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Original Article

Correlation Between Body Mass Index, Gender, and Age with Cholelithiasis

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Abstract

Background : Gallstones are formed due to deposit or hypersaturation of one or more of the bile components, namely cholesterol, bilirubin, bile salts, calcium, protein, fatty acids, and phospholipids. BMI, gender, and age are the factors that can trigger the formation of gallstones. In Indonesia, cholelithiasis cases have received less attention because they are often asymptomatic, making it difficult to detect and often misdiagnosed, resulting in a lack of official publication about the incidence of gallstones in Indonesia. This study was aimed to determine the correlation between BMI, Gender, and Age with cholelitiasis in Dr. Kariadi Hospital.
Methods : This was an observational study using cross-sectional design. Data were taken from medical records of patients in Digestive Surgery Department Dr. Kariadi Hospital from January 2018 until March 2020. A total of 100 patients were selected as subjects (50 patients with cholethiasis and 50 patienst without cholelithiasis). Pearson Chi-Square correlation was used for statistical analysis.
Results : Pearson Chi-Square test of BMI (p = 0.001) and Age (p = 0.041) was statistically significant for cholelithiasis risk (p < 0.05). While Gender (p = 0.224) was not statistically significant for cholelithiasis risk.
Conclusion : There wa a significant correlation between BMI and Age with Cholelithiasis and there was no significant correlation between Gender with Cholelithiasis.

Keywords : Body Mass Index (BMI), Gender, Age, Cholelithiasis.

INTRODUCTION

Cholelithiasis is a gallstone disease found in the gallbladder or in the bile duct, or both.[1] Cholelithiasis is a precipitate of one or more components of bile, namely cholesterol, bilirubin, bile salts, calcium, protein, fatty acids, and phospholipids.[2]

In the United States, as many as 10–15% of the adult population suffer from gallstones. and approximately 5.5 million people have gallstones and more than 50,000 cholecystectomies are performed annually.[3] In Asia the incidence of cholelithiasis ranges from 3% to 10%, based on the latest data obtained in Japan, the prevalence of cholelithiasis is around 3.2%, China 10.7%, North Indian 7.1% and Taiwan 5.0%.[4] In Indonesia the prevalence of gallstones sufferers is not known with certainty, because there are not many official publications about the incidence rate of gallstones in Indonesia, but it is suspected that the incidence rate is not much different from other countries in Asia, most of the incidence of cholelithiasis in Asia are asymptomatic.[1]

The risk factors for cholelithiasis are four F: female, fat, forty, fertile. The formation of cholelithiasis occurs from various complex interactions between genetics, environment, metabolism and risk factors.[5] Currently cholelithiasis patients in Indonesia tend to increase due to lifestyle changes such as consuming fast food which can lead to obesity due to fat deposits and trigger cholelithiasis. But no exact number of galls stone incidence was published due to the lack of study on cholelithiasis in Semarang.[6]

The case of cholelithiasis in Indonesia has received less attention because it is often asymptomatic therefore, it is difficult to detect or misdiagnosis often occurs.[1] Due to the lack of study on cholelithiasis in Semarang, this study will be conducted at Dr. Kariadi Hospital to determine the correlation of several risk factors such as BMI, sex, and age to cholelithiasis in Dr. Kariadi Hospital as a referral hospital in Central Java.

METHODS

This study method was an analytic observational study with a cross-sectional design. Sampling in the study was carried out by consecutive sampling which met the inclusion and exclusion criteria of the study. Based on the calculation of the sample size, the number of samples needed for each group is 45 people. The sample in this study were 50 cholelithiasis patients and 50 non-cholelithiatic patients in the Digestive Surgery Department.

This study was conducted in August-September 2020 at the Medical Records Installation at Dr. Kariadi Hospital, Semarang. This study is a research within the scope of Digestive Surgery.

This study has been reviewed and approved by the Health Research Ethics Commission (KEPK), Faculty of Medicine, Diponegoro University and has received permission from the education and training (Diklit) department of Dr. Kariadi Hospital, Semarang. To fulfill the principles of study ethics, the researcher maintains the confidentiality of patients as research subjects by not including the patient's identity.

The data collected in this study were secondary data. Secondary data were obtained from the medical records of patients at Dr. Kariadi Hospital, Semarang in the form of weight, height, age and sex of cholelithiasis and non-cholelithiasis patients in the Digestive Surgery Department for the period January 2018 – March 2020. Inclusion criteria was patients with a diagnosis of cholelithiasis with ICD code 10 K80.2 who undergo hospitalization, patients other than cholelithiasis in the Digestive Surgery department who undergo hospitalization, patients with a minimum age of 19 years and exclusion criteria are patients whose medical record data was incomplete and cholelithiasis patients with comorbidities such as cholecystitis, cholangitis, etc.

The independent variables of this study were BMI, sex, and age. The dependent variable of this study is cholelithiasis. Hypothesis testing was done using the chi square test. Data that did not meet the requirements of the chi square test were analyzed using Fisher's exact test. Determination of the results of the test using the p value. The p value is considered significant if p <0.05 with the 95% confidence interval. If there are more than 2 independent variables which are significant p <0.05, then the multivariate analysis is used with logistic regression test.

RESULTS

There were a total of 212 study subjects consisting of 102 cholelithiasis patients and 110 non-cholelithiasis patients. From the 102 cholelithiasis patients, 70 patients met the inclusion and exclusion criteria, 9 patients were excluded because of data incompletion, and 23 patients were excluded because of the existance of comorbidities (cholecystitis and cholangitis). From the 110 patients without cholelithiasis, 50 patients met the inclusion and exclusion criteria, 21 patients under 19 years old were excluded and 39 patients were excluded because of data incompletion. So that in this study, 50 cholelithiasis patient subjects were taken randomly from 70 patients who met the inclusion and exclusion criteria and 50 non-cholelithiatic patients who met the inclusion and exclusion criteria were taken. The selection of study subjects is shown in figure 1.

Subject Characteristics Data

The research subjects were cholelithiasis and not cholelithiasis patients in the Digestive Surgery department of Dr. Kariadi Hospital, Semarang with the

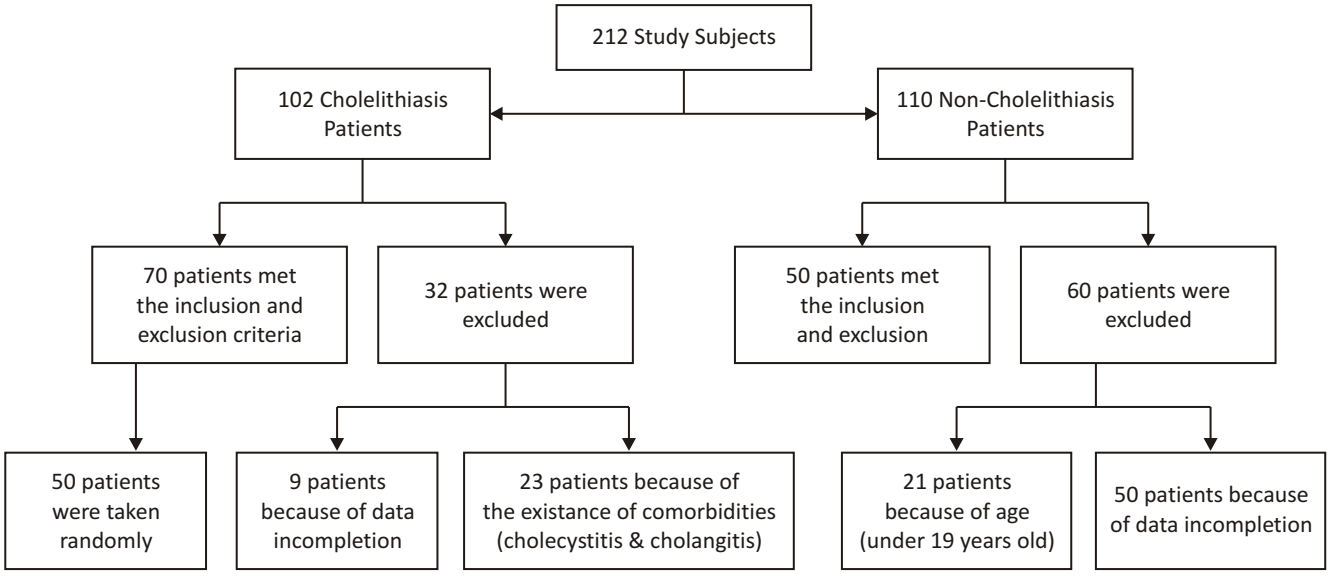

Figure 1. Selection of Study Subjects

TABLE 1
Data on the characteristic of research subjects

Variable			Mean ± SD n (%)
Age (years)	All subjects		44.56 ± 15.51
	Cholelithiasis		51.05 ± 13.84
	Non-Cholelithiasis		39.09 ± 14.97
Gender	Male	All Subjects	42 (42)
		Cholelithiasis	18 (36)
		Non-Cholelithiasis	24 (48)
	Female	All Subjects	58 (58)
		Cholelithiasis	32 (64)
		Non-Cholelithiasis	26 (52)
Weight (kg)	All Subjects		62.33 ± 13.34
	Cholelithiasis		67.07 ± 14.12
	Non-Cholelithiasis		57.59 ± 10.69
Height (m)	All Subjects		1.60 ± 0.07
	Cholelithiasis		1.59 ± 0.06
	Non-Cholelithiasis		1.60 ± 0.07
BMI (kg/m^2)	All Subjects		24.23 ± 4.32
	Cholelithiasis		26.20 ± 4.39
	Non-Cholelithiasis		21.80 ± 4.51
Cholelithiasis	Yes		50 (50)
	No		50 (50)

TABLE 2
Chi-Square test result of BMI, Gender, and Age with Cholelithiasis

Variable		Cholelithiasis		Non-Cholelithiasis		*p*
		n	%	n	%	
BMI (kg/m^2)	Obesity (≥ 25,1)	27	54	11	22	0.001*#
	Non-Obesity (< 25,1)	23	46	39	78	
Gender	Female	32	64	26	52	0.224#
	Male	18	36	24	48	
Age (years)	≥ 50	25	50	15	30	0.041*#
	< 50	25	50	35	70	

*#Pearson Chi-Square;*Significant*

demographic and clinical characteristics of research subjects is shown in Table 1.

Hypothesis Testing
Pearson Chi-Square test between BMI and cholelithiasis was obtained $p = 0.001$ ($p < 0.05$), this indicates that there is a significant correlation between BMI and the incidence of cholelithiasis. The Pearson Chi-Square test between gender and cholelithiasis was obtained $p = 0.224$ ($p > 0.05$), this indicatetes that there was no significant correlation between gender and the incidence of cholelithiasis. Pearson Chi-Square test between age and cholelithiasis was obtained $p = 0.041$ ($p < 0.05$), this indicates that there is a significant correlation between age and the incidence of cholelithiasis.

DISCUSSION

Correlation Between BMI and Cholelithiasis
The results of data analysis between BMI and cholelithiasis using the Pearson Chi-Square correlation test showed that the patient's BMI had a significant effect or there was a significant correlation with cholelithiasis. In this study, the average BMI of cholelithiasis patients was 26.20 ± 4.39 kg/m^2 included in the category of light fat – heavy fat according to the classification of the Ministry of Health Indonesia and included in the category of Obesity I – Obesity II according to the WHO classification.[7]

The results of this study are consistent with previous studies conducted by Liu *et al*. In 2018, it was found that an increase in BMI, waist circumference, and waist to hip ratio (WtHR) were significantly associated with an increased risk of cholelithiasis ($p<0.001$).[8] Nurhikmah *et al* in 2018 also stated that there was a correlation between an increase in BMI and the incidence of cholelithiasis ($p = 0.001$) where the results showed that the frequency of increase in BMI in cholelithiasis patients was higher than non-cholelithiasis patients.[9]

Study conducted by Kiani *et al* in 2020 is also in accordance with this study, namely the average BMI of cholelithiasis patients was 27.576 ± 5.753 kg/m^2 ($p = 0.08$) where the formation of gallstones was significantly associated with high BMI.[10]

Obesity is associated with more lithogenic bile, which is bile that contains more cholesterol than the bile acids or phospholipid content can dissolve. Research shows that the hypersecretion of cholesterol by the liver into the bile in obese or obese people is due to upregulation of HMG-CoA reductase activity, but it is also caused by reduced production of bile acids and phospholipids so that bile is more lithogenic. Because the level of secretion of cholesterol into the bile exceeds other lipids secreted, cholesterol is supersaturated in the bile causing increased flux into the gallbladder muscle cells which interferes with normal gallbladder function leading to higher gallbladder volume and residual volume and gallbladder motility to be lower in obese or obese women.[11]

In individuals who are obese and consume high-calorie foods, it can interfere with the emptying of the gallbladder, which causes the motility of the gallbladder to be inhibited, so that the amount of bile stored in the gallbladder increases, normally bile is flowed into the intestine, but because the motility of the gallbladder is disturbed so that deposition occurs.[12]

In obese people cholesterol levels increase which can support the formation of gallstones due to cholesterol super saturation and hypo motility in the gallbladder. Increased cholesterol levels result in an increase in the levels of the HMG CoA Reductase enzyme so that the amount of cholesterol uptake from the blood to the liver increases so that the amount of cholesterol secretion into the bile increases so that cholesterol super saturation occurs in the gallbladder. In addition, an increase in cholesterol levels also results in an increase in the release of Cholecystokinin hormone levels so that the stimulation of gallbladder contraction decreases, resulting in

gallbladder hypo motility.[12]

Correlation Between Gender and Cholelithiasis

The results of data analysis between sex and cholelithiasis using the Pearson Chi-Square correlation test showed that the patient's gender was not significant or there was no significant correlation with cholelithiasis.

Previous study conducted by Ansari-Moghaddam et al in 2016 found that women were 2.73 (95% CI; 1.34 – 5.56) times more likely to suffer from gallstones than men.[13] Research conducted by Sueta *et al* in 2017, the results showed the correlation between sex and the incidence of gallstones, a significant correlation ($p = 0.001$) was obtained between female sex and the incidence of gallstones where the prevalence ratio value was 3.38, which means gender women are a potential risk for cholelithiasis, where women have a potential risk of suffering from gallstones 3 times greater than men.[14] In addition, study by Hu *et al* in 2018 also shows a significant correlation between cholelithiasis and age / sex (OR = 0.517 for age > 55 vs <45, and for sex $P = 0.011$).[15]

Study conducted by Figueiredo *et al* in 2017 found that parity is a significant risk factor in women. The risk for women who had given birth to 4 or more children was 14% higher than those with nulliparity (HR = 1.14; 95% CI = 1.05–1.23, *p*-trend = 0.0036) of developing cholelithiasis. Women who had their first child before age 20 were at a higher risk of developing cholelithiasis (HR = 1.10; 95% CI = 1.01–1.20) than those who had never had children. The use of postmenopausal hormones only estrogen increases the risk of cholelithiasis (HR = 1.09; 95% CI: 1.02–1.17). Postmenopausal use of estrogen and progesterone was not significant (HR = 1.06; 95% CI = 0.99–1.14).[16]

This study shows different results from previous studies because the population of cholelithiasis patients at Dr. Kariadi Hospital found that the average age of cholelithiasis patients was 51.05 ± 13.84 years consisting of 32 (64%) female patients and 18 (32%) male patients. Asian women have a faster menopause (42.1–49.5 years old) than European (50.1–52.8 years old), North American (50.5 - 51.4 years old), and Latin American (43.8 –53 years old).[17] Study in Indonesia, states that the average age of menopause for Indonesian women is 49.98 years.[18] This shows that the average female cholelithiasis patient at Dr. Kariadi Hospital has menopause, where estrogen levels in the body is very low, even though estrogen and parity play an important role in the formation of gallstones so that in this study, the results showed that there was no correlation between sex and cholelithiasis.

Women have twice the risk of developing cholelithiasis than men. This is because the hormone estrogen is a derivative of cholesterol so that the increase in estrogen hormone increases the levels of the HMG CoA Reductase enzyme, which this enzyme has an effect on increasing the secretion of cholesterol into the gallbladder resulting in super saturation of cholesterol in the gallbladder.[17]

Correlation Between Age and Cholelithiasis

The results of the data analysis between age and cholelithiasis using the Pearson Chi-Square correlation test showed that the patient's age had a significant effect or there was a significant relationship to Cholelithiasis. In this study, the average age of cholelithiasis patients was 51.05 ± 13.84 years, which was included in the category of Early Elderly – Late Elderly according to the classification of the Ministry of Health Indonesia.

This study is in accordance with several previous studies conducted by Sevinç *et al*. In 2016, it was found that the age distribution of cholelithiasis patients was at most over 65 years old and the age group under 20 years was the group least at risk for gallstone formation.[19] This study also supported by Ansari-Moghaddam's study in 2016, the results showed that the risk of cholelithiasis was 2.60 times higher in people aged 45 years and over compared to people aged 30–44 years (Odds Ratio = 2.60, 95% CI; 1.22–5.55).[13]

People more than 40 years of age are more likely to develop cholelithiasis than those of younger ages. This is because with age the increased secretion of cholesterol by the liver into the bile increases and decreases the synthesis of bile acids so that bile becomes more lithogenic and gallstones rarely experience spontaneous dissolution. Gradually the ability of the tissue to repair itself or replace itself and maintain its normal structure and function so that it cannot withstand injuries and repair the damage suffered.[2,20]

The amount of cholesterol in bile increases with age. This is caused by a dyslipoproteinemia process which causes an increase in the secretion of cholesterol into the bile and a decrease in bile acid synthesis due to a decrease in the activity of the cholesterol 7α-hydroxylase enzyme (CYP7A1). The decrease in bile acid synthesis results in a longer digestion time of fat in the gallbladder, thereby increasing the occurrence of cholesterol super saturation in the gallbladder. Decreasing the enzyme 7α-hydroxylase cholesterol (CYP7A1) lowers HDL levels, raises LDL levels, and increases cholesterol levels. Decreasing HDL levels affect the decrease in Apo-protein A levels thereby increasing nucleation in the gallbladder due to deficiency of anti-nucleating substances that dissolve cholesterol in the gallbladder such as bile salts, lecithin, and phospholipids. The increase in LDL and Cholesterol levels increases the amount of cholesterol uptake in the liver so that the amount of cholesterol secretion into the bile increases which makes a saturated state of cholesterol in the gallbladder.[21]

CONCLUSION

There was a significant correlation between BMI and Age with Cholelithiasis and there was no significant

correlation of Gender with Cholelithiasis.

REFERENCES

1. Lesmana LA. Hepatobilier : Penyakit Batu Empedu. In: Aru W. Sudoyo, Bambang Setiyohadi, Idrus Alwi, Marcellus, Simadibrata SS, editor. Buku Ajar Ilmu Penyakit Dalam Jilid II. 6th ed. Jakarta: Interna Publishing; 2015. p. 2027–2022.
2. Price SA, Wilson LMC, Anugrah P, Dharma A, Wijaya C. Kolelitiasis. In: Widjaja C, editor. Patofisiologi Konsep Proses-Proses Penyakit. 6th ed. Jakarta: Penerbit Buku Kedokteran EGC; 2015. p. 530–515.
3. Stinton LM, Shaffer EA. Epidemiology of gallbladder disease: Cholelithiasis and cancer. Gut Liver. 2016;6(2):172–87. Available form : https://pubmed.ncbi.nlm.nih.gov/22570746/
4. Chang YR, Jang J-Y, Kwon W, Park JW, Kang MJ, Ryu JK, et al. Changes in Demographic Features of Gallstone Disease: 30 Years of Surgically Treated Patients. Gut Liver. 2016;7(6):719–24. Available from : https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3848536/
5. Pak M, Lindseth G. Risk factors for cholelithiasis. Gastroenterol Nurs. 2016;39(4):297309. Available from : https://pubmed.ncbi.nlm.nih.gov/27467059/
6. Purwanti A, Maliya A, Zulaicha E. Hubungan Gaya Hidup Dengan Kejadian Penyakit Cholelitiasis di Ruang Rawat Inap RSI Surakarta [Internet]. Publikasi Ilmiah Universitas Muhammadiyah Surakarta. 2016 [cited 2020 Feb 15]. Available from: http://eprints.ums.ac.id/id/eprint/43021
7. Depkes RI. Sistem Kesehatan Nasional [Internet]. 2015 [cited 2020 Feb 26]. Available from: http://www.depkes.go.id
8. Liu T, Wang W, Ji Y, Wang Y, Liu X, Cao L, *et al.* Association between different combination of measures for obesity and new-onset gallstone disease. PLoS One. 2018;13(5):1–11. Available from : https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0196457
9. Nurhikmah R, Efriza, Abdullah D. Hubungan Peningkatan Indeks Massa Tubuh dengan Kejadian Kolelitiasis di Bagian Bedah Digestif RSI Siti Rahmah Padang Periode Januari–Juni 2018. Heal Med J. 2018;I(2):1–6. Available from : https://jurnal.unbrah.ac.id › article › download
10. Kiani Q, Farooqui F, Khan MS, Khan AZ, Nauman Tariq M, Akhtar A. Association of Body Mass Index and Diet with Symptomatic Gall Stone Disease: A Case-Control Study. Cureus. 2020;12(3):1–8. Available from : https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7135725/
11. Lavoie JM. Dynamics of hepatic and intestinal cholesterol and bile acid pathways: The impact of the animal model of estrogen deficiency and exercise training. World J Hepatol. 2016;8(23):961–975. Available from : https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4990760/
12. Kharga B, Sharma BK, Singh VK, Nishant K, Bhutia P, Tamang R, *et al*. Obesity Not Necessary, Risk of Symptomatic Cholelithiasis Increases as a Function of BMI. J Clin Diagnostic Res. 2016;10(10):PC28–32. Available from : https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5121732/
13. Ansari-Moghaddam A, Khorram A, Miri-Bonjar M, Mohammadi M, Ansari H. The Prevalence and Risk Factors of Gallstone Among Adults in South-East of Iran: A Population-Based Study. Glob J Health Sci. 2016;8(4):60–7. Available from : https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4873599/
14. Sueta MAD, Warsinggih. Risk Factors of Gallstones At Dr . Wahidin Sudirohusodo General Hospital Makassar. J Bedah Nas. 2017;1(1):20–6. DOI :10.24843/JBN.2017.V01.I01.P04
15. Hu J, Chen M, Yeh C, Chiu W, Chiang M, Chang M. Effects of gender and age on prevalence of cholelithiasis in patients with chronic HCV infection. Med Balt. 2018;97(22):e10846. Available from : https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6392741/
16. Figueiredo JC, Haiman C, Porcel J, Buxbaum J, Stram D, Tambe N, *et al.* Sex and ethnic/racial-specific risk factors for gallbladder disease. BMC Gastroenterol. 2017;17:153. Available from : https://bmcgastroenterol.biomedcentral.com/articles/10.1186/s12876-017-0678-6
17. Palacios S, Henderson VW, Siseles N, Tan D, Villaseca P. Age of menopause and impact of climacteric symptoms by geographical region. Climacteric. 2016;13(5):419–28. Available from : https://pubmed.ncbi.nlm.nih.gov/20690868/
18. Rosenthal MS. The Gynecological Sourcebook: When They Tell You It's Cancer. USA: McGraw-Hill; 2017. 272–279 p.
19. Sevinç H, Demir MS, Mercan C, Yüksel F, Çaylan A. The Age and Gender Presentation In The Formations Of Gallstones. Turkish Med Student J. 2017;4:11–3. Available from : https://dergipark.org.tr/tr/download/article-file/404693
20. Douglas M Heuman. Epidemiology of Gallstones (Cholelithiasis) [Internet]. Medscape. 2020 [cited 2020 Feb 25]. Available from: https://emedicine.medscape.com/article/175667-overview#a5
21. Wibiwo S, Kanandihardja W, Sjamsuhidayat R, Syukur A. Saluran Empedu dan Hati. In: Wibiwo S, Kanandihardja W, Sjamsuhidayat R, Syukur A, editors. Buku Ajar Ilmu Bedah. 3rd ed. Jakarta: Penerbit Buku Kedokteran EGC; 2012. p. 767–73.