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To Assess the Ejection Fraction of Gallbladder in Patients of Cholelithiasis in a Tertiary Care Centre: A Case–control Study

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Abstract

Background: The gallbladder (GB) stores and concentrates bile and ejects it under the influence of cholecystokinin; disordered motility contributes to gallstone pathogenesis. GB ejection fraction (GBEF), measured after physiologic stimulation, serves as a key indicator of GB function. Ultrasound-based estimation provides a safe, accessible, and radiation-free alternative to scintigraphy. **Objective:** The aim of the study was to assess and compare the GBEF in patients with cholelithiasis and in age- and sex-matched healthy controls in a tertiary care setting. **Materials and Methods:** This case–control study was conducted in the Department of General Surgery, Bhagat Phool Singh Government Medical College for Women, Khanpur Kalan, Haryana. Seventy-two adults with sonographically confirmed cholelithiasis and 72 matched controls were included over 18 months after ethical approval and informed consent. Patients with acute cholecystitis, mucocele, pyocele, acalculous cholecystitis, carcinoma GB, or outside the 18–65-year age range were excluded. After overnight fasting, baseline GB volume was measured ultrasonographically and recalculated 60 min after a standard fatty meal (half-and-half milk). Volumes were determined using the ellipsoid formula ($V = L \times W \times H \times 0.5$), and GBEF was computed as ([Preprandial–Postprandial]/Pre-prandial) × 100. Statistical analysis was performed using Statistical Package for the Social Sciences version 21.0; $P < 0.05$ was considered significant. **Results:** The case and control groups were comparable for age ($P = 0.328$) and sex ($P = 0.655$). Laboratory parameters, including hemoglobin, liver enzymes, and bilirubin, showed no significant differences (all $P > 0.05$). Mean preprandial GB volume was significantly higher in cases (22.79 ± 12.43 cc) than in controls (15.38 ± 4.94 cc) ($P = 0.0001$), as was postprandial volume (13.26 ± 11.76 vs. 10.19 ± 4.38 cc; $P = 0.040$). GB wall thickness was also greater in cases (3.42 ± 1.84 mm) compared to controls (2.78 ± 0.75 mm; $P = 0.007$). GBEF was markedly reduced in cholelithiasis patients (33.42 ± 6.26%) versus controls (52.56 ± 9.78%) ($P = 0.0001$), indicating significant contractile dysfunction. Common bile duct diameter did not differ significantly ($P = 0.895$). **Conclusion:** Patients with cholelithiasis demonstrated significantly impaired GB contractility, increased wall thickness, and higher fasting and residual volumes compared to healthy individuals. These findings indicate that GB dysmotility may both contribute to and result from gallstone formation. Ultrasound-based assessment of GBEF using a fatty meal stimulus is a reliable, non-invasive tool for evaluating GB function and may aid early diagnosis, prognosis, and management in cholelithiasis.

Keywords: Cholelithiasis, Fatty meal test, Gallbladder dyskinesia, Gallbladder ejection fraction, Gallbladder wall thickness, Ultrasound

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Introduction

The gallbladder (GB), a pear-shaped organ beneath the liver, stores and concentrates bile – a fluid composed of water, electrolytes, bile acids, cholesterol, phospholipids, and bilirubin – essential for fat digestion and cholesterol excretion. It contracts under the influence of cholecystokinin (CCK) to release bile into the intestine. Proper coordination between the GB, cystic duct, and sphincter of Oddi ensures efficient bile flow.[1]

Cholelithiasis, or gallstone disease, is a common hepatobiliary disorder resulting from bile supersaturation with cholesterol, bilirubin, or calcium salts. Gallstones are classified as cholesterol, pigment, or mixed stones. Cholesterol stones are most prevalent and form due to hepatic cholesterol hypersecretion and GB hypomotility, while pigment stones result from excess bilirubin secondary to hemolysis. Risk factors include obesity, rapid weight loss, high-fat diet, sedentary habits, and medical conditions such as cirrhosis and Crohn's disease.[2]

Epidemiologically, 10–15% of adults in Western populations develop gallstones, with a female predominance attributed to estrogen-induced cholesterol secretion and progesterone-mediated bile stasis.[2] While many remain asymptomatic, others present with biliary colic, nausea, vomiting, or jaundice due to ductal obstruction. Complications include cholecystitis, cholangitis, pancreatitis, or, rarely, GB carcinoma.[2]

GB dyskinesia – functional motility disorder without structural abnormality – can accompany cholelithiasis or occur independently.[3] It manifests as right upper quadrant pain due to abnormal contractility or sphincter dysfunction. Dyskinesia is classified as hypokinetic (low ejection fraction with bile stasis) or hyperkinetic (excessive contraction). Whipple first described biliary dyskinesia in patients with biliary pain but no stones, many of whom improved post-cholecystectomy.[4]

Pathophysiologically, GB dyskinesia involves impaired smooth muscle contractility, altered CCK receptor sensitivity, and bile composition changes. Dysmotility leads to bile concentration, chemical cholecystitis, and potential stone formation.

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Hypersensitivity to CCK can produce excessive contraction and mucosal injury, while reduced sensitivity results in bile stasis.[5]

Diagnosis is challenging, as symptoms overlap with peptic ulcer or reflux disease. Rome IV criteria define functional GB disorder as biliary pain with low ejection fraction (<40%) and no structural abnormality.[3] GB ejection fraction (GBEF), the ratio of postprandial to fasting volume, quantifies contractility. A GBEF below 35% indicates hypokinetic dyskinesia.[6]

Cholescintigraphy with sincalide (synthetic CCK) is the gold standard for assessing GBEF but is costly and involves radiation exposure. Alternatively, fatty meals provide a physiological, inexpensive, and radiation-free stimulus for GB contraction. Studies such as Ziessman *et al*. demonstrated comparable GBEF values between fatty meal (mean 67%) and sincalide stimulation (mean 70%).[6] Despite variability in composition and timing, fatty meals simulate natural physiology, making them useful in clinical practice.[7]

Ultrasound is now the preferred non-invasive method for GB function evaluation due to its availability, safety, and cost-effectiveness.[8] After an overnight fast, baseline GB volume is measured, followed by post-fatty meal imaging to calculate GBEF. A value below 35% confirms dyskinesia.[9,10]

This study, conducted at BPS Government Medical College, Khanpur Kalan, Haryana, aims to assess the GBEF in patients with cholelithiasis using ultrasound. By comparing GBEF between cases and controls, the study seeks to elucidate the relationship between gallstones and impaired GB motility, supporting ultrasound as a reliable diagnostic tool for evaluating GB function and guiding management strategies in cholelithiasis.

Materials and Methods

This case–control study was conducted in the Department of General Surgery, Bhagat Phool Singh Government Medical College for Women, Khanpur Kalan, Haryana. The study population included patients diagnosed with cholelithiasis attending the Department of Surgery. Age- and sex-matched healthy individuals without any GB disease served as the control group. The study was conducted over a period of 1½ years following approval from the Institutional Scientific and Ethical Committee. Written informed consent was obtained from all participants after explaining the purpose and nature of the study. Confidentiality of personal data was maintained, and participants were given the right to withdraw at any stage without prejudice.

Patients aged between 18 and 65 years with a confirmed diagnosis of cholelithiasis were included in the study. Individuals younger than 18 years or older than 65 years, and those with acute cholecystitis, mucocele, pyocele, acalculous cholecystitis, or carcinoma of the GB were excluded. The sample size was 72 participants in each group, resulting in a total of 144 subjects.

For each participant, GBEF was measured ultrasonographically. The assessment was performed after an overnight fast to ensure full GB distension. Baseline (preprandial) GB volume was measured, followed by administration of a standard fatty meal (half-and-half milk). Sixty minutes after meal ingestion, a postprandial ultrasound was performed to measure the GB volume again. The GB volume (V) was calculated using the ellipsoid formula:

$$V = L \times W \times H \times 0.5,$$

where L is length, W is width, and H is height. The GBEF was then determined using the formula:

$$\text{GBEF} = (\text{Preprandial volume} - \text{Postprandial volume}] / \text{Preprandial volume}) \times 100.$$

A reduced GBEF indicated impaired GB contractility, suggestive of dyskinesia or functional compromise.

All collected data were verified for completeness, and errors or missing values were corrected. The cleaned dataset was entered into Microsoft Excel, and a master chart was prepared. Statistical analysis was performed using the Statistical Package for the Social Sciences version 21.0 (Chicago, Illinois). Descriptive statistics, including frequencies and percentages for categorical variables and mean ± standard deviation for continuous variables, were calculated. Comparative analysis between cases and controls was conducted using the Chi-square or Fisher's Exact test for categorical variables and the unpaired *t*-test for continuous variables. A $P < 0.05$ was considered statistically significant.

Results

The case and control groups demonstrated comparable baseline characteristics with no significant differences in age distribution (Table 1) ($P = 0.328$ for mean age, $P = 0.841$ for age groups) or gender distribution ($P = 0.655$), ensuring that these demographic factors did not confound the study results (Table 2). Laboratory parameters including hemoglobin, total leukocyte count, liver enzymes (serum glutamate oxaloacetate transaminase [SGOT], serum glutamate pyruvate transaminase [SGPT], alkaline phosphatase [ALP]), and serum bilirubin showed no statistically significant differences between groups (all $P > 0.05$), indicating similar baseline biochemical profiles. However, ultrasonographic evaluation revealed highly significant differences in GB parameters (Table 3): Preprandial volume was significantly higher in cases ($P = 0.0001$), postprandial volume was increased in cases ($P = 0.040$), GB wall thickness was significantly greater in cases ($P = 0.007$), and most importantly, GBEF was markedly reduced in cases compared to controls (33.42% vs. 52.56%, $P = 0.0001$), indicating severe impairment of GB contractility. Table 4 showed Clinical presentation analysis showed that pain was universal (100%), predominantly colicky in nature (81.9%), located in the right hypochondrium (83.3%), with a mean symptom duration of 7.4 months before presentation.

Discussion

Cholelithiasis is one of the most common gastrointestinal disorders globally, with a higher prevalence among females and strong associations with age, obesity, hormonal factors, and sedentary habits. Although many cases remain asymptomatic, complications such as biliary colic and cholecystitis are frequent. The GB's function, primarily bile storage and ejection, can be quantitatively assessed using GBEF. Impaired motility is implicated in gallstone pathogenesis, and evaluating GBEF helps clarify disease mechanisms and management strategies.

In the present study, the mean age of patients with cholelithiasis (40.63 ± 14.51 years) and controls (38.24 ± 14.71 years) showed no significant difference ($P = 0.328$), confirming age-matching. Most participants were aged 18–30 years, indicating a rising incidence of gallstones among younger adults, a trend possibly linked to obesity and dietary changes. Similar findings were observed by Pauletzki *et al*.,[11] who also maintained age-matched groups to minimize bias. Female predominance was seen in both groups

Table 1: Baseline demographic and clinical characteristics of study participants

Parameter	*Case (n=72)*	*Control (n=72)*	*P-value*
Age (years)			
Mean±Standard deviation	40.63±14.51	38.24±14.71	0.328
Median (Range)	37.5 (19–65)	35.5 (19–66)	
Age groups, *n* (%)			0.841
18–30 years	23 (31.9)	28 (38.9)	
31–40 years	19 (26.4)	15 (20.8)	
41–50 years	10 (13.9)	12 (16.7)	
51–60 years	10 (13.9)	8 (11.1)	
>60 years	10 (13.9)	9 (12.5)	
Gender, *n* (%)			0.655
Female	61 (84.7)	59 (81.9)	
Male	11 (15.3)	13 (18.1)	

Table 2: Comparison of laboratory parameters between case and control groups

Laboratory parameter	*Case (n=72)*	*Control (n=72)*	*P-value*
	Mean±SD	*Mean±SD*	
Hemoglobin (g/dL)	11.80±1.75	11.89±1.50	0.469
Total leukocyte count (cells/μL)	7454.17±1942.12	7058.33±1970.97	0.298
SGOT (U/L)	39.33±22.32	35.74±10.41	0.623
SGPT (U/L)	45.89±39.70	592.14±4721.77	0.328
Alkaline phosphatase (U/L)	104.36±34.35	96.97±23.04	0.134
Serum bilirubin (mg/dL)	0.70±0.25	0.88±1.38	0.274

SGOT: Serum glutamate oxaloacetate transaminase, SGPT: Serum glutamate pyruvate transaminase, SD: Standard deviation

Table 3: Comparison of ultrasonographic GB parameters between groups

USG parameter	*Case (n=72)*	*Control (n=72)*	*P-value*
	Mean±SD	*Mean±SD*	
Preprandial GB volume (cc)	22.79±12.43	15.38±4.94	0.0001*
Postprandial GB volume (cc)	13.26±11.76	10.19±4.38	-
GB wall thickness (mm)			
Mean±SD	3.42±1.84	2.78±0.75	0.007*
Median (Range)	3.0(1.2–15.1)	2.5 (2.0–4.6)	
CBD diameter (mm)			
Mean±SD	3.40±1.16	3.38±1.11	0.895
Median (Range)	4.0 (1.4–6.0)	4.0 (1.2–5.0)	
GB ejection fraction (%)			
Mean±SD	33.42±6.26	52.56±9.78	0.0001¨
Median (Range)	34.0 (13.2–44.0)	52.0 (30.0–80.0)	

SD: Standard deviation, USG: Ultrasonography, GB: Gallbladder, CBD: Common bile duct. *postprandial GB Volume is statistically significant in case. ¨GB ejection fraction is decreased in cases(statistically significant)

Table 4: Clinical presentation and characteristics of cases (*n*=72)

Clinical parameter	*Frequency*	*Percentage*
Presenting symptoms		
Pain	72	100.0
Vomiting	36	50.0
Dyspepsia	21	29.2
Fever	23	31.9
Jaundice	16	22.2
Pain location		
Epigastric	12	16.7
Right hypochondrium	60	83.3
Pain character		
Colicky	59	81.9
Dull	11	15.3
Gripping	2	2.8
Pain radiation		
No radiation	59	81.9
Radiating to back	13	18.1
Duration of symptoms (months)		
Mean±SD	7.4±4.1	
Median (Range)	6.0(3.0–36.0)	

SD: Standard deviation

(84.7% in cases, 81.9% in controls), aligning with the classical "5F" profile – female, forty, fat, fertile, and fair – and consistent with prior epidemiological data.[11-17]

Laboratory parameters were comparable across groups. Hemoglobin, liver enzymes (SGOT, SGPT, ALP), and bilirubin levels showed no significant variation, suggesting the absence of hepatobiliary inflammation or obstruction. Slightly higher total leukocyte counts in cholelithiasis cases, though within normal limits, may indicate subclinical inflammation. These comparable biochemical profiles strengthen the reliability of the study, as hepatobiliary dysfunction could otherwise confound GBEF assessment. Similar biochemical uniformity was not emphasized in earlier studies such as those by Misra *et al*.,[18] which mainly targeted diabetic populations.

A key finding was the significant difference in GB volume between groups. The mean fasting volume was 22.79 ± 12.43 cc in cholelithiasis cases versus 15.38 ± 4.94 cc in controls ($P = 0.0001$), while postprandial volume was 13.26 ± 11.76 cc in cases versus 10.19 ± 4.38 cc in controls ($P = 0.040$). These results align closely with Pauletzki *et al*.,[11] who reported similar fasting volumes (23.6 mL in cases, 15.3 mL in controls). Increased fasting and postprandial volumes reflect reduced contractility, leading to bile stasis and stone formation. Misra *et al*.[18] found even higher fasting volumes in diabetics, suggesting that metabolic dysfunctions further impair GB tone.

GB wall thickness was significantly higher in patients (3.42 ± 1.84 mm) than in controls (2.78 ± 0.75 mm) ($P = 0.007$). This increase may indicate chronic inflammation, fibrosis, or muscular hypertrophy secondary to gallstones. Lim *et al*.[15] showed that fibrosis in the GB wall correlates inversely with GBEF, while Thiyagarajan *et al*.[16] observed reduced ejection fraction in 78.8% of patients with histopathological cholecystitis. These findings suggest that structural wall changes contribute to functional impairment, forming a vicious cycle of reduced contractility and chronic inflammation.

No significant difference was noted in common bile duct (CBD) diameter between groups (3.40 ± 1.16 mm vs. 3.38 ± 1.11 mm, $P = 0.895$), indicating the absence of obstructive complications such as choledocholithiasis. The normal CBD diameter validates that functional impairment observed in gallstone patients was intrinsic to the GB rather than secondary to biliary obstruction.[14]

The central finding was a significantly reduced GBEF in cholelithiasis patients (33.42 ± 6.26%) compared to controls (52.56 ± 9.78%) ($P = 0.0001$), indicating marked impairment of GB contractility. These findings parallel those of Bartel *et al*.[12] and Misra *et al*.,[18] who reported normal GBEF values around 47–51% in controls. Mann *et al*.[19] used <35% as the diagnostic cutoff for biliary dyskinesia – remarkably close to the mean value in our case group – suggesting significant overlap between gallstone disease and functional dyskinesia. Lim *et al*.[15] similarly linked reduced ejection fraction with wall fibrosis, reinforcing a structural-functional association.

The clinical implications of reduced GBEF are noteworthy. Diminished contractility leads to bile stasis and prolonged bile

residence, fostering crystal nucleation and stone growth—a self-perpetuating cycle of dysfunction and lithogenesis. Thiyagarajan *et al*.[16] highlighted that lower GBEF correlated with multiple or larger stones and histopathological cholecystitis, indicating that GB dysfunction may predict disease severity. Furthermore, Pauletzki *et al*.[11] demonstrated that fasting GB volume alone could provide meaningful functional insights, suggesting that even simple ultrasound-based assessments may help stratify patients.

Mann *et al*.[19] explored whether GBEF predicts pain persistence after cholecystectomy and found no linear association, but extremely low ejection fractions (<16%) had limited prognostic value. This complexity underscores that while GBEF reflects mechanical function, symptoms may depend on multifactorial mechanisms, including neural and inflammatory factors.

This study confirms that patients with cholelithiasis exhibit significantly increased GB wall thickness, larger fasting and postprandial volumes, and reduced ejection fraction compared to healthy individuals. These findings reinforce the concept that impaired GB motility is both a contributor to and a consequence of gallstone formation. Functional assessment through ultrasonographic GBEF estimation offers valuable insights into GB physiology, potentially aiding early diagnosis, risk stratification, and treatment planning in patients with cholelithiasis.

Conclusion

The present case–control study demonstrated a significantly reduced GBEF in patients with cholelithiasis compared to healthy individuals, indicating impaired GB contractility. Although other laboratory and anatomical parameters showed no statistically significant differences, GB wall thickness and pre and postprandial GB volumes were also significantly increased in cases. These findings suggest that GB dysfunction may play a contributory role in the pathogenesis of cholelithiasis and support the utility of GBEF assessment in clinical evaluation.

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