

Reduced Gallbladder Emptying in Diabetic (NIDDM) Patients Evaluated by Cholescintigraphy and Ultrasonography

Ali J, Ahmed A, Memon R

Nuclear Institute of Medical Radiotherapy (NIMRA), Jamshoro Pakistan

Abstract

Non-insulin-dependent diabetes mellitus (NIDDM) is considered to predispose impaired gallbladder emptying and an increased prevalence of gallbladder diseases. The aim of the current study was to study the gallbladder emptying in diabetic (NIDDM) patients by quantitative ultrasonography and cholescintigraphy using Tc-99m DISIDA. Twenty-four diabetic patients and five control subjects underwent ultrasonography and cholescintigraphy, and gallbladder ejection fractions (GBEF%) were calculated by both techniques after 30 min of taking standard fatty meal. Mean GBEF (ultrasonography/cholescintigraphy) values were found to be reduced in diabetic patients as compared to control subjects ($41.9 \pm 11.1\%$ / 49.2 ± 14.5 Vs 54.2 ± 8.7 / $63.8 \pm 7.5\%$). The difference between the groups was statistically significant ($p < 0.05$). No statistically significant difference was found in GBEF values between longer versus shorter disease duration of NIDDM patients and poor versus good blood sugar control of NIDDM patients. We concluded that gallbladder emptying was reduced in diabetic patients & did not relate to duration & control of diabetes.

Keywords: Gallbladder Emptying, Diabetes mellitus, Cholescintigraphy, Ultrasonography

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Introduction

Diabetes is the single most important metabolic disease, which can affect nearly every organ system in the body. Gastrointestinal manifestations of diabetes mellitus are recognized to be an important cause of morbidity in diabetics (1). They include dysphagia, gastroparesis, constipation, nocturnal diarrhea and gallbladder dysfunction. (2, 3). Various studies have reported an increased prevalence of gallbladder disease in diabetic patients (4-6). This has been attributed to impaired gallbladder contraction, commonly seen in diabetics (7).

The use of cholescintigraphy and ultrasonography, combined with exogenous cholecystokinin infusion or ingestion of well defined fatty meal, to determine GBEF are non invasive methods of studying biliary dynamics and gallbladder motility (8).

The aim and objective of the current study was to observe gallbladder emptying in patients with non-insulin dependent diabetes mellitus (NIDDM) by quantitative cholescintigraphy (Tc-99m DISIDA) and ultrasonography by using standard fatty meal, and compare it with control subjects. Our study is important in the sense that: there are few studies in which gallbladder function in diabetics was assessed by both cholescintigraphy & ultrasonography at the same time. Further more diabetics patients were evaluated as whole in the large number of studies and cholecystokinin was used instead of fatty meal as gallbladder contraction stimulant.

Materials and Methods

The study was conducted at NIMRA Jamshoro in age, sex and weight matched twenty four diabetic (NIDDM) patients and five control subjects. Control subjects consisted of five male subjects (mean age 45.4 ± 7). Inclusion criteria for control subjects were absence of gastrointestinal disorders, cholelithiasis and diabetes mellitus.

The patient group consisted of 24 male patients (mean age 47.2 ± 6.2). Inclusion criteria for patient group were diagnosed cases of NIDDM. The following patients were considered diabetic having;

- Fasting plasma glucose level of 126mg/dl and/or
- 2h post prandial plasma glucose level of 200 mg/dl on more than one occasion

Patients having IDDM, hepatobiliary disorders (e.g. liver cirrhosis, cholelithiasis), gastrointestinal functional

Correspondence:

Dr. Jawad Ali

Assistant Professor

Nuclear Institute of Medical Radiotherapy (NIMRA)

Jamshoro Pakistan

E-mail: jawad_nimra@yahoo.com

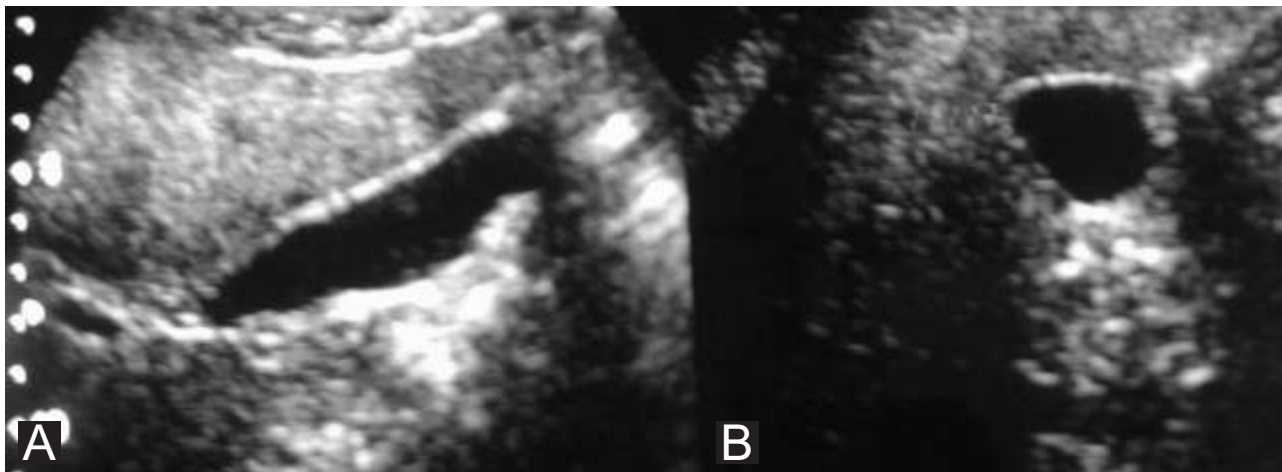


Figure 1. Ultrasonographic Gallbladder Image (A) Longitudinal Section and (B) Transverse Section

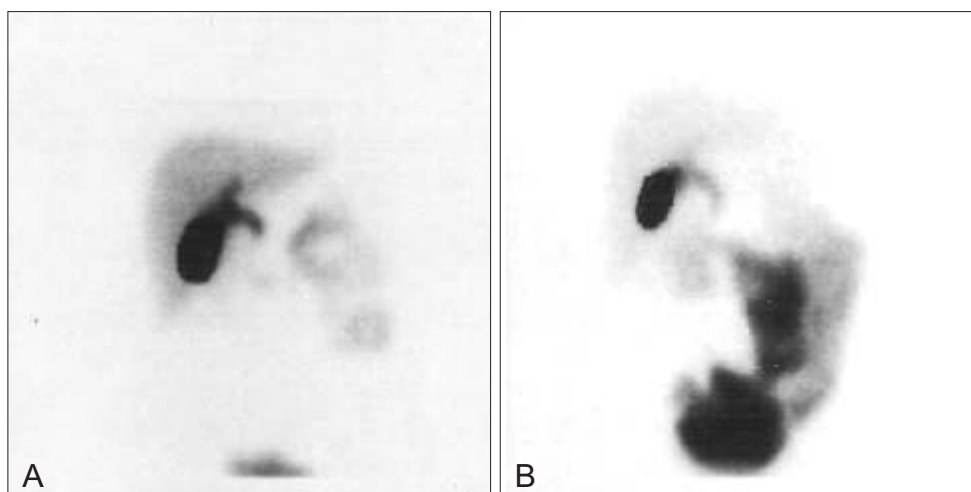


Figure 2. Cholescintigraphy Image of Gallbladder (A) Before Fatty Meal (B) After Fatty Meal (30min)

disorders (e.g., irritable bowel disease) and patients taking drugs that alter hepatobiliary function. (e.g., morphine, erythromycin), were excluded.

Each study subject was evaluated through detailed history, clinical examination and relevant investigations, i.e., LFT and blood sugar (fasting & random). The procedure was briefed to the patient and informed consent was taken. Each study subject was called for two days in fasting of 10 to 12 hours. On the first day ultrasonography and on the second day cholescintigraphy was performed.

Gallbladder volumes were estimated from the ultrasound images in fasting state and after 30 minutes of taking standard fatty meal (post prandial). The fatty meal was consisting of two bread slices, an egg and & 250 ml of milk (16gm fat, 19gm proteins, 37gm carbohydrates and 266 kcal). The gallbladder volume was estimated using a real time ultrasound system (Nemio-20, Toshiba) with a 3.5 MHz transducer using the ellipsoid method which is given by;

$$GBV = 0.52 \times L \times W \times H \quad (1)$$

Where “L” is the greatest length, “W” greatest transverse width, and “H” antero-posterior diameter of gallbladder.

The largest longitudinal and transverse gallbladder images

were recorded with the subjects lying supine or turned partially on their sides (Figure 1). The percentage of gallbladder emptying (ejection fraction GBEF) was calculated as follows:

$$GBEF (\%) = \frac{\text{Fasting GB volume} - \text{Post-prandial GB volume}}{\text{Fasting GB volume}} \times 100 \quad (2)$$

Cholescintigraphy was performed in fasting state on the second day. 148 MBq (4mCi) of Tc-99m DISIDA was injected intravenously and images were taken at every 5 minutes for 1 hour in anterior projection under large field of view gamma camera (ECAM- Siemens) equipped with leap collimator. This was followed by ingestion of the standard fatty meal and all study subjects then underwent imaging for an additional view after 30 min of taking fatty meal. The GBEF (%) was calculated by icon soft ware using the following formula;

$$GBEF (\%) = \frac{\text{Fasting GB counts} - \text{Post-prandial GB counts}}{\text{Fasting GB counts}} \times 100 \quad (3)$$

Gallbladder counts were measured by drawing visually

Sr. No.	DD (Years)	HBA _{1c}	U Sound EF (%)	Cholescint: EF (%)
CONTROL SUBJECTS				
1	NA	NA	55	76
2	=	=	43	84
3	=	=	63	71
4	=	=	62	90
5	=	=	48	61
Mean ± std			54.2 ± 8.7	63.8 ± 7.5
DIABETIC PATIENTS				
1	1	8	60	50
2	5	7.9	59	41
3	4	7.8	47	20
4	1	7.4	51	71
5	5	7.1	27	60
6	1	7	41	65
7	5	6.4	37	56
8	2	7.5	49	58
9	5	7.4	27	60
10	3	6.5	29	25
11	1	6.2	27	40
12	5	6.2	62	53
13	2	13	42	46
14	5	12.8	42	48
15	2	11.2	51	46
16	8	11	40	22
17	10	10.9	33	66
18	6	10.6	43	58
19	7	9.5	38	48
20	12	9	47	59
21	14	11.6	27	26
22	8	10.8	40	66
23	8	9.7	30	56
24	7	8.8	57	41
Mean ± std			41.9 ± 11.1	49.2 ± 14.5

Table 1. Gallbladder Ejection Fraction (%) in control subjects and all Study Patients

tight region of interest (ROI) over gallbladder activity on computer display images acquired at 1 hour of the administration of Tc-99m DISIDA and at 30 min after breaking fast (Figure 2). Mean and Standard deviation (STD) for every result was calculated. The statistical difference between the groups was analyzed using student's t-test for unpaired value. P value < 0.05 was considered significant. Results obtained by both techniques were compared and correlated with duration and control of diabetes.

Results

Gallbladder ejection fraction values determined by US and Radionuclide cholescintigraphy in control subjects varied between 43-63% (54.2±8.7) and 53-73% (63.8±7.5) respectively. In diabetic patients these values were 27-62% (41.9±11.1) and 20-71% (49.2±14.5) respectively (Table 1). The difference between the groups was statistically significant (Figure-3).

When diabetic patients were categorized on the basis of diabetic duration and blood sugar control, no statistically significant difference was found in GB EF (cholescintigraphy/ultrasonography) values between longer versus shorter duration of diabetic patients and good

versus poor blood sugar control diabetic patients (p < 0.05). Gallbladder ejection fraction values calculated by cholescintigraphy shows higher values than that by ultrasonography, but the difference were not statistically significant.

Discussion

Various studies have reported that gallbladder emptying was reduced in diabetic patients (9-11). Two major factors have been suggested for this abnormality; autonomic neuropathy and hyperglycemia. (12, 13)

The vagus nerve stimulation and cholecystokinin (CCK) in plasma are the main factors causing the contraction of gallbladders (14, 15). The failure of the gallbladder to respond to a meal may be due to impaired cholinergic innervations seen in diabetic patients (16). Other possible explanation for the impaired gallbladder contraction in diabetics includes decreased post-prandial cholecystokinin release, decreased sensitivity of gallbladder smooth muscle to CCK and decreased number of CCK receptors in the gallbladder wall (17, 18).

Both cholecystokinin (Sinicalide) and fatty meals have been used to induce gallbladder contraction enabling the gallbladder ejection fraction (GBEF) to be estimated during

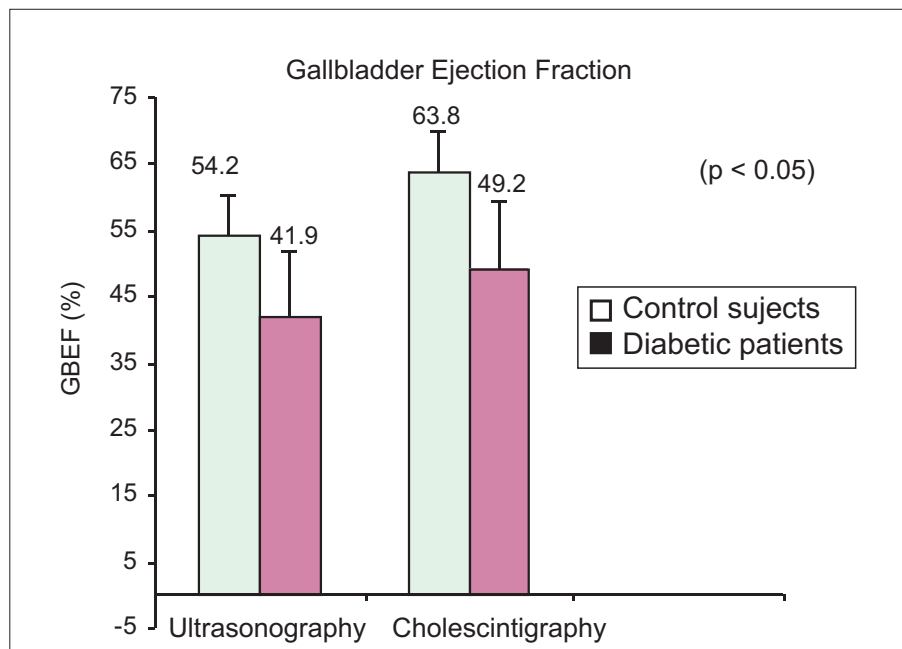


Figure-3. Mean Gallbladder Ejection Fraction (%) in Controls & Diabetics

ultrasonography and cholescintigraphy studies. In this study we have used standard fatty meal (an egg, 240ml of milk and 2 slices of bread). Dried egg yolk and milk also have been studied in large number of studies & clear methodology determined (19,20). The fatty meal has certain advantages over the conventional CCK; (a) being more physiological (b) cheap & widely available (c) having more progressive and consistent effect (d) side effects (bradycardia, hypotension, nausea and abdominal pain) observed with CCK, are not seen (21). We found our standard fatty meal to be an effective cholecystagogue and free of side effects.

We have demonstrated that gallbladder emptying was significantly less at 30 min after standard fatty meal in diabetic patients as compared to normal subjects assessed by ultrasonography and cholescintigraphy. Our results are in concurrence with that of Shreiner et al (22) in cholescintigraphy and PG Raman et al (23) in ultrasonography.

However the results of studies of gallbladder function in diabetic patients have not been consistent (24). Kronerl et al (25) reported no statistically significant difference between controls and diabetic patients. Variation in results was due to heterogeneity in the patients studied, emptying stimulus and method used to assess gallbladder function (26).

No correlation was found between GBEF values determined by ultrasonography & cholescintigraphy. This may be due to entirely different methods used to assess gallbladder kinetics.

In conclusion, the standard fatty meal was found to be effective gallbladder contraction stimulant & gallbladder ejection fraction is reduced in diabetic patients assessed by ultrasonography & cholescintigraphy

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