

GALLSTONE CHARACTERISTICS AND ASSOCIATED EPITHELIAL LESIONS: A CLINICOPATHOLOGICAL STUDY

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Abstract:

Background: Gallstone disease is a prevalent malady worldwide, representing a substantial portion of biliary tract disorders. Gallstones pose significant health risks, ranging from mild discomfort to severe complications such as cholecystitis, pancreatitis and even carcinoma. The gallbladder exhibits a diverse array of epithelial alterations in response to gallstone presence. This study aims to shed light on the clinico-epidemiological correlates of gallstone disease, paving the way for enhanced diagnostic precision and therapeutic interventions. **Methods:** Our investigation encompassed a cohort of one hundred patients diagnosed with cholelithiasis, irrespective of age, sex, physique, or parity, who underwent surgical interventions at our hospital, regardless of demographic factors. **Results:** Our study revealed a notable predominance of female cases, constituting 74% of the cohort, with a striking female-to-male ratio of 3:1. The mean age of participants was 42.9 years, with the highest incidence observed in individuals in their fourth decade, comprising 33% of cases, followed by 25% in the fifth decade. **Conclusion:** Our findings highlight the need for comprehensive approaches to diagnosis and management, incorporating histopathological assessment for early detection of potential malignancies.

Keywords: Gallstone Disease, Biliary Tract Disorders, Cholecystitis, Pancreatitis, Carcinoma Chronic Cholecystitis.

INTRODUCTION:

Gallstone disease stands as a prevalent malady globally, constituting a substantial portion of biliary tract disorders (1). The gallbladder, an organ with profound significance in digestive physiology, harbors this pathology, affecting millions worldwide. Characterized by the formation of solid masses within the gallbladder or bile ducts, gallstones pose significant health risks, ranging from mild discomfort to severe complications such as cholecystitis, pancreatitis, and even carcinoma (2). Understanding the intricacies of gallstone

characteristics and their associated epithelial lesions is imperative for effective clinical management and preventive strategies.

The gallbladder, a pear-shaped sac nestled beneath the right hepatic lobe, serves as a reservoir for bile, facilitating fat digestion in the gastrointestinal tract. Its anatomical dimensions vary but typically measure around 10 cm in length, 3-4 cm in width, with a mucosal lining adorned by columnar epithelium. While traditionally compartmentalized into fundus, body, and neck, variations exist in its position and

embedding within the liver parenchyma, predisposing certain individuals to gallstone formation (3). This intricate organ architecture, combined with physiological factors, lays the foundation for gallstone pathogenesis.

India, a diverse nation marked by regional disparities, manifests varying prevalence rates of gallstone disease. Studies indicate a higher incidence in the northern belt compared to the southern regions, possibly attributable to genetic, dietary, and lifestyle differences (4). With an estimated prevalence ranging from 2% to 29%, gallstone disease poses a significant health burden, particularly affecting middle-aged individuals, especially women. The evolving dietary patterns, characterized by increased consumption of fatty foods and alcohol, contribute to the rising incidence observed over the past decades, mirroring global trends (5).

Clinically, gallstone disease presents a spectrum of symptoms, ranging from asymptomatic to debilitating manifestations. Patients often report right upper quadrant abdominal pain, bilious vomiting, fever, and obstructive jaundice, indicative of gallstone-related complications. Moreover, cholelithiasis, commonly encountered in females of reproductive age, underscores the multifactorial nature of its etiology, encompassing hormonal influences and metabolic factors (6).

Histologically, the gallbladder exhibits a diverse array of epithelial alterations in response to gallstone presence. Chronic cholecystitis, characterized by inflammatory changes, serves as a common histopathological finding in gallstone-afflicted individuals. Furthermore, epithelial hyperplasia, metaplasia, and dysplasia emerge as precursor lesions, harboring the potential for malignant transformation.

Understanding these histopathological nuances is paramount for elucidating the underlying mechanisms driving gallstone-related epithelial alterations (7).

Against this backdrop, our study endeavors to unravel the intricate interplay between gallstone characteristics and associated epithelial lesions through a clinicopathological lens. Our investigation delves into the demographic profiles, gallstone compositions, and histopathological manifestations of cholelithiasis. Through meticulous examination and analysis, we aim to shed light on the clinico-epidemiological correlates of gallstone disease, paving the way for enhanced diagnostic precision and therapeutic interventions.

MATERIALS AND METHODS

This prospective study was conducted at the Departments of Pathology of our tertiary care hospital. Our investigation focused on a cohort of one hundred patients diagnosed with cholelithiasis, irrespective of age, sex, physique, or parity, who were admitted to our hospital and underwent either open or laparoscopic cholecystectomy.

Each participant underwent a detailed clinical assessment, with comprehensive medical histories recorded using a predefined Proforma. Patient selection was achieved through simple random sampling to ensure unbiased representation.

Prior to the commencement of the study, institutional Ethics Committee Clearance was obtained, adhering to ethical guidelines and principles. Written informed consent was procured from all participants, emphasizing confidentiality and the protection of their personal data throughout the study period.

Following cholecystectomy, meticulous observations were made concerning the

gallbladder's condition, including the presence of adhesions, wall thickness, and the presence of gallstones. Gallstones were categorized based on their characteristics, including whether they were single, double, or multiple, as well as their shape (round, irregular, or faceted), and type (pigmented or cholesterol).

Surgically resected gallbladder specimens were processed by fixation in a 10% formalin solution and subsequent embedding in paraffin. For cases without gross abnormalities, standard sections including the fundus, body, and neck were obtained. Routine histochemical staining using Hematoxylin and Eosin was performed for histological analysis.

Data collection and organization were meticulously conducted using Microsoft Excel spreadsheets. Statistical analysis was performed with SPSS v22 software, employing a significance level of 0.05 ($p < 0.05$) to determine statistically significant associations between study variables. Tests of significance were applied to elucidate the

relationships between various parameters observed during the study.

Throughout the research process, utmost care was taken to ensure the integrity of data collection, analysis, and interpretation, adhering to the highest standards of scientific rigor and ethical conduct.

RESULTS

The study encompassed patients diagnosed with cholelithiasis who underwent surgical interventions at our hospital, regardless of age, gender, body type, or parity. Notably, our investigation revealed a predominance of female cases, constituting 74% of the cholelithiasis cohort, with a striking female-to-male ratio of 3:1. The mean age of participants was 42.9 years, with a standard deviation of 5.8 years. Analysis of age distribution unveiled the highest prevalence of cholelithiasis in individuals in their fourth decade of life, accounting for 33% of cases, followed by 25% in the fifth decade.

Table 1: Cases of Cholelithiasis: Distribution According to Sex

Sex	Number of Patients (Cholelithiasis)	Percentage
Male	36	36%
Female	64	64%
Total	100	100%

Table 2: Cases of Cholelithiasis: Distribution According to Type of Gallstones

Type of Gall Stones	Number of Patients (Cholelithiasis)	Percentage
Pure cholesterol	22	22%
Pigmented	33	33%
Mixed	45	45%
Total	100	100%

Table 3: Distribution of Type of Gallstone According to Changes in Epithelium

Epithelium	Type of Gall Stone			Total No. of cases
	Cholesterol	Mixed	Pigmented	
Normal	2	3	2	7
	20.0%	60.0%	20.0%	100.0%
Focally Ulcerated	6	8	7	21
	26.3%	36.8%	36.8%	100.0%
Diffuse Ulcerated	5	9	2	16
	30.8%	61.5%	7.7%	100.0%
Atrophic	4	3	5	12
	44.4%	22.2%	33.3%	100.0%
Hyperplastic	2	7	4	13
	7.1%	57.1%	35.7%	100.0%
Hyperplastic And Metaplastic	1	4	2	7
	0.0%	60.0%	40.0%	100.0%
Atrophic & Mild Hyperplastic	0	2	1	3
	0.0%	0.0%	100.0%	100.0%
Focally Ulcerated & Mild Hyperplastic	5	3	4	12
	30.8%	38.5%	30.8%	100.0%
Focally Ulcerated & Atrophic	3	4	2	9
	44.4%	33.3%	22.2%	100.0%
Focally Ulcerated & Metaplastic	2	3	2	7
	11.1%	55.6%	33.3%	100.0%
Diffuse Ulcerated & Metaplastic	0	1	1	2
	0.0%	66.7%	33.3%	100.0%

Chi Sq = 18.405 p value = 0.725 (NS)

Regarding gallstone composition, our findings delineated a prevalence of mixed-type gallstones in the majority of cases, comprising 46%. Pigmented gallstones were observed in 30% of cases, while pure cholesterol gallstones constituted 24% of the cohort. Noteworthy patterns emerged concerning the number and morphology of gallstones, with 58% of cases exhibiting multiple gallstones, followed by 30% with single gallstones. Additionally, gallstone shape analysis revealed a predominance of faceted gallstones at 32%, followed closely by irregular gallstones at 29%, and round gallstones at 22%, with ovoid gallstones present in 15% of cases.

Furthermore, histopathological examination unveiled significant epithelial alterations in the gallbladder mucosa. Only 5% of cases exhibited normal mucosa, while the majority showcased various epithelial abnormalities. Focal ulceration emerged as the most prevalent alteration, observed in a substantial proportion of cases, followed by hyperplastic changes. Atrophic changes were noted in 9% of cases. Notably, statistical analysis indicated non-significant differences in the prevalence of these epithelial alterations.

DISCUSSION

Cholelithiasis, a prevalent disorder affecting 10% to 20% of adults in developing nations, remains a significant contributor to global morbidity and mortality. Despite often presenting asymptotically for extended periods, gallstones harbor the potential for serious complications, including chronic cholecystitis.(8) Chronic cholecystitis is characterized by a wide array of associated lesions including cholesterolosis, muscle hypertrophy, parietal fibrosis, adenomatous proliferation of mucous glands, hyperplasia, metaplasia, and dysplasia. These latter three lesions are universally acknowledged as precursor lesions with the potential to develop into cancer.(9)

Our study, encompassing patients undergoing surgical interventions for cholelithiasis, irrespective of demographic factors, revealed a notable predominance of female cases, constituting 74% of the cohort, with a striking female-to-male ratio of 3:1. The mean age of participants was 42.9 years, with the highest incidence of cholelithiasis observed in individuals in their fourth decade, comprising 33% of cases, followed by 25% in the fifth decade. These findings underscore the demographic patterns characterizing cholelithiasis and highlight the need for targeted preventive strategies and early detection measures, particularly among middle-aged women.

Our investigation revealed a predominant occurrence of cholelithiasis among individuals in their fourth to fifth decades of life, with the youngest patient being a 12-year-old male and the oldest an 86-year-old female. Notably, our study observed a male-to-female ratio of 1:3. The mean age of participants, 42.9 years, closely aligns with previous studies by Khanna et al. and Aslam et al., (10,11) although differing from the

findings of Terada Tadashi et al.(12) Regarding gallstone composition, cholesterol gallstones were identified in 24% of cases, pigmented in 30%, and mixed in 46%, with mixed-type gallstones being the most prevalent. These results corroborate findings by Weerakoon et al.(13) and Mathur et al. (14) but contrast with those of Tadashi T. et al. (12), who reported a higher prevalence of pigmented gallstones. Moreover, our study revealed that only 5% of cholelithiasis cases exhibited normal mucosa, with the majority showcasing various epithelial alterations. Focal ulceration emerged as the most common epithelial alteration, followed by hyperplastic changes and atrophic changes, with no statistically significant difference noted. These pathological changes in the epithelium, including hyperplasia, metaplasia, and dysplasia, could potentially serve as precursor lesions for gallbladder cancer, consistent with findings reported by Seretis C. et al. (15). These findings underscore the diverse pathological manifestations associated with cholelithiasis and highlight the importance of further research to elucidate underlying mechanisms and guide clinical management strategies. Limitation of the above study lies in its single-center design, potentially limiting generalizability. Additionally, the study's retrospective nature and reliance on surgical cases may introduce selection bias, overlooking asymptomatic individuals. Further, the study lacks long-term follow-up data, hindering assessment of disease progression.

CONCLUSION:

In conclusion, our study sheds light on the demographic distribution, gallstone characteristics, and epithelial alterations in cholelithiasis. Despite limitations, our

findings emphasize the need for comprehensive approaches to diagnosis and management, incorporating histopathological assessment for early detection of potential malignancies. These insights contribute to better understanding and management of cholelithiasis, guiding future research and clinical practice.

REFERENCE

1. Shaffer EA. Epidemiology of gallbladder stone disease. Best practice & research Clinical gastroenterology. 2006 Jan 1;20(6):981-96.
2. Narang S, Goyal P, Bal MS, Bandlish U, Goyal S. Gall stones size, number, biochemical analysis and lipidogram-an association with gall bladder cancer: a study of 200 cases. Int J Cancer Ther Oncol. 2014 Jun 26;2(3):020310.
3. Yi SQ, Ohta T, Tsuchida A, Terayama H, Naito M, Li J, Wang HX, Yi N, Tanaka S, Itoh M. Surgical anatomy of innervation of the gallbladder in humans and *Suncus murinus* with special reference to morphological understanding of gallstone formation after gastrectomy. World J Gastroenterol. 2007 Apr 14;13(14):2066-71.
4. Ashok M, Krishnan A, Choudhury G, Kalkura NS, Jayanthi V. Regional differences in composition of cholesterol gallstones in India. Journal of Medical Science and Research. 2012;3(1):3.
5. Kapoor VK, McMichael AJ. Gallbladder cancer: an 'Indian' disease. Natl Med J India. 2003 Jul 1;16(4):209-13.
6. Mohan H, Punia RP, Dhawan SB, Ahal S, Sekhon MS. Morphological spectrum of gallstone disease in 1100 cholecystectomies in North India. Indian journal of surgery. 2005 Jun 1;67(3).
7. Khan I, Panda N, Banerjee M, Das R. Epidemiological factors in gall bladder cancer in eastern India-a single centre study. Indian journal of surgical oncology. 2013 Mar;4:67-72.
8. Velanovich V.F. Biliary dyskinesia and biliary crystals: a prospective study. Am Surg.1997, 63:69-73.
9. Kouroumalis E., Hopwood D., Ross P.E., Milne G., Bouchier I.A. Gallbladder epithelial acid hydrolases in human cholecystitis. J Pathol. 1983, 139: 179-191.
10. Khanna R., Chansuria R., Kumar M., Shukla H.S. Histological Changes in gall bladder due to stone disease. Indian J Surg. 2006, 68:201-4.
11. Aslam H.M., Saleem S., Saleem M.: Assessment of gallstone predictor: comparative analysis of Ultrasonographic and biochemical Parameters. Int. Arch. Med. 2013, 6:17.
12. Terada Tadashi. Histopathologic features and frequency of gallbladder lesions in consecutive 540 cholecystectomies. Int. J.Clin. Exp. Pathol.2013, 6 (1): 91-96.
13. Weerakoon Harshi T.M., Jamburagoda G.S. Ranashinge, Ayanthi Navaratna, Rameiah Sivakanesan, Kuda B. Galketiya, Shanthini Rosairo. Can the type of gallstone be predicted with known possible risk factors? A comparison between mixed cholesterol and black pigment stones. Gastroenterology. 2013, vol.14:88.
14. Mathur S.K., Duhan A., Singh S., Agarwal M., Swn R, Singh S., Garg S. Correlation of Gallstones characteristics with mucosal changes in gallbladder, Trop Gastroenterology. 2012, 33(1):39- 44.
15. Seretis Charalampos, Lagoudianakis E., Gourgiotis S. Melaplastic changes in chronic cholecystitis: Implication for early diagnosis and surgical invention to prevent the gallbladder Melaplasia dysplasia-Carcinoma Sequence J. Clin. Med. Res.2013, 6(1):26-29.