 41% to 100% in cases, with the mean being $76.23 \pm 15.41\%$. The mean percentage of gastric emptying at 2 h was $93.18 \pm 8.56\%$ (68–100). By 4 h, almost all cases had 100% emptying except 1 male and 3 females [Table 3].

Scan findings of controls

Among the 30 controls, none had delayed gastric emptying for solids. The mean FBS on the day of scan was 98.26 ± 18.68 (78–161) mg/dl for males, and 94.27 ± 10.04 (77–116) mg/dl for females. The mean FBS for the control population was 96.8 ± 15.97 (77–161) mg/dl with no significant difference between males and females ($P = 0.51$). The mean HbA1c for control population was $5.09\% \pm 0.54\%$ (3.9–5.8).

Comparison between cases and controls

When biochemical, glycemic parameters and scintigraphic findings were compared between cases and controls, no significant difference in mean FBS and HbA1c levels was observed between them ($P \leq 0.01$). However, scintigraphic mean T1/2 values compared among cases and controls, there was a notable difference, which is 44.11 ± 10.52 min versus 49.56 ± 13.44 min with $P = 0.056$. Similarly, there was a significant difference in percentage of gastric emptying at 1 h between cases and controls ($P = 0.003$). Emptying by 2 h and 4 h showed a minimal difference between cases and controls with $P = 0.34$ and 0.42 , respectively [Table 4]. 8/43 (18.6%) cases had rapid gastric emptying, with a mean T1/2 of 37.2 ± 3.3 min which is significantly less when compared to normal controls ($P = 0.0003$) [Table 4].

Parameters such as duration of diabetes, HbA1c, and FBS on the day of scan were compared with T1/2. BMI was compared with duration of T1/2 in both cases and controls. All the parameters showed either a weak or no correlation. HbA1c

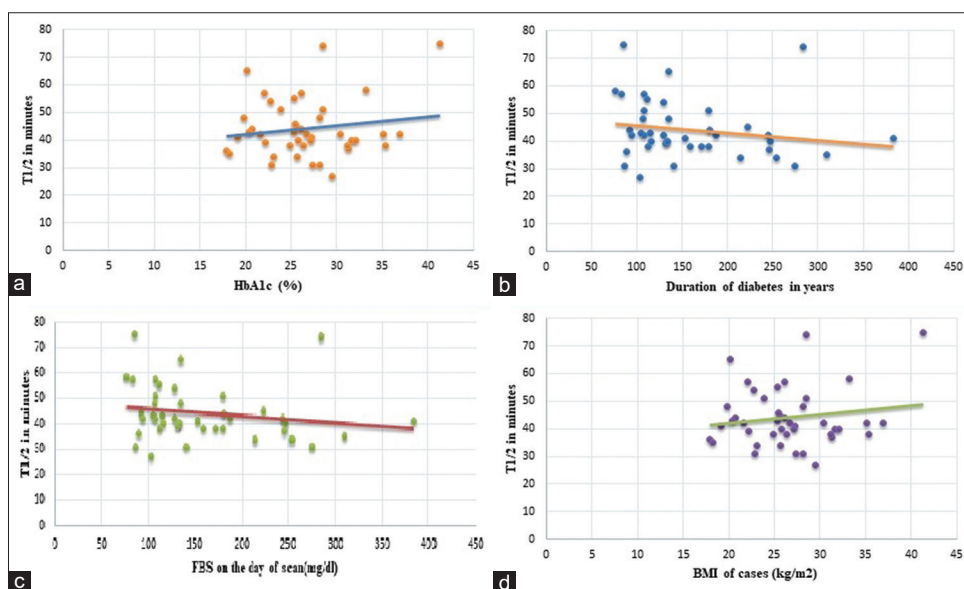


Figure 2: Scatter plots showing very weak or no correlation between T1/2 and HbA1c (R value 0.04, $P = 0.76$) (a), T1/2 and duration of diabetes ($R = -0.11$, $P = 0.47$) (b), T1/2 and FBS ($R = -0.18$, $P = 0.24$) (c), and between T1/2 and BMI in cases ($R = 0.15$, $P = 0.31$) (d)

Table 1: Demographic parameters of cases and controls

Parameter	Male	Female	Total	Significance (P)
Cases				
Mean age \pm 1SD (years)	52.88 \pm 4.85	51.46 \pm 7.48	51.60 \pm 6.0	0.44
Mean BMI \pm 1SD (kg/m ²)	25.01 \pm 4.28	28.86 \pm 5.72	26.53 \pm 5.13	0.01
Controls				
Mean age \pm 1SD (years)	46.94 \pm 6.7	41.27 \pm 4.47	44.86 \pm 6.55	0.01
Mean BMI \pm 1SD (kg/m ²)	25.45 \pm 4.0	25.09 \pm 3.85	25.29 \pm 3.88	0.76

SD: Standard deviation, BMI: Body mass index

Table 2: Comparison of demographic parameters of cases and controls

Parameter	Cases	Controls	Significance (P)
Mean age \pm 1SD (years)	51.60 \pm 6.0	44.86 \pm 6.55	<0.01
Mean BMI \pm 1SD (kg/m ²)	26.53 \pm 5.13	25.29 \pm 3.88	0.26

SD: Standard deviation, BMI: Body mass index

was found to have a positive correlation with T1/2 ($R = 0.04$) which was not significant, $P = 0.76$ [Figure 2a]. While, duration of diabetes was found to have a negative correlation ($R = -0.11$) with $P = 0.47$ [Figure 2b]. FBS has showed a negative correlation with T1/2 ($R = -0.18$) with no statistical significance, $P = 0.24$ [Figure 2c]. BMI on correlation with T1/2 showed mixed results in cases and controls with positive correlation in cases ($R = 0.15$) and negative correlation in control population ($R = -0.20$), $P = 0.31$ [Figure 2d] and 0.32, respectively.

Inter-group comparison of cases

The cases were subdivided into categories, based on glycemic control, use of insulin, and presence of symptoms. There was no significant difference in 1-h gastric emptying

between cases with good glycemic control (17/43 cases) or poor glycemic control (26/43 cases) ($P = -0.72$). The mean 1-h gastric emptying was 75.18% \pm 14.4% for cases with good glycemic control and with poor glycemic control was 76.2% \pm 16.9%. Mean HbA1c values between the two groups were statistically significant, $P \leq 0.01$. The mean HbA1c in cases with poor glycemic control was 10.22% \pm 1.35% and the mean HbA1c in cases with good glycemic control was 6.82 \pm 0.67. However, there was no significant difference between FBS on the day of scan in the two groups, $P = 0.17$.

There was no significant difference in 1-h gastric emptying between cases who were on insulin (18/43 cases) and who were not on insulin (25/43) cases, with $P = 0.286$. The mean 1-h gastric emptying for cases on insulin was 79.2 \pm 17.1 (47–100)% and for cases not on insulin was 74.08 \pm 13.9 (41–100)%. Similarly, no significant difference was found between the two groups in mean HbA1c levels and mean FBS on the day of scan with $P = 0.56$ and 0.27, respectively.

One-hour gastric emptying when compared between symptomatic, 7/43, and asymptomatic cases, 36/43, showed no significant change ($P = 0.90$). The 1-h emptying in symptomatic cases was 76.86% \pm 18.4% and in asymptomatic cases was 76.11% \pm 15.04%, respectively.

Table 3: Biochemical and scintigraphic findings among cases and controls

Parameter	Male	Female	Total	Significance (P)
Cases				
Mean FBS±1SD (mg/dl)	158.73±77.46	156.23±62.09	157.74±71.0	0.91
Mean HbA1c±1SD (%)	8.81±2.06	8.98±2.01	8.88±2.02	0.78
Mean T1/2±1SD (min)	42.92±8.66	45.94±12.94	44.11±10.52	0.36
1 h emptying±1SD (%)	77.69±14.05	74±17.49	76.23±15.41	0.44
2 h emptying±1SD (%)	93.76±6.12	92.29±11.50	93.18±8.56	0.58
4 h emptying±1SD (%)	99.73±1.04	99.35±2.66	99.58±1.84	0.51
Positive scans	0/26	2/17	2/43	
Negative scans	26/26	15/17	41/43	
Controls				
Mean FBS±1SD (mg/dl)	98.26±18.68	94.27±10.04	96.8±15.97	0.51
Mean HbA1c±1SD (%)	4.96±0.58	5.31±0.36	5.09±0.54	0.08
Mean T1/2±1SD (min)	48.42±14.36	51.54±12.09	49.56±13.44	0.54
1 h emptying±1SD (%)	67.26±15.22	61±17.19	64.96±15.97	0.30
2 h emptying±1SD (%)	90.36±10.0	92.54±8.25	91.16±9.31	0.54
4 h emptying±1SD (%)	99.78±0.91	100	99.86±0.73	0.45
Positive scans	0/19	0/11	0/30	
Negative scans	19/19	11/11	30/30	

FBS: Fasting blood sugar, HbA1c: Glycated hemoglobin, SD: Standard deviation

Table 4: Comparison of scintigraphic findings between cases and controls

Parameter	Cases	Controls	Significance (P)
Mean FBS±1SD (mg/dl)	157.74±71.0	96.8±15.97	<0.01
Mean HbA1c±1SD (%)	8.88±2.02	5.09±0.54	<0.01
Mean T1/2±1SD (min)	44.11±10.52	49.56±13.44	0.056
Mean 1 h emptying±1SD (%)	76.23±15.41	64.96±15.97	0.003
Mean 2 h emptying±1SD (%)	93.18±8.56	91.16±9.31	0.34
Mean 4 h emptying±1SD (%)	99.58±1.84	99.86±0.73	0.42

FBS: Fasting blood sugar, HbA1c: Glycated hemoglobin, SD: Standard deviation

When mean HbA1c levels and FBS on the day of scan were compared, no statistical significance was found, $P = 0.14$ and 0.06 , respectively.

Chi-square test applied to know if there was any association between glycemic control and delay in gastric emptying for solids showed $P = 0.24$. Duration of T1/2 when compared between symptomatic and asymptomatic cases showed no significant change ($P = 0.92$). The mean T1/2 in symptomatic cases was 44.57 ± 13.7 min and the mean T1/2 in controls was 44.02 ± 10.03 min, respectively. When mean HbA1c levels and FBS on the day of scan were compared, no significance was found with $P = 0.14$ and 0.06 , respectively.

In order to assess the relation of gastric emptying with glycemic control, our cases were divided into tertiles based on FBS on the day of scan. FBS ranged from 76 to 111 mg/dl in the 1st tertile indicating euglycemic state, 112–159 mg/dl in the 2nd tertile, indicating controlled hyperglycemic state, and 160–384 mg/dl in the 3rd tertile, indicating poorly controlled hyperglycemic state, respectively. Moreover, the mean T1/2 of the tertiles was 47.26 ± 10.27 , 43.23 ± 12.05 , and 41.73 ± 8.22 min, respectively. Cases were further subcategorized into groups

as tertiles, based on their HbA1c levels and duration of diabetes [Table 5]. No significant difference was seen between the tertiles with $P = 0.85$ and 0.58 , respectively.

Discussion

As per these recommendations, in the current study, we prepared a Tc-99m-SC-labeled standard test meal, idly (rice cake), using ingredients commonly consumed in the local population. The meal was first validated in 30 controls. The mean age of controls was 44.86 ± 6.55 years. The mean T1/2 among controls was $49.56 \text{ min} \pm 13.44 \text{ min}$ and the mean gastric emptying at 1 h was $64.96\% \pm 15.97\%$. Majority of the controls showed uniform distribution of the radiotracer in all four parts of the stomach. However, visually, only fundus dilatation was seen in 2/30 (6.66%) and pyloric regions dilatation was seen in 3/30 (10%) patients. A similar study was conducted by VD Aswathi *et al.* 1992, with Tc-99m SC-labeled Indian bread (Chapati), and found the mean T1/2 among 20 normal subjects to be $81.9 \pm 15.5 \text{ min}$.^[11] The difference in the mean T1/2 between the two studies indicates that gastric emptying parameter varies with test meal used, hence the test meal needs to be standardized in volunteers.

Table 5: Comparison of T1/2 between cases categorized into tertiles based on their glycated hemoglobin levels, duration of diabetes, and fasting blood sugar on the day of scan

Tertiles	Parameter	Mean values±1SD (%)	Number of patients	Mean T1/2 (min)±SD
HbA1c				
1 st tertile	5.7-7.5	6.62±0.54	14	42.78±7.22
2 nd tertile	7.5-9.8	8.64±0.67	14	44.92±12.02
3 rd tertile	10-12.8	11.2±0.80	15	44.66±12.12
Duration of diabetes				
1 st tertile	0.5-8	4.67±2.64	14	45.78±11.01
2 nd tertile	8-11	9.92±0.73	14	44.85±7.81
3 rd tertile	12-20	16.1±2.53	15	41.86±12.42
FBS on day of scan				
1 st tertile	76-111	96.78±11.63	14	47.26±10.27
2 nd tertile	112-159	132.14±13.19	14	43.23±12.05
3 rd tertile	160-384	238.53±58.94	15	41.73±8.22

FBS: Fasting blood sugar, HbA1c: Glycated hemoglobin, SD: Standard deviation

Obesity is the factor with the highest risk attributed to DM.^[3] The prevalence of obesity among Type 2 DM patients showed a significant variation in urban and rural populations. In a study conducted by Patil and Gothankar, the prevalence of obesity among urban population of Pune, Maharashtra, India, was found to be 21.43%.^[12] A similar study was conducted by Padmanabha *et al.* among rural population of Mangalore, Karnataka, India, and found the prevalence to be 15.6%.^[13] In our study, 9/43 (20.9%) cases were found to be obese (20.9%). Six cases were females and 3/9 cases were males with a female-to-male ratio of 2:1. The mean BMI of both men and women was further analyzed and found to be significantly different with $P = 0.01$.

The mean duration of diabetes was 10.28 ± 5.21 years, with no statistically significant difference between males and females. The duration of diabetes was 10 years or less in 26/43 (61.5%) cases and more than 10 years in 17/43 (39.5%). Any part of the GI system can be affected by diabetes and cause symptoms such as abdominal pain, nausea, vomiting constipation, and diarrhea. Seven cases presented with symptoms such as flatulence, hyperdefecation, and abdominal pain. Both rapid and delayed gastric emptying can occur in diabetes.^[14] Rapid gastric emptying is seen in early stages of Type 2 DM, where there is increased GI motility and hunger in patient as glucose cannot enter into cells due to insulin resistance. Delayed gastric emptying occurs at later stages when autonomic neuropathy develops due to deranged microvasculature. Clinically, it is difficult to differentiate between rapid and delayed gastric emptying based on symptoms.

In 1992, WT Phillips *et al.* conducted gastric emptying studies among 9 recently diagnosed Type II DM patients with age ranging between 32 and 62 years and compared the results with 9 healthy age-matched controls. The mean T1/2 for cases was significantly lower than controls in the

study ($P = 0.0005$). Further, cases had significantly rapid emptying at 1 h and 2 h ($P = 0.001$).^[15] Similar results were observed in a study by Linda E Watson *et al.* among 111 Type 2 DM patients, with a mean age of 64.8 years and a mean duration of diabetes of 5.5 years. In that study, diabetic patients had rapid gastric emptying compared to controls ($P = 0.0005$).^[16] Similar to these studies, in our study, the mean percentage emptying at 1 h was more in cases compared to controls, $P = < 0.01$ in our study. Although not significantly different, with $P = 0.056$, the mean T1/2 for cases was lower than that of controls. The observations of these studies further support that rapid gastric emptying can occur in early stages of Type 2 DM.

Jung *et al.* conducted a study in Minnesota, USA, from 1996 to 2006, to know the incidence and prevalence of gastroparesis among diabetic patients. The cumulative incidence was found to be 4.8% among Type 1 DM and 1% among Type 2 DM, respectively.^[17]

Somasundaram *et al.* conducted a study at Kochi, Kerala, India, using labeled rice cakes as standard test meal and found the prevalence of gastroparesis to be around 76% among 70 patients who had GI symptoms and were suspected to have diabetic gastroparesis.^[18] Anudeep *et al.* conducted a similar study with labeled rice cakes among 140 Type 2 DM patients presenting with GI symptoms at Pondicherry, India, and found the incidence of gastroparesis to be around 29%.^[19] In our study, no cases had delayed gastric emptying at 1 and 2 h according to the criteria [Figure 3]; however, 2/43 cases had delayed gastric emptying at 4 h [Figure 1]. The prevalence of gastroparesis was calculated as 4.6%. Furthermore, two cases had symptoms of flatulence and abdominal pain. Hence, the calculated prevalence of gastroparesis among symptomatic Type 2 DM was 2/7, i.e., 28.5%. These findings are similar to the observations of among symptomatic Type 2 DM patients.

8/43 cases (18.6%) in our study had visualization of large bowel by 2 h of imaging [Figure 4]. In a study by Manish

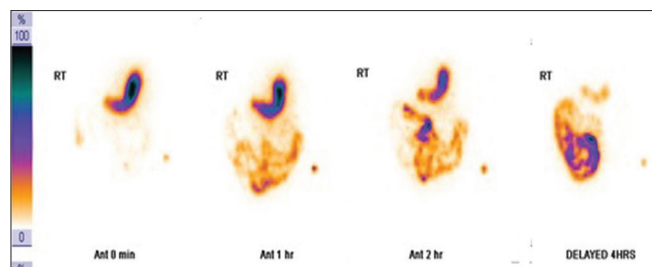


Figure 3: An asymptomatic case of Type 2 diabetes mellitus for 10 years, with Tc-99m SC-labeled meal gastric emptying study scintigraphic findings showing normal gastric emptying with immediate visualization of stomach at 0 min image, 57% emptying at 1 h, 86% emptying at 2 h, and 100% emptying by 4 h. The T1/2 in the study was 56 min

Ora *et al.*, a phenomenon called rapid gastric hurrying was described where rapid visualization of large bowel on gastric emptying scintigraphy is seen in Type 2 DM patients possibly due to early Wallerian degeneration causing vagal nerve damage.^[10]

According to a review article by Goyal *et al.*, hyperglycemia is associated with transient slow gastric emptying.^[20] Contrary to these findings, Bharucha *et al.* studied the relationship between glycemic control and gastric emptying among 30 poorly controlled Type 2 diabetic patients. They found higher fasting blood levels of glucose to be associated with rapid gastric emptying and shorter T 1/2 ($r = -0.46$; $P = 0.01$).^[21]

There was a decreasing trend in mean T1/2 among the groups with increasing FBS levels on the day of scan, although with no statistical significance ($P = 0.31$). Furthermore, FBS was found to be negatively correlating with T1/2 ($R = -0.18$), with no statistical significance ($P = 0.24$). Hayashi *et al.* conducted a study on diabetic mice and found that rapid gastric emptying can occur in Type 2 DM mice with hyperglycemia, due to hyperplasia of interstitial cells of Cajal within the gut mucosa.^[22] Similar pathophysiology could occur in humans with Type 2 DM and hyperglycemia, resulting in rapid gastric emptying.

The WHO recommends the use of HbA1c levels in the diagnosis of DM and to know the glycemic control of the patient.^[23] Izzy *et al.*, in 2017, conducted a retrospective study on correlation between HbA1c and diabetic gastroparesis among 299 patients. The patients were divided into three groups: ninety-four patients in Group A (HbA1c 6.1 ± 0.4), 131 patients in Group B (HbA1c 7.9 ± 0.5), and 74 patients in Group C (HbA1c 10.9 ± 1.6). The mean gastric retention value at 4 h was different between the three study groups, $8.3\% \pm 17$, $11.5\% \pm 19$, and $14.4\% \pm 21$, respectively ($P = 0.03$).^[24] This shows that the patients with poor glycemic control have delayed gastric emptying. In our study, we divided patient groups into tertiles based on their HbA1c levels. The mean HbA1c levels of the tertiles were 6.62 ± 0.54 , 8.64 ± 0.67 , and $11.2 \pm 0.80\%$, respectively. The mean

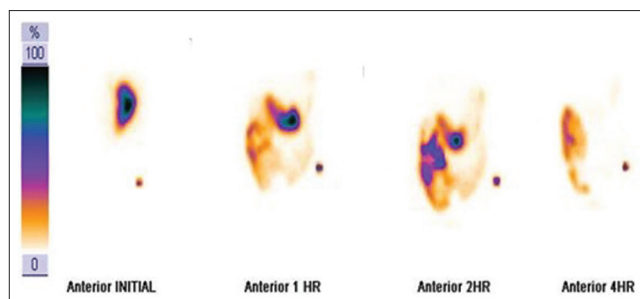


Figure 4: An asymptomatic case of Type 2 diabetes mellitus for 15 years with Tc-99m SC-labeled meal gastric emptying study scintigraphic findings showing rapid emptying with immediate visualization of stomach at 0 min image, and 91% emptying at 1 h and 100% emptying at 2 h. The T1/2 in the study was 35 min

T1/2 of the tertiles were 42.78 ± 7.22 , 44.92 ± 12.02 , and 44.66 ± 12.12 , respectively, with no statistically significant difference ($P = 0.85$). 42/43 cases showed $>90\%$ clearance by 4 h with 1/43 patient showing 89% clearance. No statistically significant association was found between gastric dysmotility and glycemic control based on HbA1c levels.

Conclusion

Radionuclide gastric emptying study, when performed with a locally prepared standard test meal, is an excellent technique for the evaluation of gastric dysmotility among Type 2 DM patients. In comparison to controls, diabetic patients showed faster gastric emptying with no correlation with duration of diabetes or HbA1c levels and a weak correlation with FBS on the day of scan. Faster gastric emptying in patients may influence satiety and directly or indirectly may affect the glycemic control. Fluctuating FBS levels in Type 2 DM patients may contribute to gastric dysmotility leading to hyperphagia and further enhancement of hyperglycemic state. However, these observations need to be verified in large patient population.

Limitations of the study

1. Small sample size, time-bound study
2. Demographic profile (age) of diabetic patients not matched with control group.

Acknowledgments

We would like to thank Sri Balaji Arogya Vara Prasadini Scheme, Sri Venkateswara Institute of Medical Sciences, for financially supporting this work. We extend our gratitude to Mr. Parthasarathi Ravi, Nuclear Medicine Technologist, Department of Nuclear Medicine, for his assistance in conducting this study.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

- Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, *et al.* Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas, 9th edition. *Diabetes Res Clin Pract* 2019;157:107843.
- Gupta A, Gupta R, Sharma KK, Lodha S, Achari V, Asirvatham AJ, *et al.* Prevalence of diabetes and cardiovascular risk factors in middle-class urban participants in India. *BMJ Open Diabetes Res Care* 2014;2:e000048.
- Deshpande AD, Harris-Hayes M, Schootman M. Epidemiology of diabetes and diabetes-related complications. *Phys Ther* 2008;88:1254-64.
- Aggarwal S, Tonpay PS, Trikha S, Bansal A. Prevalence of autonomic neuropathy in diabetes mellitus. *Curr Neurobiol* 2011;2:101-5.
- Vinik AI, Maser RE, Mitchell BD, Freeman R. Diabetic autonomic neuropathy. *Diabetes Care* 2003;26:1553-79.
- Chojnowski M, Kobylecka M, Olesińska M. Esophageal transit scintigraphy in systemic sclerosis. *Reumatol Clin* 2016;54:251-5.
- Saleh CM, Smout AJ, Bredenoord AJ. The diagnosis of gastro-esophageal reflux disease cannot be made with barium esophagograms. *Neurogastroenterol Motil* 2015;27:195-200.
- Bharucha AE, Camilleri M, Veil E, Burton D, Zinsmeister AR. Comprehensive assessment of gastric emptying with a stable isotope breath test. *Neurogastroenterol Motil* 2013;25:e60-9.
- Abell TL, Camilleri M, Donohoe K, Hasler WL, Lin HC, Maurer AH, *et al.* Consensus recommendations for gastric emptying scintigraphy: A joint report of the American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine. *Am J Gastroenterol* 2008;103:753-63.
- Ora M, Nazar AH, Parashar A, Kheruka S, Gambhir S. Gastric emptying scintigraphy: Beyond numbers – An observational study to differentiate between various etiologies and a step toward personalized management. *Indian J Nucl Med* 2019;34:194-200.
- Awasthi VD, Sewatkar AB, Gambhir S, Mittal B, Das BK. Gastric emptying in normal adult males: A radionuclide study. *Indian J Pharmacol* 1992;24:238-40.
- Patil R, Gothankar J. Risk factors for type 2 diabetes mellitus: An urban perspective. *Indian J Med Sci* 2019;71:16-21.
- Padmanabha UR, Nalam U, Badiger S, Nagarajaiah P, Rani U. Prevalence and risk factors of type 2 diabetes mellitus in the rural population of Mangalore, South India. *Natl J Community Med* 2017;8:456-61.
- Verne GN, Sninsky CA. Diabetes and the gastrointestinal tract. *Gastroenterol Clin North Am* 1998;27:861-74, vi-vii.
- Phillips WT, Schwartz JG, McMahan CA. Rapid gastric emptying of an oral glucose solution in type 2 diabetic patients. *J Nucl Med* 1992;33:1496-500.
- Watson LE, Xie C, Wang X, Li Z, Phillips LK, Sun Z, *et al.* Gastric emptying in patients with well-controlled type 2 diabetes compared with young and older control subjects without diabetes. *J Clin Endocrinol Metab* 2019;104:3311-9.
- Jung HK, Choung RS, Locke GR 3rd, Schleck CD, Zinsmeister AR, Szarka LA, *et al.* The incidence, prevalence, and outcomes of patients with gastroparesis in Olmsted County, Minnesota, from 1996 to 2006. *Gastroenterology* 2009;136:1225-33.
- Somasundaram VH, Subramanyam P, Palaniswamy SS. A gluten-free vegan meal for gastric emptying scintigraphy: Establishment of reference values and its utilization in the evaluation of diabetic gastroparesis. *Clin Nucl Med* 2014;39:960-5.
- Anudeep V, Vinod KV, Pandit N, Sharma VK, Dhanapathi H, Dutta TK, *et al.* Prevalence and predictors of delayed gastric emptying among Indian patients with long-standing type 2 diabetes mellitus. *Indian J Gastroenterol* 2016;35:385-92.
- Goyal RK, Cristofaro V, Sullivan MP. Rapid gastric emptying in diabetes mellitus: Pathophysiology and clinical importance. *J Diabetes Complications* 2019;33:107414.
- Bharucha AE, Kudva Y, Basu A, Camilleri M, Low PA, Vella A, *et al.* Relationship between glycemic control and gastric emptying in poorly controlled type 2 diabetes. *Clin Gastroenterol Hepatol* 2015;13:466-76.e1.
- Hayashi Y, Toyomasu Y, Saravanaperumal SA, Bardsley MR, Smestad JA, Lorincz A, *et al.* Hyperglycemia increases interstitial cells of Cajal via MAPK1 and MAPK3 signaling to ETV1 and KIT, leading to rapid gastric emptying. *Gastroenterology* 2017;153:521-35.e20.
- American Diabetes Association. Diagnosis and classification of diabetes mellitus. *Diabetes Care* 2014;37:81-90.
- Izzy M, Lee M, Johns-Keating K, Kargoli F, Beckoff S, Chun K, *et al.* Glycosylated hemoglobin level may predict the severity of gastroparesis in diabetic patients. *Diabetes Res Clin Pract* 2018;135:45-9.