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Original Research Article

Clinicopathological Evaluation of Gallstone Variants: An Integrated Approach to Risk Factor Correlation and Histopathological Findings

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Abstract

Introduction: Gallstone disease is one of the most common hepatobiliary disorders and is associated with significant morbidity worldwide. The disease shows considerable variation in incidence, gallstone morphology, and histopathological manifestations across different populations. Identification of associated risk factors and pathological changes is important for early diagnosis and appropriate management. The study aimed to assess the clinicopathological spectrum of gallstone variants and correlate them with risk factors and histopathological findings.

Materials and Methods: This retrospective observational study was conducted in the Department of Pathology, Government Medical College, Anantapuramu, over a period of 18 months from December 2023 to June 2025. A total of 112 cholecystectomy specimens with gallstones from patients of all age groups were included in the study. Gross examination was performed to classify gallstones into pigmented, cholesterol, and mixed variants based on morphology. Histopathological examination was carried out using hematoxylin and eosin-stained sections. Clinicodemographic parameters, risk factors, presenting complaints, and histopathological findings were analyzed using descriptive statistics.

Results: The majority of patients belonged to the 31–40 years age group [35 (31.3%)], with a female predominance [80 (71%)]. Urban residents constituted 87 (78%) cases. Pigmented stones were the most common variant [65 (58%)], followed by cholesterol stones [32 (28.6%)] and mixed stones [15 (13.4%)]. Most patients were asymptomatic [72 (64.3%)], while right hypochondrial pain was the most common presenting complaint among symptomatic cases [16 (14.3%)]. Chronic cholecystitis was the predominant histopathological lesion [82 (73.2%)], followed by acute cholecystitis [25 (22.3%)]. Carcinoma gallbladder was identified in 2 (1.7%) cases.

Conclusion: Gallstone disease is strongly associated with demographic and metabolic risk factors, particularly female gender, middle age, urban residence, and dyslipidemia. Histopathological evaluation of cholecystectomy specimens remains essential for identifying inflammatory lesions and detecting clinically silent malignancies.

Keywords: Gallstone disease; Cholecystectomy; Chronic cholecystitis; Pigmented gallstones; Histopathology.

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Introduction

Gallstone disease is one of the most prevalent gastrointestinal disorders and contributes a significant burden to healthcare systems worldwide [1]. The estimated prevalence of gallstones in India ranges from 2–29%, with the disease being nearly seven times more common in North India compared to South India [2]. The prevalence of gallstone disease varies according to age, sex, dietary habits, socioeconomic status, and lifestyle factors [3]. Females are more commonly affected, and the incidence increases with advancing age due to alterations in cholesterol metabolism and biliary secretion [4]. Gallstones are broadly classified into cholesterol, pigment, and mixed stones based on

their composition and morphology [5]. Regional variations in the pattern of gallstones have been observed in India, with cholesterol stones being more common in North India, whereas pigmented stones predominate in South India [6]. Multiple risk factors such as obesity, dyslipidemia, sedentary lifestyle, dietary habits, and metabolic disturbances have been implicated in the pathogenesis of gallstone formation [7].

The diseased gallbladder associated with gallstones exhibits a wide spectrum of morphological and histopathological changes ranging from acute and chronic inflammatory lesions to premalignant and malignant conditions [8]. Chronic irritation and inflammation caused by gallstones may result in chronic cholecystitis, xanthogranulomatous cholecystitis, mucosal dysplasia, and carcinoma gallbladder [9]. Histopathological examination of cholecystectomy specimens therefore plays an important role in identifying associated pathological alterations and detecting incidental malignancies [10]. In view of the clinical importance and pathological diversity of gallstone disease, the present study was undertaken to evaluate the clinicopathological spectrum of gallstone variants and correlate them with associated risk factors and histopathological findings. The objectives of the study were to determine the incidence of various gallstone types and to analyze the risk factors and clinicopathological spectrum associated with different gallstone variants.

Materials and Methods

This retrospective observational study was conducted in the Department of Pathology, Government Medical College, Anantapuramu, over a period of 18 months from December 2023 to June 2025. The study was undertaken to evaluate the clinicopathological spectrum of gallstone disease with emphasis on demographic characteristics, risk factor correlation, gallstone morphology, and associated histopathological lesions. A total of 112 cholecystectomy specimens from patients of all age groups diagnosed with gallstone disease were included in the study. Relevant clinical and demographic details such as age, gender, body mass index (BMI), area of residence, presenting complaints, and serum lipid profile were obtained from pathology requisition forms and hospital records. All cholecystectomy specimens with gallstones were included in the study, whereas autolyzed or inadequately preserved specimens were excluded.

All specimens were subjected to detailed gross examination with documentation of the number, size, shape, color, and consistency of gallstones. Based on morphological appearance, gallstones were classified into pigmented, cholesterol, and mixed variants. Representative sections were taken from the fundus, body, neck, and any grossly suspicious areas of the gallbladder. The tissues were processed routinely, embedded in paraffin, sectioned, and stained with hematoxylin and eosin for histopathological evaluation. Microscopic examination was performed to identify various inflammatory and neoplastic lesions including acute cholecystitis, chronic cholecystitis, xanthogranulomatous cholecystitis, and carcinoma gallbladder. Histopathological findings were correlated with the different gallstone variants and clinicodemographic parameters. The collected data were entered into Microsoft Excel and analyzed using descriptive statistical methods. Categorical variables were expressed as frequencies and percentages. The results were presented in the form of tables and charts wherever appropriate.

Results

The majority of gallstone cases were observed in the 31–40 years age group [35 (31.3%)], followed by 41–50 years [30 (26.8%)]. Females predominated with 80 (71%) cases, while males accounted for 32 (29%) cases. Most patients had normal BMI [69 (61.6%)], whereas overweight and obese individuals constituted 37 (33%) and 6 (5.4%) cases, respectively. Urban residents formed the majority of the study population [87 (78%)]. (Table 1)

Table 1: Clinicodemographic profile of gallstone cases (n=112)

Variable	Category	Number of patients	Percentage
Age group	<20 years	5	4.5%
	21–30 years	18	16.1%
	31–40 years	35	31.3%
	41–50 years	30	26.8%
	>50 years	24	21.4%
Gender	Female	80	71.0%
	Male	32	29.0%
BMI category	Normal	69	61.6%
	Overweight	37	33.0%
	Obese	6	5.4%
Area of residence	Urban	87	78.0%
	Rural	25	22.0%

Most patients were asymptomatic [72 (64.3%)]. Among symptomatic cases, right hypochondrial pain was the most common presenting complaint [16 (14.3%)], followed by epigastric pain [10 (8.9%)]. Nausea, vomiting, and jaundice were less commonly observed. (Table 2)

Table 2: Chief complaints among gallstone cases (n=112)

Chief complaints	Number of patients	Percentage
Asymptomatic	72	64.3%
Right hypochondrial pain	16	14.3%
Epigastric pain	10	8.9%
Nausea	7	6.3%
Vomiting	5	4.5%
Jaundice	2	1.8%

Pigmented stones were the most common gallstone variant [65 (58%)], followed by cholesterol stones [32 (28.6%)]. Mixed stones accounted for 15 (13.4%) cases. (Table 3)

Table 3: Classification of gallstones based on morphology (n=112)

Type of stone	Morphology	Number of patients	Percentage
Pigmented	Multiple, small, jet black, mulberry-shaped	65	58.0%
Cholesterol	Solitary, large, oval, yellow	32	28.6%
Mixed	Multiple, varying sizes	15	13.4%
Total		**112**	**100%**

Chronic cholecystitis was the predominant histopathological lesion across all gallstone variants and was most commonly associated with mixed stones [10 (76.9%)] and pigmented stones [49 (75.3%)]. Acute cholecystitis was relatively more frequent in cholesterol stones [9 (26.4%)]. Xanthogranulomatous cholecystitis and carcinoma gallbladder were infrequently encountered. (Table 4)

Table 4: Distribution of histopathological lesions in relation to gallstone variants

Histopathological lesion	Pigmented stones (n=65)	Cholesterol stones (n=34)	Mixed stones (n=13)
Acute cholecystitis	14 (21.5%)	9 (26.4%)	2 (15.4%)
Chronic cholecystitis	49 (75.3%)	23 (67.6%)	10 (76.9%)
Xanthogranulomatous cholecystitis	1 (1.5%)	2 (5.8%)	0
Carcinoma gallbladder	1 (1.5%)	0	1 (7.7%)
Total	**65**	**34**	**13**

Pigmented gallstones were characteristically multiple, small, jet black in color, and mulberry-shaped. (Figure 1) Cholesterol gallstones were predominantly solitary, large, oval-shaped, and yellow in appearance. (Figure 2)

Mixed gallstones showed variable morphology with multiple stones of differing sizes and appearances. (Figure 3) Histopathological examination revealed features of chronic cholecystitis with prominent Rokitansky–Aschoff sinus formation. (Figure 4)

Microscopic examination demonstrated features consistent with adenocarcinoma of the gallbladder associated with gallstone disease. (Figure 5)

Figure 1: Pigmented gall stones

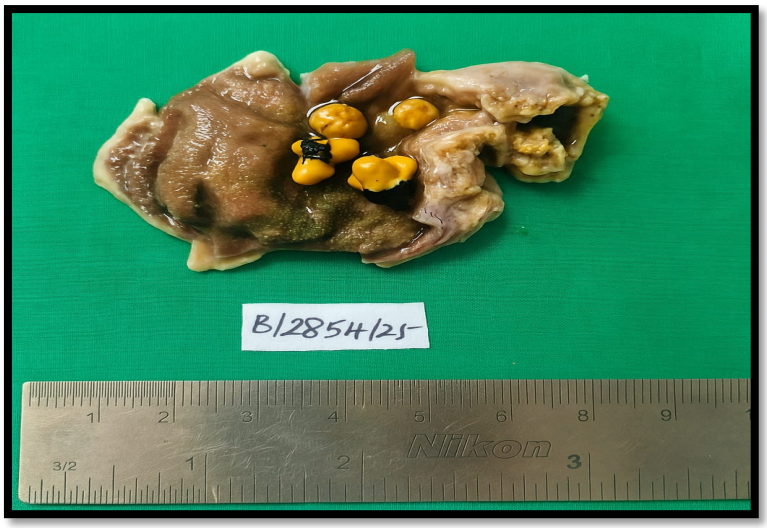

Figure 2: Cholesterol gall stones

Figure 3: Mixed gall stones

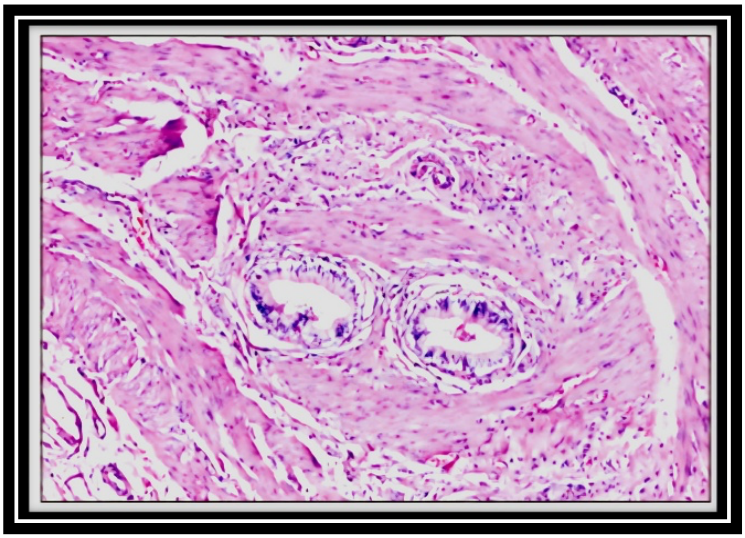

Figure 4: Chronic cholecystitis with Rokitansky Aschoff sinus

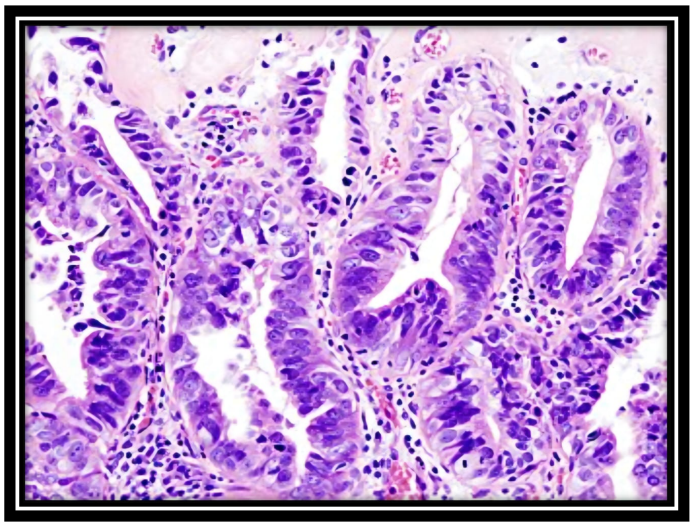

Figure 5: Adenocarcinoma of Gall bladder

Discussion

Gallstone disease is a common hepatobiliary disorder predominantly affecting middle-aged females and is influenced by multiple demographic and metabolic risk factors. In the present study, the majority of patients belonged to the 31–40 years age group [35 (31.3%)], followed by the 41–50 years group [30 (26.8%)]. Similar observations were reported by Devi Beena et al., where the highest number of patients belonged to the 41–50 years age group [11]. Female predominance was evident in the present study, with females accounting for 80 (71%) cases and males constituting 32 (29%) cases. Comparable female predominance has been documented by Hassan et al. and Noor et al., who reported higher incidence of gallstone disease among women, particularly in the third and fourth decades of life [12,13]. The increased occurrence among females may be related to hormonal influences on cholesterol metabolism and bile composition.

In the present study, urban residence was observed in 87 (78%) patients, while obesity and dyslipidemia were noted in 6 (5.3%) and 28 (25%) cases, respectively. These findings support the role of changing dietary habits, sedentary lifestyle, and altered lipid metabolism in gallstone formation. Similar observations have been reported in studies from different parts of India, where urban populations demonstrated a higher prevalence of gallstone disease and associated metabolic risk factors [11,14,15]. Hassan et al. also observed increased frequency of gallstones among urban residents and patients with dyslipidemia [12].

Most patients in the present study were asymptomatic [72 (64.3%)]. Among symptomatic individuals, right hypochondrial pain [16 (14.3%)] and epigastric pain [10 (8.9%)] were the common presenting complaints. Noor et al. reported abdominal pain as the predominant clinical presentation in 78.4% of patients undergoing cholecystectomy [13]. Morphologically, pigmented stones were the most common gallstone variant in the present study [65 (58%)], followed by cholesterol stones [32 (28.6%)] and mixed stones [15 (13.4%)]. Devi Beena et al. similarly reported pigment stones as the predominant gallstone type in their study population, whereas studies from North India demonstrated predominance of mixed stones, reflecting regional variations in dietary habits and bile composition [11].

Histopathological examination in the present study revealed chronic cholecystitis as the most common lesion [82 (73.2%)], followed by acute cholecystitis [25 (22.3%)]. Xanthogranulomatous cholecystitis and carcinoma gallbladder were identified in 3 (2.6%) and 2 (1.7%) cases, respectively. Similar findings were reported by Noor et al., who observed chronic cholecystitis in 76% of cases, and by another large Indian study where chronic cholecystitis constituted 79.8% of all histopathological lesions [13]. The incidence of carcinoma in the present study was low but clinically significant, emphasizing the importance of routine histopathological examination of all cholecystectomy specimens for early detection of incidental malignancies and premalignant lesions.

Conclusion

Gallstone disease remains a common hepatobiliary disorder with significant association with demographic and metabolic risk factors such as female gender, middle age, urban residence, obesity, and dyslipidemia. Understanding these associated risk factors is essential for improving early diagnosis, guiding preventive strategies, and optimizing patient management. The present study also demonstrated that different gallstone variants are associated with a wide spectrum of histopathological lesions, with chronic cholecystitis being the most common finding. Histopathological

evaluation of cholecystectomy specimens continues to remain the gold standard, as it not only confirms inflammatory pathology but also aids in the detection of clinically silent premalignant and malignant lesions, thereby emphasizing the importance of routine microscopic examination of all cholecystectomy specimens.

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