Open Access

Original Article

# Relationship of GallstoneDisease with Age and Gender

**Faheem, Zakaullah Khan, Muhammad Yousaf Shah, Muhammad Nafe Bin Tahir, Rohan Qamar, Saba Yousaf***

Department of Surgery, Combined Military Hospital/National University of Medical Sciences (NUMS) Rawalpindi Pakistan
*Lahore University of Management Sciences

## ABSTRACT

***Objective***: To analyze the role of age and gender in gallstones formation and their relation to the types of stones formed.
***Study Design***: Cross-sectional study.
***Place and Duration of Study***: Combined Military Hospital, Rawalpindi Pakistan, from Jan 2019 to Jun 2021.
***Methodology***: Laparoscopic cholecystectomies were performed on 400 patients with symptomatic gallstones and acute cholecystitis. Variables such as gender, number of pregnancies if female, age, stone-types, and fatty liver.
***Results***: The study included 166(41.5%) male and 234(58.5%) female patients. The mean age was 48.89±16.3 years. 106(63.9%) male patients had cholesterol stones while 32(19.3%) and 28(16.9%) had bilirubin and mixed stones, respectively. Among female patients, 182(77.8%) had cholesterol stones, 26 (11.1%) had mixed and 26(11.1%) had bilirubin stones. Patients with gall stones in age groups <25 years, 26-50 years, 51-75 years and greater than 76 years were 35(8.8%), 186(46.5%), 144(36%) and 35(8.8%) respectively. The frequency of cholesterol gallstones was 14(40%), 130(69.9%), 127(88.2%) and 17(48.6%) in all the four age groups, respectively. The relationship of cholesterol gallstones with fatty liver and number of pregnancies was positive with coefficients β=6.61 for fatty liver and β=5.9 for number of pregnancies.
***Conclusion***: The gender and age of patients had significant relationship with gallstones. The frequency of cholesterol stones positively relates to fatty liver and number of pregnancies in females.

**Keywords:** Cholecystitis, Gallstones, Laparoscopic Cholecystectomy.

***How to Cite This Article:*** *Faheem, Khan Z, Shah MY, Tahir MN, Qamar R, Yousaf S. Relationship of Gallstone Disease with Age and Gender. Pak Armed Forces Med J 2024; 74(4): 1161-1164. DOI: https://doi.org/10.51253/pafmj.v74i4.8460*



## INTRODUCTION

Gallstone disease is one of the most common health issue in the world with 10-20% prevalence, out of which more than 20% patients present with clinical symptoms.[1] These occur due to abnormal stone masses which gather in the gallbladder or the intrahepatic bile duct.[2] Multiple pathogenic factors lead to stone formation with most studies focusing on the role of biliary microbiome in the pathogenesis of gallstones.[3] Gallstone disease is prevalent in the developed world, where 80% are cholesterol gallstones. A complex interplay of dietary habits, genetic factors and other pathogenic mechanisms is suspected to be at play.[4] Jayanthi *et al*. found that the patients with cholesterol stones had markedly high cholesterol contents in their bile whereas the patients with mixed stones had cholesterol rich bile composition and patients with pigment gall stones presented with high composition of bile salts.[5] However, one study revealed that there were significant differences in the chemical elements and amino acid composition of all three types of stones that implies the different conditions through which they are formed.[6] Numerous studies have identified the factors that can cause cholesterols gallstones formation. One previous study presented a dietary model in which people with intake of highly refined sugars, fats, fast food consumption, and low fiber intake are at elevated risk for cholesterols gallstones compared to people with high fiber consumption, low fats, proteins, vegetables, and fruit are at low risk.[7] Female gender has also been identified as a major risk factor for gallstones mainly at the childbearing age that relate to the number of pregnancies and presence of sex hormones such as estrogen which increases the biliary cholesterol secretion thus leading to cholesterol supersaturation of bile.[8] The study of Hermida *et al*. indicated that the frequency of gallstones is higher in aged people than younger people.[9] The objective of our study was to see the relationship of distinct types of gallstones with age and gender.

**Correspondence: Dr Faheem,** Department of Surgery, Combined Military Hospital, Rawalpindi Pakistan
*Received: 21 Sep 2022; revision received: 29 Mar 2022; accepted: 23 Sep 2022*

## METHODOLOGY

The cross-sectional study was conducted from January 2019 to June 2021 at CMH, Rawalpindi Pakistan, after permission from the Institutional Ethics Review Board (Ser 291). Sample size was calculated by using WHO calculator with 50% population

proportion10. The data was collected through non-probability consecutive sampling technique.

**Inclusion Criteria**: Patients aged 11 to 90 years, of either gender, with symptomatic gallstones, acute cholecystitis and chronic cholecystitis were included.

**Exclusion Criteria**: Patients with choledocholithiasis, gall bladder polyps and cholangitis were excluded.

The patients selected for this study were chosen on the basis of their ultrasound reports and final diagnosis. The consent of patients was duly taken through pre-operative proforma, maintaining their rights of safety and privacy.

Statistical Package for Social Sciences version 26 was used for data analysis. Quantitative variables with normal distribution were expressed as Mean±SD and qualitative variables were expressed as frequency and percentages. Chi-square test was applied to explore the inferential statistics.

## RESULTS

In our study, 400 patients with symptomatic gallstones were assessed. The age of patients ranged from 11 to 90 years. The mean age was 48.89±16.3 years. The study included 234(58.5%) female patients and 166(41.5%) male patients. The female to male ratio was 1.5:1. Out of 400 patients 288(72%) had cholesterol stones while 58(14.5%) had bilirubin stones and the other 54(13.5%) had mixed stones. The ratio of cholesterol stones were higher in females 182(77.8%) as compared to males 106(63.9%). The percentage of bilirubin and mixed stones were higher in males that is 32(19.3%) and 28(16.9%) respectively. Whereas in females the frequency of both bilirubin and mixed stones were 26(11.1%). The reason to transform short-age into age-groups was to see the prevalence of stones in the particular age groups. Gallstones occurring in the age groups 26-50 were 186(46.5%) and in the 51-75 age group there were 144(36%) patients which were clearly more than the other groups. After ultrasound screening, 164(41%) patients showed no indication of fatty liver while, 236(59%) patients were found to have fatty liver disease. There were 29(12.3%) patients had never been pregnant, 30(12.8%) female patients had 1 child and the total of 175(74.7%) female patients out of 234 had more than 1 child (Table).

Regression was performed to ascertain the effects of age, gender, fatty liver, and number of pregnancies on the likelihood of cholesterol stones formation. The logistic regression model was statistically significant, $X^2(4)=122.9$, $p<0.05$. The model explained 38.1% (Nagelkerke R2) of the variance in cholesterol stones and correctly classified 80.8% of the cases. Males were 0.028 times less likely to develop cholesterol stones than females. Fatty liver was found to be positively associated with cholesterol stones exhibition. Patients with fatty liver were 6.61 times more inclined to cholesterol gallstones formation. Similarly, the number of pregnancies in females was 5.9 times more likely to be the reason of cholesterol stones.

**Table: Association between Stone Types with Age Groups and Gender (n=400)**

| Variables | Types of Stones | | | *p*-value |
|---|---|---|---|---|
| | Bilirubin (n=58) | Cholesterol (n=288) | Mixed (n=54) | |
| **Gender, n (%)** | | | | |
| Male | 32(19.3%) | 106(63.9%) | 28(16.9%) | 0.009 |
| Female | 26(11.1%) | 182(77.8%) | 26(11.1%) | |
| **Age-Groups, n (%)** | | | | |
| Under 25 | 11(31.4%) | 14(40%) | 10(28.6%) | 0.001 |
| 26-50 | 27(14.5%) | 130(69.9%) | 29(15.6%) | |
| 51-75 | 8(5.6%) | 127(88.2%) | 9(6.3%) | |
| 76 Above | 12(34.3%) | 17(48.6%) | 6(17.1%) | |

## DISCUSSION

Gallstones disease has been attributed to the interaction of genetic and environmental factors with some unmodifiable factors such as age and genetic makeup.[11] In the quest for minimally invasive and most effective treatment of the disease has led to development of laparoscopic modalities of treatment.[12] While cholesterol gallstones are most prevalent in the developing and developed societies owing to the presence of risk factors and shifting food habits, bilirubin stones are found commonly in patients with blood disorder and mixed stones are infected and found primarily in common bile duct.[13] In western countries, the prevalence of gallstones is composed of 75% cholesterols, 20% bilirubin stones and 5% mixed stones.[14] In our study, it was found that 288(72%) of the total gallstones were cholesterol stones. 58(14.5%) were bilirubin stones and the other 54(13.5%) were mixed stones. According to Attri *et al*. damaged gallbladder motility, excessive hepatic cholesterol secretion, lithogenes and genetics, rapid phase transition of cholesterol in bile, intestines related factors involving cholesterol absorption, slow intestinal motility and changed gut microbiota defects play important role in the pathogenesis of cholesterol stones.[15] In our study, there was a significant association between age, gender and stone types. Other studies have suggested that advanced age is one of the risk factors for gallstones formation such as Kinoo *et al*. who found that

increasing age reduces the activity of enzyme 7-alpha hydroxylase, which leads to cholesterol hyper-saturation in bile, increasing the chances of cholesterol stones formation.[16]

Similarly, females are at elevated risk for gallstones as compared to males. Littlefield *et al*. suggested that estrogen levels in females are naturally higher also, usage of oral contraceptives can lead to higher estrogens. Excessive estrogen tends to increase cholesterol in bile and thickens the bile liquid, while also altering the composition of bile acid leading to gallstone formation.[17] In our study, female patients had mostly cholesterol stones similar to males, indicating that the occurance of cholesterol gallstones is dominant in both genders. Chang *et al*. conducted a cohort study to find out the bidirectional association between fatty liver and gallstones disease and it was found that fatty liver disease and its severity was independently related to increased gallstones frequency[18], similar to our findings.

According to Celaj *et al*. the risk of gallstones disease in women increases during pregnancy due to higher hormone levels which leads to higher serum cholesterol and gallbladder emptying is delayed.[19]. Nearly 8% of women form new gallstones by the third trimester. In our study, it was found that women with 1 or more children were 5. 68 times at higher risk of exhibiting cholesterol gallstones. Although studies suggest that age is one of the major factors for cholesterol gallstones but in our model the patients mostly lie in the middle age group which could be the potential limitation for the variable of Age to be insignificantly related to binary variable cholesterol gallstones. Our study has provided an insight to the prevention of cholesterol gallstone disease. Timely lifestyle modification and anti-cholesterol trial therapy can be used in high-risk patients to decrease frequency of cholesterol gall stone disease.

## CONCLUSION

Significant relationship exists between gallstones, age, and gender, especially patients with fatty liver and multiple pregnancies are at higher risk of developing cholesterol gallstones.

**Conflict of Interest:** None.

**Authors Contribution**

Following authors have made substantial contributions to the manuscript as under:

F & ZK: Data acquisition, data analysis, critical review, approval of the final version to be published.

MYF & MNT: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

RQ & SY: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

## REFERENCES


1. Gallstone disease, towards a better understanding and clinical practice. Curr Opin Gastroenterol 2017; 2(34): 1. https://doi.org/10.1097/MOG.0000000000000357
2. Shabanzadeh DM. New determinants for gallstone disease? Dan Med J 2018; 2(65): A5456.
3. Wang Y, Qi M, Qin C, Hong J. Role of the biliary microbiome in gallstone disease. Expert Rev Gastroenterol Hepatol 2018; 2(12): 1035-1046. https://doi.org/10.1080/17474124.2018.1539785
4. De Angelis M, Di Ciaula A, Garruti G, de Bari O, Frühbeck G. The role of diet in the pathogenesis of cholesterol gallstones. Curr Med Chem 2017; 19(24): 2222-2234. https://doi.org/10.2174/0929867324666170123120847
5. Jayanthi V, Sarika S, Varghese J, Vaithiswaran V, Sharma M. Composition of gallbladder bile in healthy individuals and patients with gallstone disease from north and south India. Indian J Gastroenterol 2016; 5(35): 367-373. https://doi.org/10.1007/s12664-016-0718-8
6. Mashina EV, Amosova OE, Shanina SN. Gallstones: Chemical and amino acid composition. Miner Struct Prop Methods Investig Proc 10th Russ Youth Sci Conf 2020; 131–139. https://doi.org/10.1007/978-3-030-26749-9_21
7. Di-Ciaula A, Portincasa P. Recent advances in understanding and managing cholesterol gallstones. F1000 Res 2018; 7: 1529. https://doi.org/10.12688/f1000research.15725.1
8. Wang HH, Portincasa P, Wang DQH, Liu M, Clegg DJ. New insights into the molecular mechanisms underlying effects of estrogen on cholesterol gallstone formation. Biochim Biophys Acta 2009; 11(1791): 1037-1047. https://doi.org/10.1016/j.bbalip.2009.08.005
9. Hermida FJ. Analysis of human urinary stones and gallstones by Fourier transform infrared attenuated total reflectance spectroscopy. J Appl Spectrosc 2021; 1(88): 88-93. https://doi.org/10.1007/s10812-021-01046-3
10. Kamangar F, Islami F. Sample size calculation for epidemiologic studies: Principles and methods. Arch Iran Med 2013; 5(16): 295-300.
11. Ram M, Khan S, Soni DK, Tiwari S. Pattern of gallstone disease in an industrial township in India: Are the risk factors different? Int Surg J 2020; 5(7): 2336-2341. https://doi.org/10.18203/2349-2902.isj20202523
12. Cao AM, Eslick GD. Epidemiology, and pathogenesis of gallstones. Manag Gallstone Dis 2018; 53-66. https://doi.org/ 10.1007/978-3-319-71559-9_3
13. Yao C, Wu S, Liu Z, Li P. A deep learning model for predicting chemical composition of gallstones with big data in medical internet of things. Future Gener Comput Syst 2019; 94: 140-147. https://doi.org/10.1016/j.future.2018.11.004

14. Mustafa KN. The role of some foods and diet habits in cholecystitis and gallstones in Mosul in Iraq. J Cardiovasc Dis Res 2020; 2(11): 189-193.
15. Attri MR, Kumar IA, Mohi Ud Din F, Raina AH, Attri A. Pathophysiology of gallstones. Gallstones Rev Recent Prog 2021; https://doi.org/10.5772/intechopen.97541
16. Kinoo SM, Nagiah S, Chuturgoon AA, Singh B. Symptomatic gallstones and HIV in black South African women: Changing trends of gallstone disease? South Afr J HIV Med 2021; 1(22): 1298. https://doi.org/10.4102/sajhivmed.%20v22i1.1298
17. Littlefield A, Lenahan C. Cholelithiasis: Presentation and management. J Midwifery Womens Health 2019; 1(64): 95-101. https://doi.org/10.1111/jmwh.12917
18. Chang Y, Noh YH, Suh BS, Kim Y, Sung E. Bidirectional association between nonalcoholic fatty liver disease and gallstone disease: A cohort study. J Clin Med 2018; 11(7): 458. https://doi.org/10.3390/jcm7110458
19. Celaj S, Kourkoumpetis T. Gallstones in pregnancy. JAMA 2021; 23(325): 2410. https://doi.org/10.1001/jama.2021.6919