

Real-Time Ultrasonography for Gallbladder Volume Assessment in Type 2 Diabetes Mellitus Patients

Chandan Kishore¹, Ratna Priya²

¹MD, FRCR, Associate Professor, Department of Radiology, Narayan medical college & Hospital, Jamuhar, Sasaram, Bihar, India.

²MD, Assistant Professor, Department of Biochemistry, Patna Medical College & Hospital, Patna, Bihar, India.

Received: 13-04-2021 / Revised: 26-05-2021 / Accepted: 20-06-2021

Corresponding author: Dr. Ratna Priya

Conflict of interest: Nil

Abstract

Aim: The aim of the present study to evaluate the Gall Bladder Volume in Type 2 Diabetes Mellitus Patients Using Real Time Ultrasonography. **Methods:** A cross-sectional prospective study was conducted in the Department of Radiology, Narayan medical college & Hospital, Jamuhar, Sasaram, Bihar, India, for 1 year. Among 110, 55 were type 2 diabetes mellitus patients with duration of 5 years or more, with diabetic complications are included as cases and 50 age and sex matched healthy controls. Autonomic neuropathy was assessed by the presence of symptoms like dysphagia, abdominal fullness, nausea, vomiting, diarrhea, fecal incontinence, urinary incontinence, gustatory sweating, impotence etc. Under aseptic conditions, 3ml fasting blood samples were collected from all the subjects and used for the estimation of fasting blood sugar, post prandial blood sugar. **Results:** The mean age of the T2DM patients was 43.88 ± 4.98 and in the healthy controls 49.88 ± 5.69 ($p=0.42$). In the cases, 36 were males and 19 were females and in the control group 38 were males and 17 were females. In the present study, BMI ($25.88 \pm 2.41 \text{kg/m}^2$), FBS ($161.88 \pm 28.09 \text{mg/dl}$), PPBS ($245.41 \pm 39.01 \text{mg/dl}$), Fasting gall bladder volume ($34.43 \pm 6.52 \text{cm}^3$), post fatty meal gall bladder volume ($16.31 \pm 6.49 \text{cm}^3$), ejection fraction ($50.44 \pm 18.39 \text{cm}^3$) were significantly increased in type 2 diabetes mellitus patients compared with healthy controls. T2DM patients were also subdivided broadly into without complications and those with diabetic complications. T2DM patients without diabetic complications were reported in 28 (50.91%) patients. Peripheral neuropathy was observed in 12(21.82%), peripheral neuropathy & Autonomic neuropathy was reported in 10 (18.18%) cases. In the present study, fasting GB Volume (cm^3), post fatty meal GB Volume (cm^3) and ejection fraction (%) were compared between the T2DM patients without complications and with complications. The fasting GB Volume (cm^3) was not statistically significant between two groups ($p=0.223$). The post fatty meal gallbladder volume (cm^3) was statistically significant between the two groups ($p<0.001$). **Conclusion:** Ultrasound evaluation of gall bladder volume (fasting and post-prandial) and Ejection Fraction are efficient parameters to evaluate gallbladder function. Gallbladder function should be evaluated routinely in T2DM patients as incomplete gallbladder emptying may lead to gallstone formation and associated complications. Further studies with large sample size are recommended.

Keywords: Diabetes Mellitus, Gall Bladder, Ultrasound

This is an Open Access article that uses a fund-ing model which does not charge readers or their institutions for access and distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>) and the Budapest Open Access Initiative (<http://www.budapestopenaccessinitiative.org/read>), which permit unrestricted use, distribution, and reproduction in any medium, provided original work is properly credited.

Introduction

Since long time diabetes mellitus is one of the most common endocrine disorder and now a day it is on the rise due to advancing modern lifestyle; characterised by multiple metabolic abnormalities which leads to long term multi organ complications involving hepatobiliary system, kidneys, gastrointestinal tract, nerves, and blood vessels, thereby causing serious morbidity and mortality. Few previous studies had pointed towards an increased prevalence of gall bladder dysfunctions and its complications in diabetics[1-3]. Those have been attributed to cholecystomegaly and impaired motility of gall bladder, mainly due to autonomic neuropathy commonly seen in chronic diabetics. Though prolonged bile stasis is the most important factor for gallstone formation but other risk factors i.e. age, sex, obesity, genetic predisposition, drugs, parity, diet, hyperlipidaemia, and ileal resection also contribute in it[4]. This study was undertaken to compare gall bladder volumes in chronic diabetics and controls. Ultrasonography is preferred modality of choice to assess gall bladder volume because it is safe, non-invasive, less expensive, less time consuming, and accurate. This study was also intended to correlate gall bladder volume in patients of chronic diabetes with other parameters of patient like age, sex, body mass index (BMI), parity and hyperlipidaemia. In addition to different manifestations in many other systems of body, autonomic neuropathy is responsible to various manifestations in the gastrointestinal tract such as nocturnal diarrhoea, oesophageal dysmotility, gastropathies, constipation and gallbladder dysfunction which is consequence of vagal neuropathy and leads to decreased gastrointestinal motility. The duration of diabetes mellitus has significant positive correlation with prevalence of gallbladder disease. Type of therapy for treatment has no significant association and the fasting plasma glucose level is inversely associated with gall bladder disease[5]. Involvement of gall

bladder in diabetic autonomic neuropathy is usually manifested in the form of higher incidence of gall stones and a significant increase in gall bladder volume[6] with poor concentration and poor visualization, with lack of symptoms of gallbladder disease[7]. The present study has aim to find out the prevalence of gallbladder diseases in patients of type 2 chronic diabetes, correlation in duration of diabetes with gall bladder disease and comparison of gallbladder dysfunction in patients with and without autonomic neuropathy as well as normal individuals. Reduced gall bladder motility in chronic diabetics due to autonomic neuropathy together with hypertriglyceridemia and obesity is a major risk factor for cholelithiasis[8-10]. Gall bladder emptying is controlled by both, sympathetic and parasympathetic nervous system where parasympathetic system controls contractility and sympathetic system controls relaxation. Reduced motility of gall bladder is attributed to dysfunction of autonomic nervous system dysfunction and defective response to gastrointestinal hormones e.g. cholecystokinin, motilin and secretin[11].

Materials and Methods

A cross-sectional prospective study was conducted in the Department of Radiology, Narayan medical college & Hospital, Jamuhar, Sasaram, Bihar, India, for 1 year, after taking the approval of the protocol review committee and institutional ethics committee.

Methodology

110 patients were included. Among them, 55 were type 2 diabetes mellitus patients with duration of 5 years or more, with diabetic complications are included as cases and 50 age and sex matched healthy controls. A detailed medical history, presenting complaints, duration of diabetes mellitus, family history of diabetes mellitus, mode of treatment, exercise, diet, oral hypoglycemics, insulin, whether the treatment was regular, and history of

diabetic complications were recorded. All the study subjects were underwent detailed general and systemic examinations. Peripheral neuropathy was assessed by presence of tingling and numbness in the palms and soles. Autonomic neuropathy was assessed by the presence of symptoms like dysphagia, abdominal fullness, nausea, vomiting, diarrhea, fecal incontinence, urinary incontinence, gustatory sweating, impotence etc. Under aseptic conditions, 3ml fasting blood samples were collected from all the subjects and used for the estimation of fasting blood sugar, post prandial blood sugar.

Gall bladder volume evaluation in fasting and 45 minutes post prandial (standardized fatty meal) state were done in type 2 diabetes mellitus patients and controls using real time ultrasound. Patients who have undergone previous cholecystectomy, acute or chronic hepatocellular disease and liver cirrhosis, patients with jaundice, gall bladder anomalies or diseases were excluded. Informed consent of the patients and controls were obtained and confidentially maintained. Gall bladder was evaluated by Affinity 50 - Phillips. Gall bladder volume was measured in fasting T2DM patients and in control subjects. Gallbladder volume was again measured in post prandial (standardized fatty meal) state in T2DM patients and controls.

Statistical analysis

Independent student 't' test was used to test the significance in both type 2 diabetes mellitus patients and control subjects. $p < 0.05$ was considered as statistically significant. Data analysis was carried out using Statistical Package for Social Science (SPSS), Version 22.0

Results

In the present study, 55 type 2 diabetes mellitus patients as cases and 55 healthy subjects underwent sonographic evaluation of the gallbladder volume in both fasting state and post prandial (after standardized fatty meal) state. Laboratory parameters like fasting blood sugar and post prandial blood sugar were measured in all the subjects. In this study, mean age of the T2DM patients was 43.88 ± 4.98 and in the healthy controls 49.88 ± 5.69 ($p=0.42$). In the cases, 36 were males and 19 were females and in the control group 38 were males and 17 were females. In the present study, BMI ($25.88 \pm 2.41 \text{ kg/m}^2$), FBS ($161.88 \pm 28.09 \text{ mg/dl}$), PPBS ($245.41 \pm 39.01 \text{ mg/dl}$), Fasting gall bladder volume ($34.43 \pm 6.52 \text{ cm}^3$), post fatty meal gall bladder volume ($16.31 \pm 6.49 \text{ cm}^3$), ejection fraction ($50.44 \pm 18.39 \text{ cm}^3$) were significantly increased in type 2 diabetes mellitus patients compared with healthy controls as shown in (Table 1).

In the study group, T2DM patients were also subdivided broadly into without complications and those with diabetic complications. T2DM patients without diabetic complications were reported in 28 (50.91%) patients. Peripheral neuropathy was observed in 12 (21.82%), peripheral neuropathy & Autonomic neuropathy was reported in 10 (18.18%) cases as shown in (Table 2). In the present study, fasting GB Volume (cm^3), post fatty meal GB Volume (cm^3) and ejection fraction (%) were compared between the T2DM patients without complications and with complications. The fasting GB Volume (cm^3) was not statistically significant between two groups ($p=0.223$). The post fatty meal gallbladder volume (cm^3) was statistically significant between the two groups ($p < 0.001$). The ejection fraction (%) difference observed in the mean value between the two groups was statistically significant with a $p < 0.02$ (Table 3 & 4).

Table 1: Comparison of BMI, FBS, PPBS, FGBV, PPGVB between T2DM & Controls

Parameters	T2DM Cases (n=55) Mean±SD	Controls (n=45) Mean±SD	P Value
Body Mass Index (Kg/m ²)	25.88±2.41	23.61±3.66	0.001
Fasting Blood Sugar (mg/dl)	161.88±28.09	93.72±7.79	0.000
Post Prandial Blood Sugar(mg/dl)	245.41±39.01	116.39±5.64	0.001
Fasting Gall bladder volume(cm ³)	34.43±6.52	30.13±6.40	0.000
Post Fatty Meal GB Volume(cm ³)	16.31±6.49	8.98±8.25	0.000
Ejection Fraction (cm ³)	50.44±18.39	77.23±5.88	0.012

Table 2: T2DM patients without and with diabetic complications

Number (%)		
Without Complications	28	50.91
Peripheral Neuropathy	12	21.82
Peripheral Neuropathy + Autonomic Neuropathy	10	18.18
Peripheral Neuropathy + Retinopathy	1	1.82
Peripheral Neuropathy + Diabetic Nephropathy	2	3.64
Peripheral Neuropathy + Autonomic Neuropathy + IHD	1	4.82
Peripheral Neuropathy + Diabetic Nephropathy +post renal transplant	1	1.82

Table 3: T2DM Patients without and with diabetic complications

Parameter		No.	Mean	St. deviation	Minimum	Maximum
Fasting *GBV	Without Complication	28	30.12 cm ³	6.65	18.10 cm ³	41.50 cm ³
	With Complication	27	32.19 cm ³	6.21	25.20 cm ³	46.80 cm ³
Post Fatty Meal *GBV	Without Complication	28	13.38 cm ³	5.74	4.30 cm ³	26.00 cm ³
	With Complication	27	19.38 cm ³	5.69	5.55 cm ³	30.30 cm ³
Ejection Fraction	Without Complication	28	57.81 cm ³	16.120	31.20cm ³	82.00 cm ³
	With Complication	27	42.53 cm ³	16.13	16.00 cm ³	83.00 cm ³

Table 4: Independent Samples Test of T2DM patients without and with diabetic complications

Independent Samples Test	Student 't' test	Df Degree of freedom	P value
Fasting *GBV	-1.116	42.87	0.223
Post Fatty Meal *GBV	-3.542	42.88	0.001
Ejection Fraction	3.338	42.97	0.002

Discussion

Late complications of Diabetes mellitus are a major source of morbidity and mortality. Diabetics in particular those with T2DM have an increased prevalence of gallstones[12]. Diabetic subjects are

reported to have a two to three fold increase in the prevalence of cholesterol gall stones[13]. Chapmann et al. conducted a large study involving 271 diabetic subjects, reported that there is increased incidence of cholesterol gallstones in

T2DM patients. A highly significant increase in gall bladder volume was also observed in T2DM group. Conventional real time ultrasonography is a simple non-invasive investigation for evaluation of gall bladder volume. In a similar study C. GAUR et al who examined 40 patients of NIDDM, 10 patients of IDDM and 50 healthy controls, found that patients with NIDDM had statistically significant larger fasting gall bladder volume and these values were highly significant amongst patients with autonomic neuropathy. They also had significant larger post fatty meal gallbladder volume and these values were high in patients with autonomic neuropathy[14]. In a study by PG Raman et al[13], who studied 50 NIDDM patients and 30 controls, found that 32% of diabetic patients had ultrasonographic evidence of gallstones as compared to 6.7% in healthy controls. They also found that mean fasting gall bladder volume was significantly increased in diabetic patients (26 cm³) as compared to control population (15.8cm³). Furthermore, mean fasting gallbladder volume of diabetic patients with gallbladder disorders (28.1 cm³) was found to be significantly larger than that of those patients without gallbladder disorder (24.6 cm³) Mean percentage of contractions (Ejection fraction) of gallbladder 60 minutes after fatty meal was reduced in diabetic patients (53%) and it was further reduced in the patients with gall bladder disorder (41.8 %). Mean duration of diabetes was significantly longer in diabetic patients with gallbladder disorder. In a study by Agarwal AK et al., reported that mean fasting gallbladder volume in T2DM was 25.87 ±13.90 ml, with a minimum value of 9.30 ml and maximum value of 88 ml and higher gallbladder volumes were seen in patients with autonomic neuropathy[15]. In a study by CA Ugbaja et al., reported that diabetic patients with neuropathy have significant abnormalities of gall bladder function, presumably due to autonomic nerve dysfunction. These patients also have a higher prevalence of gallstones,

suggesting that ultrasound screening may be useful[16]. In a study conducted by Garjesh S. Rai et al., observed that higher fasting gall bladder volume and reduced percentage of contraction in T2DM patients attributed to autonomic neuropathy. Suggested that, hepatobiliary ultrasonography in chronic diabetics can be used as screening tool for early diagnosis of complication and to avoid its serious consequences when presents in emergency and undergone for surgery[17]. In our study the fasting GB Volume (cm³) difference was not statistically significant between T2DM patients without complications and T2DM patients with complications, but there was significant difference between the two in the post fatty gallbladder volume with a mean value of 13.38 cm³ in patients without complications and a mean value of 19.38 cm³ in patients with complications. Furthermore, percentage of ejection fraction showed significant difference with a mean value of 58% in patients without complications and a mean value of 42 % in patients with complications. There was significant difference in fasting gallbladder volume between the T2DM patients and the control group with a p< 0.001. Our study results matched the previous studies demonstrating the increased fasting GB Volume, post fatty meal GB Volume and decreased ejection fraction in the T2DM patients[13,14]. Longer the mean duration of T2DM, there was an increase in the mean fasting GB Volume and decrease in ejection fraction (%). In our study we also found there was a significant difference in Body Mass Index (BMI) between the T2DM patients and control group with a p<0.001.

It is known that patients with diabetes often develop cholelithiasis and gall bladder stasis is considered to be one of the causes[14]. Stasis leads to lithogenicity of bile and incomplete gall bladder emptying leading to sequestration of cholesterol and nidus formation, thereby predisposing to gallstone formation. The

mechanism responsible for cholecystoparesis is attributed to vagal neuropathy.

Conclusion

Ultrasound evaluation of gall bladder volume (fasting and post-prandial) and Ejection Fraction are efficient parameters to evaluate gallbladder function. Gallbladder function should be evaluated routinely in T2DM patients as incomplete gallbladder emptying may lead to gallstone formation and associated complications. Further studies with large sample size are recommended.

Reference

1. Agarwal AK, Miglani S, Singla S, Garg U, Dudeja RK, Goel A. Ultrasonographic evaluation of gall bladder volume in diabetics. *JAPI*. 2004; 52:962-5.
2. Gitelson J, Schwartz A, Frankel M. Gallbladder dysfunction in diabetes mellitus. The diabetic neurogenic gallbladder. *Diabetes*. 1963; 12:308-12.
3. Singh S, Chander R, Singh A, Mann S. Ultrasonographic evaluation of gall bladder diseases in diabetes mellitus type 2. *Indian Journal of Radiology and Imaging*. 2006;16(4):505.
4. Shaffer EA. Epidemiology of gallbladder stone disease. *Best Practice & Research Clinical Gastroenterology*. 2006;20(6):981-96.
5. Haffner SM, Diehl AK, Valdez R, Mitchell BD, Hazuda HP, Morales P, et al. Clinical Gallbladder Disease in NIDDM Subjects: Relationship to duration of diabetes and severity of glycemia. *Diabetes Care*. 1993;16(9):1276-84.
6. Chapman BA, Chapman TM, Frampton CM, Chisholm RJ, Allan RB, Wilson IR, et al. Gallbladder Volume (Comparison of Diabetics and Controls). *Digestive diseases and sciences*. 1998;43(2):344-8.
7. Palasciano G, Portincasa P, Belfiore A, Baldassarre G, Cignarelli M, Paternostro A. Gallbladder volume and emptying in diabetics: the role of neuropathy and obesity. *Journal of internal medicine*. 1992;231(2):123-7.
8. Ewing DJ, Clarke BF. Diagnosis and management of diabetic autonomic neuropathy. *British medical journal (Clinical research ed.)*. 1982;285(6346):916.
9. Kayacetin E, Kisakol G, Kaya A, Akpınar Z. Realtime sonography for screening of gallbladder motility in diabetic patients: relation to autonomic and peripheral neuropathy. *Neuroendocrinology Letters*. 2003;24(1/2):73-6.
10. Everson GT, Braverman DZ, Johnson ML, Kern F. A critical evaluation of real-time ultrasonography for the study of gallbladder volume and contraction. *Gastroenterology*. 1980;79(1):40-6.
11. Jorgensen T. Gall stones in a Danish population. Relation to weight, physical activity, smoking, coffee consumption, and diabetes mellitus. *Gut*. 1989;30(4):528-34.
12. Chapman TMBA, Chapman CM, Frampton RJ, Chisholm RB, Allan IR, Wilson. Gallbladder volume comparison of diabetic standard controls. *Digestive DisSci*. 1998;43(2):344-348.
13. Raman PG, Patel A, V M. Gall bladder disorder and Type 2 diabetes mellitus. A clinical based study. *J Assoc Phys India*. 2002;50:887-890
14. Gaur C, Mathur, Agarwal A, Verma K, Jain R, Swaroop A. Diabetic autonomic neuropathy causing gallbladder dysfunction. *J Assoc Phys India*. 2000; 48:603-605.
15. Agarwal AK, Miglani S, Singla S, Garg U, Dudeja RK, Goel A. Ultrasonographic evaluation of gallbladder volume in diabetics. *J Assoc Physicians India*. 2004; 52:962-967.
16. Ugbaja CA, Ayoola RTOO, Ikem BM, Idowu. Gall bladder volume and contractility in type 2 diabetes

- mellitus. Afr J Diabetes Med. 2015;23(2):9–12.
17. Rai G, Baghel V, Rai T, Vyas M. Gall bladder dysfunction in chronic diabetics (type 2): an ultrasonography based prospective study. Int J Res Med Sci. 2016;4(2):390– 397