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# Association of gall bladder ejection fraction and histopathological spectrum in patients with cholelithiasis undergoing cholecystectomy in tertiary care centre : An observational study

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## ABSTRACT

**Background:** Cholelithiasis is a common hepatobiliary disorder characterized by gallstone formation due to bile supersaturation, impaired motility, and mucin hypersecretion. Gallbladder ejection fraction (GBEF) is an important functional parameter that reflects gallbladder contractility and may correlate with disease severity. While histopathological examination after cholecystectomy remains the diagnostic gold standard, few studies have explored the association between preoperative GBEF and histopathological spectrum in gallstone disease.

**Methods:** This observational study was conducted in the Department of General Surgery at Bhagat Phool Singh Government Medical College for Women over 18 months. Ninety patients with clinically and ultrasonographically confirmed cholelithiasis undergoing cholecystectomy were included. GBEF was determined ultrasonographically before and 60 minutes after a standard fatty meal using the ellipsoid method. Postoperative gallbladder specimens were analyzed histologically using hematoxylin and eosin staining. Data were analyzed using SPSS version 21.0, applying the Chi-square and unpaired t-tests, with $p < 0.05$ considered statistically significant.

**Results:** Most participants were middle-aged females with multiple gallstones. Chronic cholecystitis was the predominant histopathological finding, followed by acute on chronic cholecystitis and chronic cholecystitis with cholesterosis. A statistically significant association was found between GBEF and histopathological diagnosis ($p = 0.0001$), indicating that lower GBEF values correlated with more severe inflammatory changes. No significant association was observed between GBEF and age or gender.

**Conclusion:** Reduced GBEF was associated with advanced inflammatory pathology, suggesting that functional impairment parallels histological severity in cholelithiasis. Preoperative GBEF evaluation may serve as a useful non-invasive marker for predicting disease chronicity and guiding management in patients undergoing cholecystectomy.

***KEYWORDS:*** *Cholelithiasis, Gallbladder ejection fraction, Chronic cholecystitis, Histopathology, Biliary dyskinesia, Gallstones, Cholecystectomy, Gallbladder motility etc.*

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## 1. INTRODUCTION

Gallstones, or cholelithiasis, are among the most common gastrointestinal disorders worldwide, characterized by the formation of calculi in the gallbladder due to bile supersaturation with cholesterol, impaired motility, and excess mucin secretion. They are frequently associated with risk factors such as obesity, diabetes, high-fat diet, and sedentary lifestyle. While many cases remain asymptomatic, complications such as acute cholecystitis, choledocholithiasis, and biliary pancreatitis often necessitate surgical removal of the gallbladder through cholecystectomy [1].

The gallbladder serves as a bile reservoir, expelling bile into the duodenum during digestion. Its contractile function is quantified by the gallbladder ejection fraction (GBEF), which represents the proportion of bile expelled after stimulation. Reduced GBEF indicates impaired gallbladder motility and has been linked to biliary dyskinesia and functional gallbladder disorders. Imaging techniques, particularly hepatobiliary scintigraphy, provide an accurate, non-invasive assessment of GBEF, making it an emerging functional biomarker for gallbladder pathology [2].

The prevalence of gallstone disease varies globally—10–20% in Western countries and approximately 5% in Asian populations—reflecting differences in genetic predisposition and dietary habits [3-4]. In India, increasing urbanization and lifestyle changes have led to a rising incidence, with women affected more frequently than men (3:1), primarily due to hormonal influences on bile composition and motility [5]. Gallstone disease contributes significantly to surgical workload, with symptomatic cases being a leading cause of emergency admissions. Laparoscopic cholecystectomy remains the treatment of choice, although understanding the underlying gallbladder dysfunction is essential for optimizing patient outcomes [6].

GBEF, typically measured using hepatobiliary scintigraphy after cholecystokinin stimulation, quantifies gallbladder contractility. A value below 35% is considered abnormal and suggests functional impairment or biliary dyskinesia [7]. Emerging evidence indicates that a low GBEF is associated with chronic inflammation and gallbladder wall fibrosis, likely due to prolonged bile stasis and impaired evacuation. [8].

Histopathological findings in cholelithiasis demonstrate a wide disease spectrum. Chronic cholecystitis, the most frequent diagnosis, exhibits fibrosis and lymphocytic infiltration, while acute inflammation is marked by edema, mucosal ulceration, and neutrophil infiltration. Cholesterolosis produces the “strawberry gallbladder” pattern, and persistent irritation may cause mucosal hyperplasia or metaplastic changes, which are potential precursors to dysplasia and carcinoma [9-10]. Recognizing these histological variations is critical for identifying early malignant transformation and understanding disease chronicity.

Despite increasing interest in functional gallbladder evaluation, limited research integrates GBEF with histopathological assessment. Hence, this observational study aims to investigate the association between preoperative GBEF and histopathological findings in patients with cholelithiasis undergoing cholecystectomy at a tertiary care center, thereby enhancing understanding of gallbladder dysfunction and guiding patient-specific management strategies.

## 2. MATERIAL AND METHODS:

This observational study was conducted in the Department of General Surgery at Bhagat Phool Singh Government Medical College for Women over a period of one and a half years following approval from the Institutional Scientific and Ethical Committee. The study included patients diagnosed clinically and radiologically with cholelithiasis who subsequently underwent cholecystectomy. Patients aged below 14 years or above 70 years and those with acalculous cholecystitis were excluded. The sample size was 90 participants.

All eligible patients presenting to the outpatient department or emergency with a diagnosis of calculus cholelithiasis and deemed fit for surgery were evaluated preoperatively. Ultrasonography of the whole abdomen was performed to confirm the diagnosis, and the gallbladder ejection fraction (GBEF) was calculated using a standard fatty meal stimulus (half-and-half milk). The gallbladder volume was measured before and 60 minutes after the meal, and GBEF was derived using the ellipsoid method:

**GBEF (%) = [(Pre-prandial Volume – Post-prandial Volume) / Pre-prandial Volume] × 100**,
where volume (V) = Length × Breadth × Height × 0.5.

Postoperative gallbladder specimens with stones were collected in 10% buffered formalin and sent to the Department of Pathology for histopathological evaluation. Each specimen underwent gross and microscopic examination using standard histopathological techniques. Three full-thickness sections—one each from the fundus, body, and neck—were prepared,

stained with hematoxylin and eosin, and examined under a microscope to assess the histopathological spectrum.

Data were analyzed using SPSS version 21.0 (Chicago, Illinois). Descriptive statistics were used to summarize categorical variables as frequencies and percentages, while continuous variables were expressed as mean ± standard deviation. Bivariate analyses were performed using the Chi-square or Fisher's exact test for categorical data and the unpaired t-test for quantitative data. A p-value of less than 0.05 was considered statistically significant.

**Results:**

The study included 90 participants with a mean age of 40.27 ± 13.69 years. The majority were in the 31-50 years age group (45.6%), followed by ≤30 years (30.0%) and 51-70 years (24.4%). Females predominated at 84.4%, while males comprised 15.6%. Multiple gallstones were observed in 70.0% of participants, and single stone in 30.0% [Table 1].

Laboratory parameters showed mean hemoglobin of 11.79 ± 1.68 g/dL, total leukocyte count of 7435.56 ± 1953.52 /mm³, and platelet count of 2.30 ± 0.74 lakh/mm³. Liver function tests revealed mean SGOT of 40.04 ± 21.34 IU/L, SGPT of 49.35 ± 49.47 IU/L, serum alkaline phosphatase of 107.91 ± 36.34 IU/L, and total bilirubin of 0.69 ± 0.24 mg/dL [Table 2].

Ultrasonographic findings showed mean CBD wall thickness of 3.25 ± 1.58 mm and CBD diameter of 2.96 ± 1.30 mm. Mean preprandial gallbladder volume was 22.57 ± 11.87 cc, which reduced to 12.94 ± 10.95 cc postprandially. The mean gallbladder ejection fraction (GBEF) was 45.99 ± 19.53%, with a median of 46.76% and range of 8.57-95.23% [Table 3]. Chronic cholecystitis was the most common diagnosis (62.2%), followed by acute on chronic cholecystitis (22.2%) and chronic cholecystitis with cholesterosis (15.6%). No significant association was found between stone number (multiple vs. single) and histopathological diagnosis (p = 0.524) [Table 4].

GBEF showed no significant differences across age groups (p = 0.242) or gender (p = 0.970). However, participants with multiple stones had significantly higher mean GBEF (47.60%) compared to single stone (42.22%), p = 0.0001. GBEF also varied significantly across diagnoses (p = 0.0001), being lowest in acute on chronic cholecystitis (42.33%), followed by chronic cholecystitis with cholesterosis (46.44%), and highest in chronic cholecystitis (47.18%) [Table 5].

**TABLE 1: DEMOGRAPHIC AND BASELINE CHARACTERISTICS OF STUDY PARTICIPANTS (n=90)**

| Parameter | Category/Statistics | Frequency (%) / Value |
|---|---|---|
| **Age (years)** | Mean ± SD | 40.27 ± 13.69 |
| | Median (Range) | 38.0 (19.0 - 70.0) |
| **Age Group Distribution** | ≤30 years | 27 (30.0%) |
| | 31-50 years | 41 (45.6%) |
| | 51-70 years | 22 (24.4%) |
| **Gender** | Female | 76 (84.4%) |
| | Male | 14 (15.6%) |
| **Stone Type** | Multiple stones | 63 (70.0%) |
| | Single stone | 27 (30.0%) |

**TABLE 2: LABORATORY PARAMETERS OF STUDY PARTICIPANTS (n=90)**

| Parameter | Mean ± SD | Median | Range |
|---|---|---|---|
| **Complete Blood Count** | | | |
| Hemoglobin (g/dL) | 11.79 ± 1.68 | 11.55 | 8.00 - 16.80 |
| Total Leukocyte Count (/mm³) | 7435.56 ± 1953.52 | 7050.00 | 4500 - 15000 |
| Platelet Count (lakh/mm³) | 2.30 ± 0.74 | 2.10 | 1.00 - 5.20 |
| **Liver Function Tests** | | | |
| SGOT (IU/L) | 40.04 ± 21.34 | 34.00 | 16.0 - 146.0 |
| SGPT (IU/L) | 49.35 ± 49.47 | 34.00 | 10.0 - 352.0 |
| Serum Alkaline Phosphatase (IU/L) | 107.91 ± 36.34 | 100.50 | 51.0 - 245.0 |
| Total Bilirubin (mg/dL) | 0.69 ± 0.24 | 0.65 | 0.4 - 1.7 |
| Conjugated Bilirubin (mg/dL) | 0.23 ± 0.10 | 0.20 | 0.10 - 0.50 |
| Unconjugated Bilirubin (mg/dL) | 0.46 ± 0.18 | 0.40 | 0.2 - 1.2 |

**TABLE 3: ULTRASONOGRAPHIC AND FUNCTIONAL FINDINGS (n=90)**

| Parameter | Mean ± SD | Median | Range |
|---|---|---|---|

| | | | |
|---|---|---|---|
| CBD Wall Thickness (mm) | 3.25 ± 1.58 | 3.00 | 1.0 - 14.0 |
| CBD Diameter (mm) | 2.96 ± 1.30 | 2.80 | 1.0 - 6.0 |
| **Gallbladder Volume** | | | |
| Preprandial Volume (cc) | 22.57 ± 11.87 | 20.00 | 7.0 - 78.0 |
| Postprandial Volume (cc) | 12.94 ± 10.95 | 10.00 | 1.0 - 70.0 |
| **Gallbladder Ejection Fraction (GBEF) (%)** | 45.99 ± 19.53 | 46.76 | 8.57 - 95.23 |

**TABLE 4: HISTOPATHOLOGICAL DIAGNOSIS AND ASSOCIATION WITH STONE NUMBER (n=90)**

| Histopathological Diagnosis | Overall | Multiple Stones (n=63) | Single Stone (n=27) | p-value |
|---|---|---|---|---|
| | n (%) | n (%) | n (%) | |
| Acute on Chronic Cholecystitis | 20 (22.2%) | 16 (25.4%) | 4 (14.8%) | 0.524 |
| Chronic Cholecystitis | 56 (62.2%) | 38 (60.3%) | 18 (66.7%) | |
| Chronic Cholecystitis with Cholesterosis | 14 (15.6%) | 9 (14.3%) | 5 (18.5%) | |
| **Total** | **90 (100%)** | **63 (100%)** | **27 (100%)** | |

**TABLE 5: COMPARISON OF GALLBLADDER EJECTION FRACTION (GBEF) ACCORDING TO CLINICAL VARIABLES (n=90)**

| Variable | Category | n | Mean GBEF ± SD (%) | Median (%) | Range (%) | p-value |
|---|---|---|---|---|---|---|
| **Age Group** | ≤30 years | 27 | 47.83 ± 19.78 | 41.66 | 13.16 - 90.90 | 0.242 |
| | 31-50 years | 41 | 45.99 ± 18.92 | 50.00 | 8.57 - 95.23 | |
| | 51-70 years | 22 | 45.49 ± 21.08 | 42.20 | 12.85 - 90.90 | |
| **Gender** | Female | 76 | 46.02 ± 19.91 | 46.76 | 8.57 - 95.23 | 0.970 |
| | Male | 14 | 45.81 ± 17.98 | 46.20 | 20.00 - 74.15 | |
| **Stone Number** | Multiple | 63 | 47.60 ± 20.73* | 47.36 | 8.57 - 95.23 | **0.0001*** |
| | Single | 27 | 42.22 ± 16.14 | 40.00 | 16.60 - 72.00 | |
| **Diagnosis** | Acute on Chronic | 20 | 42.33 ± 23.90 | 34.52 | 8.57 - 90.90 | **0.0001*** |
| | Chronic Cholecystitis | 56 | 47.18 ± 19.10 | 49.00 | 12.85 - 95.23 | |
| | Chronic with Cholesterosis | 14 | 46.44 ± 14.38 | 48.68 | 16.60 - 61.10 | |

## 3. DISCUSSION:

Cholelithiasis remains a prevalent hepatobiliary disorder, most commonly affecting middle-aged women due to hormonal and metabolic influences. Although many cases are asymptomatic, complications such as cholecystitis and pancreatitis often require cholecystectomy. Gallbladder ejection fraction (GBEF) serves as a key indicator of gallbladder motility and can be quantified via hepatobiliary scintigraphy or ultrasonography. It helps assess gallbladder function preoperatively and may correlate with chronic inflammation. Histopathological evaluation following cholecystectomy remains the diagnostic gold standard, offering valuable insights into disease chronicity and tissue changes.

In the present study, the mean age was 40.26 ± 13.69 years, with most patients aged 31–50 years, consistent with the typical peak age for gallstone disease. Similar findings were observed by Mann BK et al. (2023) [11], while Pauletzki J et al. (1993) [12] and Misra AP et al. (2021) [13] reported comparable demographic trends in different subgroups. No significant difference in GBEF was noted across age groups (p = 0.242), suggesting that gallbladder contractility remains stable in adults with cholelithiasis. Females predominated (84.4%), aligning with the established female-to-male ratio of 3–5:1, as seen in Delgado-Aros S et al. (2003) [14]. However, gender did not significantly affect GBEF (p = 0.970), indicating that while female sex predisposes to stone formation, it may not directly impair gallbladder function.

Multiple gallstones were observed in 70% of patients, consistent with the general trend in cholelithiasis. Interestingly, patients with multiple stones had a significantly higher mean GBEF (47.60 ± 20.72%) compared to those with single stones (42.22 ± 16.14%) (p = 0.0001). This finding contrasts with Thiyagarajan M et al. (2019) [15], who reported lower ejection fractions in cases with multiple stones. The discrepancy may relate to methodological differences, varying thresholds for abnormal GBEF, or differing stone characteristics. The higher GBEF in patients with multiple stones could indicate partial preservation of contractile function or compensatory responses in early disease stages.

Laboratory findings, including liver function tests and complete blood counts, were within normal limits, suggesting that most patients had uncomplicated cholelithiasis. This minimized confounding factors like biliary obstruction or acute inflammation, ensuring a more accurate assessment of the relationship between GBEF and histopathology.

The mean preprandial gallbladder volume in our study was 22.57 ± 11.87 cc, similar to Pauletzki J et al. (1993) [12], who reported comparable fasting volumes in gallstone patients. The mean postprandial volume was 12.94 ± 10.95 cc, with a mean GBEF of 45.99 ± 19.53%, consistent with Bartel TB et al. (2005) [16] and Flick KF et al. (2021) [17]. These findings confirm that GBEF values around 40–50% are typical in gallstone disease, reflecting moderate impairment of gallbladder contractility.

Histopathological examination showed chronic cholecystitis as the most frequent diagnosis (62.2%), followed by acute on chronic cholecystitis (22.2%) and chronic cholecystitis with cholesterosis (15.6%). This distribution reflects the chronic inflammatory nature of gallstone disease. A significant association was observed between GBEF and histopathological diagnosis ($p = 0.0001$), with the lowest GBEF in acute on chronic cholecystitis (42.33%), suggesting that functional impairment parallels inflammatory severity. Thiyagarajan M et al. (2019) [15] also found reduced ejection fractions in patients with histological evidence of cholecystitis ($p = 0.017$).

Ahn H et al. (2020) [18] and Lim JU et al. (2017) [19] further demonstrated that a lower muscle-to-fibrosis ratio in the gallbladder wall correlates with decreased GBEF, supporting the hypothesis that structural wall changes directly influence contractility. These findings align with our results, reinforcing the association between diminished gallbladder function and chronic inflammation.

No significant relationship was found between stone number and histopathological diagnosis ($p = 0.524$), indicating that gallbladder dysfunction is more closely linked to inflammatory processes than to stone burden. Similar to Thiyagarajan M et al. (2019) [158], who correlated multiple stones with reduced GBEF but not histological severity, our results highlight that stone number alone does not predict inflammation extent.

The overall findings suggest that reduced GBEF reflects the functional impact of chronic inflammation rather than stone quantity. Assessing GBEF preoperatively may therefore provide a useful non-invasive indicator of gallbladder pathology, complementing histopathological evaluation. In clinical practice, this can help identify patients with significant gallbladder dysfunction who may benefit most from surgical management, even when radiological findings appear mild. The study underscores the importance of integrating functional and structural assessment in the comprehensive evaluation of gallbladder disease.

## 4. CONCLUSION:

This observational study established a clear association between gallbladder ejection fraction (GBEF) and histopathological changes in patients with cholelithiasis undergoing cholecystectomy. The findings demonstrated that reduced GBEF correlated with more severe inflammatory alterations in the gallbladder, indicating that functional impairment often parallels structural damage. Chronic cholecystitis was the predominant histopathological finding, consistent with the natural progression of gallstone disease and chronic inflammation. The study also highlighted that gallbladder function, as assessed by GBEF, may serve as a reliable indicator of disease chronicity and severity. Interestingly, the relationship between gallstone characteristics and GBEF appeared complex, suggesting that factors such as stone size, distribution, and duration of disease may influence gallbladder motility beyond simple mechanical obstruction. No significant relationship was found between demographic variables and gallbladder function, emphasizing that physiological rather than external factors determine functional impairment. Incorporating functional evaluation with routine imaging and histological assessment may improve the diagnostic accuracy, guide surgical decision-making, and enhance the understanding of gallbladder disease progression in patients with cholelithiasis.

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