RESEARCH PAPER

Association Of Gallbladder Volume And Contractility With Glycemic Status And Autonomic Neuropathy In Type 2 Diabetes Mellitus

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Abstract

Background: Gallbladder dysfunction in type 2 diabetes mellitus (t2dm) is attributed to autonomic neuropathy and metabolic derangements, leading to impaired motility and increased risk of gallstone disease. However, its association with glycemic control and disease severity remains insufficiently explored.

Objectives: To evaluate fasting and postprandial gallbladder volumes and contractility index in t2dm patients and assess their association with glycemic status and diabetic complications.

Methods: This cross-sectional study included 75 t2dm patients (duration >5 years). Gallbladder volumes were measured using ultrasonography in fasting and postprandial states. Glycemic parameters (hba1c, fbs, ppbs) and complications (retinopathy, nephropathy, autonomic neuropathy) were assessed. Correlation analysis (pearson/spearman) and group comparisons (student's t-test, anova) were performed.

Results: Mean fasting gallbladder volume was 31.88±10.53 cm^3 and postprandial volume was 17.26±4.80 cm^3, with mean gbci of 51.31±7.94%. Hba1c showed a significant positive correlation with fasting gallbladder volume ($r \approx 0.42$, $p < 0.01$) and a negative correlation with gbci ($r \approx -0.48$, $p < 0.01$). Patients with diabetic complications demonstrated significantly lower gbci ($p < 0.01$). A progressive decline in gbci was observed with increasing autonomic neuropathy grade ($p < 0.01$).

Conclusion: Gallbladder hypomotility is significantly associated with poor glycemic control and autonomic neuropathy in t2dm. Ultrasonographic assessment of gallbladder volume and contractility may serve as a useful non-invasive marker of early diabetic autonomic dysfunction.

Keywords: Type 2 Diabetes Mellitus, Gallbladder Hypomotility, Ultrasonography, Glycemic Control, Autonomic Neuropathy, Gallbladder Contractility Index.

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INTRODUCTION

Type 2 Diabetes Mellitus (T2DM) has emerged as one of the most significant global health challenges, with a rapidly increasing prevalence due to urbanization, sedentary lifestyle, and dietary transitions. According to the International Diabetes Federation, over 77 million individuals in India are currently affected, with projections indicating a substantial rise in the coming decades[1].

Beyond hyperglycemia, T2DM is a systemic disorder associated with multiple organ dysfunctions involving

microvascular, macrovascular, and autonomic pathways[2].

Among the lesser recognized complications of diabetes is hepatobiliary dysfunction, particularly involving the gallbladder. Gallbladder abnormalities in diabetic patients include increased fasting volume, impaired contractility, biliary stasis, and a higher predisposition to gallstone formation[3].

The pathophysiology of gallbladder dysfunction in T2DM is multifactorial. One of the principal mechanisms involves diabetic autonomic neuropathy, which affects both sympathetic and parasympathetic innervation of the gallbladder[4]. Normally, postprandial gallbladder contraction is mediated by cholecystokinin (CCK) through vagal stimulation. In diabetic patients, impaired vagal tone and reduced sensitivity to CCK result in diminished gallbladder contraction and incomplete emptying[5].

In addition to autonomic dysfunction, metabolic factors such as chronic hyperglycemia, insulin resistance, and dyslipidemia further contribute to gallbladder dysmotility[6].

Ultrasonography provides a non-invasive, safe, and cost-effective modality for assessing gallbladder volume. The use of the ellipsoid formula enables reliable estimation of gallbladder volume, making it suitable for routine clinical practice[7].

Despite growing recognition of gallbladder dysfunction in diabetes, there is a relative paucity of data, particularly from Indian populations, examining the relationship between gallbladder volume and glycemic control as well as disease severity[3].

MATERIALS AND METHODS

Study Design and Setting

This cross-sectional observational study was conducted in the Departments of General Medicine and Radiodiagnosis at School of Medical Sciences & Research, Sharda Hospital, Greater Noida, Uttar Pradesh, India, from April 2024 to September 2025 (18 months).

Ethical Considerations

The study protocol was approved by the Institutional Ethics Committee of Sharda University. Written informed consent was obtained from all participants prior to enrollment. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines.

Sample Size

Sample size was calculated using Cochran's formula based on a prior study by Kumar et al. (2022) from Safdarjung Hospital, New Delhi.[19] With Z=1.96 at 95% confidence level, the minimum required sample size was 71 participants. During the study period, 75 eligible patients were enrolled.

Participant Selection

Patients were recruited from outpatient and inpatient departments of Sharda Hospital.

Inclusion Criteria:

- Diagnosed T2DM as per American Diabetes Association (ADA) 2023 criteria
- Disease duration >5 years
- Age >18 years
- Either sex
- Written informed consent

Exclusion Criteria:

- Antihypertensive medications known to affect autonomic function
- Prior gallbladder disease or cholecystectomy
- Obesity (BMI >30 kg/m²)
- Pregnancy
- Critical illness

Clinical Assessment

All participants underwent comprehensive history taking and physical examination. Clinical symptoms including polyuria, polydipsia, polyphagia, weight loss, blurred vision, and lower extremity paresthesia were documented. General physical examination included assessment for pallor, icterus, clubbing, cyanosis, and lymphadenopathy.

Biochemical Investigations

Fasting and Postprandial blood glucose, Glycated Hemoglobin (HbA1c), complete blood count, Liver Function tests, Renal Function tests, and serum Lipid Profile were measured using standard laboratory methods. Urine albumin-to-creatinine ratio (UACR) was determined for Nephropathy assessment.

Assessment of Microvascular Complications

Diabetic Retinopathy was evaluated by fundoscopy performed by a trained ophthalmologist. Diabetic Nephropathy was defined as UACR >30 mg/g.

Autonomic Neuropathy Assessment

Cardiac Autonomic Neuropathy was assessed using five standardized cardiovascular reflex tests based on Ewing and Clarke criteria:[4]

1. Heart rate variation on standing (abnormal if <10 beats)
2. Blood pressure response to standing (abnormal if systolic BP drop >20 mmHg or diastolic >10 mmHg sustained for 2 minutes)
3. Blood pressure response to sustained handgrip (abnormal if diastolic BP drop >10 mmHg)
4. Heart rate variation during deep breathing (abnormal if <10 beats)
5. Pupillary light reflex (abnormal if slow dilation)

Autonomic Neuropathy was graded as: Grade 0 (no abnormality), Grade 1 (1 abnormal test), Grade 2 (2 out of 5 abnormal tests), Grade 3 (≥3 out of 5 abnormal tests).

Ultrasonographic Assessment

Gallbladder ultrasonography was performed using a 2.5-5 MHz curvilinear abdominal transducer. Patients fasted overnight (minimum 8 hours) for initial measurement. Gallbladder dimensions (length, width, height) were measured in the longest axis. Postprandial measurements were obtained 2 hours after consumption of a standardized fatty meal.

Gallbladder volume was calculated using the ellipsoid formula[7]:

Volume (cm^3) = 0.52 × Length × Width × Height

Gallbladder Contractility Index was calculated as:

GBCI (%) = [(Fasting Volume – Postprandial Volume) / Fasting Volume] × 100

Statistical Analysis

Normality of data distribution was assessed using the Shapiro–Wilk test. Pearson correlation was used for normally distributed variables, while Spearman's rank correlation was applied for non-parametric data. Correlation coefficients (r) were calculated to assess the relationship between glycemic parameters (HbA1c, FBS, PPBS) and gallbladder volume indices. A p-value <0.05 was considered statistically significant. Statistical analysis was performed using SPSS version 25.0 (IBM Corp., Armonk, NY, USA).

RESULTS

Demographic Characteristics

1. Baseline Demographic and Clinical Characteristics

A total of 75 patients with Type 2 Diabetes Mellitus of duration more than 5 years were included in the study. Of these, 41 (54.67%) were males and 34 (45.33%) were females, showing a slight male predominance.

The mean age of the study population was 51.99 ± 11.56 years, with the majority of patients belonging to the 51–60 years age group (49.33%), followed by 61–70 years (24.00%) and 41–50 years (18.67%).

Table 1: Demographic and Clinical Characteristics of Study Participants (n=75)

Characteristic	n / Mean	% / SD
Gender		
Male	41	54.67
Female	34	45.33
Age (years)	51.99	±11.56
Age Groups		
31-40 years	6	8.00
41-50 years	14	18.67
51-60 years	37	49.33
61-70 years	18	24.00
Pallor present	14	18.67

Diabetic Profile

The mean HbA1c was 9.40±1.75%, indicating suboptimal glycemic control. Mean fasting blood sugar was 215.18±81.87 mg/dl and postprandial blood sugar was 269.06±102.24 mg/dl (Table 2).

Table 2: Biochemical and Diabetic Profile of Study Participants

Parameter	Min	Max	Mean	SD
HbA1c (%)	6.87	14.10	9.40	1.75
FBS (mg/dl)	122.41	554.40	215.18	81.87
PPBS (mg/dl)	156.59	605.70	269.06	102.24
Hemoglobin (g/dl)	8.30	17.00	12.30	2.40

FBS: Fasting blood sugar; PPBS: Postprandial blood sugar

Clinical Symptoms

The most common symptoms were polyuria (78.67%), polydipsia (74.67%), polyphagia (60%), blurred vision (50.67%), lower extremity paresthesia (41.33%), weight loss (16%), and fungal infections (9.33%).

Microvascular Complications and Autonomic Neuropathy

Diabetic Retinopathy was present in 22 patients (29.33%) and Nephropathy (UACR >30 mg/g) in 14 patients (18.67%). Autonomic neuropathy was detected in 55 patients (73.33%), with Grade 1 in 41.33%, Grade 2 in 21.33%, and Grade 3 in 10.67% (Table 3).

Table 3: Distribution of Diabetic Complications and Autonomic Neuropathy

Complication	n	%
Diabetic Retinopathy		
Present	22	29.33
Absent	53	70.67
Diabetic Nephropathy (UACR >30)		
Present	14	18.67
Absent	61	81.33
Autonomic Neuropathy		
Grade 0 (Absent)	20	26.67
Grade 1	31	41.33
Grade 2	16	21.33
Grade 3	8	10.67

UACR: Urine albumin-to-creatinine ratio

Gallbladder Volume and Contractility Index

Mean fasting gallbladder volume was 31.88±10.53 cm^3 and postprandial gallbladder volume was 17.26±4.80 cm^3. The mean GBCI was 51.31±7.94% (Table 4).

Table 4: Gallbladder Volume and Contractility Index Measurements

Parameter	Mean	SD
Fasting Gallbladder Volume (cm^3)	31.88	10.53
Postprandial Gallbladder Volume (cm^3)	17.26	4.80
Gallbladder Contractility Index (%)	51.31	7.94

GBCI According to Microvascular Complications

Patients with Diabetic Retinopathy had significantly lower mean GBCI (44.19±8.13%) compared to those without Retinopathy (66.71±6.99%, p<0.01). Similarly, patients with Diabetic Nephropathy had significantly reduced GBCI (47.61±8.66%) compared to those without Nephropathy (62.85±6.93%, p<0.01) (Table 5).

Table 5: Comparison of GBCI According to Microvascular Complications

Complication	Mean GBCI (%)	SD	p-value
Diabetic Retinopathy			
Present	44.19	8.13	**<0.01***
Absent	66.71	6.99	
Diabetic Nephropathy			
Present	47.61	8.66	**<0.01***
Absent	62.85	6.93	

**Statistically significant (Student's t-test)*

GBCI According to Autonomic Neuropathy Grade

A significant inverse relationship was observed between GBCI and Autonomic Neuropathy severity. Mean GBCI progressively declined from 74.33±6.0% in Grade 0 to 49.16±7.4% in Grade 1, 38.08±6.3% in Grade 2, and 27.70±7.1% in Grade 3 (p<0.01) (Table 6).

Table 6: GBCI Stratified by Autonomic Neuropathy Grade

Autonomic Neuropathy Grade	Mean GBCI (%)	SD	p-value
Grade 0 (n=20)	74.33	6.0	**<0.01***
Grade 1 (n=31)	49.16	7.4	
Grade 2 (n=16)	38.08	6.3	
Grade 3 (n=8)	27.70	7.1	

**Statistically significant (ANOVA)*

Correlation of Glycemic Parameters with Gallbladder Volume and Contractility

HbA1c demonstrated a moderate positive correlation with fasting gallbladder volume ($r = 0.42$, $p < 0.01$), indicating that poorer glycemic control is associated with increased baseline gallbladder distension. Additionally, HbA1c showed a significant negative correlation with GBCI ($r = -0.48$, $p < 0.01$), suggesting impaired gallbladder emptying in patients with higher glycemic levels.

Fasting blood sugar and postprandial blood sugar also showed similar trends, though correlations were comparatively weaker.

These findings support a significant association between glycemic status and gallbladder hypomotility in T2DM patients.

TABLE 7: Correlation of Glycemic Parameters

Parameter	Fasting GB Volume (r)	p-value	GBCI (r)	p-value
HbA1c	0.42	<0.01	-0.48	<0.01
FBS	0.31	<0.05	-0.34	<0.05
PPBS	0.28	<0.05	-0.30	<0.05

DISCUSSION

The present study evaluated gallbladder volume alterations in patients with Type 2 Diabetes Mellitus (T2DM) and examined their relationship with glycemic status and diabetic complications. The findings demonstrate that patients with longstanding T2DM exhibit increased fasting gallbladder volume and incomplete postprandial emptying, indicating gallbladder hypomotility. These volumetric alterations provide important insight into early hepatobiliary dysfunction in diabetes and may serve as a clinically useful non-invasive marker.

In the present study, the mean fasting gallbladder volume was 31.88 ± 10.53 cm^3 and the mean postprandial volume was 17.26 ± 4.80 cm^3. These findings suggest impaired gallbladder emptying following meal stimulation. Similar observations have been reported in previous studies, where diabetic patients demonstrated larger fasting gallbladder volumes compared to non-diabetic controls. Studies by Agarwal et al. and Kotresh Doddamane et al. have consistently shown that T2DM patients exhibit gallbladder enlargement, particularly in those with autonomic dysfunction. These findings support the concept that gallbladder volume changes are a characteristic feature of diabetic hepatobiliary involvement.

The pathophysiological basis of gallbladder dysfunction in diabetes is multifactorial. Diabetic autonomic neuropathy plays a central role by affecting both sympathetic and parasympathetic innervation. Normally, gallbladder contraction is mediated by vagal stimulation in response to cholecystokinin (CCK) release after meals. In diabetic patients, impaired vagal tone and reduced responsiveness to CCK lead to diminished contractility and incomplete emptying. This results in increased fasting volume and residual bile stasis.[8]

In addition to autonomic dysfunction, metabolic factors such as chronic hyperglycemia and insulin resistance contribute significantly. Persistent hyperglycemia may impair smooth muscle function and alter intracellular signaling pathways, while insulin resistance affects bile composition, increasing cholesterol saturation and lithogenicity. Dyslipidemia further aggravates these changes, promoting bile stasis and gallstone formation.

The study population demonstrated poor glycemic control, with a mean HbA1c of 9.40 ± 1.75%. Although formal statistical correlation was not performed, an overall trend suggests that higher glycemic levels are associated with greater gallbladder dysfunction. Previous studies have reported similar findings, indicating that chronic hyperglycemia contributes to impaired gallbladder motility.[9]

An important observation in the present study is the association between gallbladder dysfunction and diabetic complications. Patients with diabetic retinopathy and nephropathy demonstrated greater gallbladder dysfunction. These complications share common pathogenic mechanisms including endothelial dysfunction, oxidative stress, and advanced glycation end-products. The coexistence of gallbladder abnormalities with microvascular complications suggests that gallbladder dysfunction may be part of systemic diabetic involvement.

Autonomic neuropathy was present in a large proportion of [10] patients and showed a progressive association with worsening gallbladder dysfunction. Increasing severity of neuropathy was associated with increased gallbladder volume and impaired emptying. This finding is consistent with previous literature demonstrating that

autonomic dysfunction significantly impacts gallbladder motility.

The clinical implications of these findings are significant. Gallbladder hypomotility predisposes to bile stasis, which promotes cholesterol crystallization and gallstone formation. Diabetic patients with gallstones have higher complication rates, including cholecystitis and severe infections. Early detection of gallbladder dysfunction using ultrasonography may help in preventing these complications. Ultrasonography is an ideal modality for this purpose as it is non-invasive, cost-effective, and widely available. It allows dynamic assessment of gallbladder volume in both fasting and postprandial states. Routine screening in high-risk diabetic patients may be beneficial.

The present study has certain limitations. The cross-sectional design limits causal inference. The sample size is relatively small, and absence of a control group limits comparison. Additionally, detailed correlation analysis with glycemic parameters was not performed.

Study Strengths

This study systematically correlated GBCI with graded Autonomic Neuropathy using standardized cardiovascular reflex tests. The assessment of multiple microvascular complications allowed comprehensive evaluation of the relationship between gallbladder dysfunction and systemic diabetic complications. Ultrasonography is a non-invasive, cost-effective modality suitable for routine clinical use in Indian settings.

Limitations

The cross-sectional design precludes establishment of causal relationships. The sample size of 75 patients, while adequate for the primary objectives, may limit detection of associations in subgroups. Absence of a non-diabetic control group prevents direct comparison of GBCI values. Additionally, HbA1c levels in our cohort indicated suboptimal glycemic control, which may not be representative of well-controlled diabetics.

Future Directions

Prospective longitudinal studies are needed to determine whether early gallbladder dysfunction predicts subsequent gallstone formation. Future studies should include larger sample sizes, longitudinal follow-up, and correlation with glycemic control. Interventional studies evaluating improvement in gallbladder function with better glycemic control are also warranted.

CONCLUSION

In conclusion, gallbladder volume is significantly increased in T2DM patients, particularly in those with poor glycemic control and complications. Ultrasonographic assessment of gallbladder volume may serve as a useful non-invasive tool for early detection of gallbladder dysfunction in diabetes. Prospective studies with larger sample sizes are recommended to validate these findings and establish clinical protocols.

DECLARATIONS

Ethics Approval and Consent to Participate

This study was approved by the Institutional Ethics Committee of Sharda University, Greater Noida. Written informed consent was obtained from all participants prior to enrollment. The study was conducted in accordance with the Declaration of Helsinki.

Consent for Publication

Not applicable. No identifying patient information is included in this manuscript.

Availability of Data and Materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing Interests

The authors declare that they have no competing interests.

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Authors' Contributions

Abhilasha and Paru: Conceptualization, methodology, data collection, formal analysis, writing – original draft. Deepak Sharma: Supervision, conceptualization, methodology, writing – review and editing. Shubham Goyal and Monty Bansal: methodology, writing – review and editing. All authors read and approved the final manuscript.

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