



ULTRASONOGRAPHIC EVALUATION OF GALLBLADDER VOLUME IN TYPE 2 DIABETICS AND ITS CORRELATION WITH AUTONOMIC NEUROPATHY

Dr. Vishal gupta, Dr. Sureshkumar yadav & Dr. Shrikant sharma

S M S Medical College and Hospital, Jaipur, Rajasthan, India.

ABSTRACT

Aims and Objective: Ultrasonographic determination of gallbladder volume in type 2 diabetics with 5 to 10 year duration and it's comparison with a control group, and correlation of gallbladder volume in type 2 diabetics with autonomic neuropathy. **Materials and Method:** Fifty cases of diabetes mellitus and 50 healthy controls were recruited for the study. A detailed history and physical examination were recorded. Laboratory investigations done were - fasting and postprandial blood sugar, glycosylated haemoglobin, and serum lipid profile. Autonomic neuropathy was determined by using simple non-invasive bedside tests. Fasting gallbladder volume was measured by ultrasonography (calculated by ellipsoid formula). **Results:** The mean fasting gall bladder volume has been detected as 29.20 ± 12.74 ml in diabetics with a minimum value of 10 and maximum value of 78 ml. and 17.50 ± 2.206 ml in control subjects. When type 2 diabetics were subgrouped according to the presence of autonomic neuropathy, higher gallbladder volumes were seen in patients with autonomic neuropathy. **Conclusions:** Cholecystomegaly, to a significant degree, was documented in type 2 diabetics in the present study. It emphasized that duration of diabetes in these cases were 5 to 10 years. Gall bladder volume enlargement in type 2 diabetics as a whole is significantly correlated with severity of autonomic neuropathy ($p < 0.001$). The mean gall bladder volume in type 2 female diabetics is higher than that found in type 2 male diabetics, but the difference in the gall bladder volume between the two sub groups is not statistically significant ($p > 0.05$).

Key words: Cholecystomegaly (sonographically determined increased gall bladder volume), Autonomic neuropathy, gall bladder volume, squatting test.

INTRODUCTION

Diabetes mellitus is the most common endocrine disorder of humans characterised by metabolic abnormalities leading to long-term macro and microvascular complications involving kidneys, gastrointestinal tract, nerves, and blood vessels, thereby causing profound morbidity and mortality. Various previous studies point towards an increased prevalence of gall bladder disease in diabetics¹⁻³. This has been attributed to increase gall bladder volume and impaired gall bladder contraction, mainly due to autonomic neuropathy seen in diabetics. Though gall bladder stasis is the most necessary pre-requisite for gallstone formation, other risk factors include sex, genetic factors, obesity, parity, diet, drugs, hyperlipidaemia, and ileal resection⁴. The present study was undertaken to compare gall bladder volumes in diabetics and controls. Ultrasonography was chosen as the modality to assess gall bladder volume, as it is safe, noninvasive, inexpensive, less time consuming, and accurate. It was also intended to correlate gall bladder volume in diabetics with autonomic neuropathy.

Material and methods: The study was conducted on type 2 diabetic patients attending the diabetic clinic of the Department of Medicine, Sawai Man Singh Hospital, Jaipur. Fifty patients (25 type II female diabetics, 25 type II male diabetics) were recruited for the study. An informed consent was taken from all the subjects in the study and control groups. The study protocol was approved by the ethical committee of the hospital.

Selection of study group

The diabetic patients recruited to the study group were Type 2 diabetic patients with 5 to 10 yrs. duration, age of onset in type 2 diabetics > 35 yr. Patients have a functioning gall bladder, well controlled blood sugar, no evidence of gastrointestinal or hepatobiliary disease and no previous history of cholecystectomy. The diabetic patients taking antihypertensive drugs which interfere with autonomic functions, those with a history of major cardiac arrhythmias, obese subjects, those with a past history of CVA, pregnant ladies and type I diabetics were excluded from the study.

Selection of control group;

Fifty healthy, non-obese, non-pregnant healthy volunteer without gastrointestinal, renal, and cardiac disease were recruited to the control group.

A detailed history was recorded with special reference to symptoms of autonomic neuropathy like nocturnal diarrhoea or constipation, hypoglycaemic unawareness, sphincter disturbances, orthostatic hypotension, and impotence. Apart from the anthropometric measurements like standing height, weight, waist circumference and hip circumference, indirect auscultatory arterial blood pressure and resting 12-lead electrocardiogram were performed. Biochemical investigations conducted on the patients included blood glucose (fasting and postprandial), blood urea, serum creatinine, glycosylated haemoglobin, and serum lipid profile. Clinical assesment of Cardiac autonomic neuropathy in diabetic patients by using simple non-invasive bedside tests, which included heart rate variation during squatting, heart rate variation during deep breathing, immediate heart rate response to standing, blood pressure response to standing, and blood pressure response to sustained handgrip. The cardiac autonomic neuropathy was graded into four categories:

1. No test abnormal -Grade 0/ No autonomic neuropathy
2. One test abnormal -Grade I/ Mild autonomic neuropathy
3. Two tests abnormal -Grade II/ Moderate autonomic neuropathy
4. Three or more tests abnormal - Grade III/ Severe autonomic neuropathy

The greatest length (L), greatest transverse width (W), and anteroposterior (H) dimensions of fasting gall bladder were recorded by ultrasonography. All the measurements were recorded by a single, experienced observer on two consecutive days, and the average of the two readings was taken as the final fasting gall bladder volume for the case or control. The gall bladder volume was calculated by the ellipsoid formula = $\pi \times L \times W \times H / 6$

DATA ANALYSIS

All relevant details including history, examination, investigations, etc. were enlisted in the performa and further analysed with Student's t-test for comparison between the study and control groups. The association between gallbladder volume and parameters such as sex, body mass index, hyperlipidaemia, and autonomic neuropathy was determined using the Karl Pearson coefficient of correlation.

OBSERVATIONS

A total of 50 cases type 2 diabetes of 5 – 10 year duration and 50 healthy controls were included in the present study. Cases comprised of 25 males and 25 females. Out of the 5 test conducted for cardiac autonomic neuropathy(CAN), squatting test has been found to be the most sensitive, and is observed to be abnormal in 88% of the study group cases. All patients with CAN show abnormal squatting test. Table 1 shows the prevalence of CAN in diabetics and controls.

TABLE 1
Prevalence of CAN in cases and controls

CAN	CASES	CONTROLS
Grade I (No CAN)	6	50
Grade II (mild CAN)	9	-
Grade III (moderate CAN)	19	-
Grade IV (severe CAN)	16	-

Table 2
Comparison between Case & Control

	Group	Mean	Std. Deviation	P-Value
Gall bladder volume (ml.)	Case	29.20	12.744	.0000
	Control	17.50	2.206	

The mean fasting gall bladder volume has been detected as 29.20±12.744 in diabetics with a minimum value of 10 and maximum value of 78 ml. and 17.50±2.206 in control subjects. (Fig. 1)

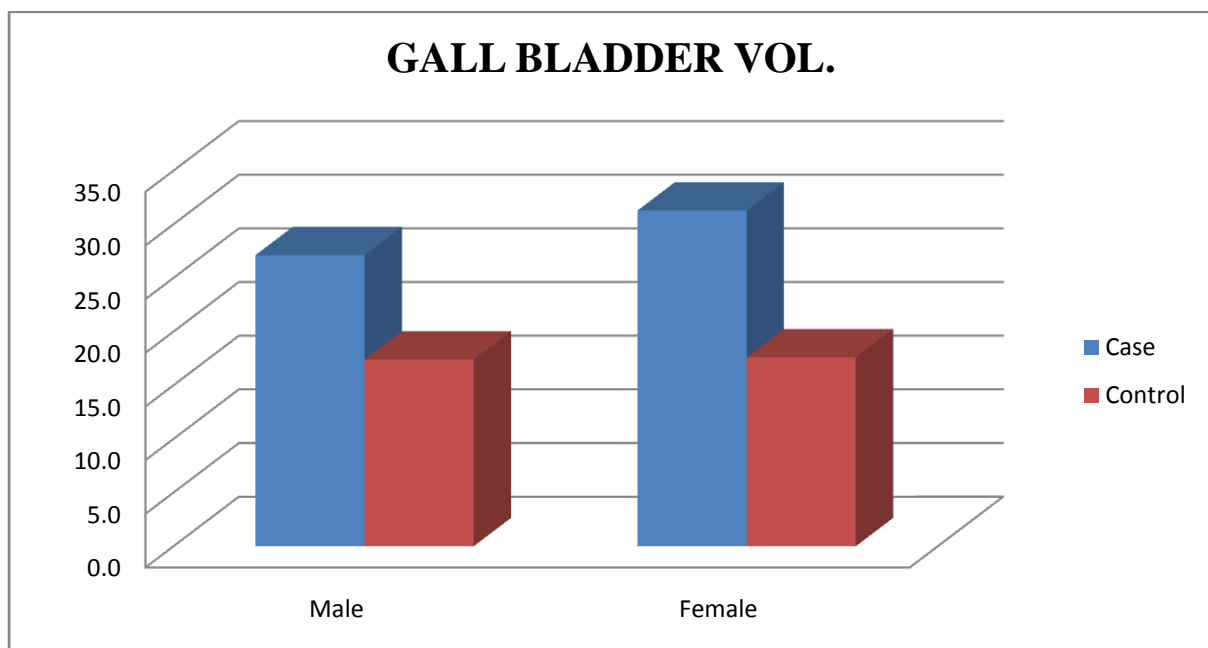


Fig.1 Comparison between Case & Control

Grading of cardiac autonomic neuropathy	Gall bladder volume
Mild autonomic neuropathy	20.33 ml
Moderate autonomic neuropathy	25.95 ml
Severe autonomic neuropathy	45.38 ml

When cases are sub grouped according to the presence of cardiac autonomic neuropathy, a higher gall bladder volume are seen in patients with cardiac autonomic neuropathy. The mean gall bladder volume has been detected as 20.33 ml in cases with mild autonomic neuropathy, 25.95 ml with moderate autonomic neuropathy, and 45.38 ml with severe autonomic neuropathy ($p < 0.001$). (Table-3, fig-2).

Table 3: Comparison between gall bladder volume and grading of cardiac autonomic neuropathy.

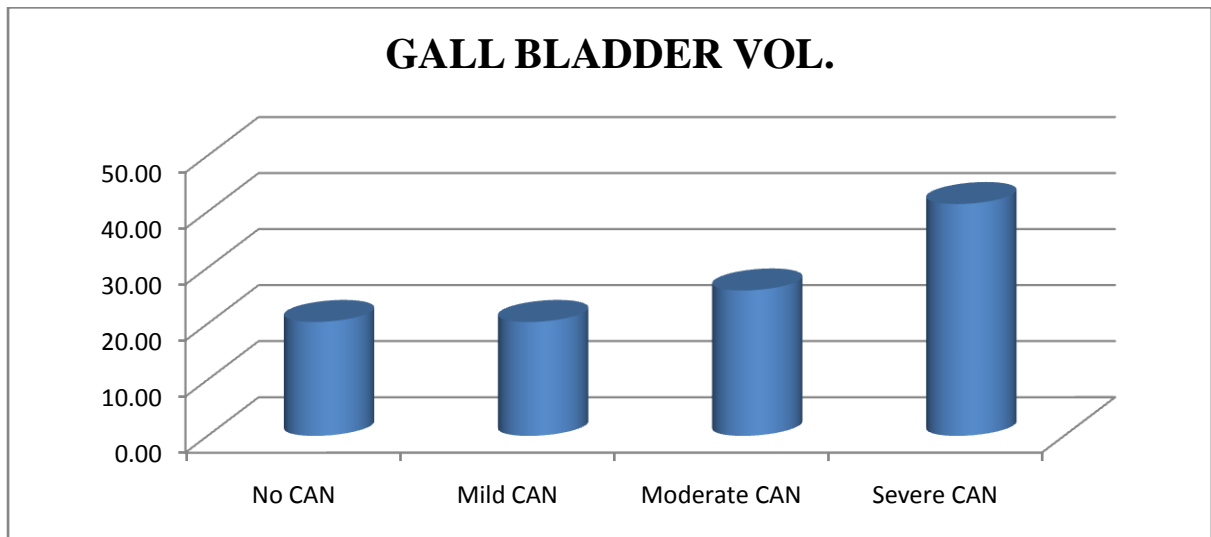


Fig.2 Comparison between gall bladder volume and grading of cardiac autonomic neuropathy

When Karl-Pearson coefficients of correlation are calculated for gall bladder volume with cardiac autonomic neuropathy, it is found that-Gall bladder volume enlargement in type two diabetics as a whole is significantly correlated with severity of autonomic neuropathy.

TABLE 4: Gall bladder volume correlation with cardiac autonomic neuropathy

Parameter	ALL CASES			MALE			FEMALE		
	S			P/C#			P/C #		
	P/C#	P value	N	P/C#	P value	N	P/C #	P value	N
CAN	.613**	.000	50	.660**	.000	25	.544**	.000	25

N- No. of patients in group

CAN-Cardiac autonomic neuropathy

P/C# Pearson correlation

**. Correlation is significant at the 0.01 level (2-tailed).

DISCUSSION

Diabetes mellitus is the most common endocrine disorder of humans characterized by metabolic abnormalities leading to long term complications involving kidneys, GIT, nerves, and blood vessels, thereby causing profound morbidity and mortality. By general consensus, the neuropathy is the most common among the complications of diabetes, yet it remains the least investigated. One of the dreaded subtypes of neuropathy is diabetic autonomic neuropathy. It manifests as abnormal cardiovascular, gastrointestinal, genitourinary, cutaneous, papillary, and metabolic functions. Involvement of alimentary canal in diabetics patients with autonomic neuropathy takes several forms: (a) oesophagopathy; (b) gastroparesis; (c) enteropathy; and (d) biliary tract disorders

Gallbladder emptying is mediated by both parasympathetic and sympathetic innervation; the former increases gallbladder contractility and the latter causes relaxation. Meal-related release of CCK causes gallbladder contraction. In previous study increased gall bladder volume and impaired contractility have been documented in diabetes mellitus⁵⁻¹¹. Diabetic patients are at increased risk for gall stone formation, which is supposed to be related to increased lithogenicity of the bile and to incomplete gall bladder emptying. Vagal neuropathy has been postulated as a major cause of gall bladder dysfunction. Our study has shown increased fasting gallbladder volumes in type 2 diabetics as compared to healthy controls. This has been supported by earlier studies⁵⁻¹¹. These studies also found that the gallbladder emptying rate and/or the gallbladder emptying were also reduced in diabetics.

However, autonomic neuropathy cannot entirely account for the cholecystoparesis. Braverman found that diabetic cholecystoparesis was not corrected by metoclopramide, a known cholinergic stimulant¹². In contrast, Dhiman et al have shown improved gallbladder emptying response to cisapride, another cholinergic stimulant¹³.

A definite association of autonomic neuropathy with cholecystomegaly has been demonstrated in our study and it implies a thorough evaluation for autonomic impairment in all diabetics because autonomic neuropathy in diabetic patient is important cause of morbidity and is routinely not diagnosed.

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