

Relationship of gallbladder histopathology towards types of stones in cholelithiasis patients at Universitas Sumatera Utara Hospital, Medan, Indonesia



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ABSTRACT

Background: Cholelithiasis is a common disease of the gallbladder. It is estimated that around 10-15% of the population in western countries suffer from cholelithiasis. Types of gallbladder stones can be classified into cholesterol stones (containing cholesterol > 50%), mixed stones (containing 20-50% cholesterol), and pigment stones (containing cholesterol < 20%). Cholelithiasis causes various histopathological changes in the gallbladder mucosa such as acute and chronic inflammation, Cholelithiasis, hyperplasia and carcinoma. The general objective of this study was to determine the histopathological relationship of the gallbladder to the type of stone in cholelithiasis patients at USU Hospital.

Method: The design in this study was cross sectional. The sample of this study was 49 samples of patients with cholelithiasis who underwent cholecystectomy either by open cholecystectomy or per-laparoscopic cholecystectomy at Universitas Sumatera Utara (USU) Hospital. Gallstones and gallbladder will be examined in the laboratory. Data analysis will use the chi-square test.

Result: From 49 research samples found the most types of stones were mixed stones with 24 (49%) and histopathological results showed 18 examples (36.7%) were chronic inflammation. Based on the Chi-Square test found a significant relationship between the types of stones with histopathology of the gallbladder with a p-value of 0.001.

Conclusion: There is a significant relationship between the type of stone with histopathology in patients with cholelithiasis.

Keywords: cholelithiasis, histopathology, gallbladder

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INTRODUCTION

Cholelithiasis is the most common disease in the gallbladder. It is estimated that 10-15% of the population in western countries suffer from cholelithiasis.¹ Eighty-five percent of these cases are cholesterol stones.² According to Abbas et al.³ the prevalence of cholelithiasis occurs in 17% of the Asia population and 11-36% around the world. In Indonesia, the incidence of cholelithiasis per year has not been officially published.

Types of gallbladder stones can be classified into cholesterol stones (containing cholesterol > 50%), mixed stones (containing 20-50% cholesterol), and pigment stones (containing < 20% cholesterol).⁴ Cholesterol stones will be brownish yellow, pigment stones are

amorphous, brittle, calcium carbonate stones are shaped like black granules, green grains like mud or black, and others.⁵

Cholelithiasis causes various histopathological changes in the gallbladder's mucosa, such as acute and chronic inflammation, cholesterosis, hyperplasia and carcinoma. due to persistent irritation, trauma and, chronic inflammation.⁸

According to Bidaya et al.⁹ study Histopathological changes in the gallbladder have an important role in the process of stone formation. In contrast to the study of Kereh et al.¹⁰ stated that there was no relationship between the type of stones and changes in the gallbladder mucosa. As far as the knowledge of researchers in North Sumatra has never conducted this research. Because there

are still differences of opinion, the authors are interested in knowing the histopathological relationship to the type of stones in cholelithiasis patients at USU Hospital.

METHOD

This study used a cross sectional design, which was conducted during the period 2017 to 2018 at the Universitas Sumatera Utara. Hospital. The study population was all patients with a diagnosis of cholelithiasis. The sample of this study is a population that fits the inclusion and exclusion criteria of the study. The inclusion criteria in this study were cholelithiasis patients who underwent cholecystectomy either by open cholecystectomy or laparoscopic cholecystectomy. The exclusion criteria in

this study were cholelithiasis accompanied by cholecystitis and no gallstones were found after surgery. Data analysis in this study used SPSS version 25.0 for Windows (IBM Corporation, Armonk, USA), the chi-square test was used to assess the relationship of gallstones to the histopathological features of the gallbladder. All values are considered significant if $p < 0.05$.

RESULT

The mean age of the sample in this study was 48.76 (± 6.46) years, consisting of 16 men (32.7%) and 33 women (67.3%). Whereas for stone types, mixed stones were the most stone types with 24 people (49.0%), followed by 16 people (32.7%), and cholesterol with 9 people (18.4%). The last characteristic assessed in this study was histopathology, where chronic inflammation was the most common type with 18 people (36.7%), followed by acute inflammation, hyperplasia, and cancer, respectively, namely 16 people (32.7%), 11 people (22.4%), and 4 people (8.2%)

(Table 1).

The type of stone has a relationship to the histopathology of the gallbladder tissue. In cholesterol stones, from 9 samples, from the histopathological results it had 5 acute inflammation and 4 chronic inflammation, whereas for hyperplasia and cancer were not found. In pigment stones, there were respectively 8 acute and chronic inflammation and no hyperplasia and cancer were found. As for mixed stones, there were 3 samples with acute inflammation, 6 with chronic inflammation, 11 with hyperplasia, and 4 with cancer. There is statistically significant relationship between type of stone and the histopathology of the gallbladder tissue ($p=0.001$) (Table 2).

DISCUSSION

Cholelithiasis or gallstones are essentially deposits of one or more bile components (cholesterol, bilirubin, bile salts, calcium, and protein).¹¹ Gallstones occur when there is an imbalance in the chemical elements of bile which results in the

deposition of one or more components.¹² There are many factors, which cause stone formation, namely impaired gallbladder function, supersaturated bile, cholesterol nucleation factors, and circulating absorption of bile acids.

It is estimated that 10-15% of the population in western countries has cholelithiasis. According to Abbas et al.³ the prevalence of cholelithiasis occurs in 17% of the Asian population, 10% of the population in Western countries and 11-36% of all world countries. In Indonesia, the incidence of cholelithiasis per year has not been officially published. In this study, 49 patients had cholelithiasis, with the mean age being 48.76 \pm 6.46 years. The cholelithiasis frequency increases with age, increasing sharply to 4 to 10 times more often in patients over 40 years of age.¹³ In this study, it was found that the number of female patients was more than the number of male patients (16 men (32.7%) and 33 women (67.3%). Female sex is twice as likely to develop cholelithiasis during fertile/pre-menopausal periods (< 40 years) than men, related to female sex hormones (estrogen), parity, use of oral contraceptives and estrogen replacement therapy.¹⁴

In this study, mixed stones were the most common type of stone, found in 24 people (49.0%), followed by pigment stones (16 people (32.7%), and cholesterol with 9 people (18.4%). Similar findings by Chandran et al.⁵ study stated that in 200 gallstones studied in Haryana, India, 76 of them were mixed stones (38%). Research conducted in Belagavi, India also showed that mixed types of stones as many as 81.12% cases.¹⁴ However, study in Pakistan by Atamanalp et al.¹⁵ was found that the most common stone type was cholesterol stones (58.7%), where high serum cholesterol and LDL levels were associated with a high incidence of cholesterol stones.

Table 1. Study characteristics

Characteristics	Mean (\pm SD)	n (%)
Age	48,76 (\pm 6,46)	
Gender		
Male		16 (32.7)
Female		33 (67.3)
Stone type		
Cholesterol		9 (18.4)
Pigmented		16 (32.7)
Mixed		24 (49.0)
Histology		
Acute inflammation		16 (32.7)
Chronic inflammation		18 (36.7)
Hyperplasia		11 (22.4)
Cancer		4 (8.2)

Table 2. Relationship between stone types and histology of gallbladder

		Histopathology				p-value
		Acute inflammation	Chronic inflammation	Hyperplasia	Cancer	
Stone type	Cholesterol	5	4	0	0	0.001
	Pigmented	8	8	0	0	
	Mixed	3	6	11	4	

Chronic cholecystitis is the most common inflammation of the gallbladder. In this study, the histopathological results showed that chronic inflammation was the most common type (18 people (36.7%)), followed by acute inflammation, hyperplasia, and cancer, respectively, namely 16 (32.7%), 11 people (22.4%), and 4 people (8.2%). This is in accordance with the results of a study conducted by Unisa et al.¹⁶ which showed that mononuclear infiltrates' inflammation was found in all studied cases (100 cases). In this study gallbladder malignancy was seen in 4 cases, with 1 case of mild dysplasia and 3 severe dysplasia cases. The study of Barcia et al.¹⁷ also showed that the incidence of mild inflammation was present in 26% of cases, moderate in 62% of cases, and severe in 12% of cases.

Our study shows that the type of stone has a relationship with the histopathology of the gallbladder tissue. In cholesterol stones, from 9 samples, from the histopathological results it had 5 acute inflammation and 4 chronic inflammation, whereas for hyperplasia and cancer were not found. In pigment stones, there were respectively 8 acute and chronic inflammation and no hyperplasia and cancer were found. As for mixed stones, there were 3 samples with acute inflammation, 6 with chronic inflammation, 11 with hyperplasia, and 4 with cancer. The p-value of 0.001 indicates that there is a statistically significant relationship between the type of stones and the histopathology of the gallbladder tissue. This is consistent with the results of a study conducted by Sunder et al.¹⁸ which stated that metaplastic changes were common in patients with multiple mixed stones, where there was a significant relationship between changes in the histology of gallbladder tissue and the incidence of malignancy. There is a strong correlation between the duration of the symptoms and the severity of the disease, where the prolonged duration of the symptoms significantly influences the severity of the histopathological changes. In patients with chronic inflammation, patients with a duration of symptoms of less than 4 months, the severity of histopathological changes were mild. Histopathologic changes increased over

a duration lasting more than one year. Similar developmental patterns were seen in fibrosis and dysplasia.¹⁸ As with Sunder's study, patients with mixed stones developed hyperplasia, metaplasia, and gallbladder carcinoma.

CONCLUSION

Mixed stones type still dominated (49%) and histopathological results showed 18 samples (36.7%) were chronic inflammation, and there was a significant relationship between stone type and histopathology appearance in cholelithiasis patients.

CONFLICT OF INTEREST

The author declares there is no conflict of interest regarding publication of this article.

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ETHICAL CONSIDERATION

This study has been approved by the Ethical Committee Faculty of Medicine Universitas Sumatera Utara/Haji Adam Malik Hospital, Medan, Indonesia. All study procedures in accordance to the Helsinki Declaration of human rights.

AUTHOR CONTRIBUTION

Adi Muradi Muhar responsible for data gathering, project administration, supervision, and writing the original draft. Denny Rifsal Siregar and Doddy Prabisma responsible for statistical analysis, and writing the original draft. All authors had reviewed the final version of the manuscript.

REFERENCES

1. William NS, O'Connell PR, Mc Caskie AW. The Gallbladder and Bile Duct. In: Bailey & Love's Short Practice of Surgery 27th Edition. CRC Press; 2018. p. 1188-1199.
2. Stinton LM, Shaffer EA. Epidemiology of Gallbladder Disease: Cholelithiasis and Cancer. Gut Liver. 2012;6(2):172-187.
3. Abbass S, Ahmad I, Gyedu A, Adaye Aboagye K, Badu-Peprah A. Prevalence of Cholelithiasis

- among persons undergoing abdominal ultrasound at the Komfo Anokye Teaching Hospital, Kumasi, Ghana. Africa Health Science. 2015;15:246-252.
4. Kim SB, Kim KH, Kim TN, Heo J, Min KJ, Jung K. Sex Differences in Prevalence and Risk Factors of Asymptomatic Cholelithiasis in Korea Health Screening Examine: A Retrospective Analysis of A Multicenter Study. Medicine (Baltimore). 2017;96(13):e6477.
5. Chandran PNK, Kuchhal M. An Extended Chemical Analysis Of Gallstone. Indian Journal of Clinical Biochemistry. 2007;22(2):145-150.
6. Beena D, Shetty J, Bose V. Histopathological Spectrum of Diseases in Gallbladder. National Journal of Laboratory Medicine. 2017;6(4):6-9.
7. Zaki M, Al Refeidi A. Histological changes in the human gallbladder epithelium associated with gallstones. OMI. 2009;24(4):269-73.
8. Baidya R, Sigdel B, Baidya NL. Histopathological Changes in Gallbladder Mucosa Associated with Cholelithiasis. Journal of Pathology of Nepal. 2012;2:224-225.
9. Kereh DS, Lampus H, Sapan H, Loho LL. Correlation between stone type and mucosal histology change of gall bladder in gall stone patient. Biomedical Journal. 2015;7:41-47.
10. Bravo E, Contardo J, Cea J. Frequency of cholelithiasis and biliary pathology in the easter island rapanui and non-rapanui population. Asian Pac J Cancer Prev. 2016;17(3):14588.
11. Njeze GE. Gallstone. Nigerian Journal of Surgery. 2013;19(2):49-55.
12. Völzke H, Baumeister SE, Alte D, et al. Independent risk factors for gallstone formation in a region with high cholelithiasis prevalence. Digestion. 2005;71:97-105.
13. Cirillo DJ, Wallace RB, Rodabough RJ, et al. Effect of estrogen therapy on gallbladder disease. JAMA. 2005;293:330-339.
14. Karlatti SS, et al. Incidence of Various Types of Gallstones in Patients of Cholelithiasis in Belagavi. International Journal of Scientific Study. 2016;4:7: 21- 23.
15. Atamanalp SS, Keles MS, Atamanalp RS, Acemoglu H, Laloglu E. The effects of serum cholesterol, LDL, and HDL levels on gallstone cholesterol concentration. Pak J Med Sci. 2013;29(1):187-190.
16. Unisa S, Jagannath P, Dhir V, Khandelwal C, Sarangi L, Roy TK. Population-based study to estimate prevalence and determine risk factors of gallbladder diseases in the rural Gangetic basin of North India. HPB (Oxford). 2011;13(2):117-25.
17. Barcia JJ. Histologic analysis of chronic inflammatory patterns in the gallbladder:diagnostic criteria for reporting cholecystitis. Ann Diagn Pathol 2003;7:147-53.
18. Sunder G, Sanjeevsingh AD. Correlation between gallstones characteristics and gallbladder mucosal changes : A retrospective study of 313 cases. Clin Cancer Investig J. 2014;3:157-161.



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