ORIGINAL ARTICLE

Morphological Spectrum of Gall Bladder Diseases at a Tertiary Care Hospital of Karachi

Asma Shabbir[1], Zareen Irshad[1], Saba Javed[2], Fakiha Nadeem[2], Nazish Jaffar[1], and Syed Mehmood Hasan[3]

ABSTRACT

Objectives: To determine morphological spectrum of gall bladder diseases at a tertiary care centre of Karachi and to correlate with age and gender.

Methodology: Data was collected from histopathological records between June 2017 to June 2019. Relevant data including registration number, age, gender of the patients and diagnosis were recorded. Data was entered and analyzed using SPSS version 21. P-value < 0.05 was considered as significant.

Results: In our study, patients 26-35 years of age were predominantly found to be susceptible to gall bladder diseases and male to female ratio was 1:3.7. Out of the total 150 cases, 75 were identified as chronic cholecystitis with cholelithiasis whereas 32 cases of chronic cholecystitis were without stones or any other associated pathology. Out of 150 cases, 40 were seen in combination with different pathologies. Our series also included three cases of adenocarcinoma and all of these were diagnosed in females. Significant association of diagnosis was seen with gender and type of stones (p-value = 0.03) (p-value = 0.01) respectively.

Conclusion: In our study, chronic cholecystitis with cholelithiasis was the most common finding which was most predominantly seen in females. Younger age group was mainly affected in both genders. Mixed type of gall stones were the most common stones found in our series.

Key words: Cholelithiasis, cholecystitis, adenocarcinoma

How to cite this article: Shabbir A, Irshad Z, Javed S, Nadeem F, Jaffar N, Hasan SM. Morphological spectrum of gall bladder diseases at a tertiary care hospital of Karachi. Ann Jinnah Sindh Med Uni 2020; 6(1):24-28

DOI:https://doi.org/10.46663/ajsmu.v6i1.24-28

INTRODUCTION

One of the most common diseases among gastrointestinal disorders are those arising from gall bladder. The disease entity varies from cholecystitis (acute, chronic, follicular and xanthogranulomatous), cholelithiasis, cholesterolosis, adenomatous hyperplasia, metaplasia and carcinoma[1]. According to recent epidemiologic study, there is evidence of strong association of Helicobacter pylori species with chronic cholecystitis, gall bladder carcinoma and cholesterol stones.[2] Cholelithiasis has been the most common gastrointestinal disorder which presents with acute abdominal pain that may require hospitalization in otherwise healthy people, however, more than half of the cases are asymptomatic.

Assistant Professor[1] / 3rd year MBBS student[2] / Professor, Head of the Department[3], Department of Pathology, Sindh Medical College, Jinnah Sindh Medical University, Karachi, Pakistan

Correspondence: Asma Shabbir, Assistant Professor, Department of Pathology, Sindh Medical College, Jinnah Sindh Medical University, Karachi, Pakistan

Email: drasma52@gmail.com

Prevalence of gallstones is the highest in the West, particularly in elderly women.[3,4] Increased incidence of gallstones in western countries is most likely due to an ageing population and obesity.[5] In western countries, 70-80% are pure cholesterol gallstones whereas in Asian countries, mixed stones are predominant.[6,7] The common risk factors of gallstones formation in Asia are middle age, fertility, female gender, and flatulence.[8] According to Globocan 2018 data, gall bladder cancer accounts for 1.2% of all global cancer diagnosis and 1.7% of all cancer death.[9] Though gall bladder carcinoma is rare but it is an aggressive disease with poor prognosis. Less than 5% of the patients survive for up to 5 years, but if diagnosed and treated at early stage, 75% of the patients can survive for 5 years.[10] The presenting symptoms of gall bladder carcinoma are mostly related to invasion of adjacent organs involving liver as the most common site, other organs might be involved through distant metastasis. Hence, extensive tumour sampling is required for accurate staging of invasive cancers which is essential to determine the prognosis and treatment.

Acute pancreatitis is the other severe complication of cholelithiasis.[11] Moreover, literature shows that gall bladder diseases are the major risk factor for developing hepatocellular carcinoma independent of cirrhosis and viral hepatitis.[12] The study of gall bladder diseases has gained importance because of its associated co-morbidities. Females with rheumatoid arthritis older than 60 years of age were found to be associated with significantly higher prevalence of gall stones compared with general population and the most probable reason is hyperlipidemia and chronic inflammation.[13] The other co-morbidities with cholelithiasis include Crohn's disease, ileal resection or other diseases of ilium, hence it is important to know the frequency of gall bladder diseases which might provide the clue about co-morbidities as well.

The aim of this study is to identify the morphological spectrum of different gall bladder diseases at a tertiary care hospital of Karachi.

METHODOLOGY

This descriptive study was conducted after ethical approval from Institutional Review Board of Jinnah Sindh Medical University (Reference no: JSMU/IRB/2019-244) and Dr. Tahir laboratory, Hamdard University and Hospital, Karachi. Data was collected from the records available between June 2017 to June 2019. All histopathologically diagnosed cases of gall bladder diseases reported during two years were included in the study. Relevant data including registration number, age, gender of the patients and diagnosis were recorded. Cases with incomplete data were excluded from the study. Data was entered and analysis was done using SPSS version 21. The frequency of gall bladder diseases was studied. Furthermore, association of diagnosis with age and gender of the patients were calculated using chi-square test. P-value < 0.05 was considered as significant.

RESULTS

Over the period of two years, 150 cases of gall bladder diseases were diagnosed at a tertiary care centre of Karachi, out of which 32 (21.3%) were males. The mean age of the group was 42.36±1.26. We found significant association between diagnosis and age (p=0.001). We observed that patients in 26-35 years age group were more susceptible to gall bladder diseases closely followed by 36-45 years age group as compared to older age group (65-75 years). From the total 150 cases, 75 cases were identified as chronic cholecystitis with cholelithiasis, whereas 32 cases of chronic cholecystitis were without stones or any other associated pathology. Out of 150 cases, 40 cases were seen in combination with different pathologies. Our series also included 3 cases of adenocarcinoma and all of them were diagnosed in females. We observed significant association between diagnosis and gender (p=0.03), where chronic cholecystitis with cholelithiasis was most common in females. (Table 1) (Figure 1 and Figure 2)

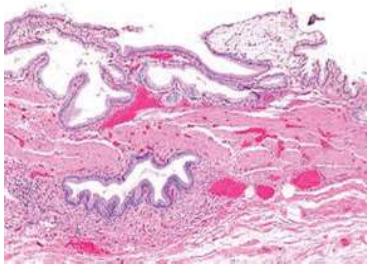

Figure 1: Chronic Cholecystitis

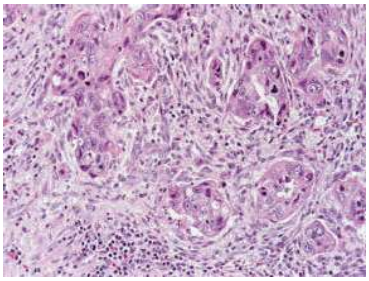

Figure 2: Adenocarcinoma gall bladder

Out of total 150 cases, 102 cases were associated with stones and 48 were without stones. From 102 cases reported with gallstones, 67 were mixed stones, 18 were pure cholesterol stones and 17 were pigmented stones. Significant association was seen between types of stones and diagnosis, where mixed type of stones were most commonly seen in chronic cholecystitis without any other associated pathology (p= 0.001). (Table 2)

DISCUSSION

Gall bladder diseases seriously affect the quality of life of the patients. In this retrospective study, we investigated different histopathological diseases of gall bladder at a tertiary care hospital of Karachi**.** Our study observed gall bladder diseases to be more common in females as compared to males with a ratio of 3.7:1. This is consistent with other studies globally which also reported females to be more susceptible to gall bladder diseases particularly cholecystitis.[14,15] The most probable reason for female predominance of cholecystitis might be assumed by the role of estrogen secretion in females. Literature shows that, estrogen

Table 1: Association Between Diagnosis and Gender

Diagnosis	Gender		Total	P-value
	Male	Female		
Acute Necrotizing Cholecystitis	1	2	3	0.03
Acute Necrotizing Cholecystitis with Cholelithiasis	1	5	6	
Chronic Cholecystitis	4	28	32	
Chronic Cholecystitis with Cholelithiasis	15	60	75	
Chronic Cholecystitis with Cholelithiasis with Cholesterolosis	2	14	16	
Chronic Cholecystitis with Cholelithiasis with Reactive Hyperplasia	2	3	5	
Adenocarcinoma	3	0	3	
Follicular Cholecystitis	4	6	10	
Total	32	118	150	

Table 2. Association Between Diagnosis and Type of Stones

Types of Gallstones	Chronic Cholecystitis	Acute Necrotizing Cholecystitis	Chronic Cholecystitis with Cholesterolosis	Chronic Cholecystitis with Reactive Hyperplasia	P- value
Pigmented	15	1	0	1	0.001
Cholesterol	0	2	16	0	
Mixed	60	3	0	4	
Total	75	6	16	5	

influences gallstone formation as it appears to increase saturation index of biliary cholesterol.[16] Iron deficiency anaemia appears to be another risk factor for cholecystitis and past studies have observed high prevalence of iron deficiency anaemia in Pakistani females which could be one of the most likely causes of cholecystitis in females of our region.[17] Other factors contributing to increased frequency of cholecystitis among females include multiparity, high Body Mass Index (BMI), frequent use of oral contraceptives and hormone replacement therapy.[18]

In our study, we found that the peak incidence for occurrence of gall bladder diseases was 26-35 years in both genders, closely followed by 36-45 years which is consistent with other studies conducted in Asian countries, including Pakistan.[19,20] Whereas this finding is contrary to the studies conducted in the West where gall bladder diseases are more common among elderly people aged above 60 years.[15] This difference might be due to the majority of the population in our region being young individuals who consume less vegetarian and high saturated fatty diet.[22] The other reason could be majority of obese individuals in elderly ages in the West. However, the exact reason for this discrepancy remains unanswered.

In our study, chronic cholecystitis with cholelithiasis is the most commonly encountered gall bladder disease which is in line with other studies done in Pakistan and neighbouring countries.[21,22] However, in developed countries, chronic cholecystitis is a common finding as compared to association with cholelithiasis.[23]

Our study is also in accordance with other studies from Asian countries where we found mixed type of stones as the most common gall stones.[24] On the contrary, in the West, pure cholesterol stones appear to be the more common type.[7] However, pure cholesterol stones are also commonly seen in different regions of Pakistan.[25,26] We assume that most probable reason for variation in types of gallstones in our country is delayed presentation and diagnosis of cholelithiasis which results in conversion of cholesterol stones into mixed type of stones. With time, gallstones may be colonized with bacteria which triggers gall bladder mucosal inflammation and cystic enzymes from bacteria and leukocytes hydrolyze bilirubin conjugates and fatty acids. As a result, cholesterol stones may accumulate the substantial proportion of calcium bilirubinate and calcium salts producing mixed stones over time. In agreement with the West, adenocarcinoma of gall bladder is less frequently seen in our region.[27] Our

study reveals that gall bladder carcinoma is common among females as compared to males which is in correspondence with literature from other regions of the world.[28] As mentioned earlier, estrogen increases the risk of gallstones thus estrogen might be the primary cause of increased incidence of gall bladder cancer in females.[28] Moreover, long standing gall stones is a probable risk factor for adenocarcinoma. Hence, symptomatic patients with cholelithiasis should be promptly treated and every specimen after cholecystectomy must be sent for histopathological reporting to confirm the diagnosis and also to reveal incidental findings.

CONCLUSION

We conclude that chronic cholecystitis with cholelithiasis was the most common finding in our study which was most predominantly seen in females. Young age was mainly affected in both genders. Mixed type of gall stones were found to be the most common stones.

With the best of our efforts, we have collected and compiled all the common and rare diseases of gall bladder broadly which have been reported during one year at a tertiary care centre of Karachi. This might help us to know the disease burden in our region and might help in future to plan the appropriate precautionary diagnostic and treatment strategies. Further studies with larger sample size are needed to focus on the gall bladder diseases associated with co morbidities.

Author's Contributions: Dr. Syed Mehmood Hasan & Dr. Asma Shabbir conceived the idea. Saba Javed and Fakeha Nadeem contributed in data collection & literature search. Saba Javed worked on introduction & methodology. Dr. Asma Shabbir did statistical analysis. Fakeha Nadeem worked on results & discussion. Dr. Zareen Irshad & Dr. Nazish Jaffar did critical review. All the authors approved the manuscript.

References

1. Sangwan, M.K., V. Sangwan, M.K. Garg, D. Singla, P. Malik, and A. Duhan, Incidental carcinoma of gall bladder in north India: is routine histopathology of all cholecystectomy specimens justified? Int J Surgery. 2016; 2(4):465-470.
2. Maurer K.J, MM Ihrig, AB Rogers, Vivian Ng, Bouchard G, MR Leonard, et al. Identification of cholelithogenic enterohepatic helicobacter species and their role in murine cholesterol gallstone formation. Gastroenterology. 2005; 128(4):1023-1033.
3. Gangwar P, Rathore LKPS, Gupta R, and Singh L. Heptoprotective Action of katuki. Eur J Biomed Pharm Sci.2018;5(1):892-895.
4. Singh PK, PK Arya, HS Khetarpal, K Goyal, HS Jolly, T Din, et al., Epidemiology of gallstone disease in a tertiary care hospital-- a changing trend in current perspective. J Evol Med & Dent Sci. 2017;6(75):5332-5337.
5. Noble F and Johnson C. Gallstones. Medicine Elsevier, 2015; 43(11):689-693.
6. Nayak AK, A Anand, and D Sahoo, Role of Pathological Organisms in Gallstone disease. J Pharm Biomed Sci. 2016; 6(3): 155-157.
7. Cariati A, Gallstone classification in western countries. Indian J Surg. 2015;77(2):376-380.
8. Jaleel F, K Rashid, N Bakhtiar and M Jawaid. Risk factors of gallstones. The Professional Med J. 2017; 24(11):1675-1679.
9. Rawla P, T Sunkara, KC Thandra and A Barsouk, Epidemiology of gall bladder cancer.Exp Clin Hep. 2019;5(2):93.
10. Goetze TO, gall bladder carcinoma: prognostic factors and therapeutic options. World J Gastroenterol. 2015; 21(43):12211-7.
11. Venneman NG, W Renooij, JF Rehfeld, GP vanBerge-Henegouwen, PM Go, IA Broeders, et al., Small gallstones, preserved gall bladder motility, and fast crystallization are associated with pancreatitis. Hepatology. 2005;41(4):738-746.
12. Al-Assi K, R Hatia, V Rallapalli, Y Abugabal, A Abdelhakeem, R Abdel-Wahab, et al. gall bladder disease in the absence of cirrhosis is a significant risk factor for hepatocellular carcinoma. J Hepatology. 2019.
13. Paulin F, JF Mercado, ME Fernández, FM Caro, ML Alberti, and LA Fassola, Correlation between Lung and Joint Involvement in Patients with Rheumatoid Arthritis and Interstitial Lung Disease: A Cross-Sectional Study. Rev Invest Clín.2018;70(2): 76-81.
14. Vahed LK and L Khedmat, Frequency of symptoms associated with gallstone disease: a hospital-based cross sectional study. Eur J Trans Myol.2018; 28(2).
15. Figueiredo JC, C Haiman, J Porcel, J Buxbaum, D Stram, N Tambe, et al., Sex and ethnic/racial-specific risk factors for gall bladder disease. BMC gastroenterol. 2017;17(1):153.
16. Wang S, Y Wang, J Xu, and Y Chen. Is the oral contraceptive or hormone replacement therapy a risk factor for cholelithiasis: A systematic review and meta-analysis. Medicine(Baltimore). 2017;96(14):6556.
17. Kshirsagar AY, Kabra MV, Reddy M, Panicker S, and Phadke A. A study to correlate low serum iron levels with gallstones. J Evol Med & Dent Sci. 2015; 4(104):16912-16915.

18. Gomati A, S Elafi, H Rafe, E Abimbola, A Willido and R Sahitha, A study on the Risk factors for gall bladder diseases in El-khoms Teaching Hospital, Libya. IOSR-JDMS. 2014: 13(2):1-4.

19. Kim HS, Cho SK, Kim CS, and Park JS. Big data and analysis of risk factors for gall bladder disease in the young generation of Korea. PloS one, 2019;14(2).

20. Mansoor S, Effan F, Ibnerasa S, Butt S and Rathore S. Morphological Spectrum of gall bladder Disease: a retrospective study in a private medical college in Lahore. Pak J Med Sci.2017; 11(4): 1505-1508.

21. Masood I, Rasheed H and Raheem A, Cohort study: occurrence rate of occult gall bladder carcinoma and its curative strategies. Pak J Surg, 2016. 32(4):245-249.

22. Sharma,RK, Bisht N, and Neki N, Histopathological examination of various lesions of gall bladder in routine 488 cholecystectomy specimens-A hospital based study. Int J Curr Res Med Sci. 2017; 3(8):112-118.

23. Turkcu G, Alabalýk U, Keles AN, Ibiloglu I, Hamidi A, and Ulger BV. Institutional experience in the histopathological characteristics and frequency of gall bladder lesions. Int J Clin Exp Pathol. 2016;9(1):176-180.

24. Nagi GS and Arora R. Incidence of various types of gallstones in patients of cholelithiasis in north Ind J Evol Med & Dent Sci.2015;4(97):16213-16215.

25. Channa NA, Khand FD, and Bhanger MI. Analysis of human gallstones by FTIR. Malaysian J Ana Sci. 2008;12(3):552-560.

26. Tassaduqe K, Ali M, Salam A, Latif M, Af-roze N, Masood S. et al., Studies on the Chemical Composition and Presentation of Gallstones in Relation to Sex and Age among Human Population of Multan, Pakistan. J Biol Sci. 2004; 4(4):470-473.

27. You Y, Bui K, Bui MM, Malafa M, and Coppola D. Histopathological and immunophenotypical features of intestinal-type adenocarcinoma of the gall bladder and its precursors. Cancer Control. 2014;21(3):247-250.

28. Rashmi H, Shivamurthy Y, Suresh K and Chatura K. Histopathological study to establish the association of gallstones with cholecystitis and carcinoma of gall bladder. MedPulse Int J Pathol.2018;5(3):56-59