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RESEARCH ARTICLE

Lack of Association between Hypercholesterolemia and Obesity Status with the Gallstones type among Cholelithiasis Patients at Sanglah General Hospital, Bali, Indonesia

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Abstract

Introduction: Gallstone disease is still one of the major health problems in the world. It is one of the most common diseases in developed countries associated with many factors. Increased total blood cholesterol, free cholesterol, LDL, triacylglycerol, obesity, and decreased HDL cholesterol levels also play an important role in the pathogenesis of gallstone formation. This study aimed to determine the relationship between hypercholesterolemia and obesity to types of gallstones. Methods: An observational cross-sectional study was conducted at Sanglah General Hospital from January-December 2017. The sample was obtained using consecutive sampling of patients with cholelithiasis that met inclusion and exclusion criteria. Data analysis was done with univariate and bivariate analysis using SPSS version 23 software. The confidence interval was set to 95% and p-value < 0.05 was considered statistically significant. Result: Twenty-six samples were included in this study. Majority of the sample was suffered from gall stone type cholesterol and was performed open cholecystectomy. There was no association found between gall stone type and obesity (p=0.618). In addition, recent findings also suggest no significant differences between gall stone type and total cholesterol status (p=0.211).Conclusion: There is no association between obesity and hypercholesterolemia with gall stone type in cholelithiasis patients.

Keywords: *Cholelithiasis, Gallstone, Hypercholesterolemia, Obesity.*

Introduction

Gallstone disease is still one of the major health problems in the world. This is one of the most common diseases in developed countries, whereas in developing countries with traditional diets the prevalence rate is still relatively small [1, 3]. In Indonesia, every year there are approximately 700,000 cholecystectomy procedures caused by gallstones with complications reaching 3,000 deaths (0.12% of all mortality) [1].

Gallstones are becoming increasingly common and can be found in all age groups. Furthermore, the incidence also increases with age. There is a shifting phenomenon in developing countries in Asia, especially in Indonesia, where the prevalence of cholesterol-type gallstones is increasing. The recurrence rate is also high. This phenomenon is happening because of changes in lifestyle in developing countries. The western culture which has influenced lifestyle and dietary patterns cause an increase in consumption of refined carbohydrates and fats as well as a lack of fiber intake. These are a potential risk factor for the formation of cholesterol-type gallstones in developing countries [2]. Increased total blood cholesterol, free cholesterol, LDL, triacylglycerol, hematological markers, and decreased HDL cholesterol levels also play an important role in the pathogenesis of gallstone formation [4, 6].

The relationship between blood cholesterol levels and lithogenesis ability is still quite controversial with several studies showing conflicting results [4, 5].Several risk factors for cholesterol gallstones formation cannot be intervened and modified such as ethnic background, increasing age (getting older), female sex, and genetic or hereditary. While obesity rapidly decreases body weight and

sedentary lifestyle, is a risk factor that can be intervened and become a critical component in the prevention strategy of gallstones formation. The epidemic of obesity and metabolic syndrome are predicted to increase the incidence of cholesterol-type gallstones [4]. Studies that have studied the relationship between cholesterol levels and obesity with cholelithiasis have been carried out in several developing and developed countries, but no studies have been found that study obesity and cholesterol levels as interrelated factors in the type of gallstones.

The conflicting results of these discrepancies and lack of understanding between hypercholesterolemia as well as obesity to the type of gallstones encourage the authors to conduct this study. Based on those mentioned earlier, this study aims to determine the relationship between hypercholesterolemia and obesity to types of gallstones.

Methods

An observational cross-sectional study was conducted at Sanglah General Hospital from January to December 2017. Consecutive sampling technique was used among patients with cholelithiasis that met inclusion and exclusion criteria. The inclusion criteria were cholelithiasis patients who performed open or laparoscopic cholecystectomy surgery and agreed to involve in this study by signing an informed consent form. The exclusion criteria were a history of consuming anti-cholesterol medicine, suffering from an infection of the gastrointestinal, pancreas, diabetes mellitus, and hepato-pancreaticobiliary malignancy. According to the formula, the minimum sample size was 23 patients and we enrolled 26 patients. Hypercholesterolemia was defined as total blood cholesterol ≥ 200 mg/dL in the peripheral vein. Obesity was defined as body mass index ≥ 30. Gallstone type cholesterol was defined as gallstone with greyish yellow color and 50-90% of its content was cholesterol in analysis result. Gallstone type non-cholesterol was classified into brown pigment type and black pigment type.

Brown pigment type was defined as brown color gallstone with 50% bilirubin as its content. Black pigment type was defined as dark brown color gallstone with > 50% bilirubin as its content. Data analysis was done with univariate and bivariate analysis. Univariate analysis was done to describe the characteristic of samples and variables.

The results of the univariate analysis were described in mean with standard deviation and frequency. Bivariate analysis was done to determine the association between variables with a Chi-Square test. Confidence interval was set to 95% and p-value < 0.05 was considered significant.

Results

The characteristic of sample can be seen in Table 1. Twenty-six samples were included in this study. Majority of the sample was suffered from gall stone type cholesterol and was performed open cholecystectomy.

Table 1: Baseline characteristics of respondents

Variables	Parameters (N=26)		P-value
	Cholesterol stone (N=20)	Non-cholesterol stone (N=6)	
Sex (%) Male Female	 12 (60.0%) 8 (40.0%)	 3 (50.0%) 3 (50.0%)	0.664[a]
Age (mean ±SD)(years)	48.80±2.76	41.17±9.40	0.292[a]
Cholecystectomy (%) Open Laparoscopic	 16 (80.0%) 4 (20.0%)	 5 (83.3%) 1 (16.7%)	0.447[a]
Body Mass Index (BMI)(kg/m^2)(mean ±SD)	24.59±3.72	23.01±2.82	0.283[a]
Cholesterol (mg/dL) (mean ±SD)	198.25±38.84	172.83±46.14	0.342[a]

[a]Shapiro-Wilk test: normally distributed if P-Value <>0.05; SD: Standard deviations

Based on Table 1, most patients were males in patients with cholesterol stone (60%) compared with 50% in patients without cholesterol stone. The average age of respondents was 48.80±2.76 years-old in patients with cholesterol and 41.17±9.40 years-old in non-cholesterol stone patients. Most of the respondents had received open cholecystectomy in both groups such as 80% and 83.3% in patients with and without cholesterol stone, respectively. The body mass index (BMI) also found approximately 24.59±3.72 kg/m^2 and 23.01±2.82 kg/m^2 in both patients with and without cholesterol stone. Also, our study also revealed that total cholesterol level slightly higher in cholesterol

group (198.25±38.84 mg/dL) compared with a non-cholesterol group (172.83±46.14 mg/dL) respectively.

All of the baseline characteristics are normally distributed based on Shapiro-Wilk test.

Table 2: The association between gall stone type with obesity-overweight and total cholesterol status

Variables	Gall stone type		OR	95% Confidence Interval		P-value
	Cholesterol N(%)	Noncholesterol N(%)		Lower	Upper	
BMI status						
Obesity-Overweight	7 (35)	1 (16.7)	2.692	0.261	27.821	0.628
Normal	13 (65)	5 (83.3)				
Cholesterol Status						
Hypercholesterolemia	9 (45)	1 (16.7)	4.091	0.402	41.658	0.211
Normocholesterolemic	11 (55)	5 (83.3)				

OR: Odds-Ratio; BMI: Body Mass Index; P-value: statistically significant if less than 0.05

Risk analysis model using Odds Ratio (OR) value has been carried out in Table 2. Our finding suggests that most patients with cholesterol-stone were in Normal BMI status (65%) as well as normocholesterolemic status (55%). Table 2 also exhibits that even the OR value showed more than one as a ratio (2.692 vs. 4.091); however these result also provided statistically insignificant based on Chi-Square analysis (P>0.05)

Discussion

The prevalence of cholesterol gallstones is 80% of all gallstones in the western, whereas in Asia the highest prevalence is brown pigment gallstones which are mostly caused by infection. In Indonesia, based on research conducted by gastrointestinal and hepatology division at Cipto Mangunkusumo hospital Jakarta, 73% of all gallstone patients were caused pigment gallstones, and 27% were cholesterol gallstones type. The association between metabolic syndrome and gallstone disease is still unclear in Asian populations, especially in China [7].The association between blood cholesterol levels and lithogenesis ability is still controversial with several studies showing conflicting results [4, 5].

It should be noted that there are many risk factors for cholesterol gallstones that cannot be intervened and modified such as ethnic background, increasing age, female gender, and genetic or hereditary. Pure cholesterol stones are rarely found, and more often found a mixture of 70% cholesterol and bile salts; the rest are bile pigments and calcium. Usually, they are multiple, varies in size and shape, with colors from yellowish white to green or black. Often these stones are radiolucent, and less than 10% are radio opaque [1].

All patients included in this study were suffering from chronic cholecystitis based on histopathology examination. This result is consistent with the pathogenesis of cholesterol gallstones that the gallbladder wall inflammation becomes a critical factor. The gallbladder wall is exposed to bile salt detergent, unesterified cholesterol and bacterial infection which all of that can cause inflammation and increased risk of developing cholesterol stones [8].

Bivariate analysis using chi-square analysis showed that there is no significant association between hypercholesterolemia and type of gallstones. In this study, we also found that there is no significant association between obesity and type of gallstones. In line with the research conducted by Stinton et al. and Mendez-Sanchez et al. our study also did not find a significant association between hypercholesterolemia and obesity to the type of gallstones [4, 9].After several evaluations, there may be several things that can affect the results of our research such as the method of determining the type of gallstones.

The method in determining the gallstones type was based on the visual examination only, so the result was subjective. Furthermore, the analysis carried out at our hospital has not been able to determine the percentage of the gallstone components. Besides, gallstones type is caused by a multifactorial risk so that one independent risk factor could not rule out the hypothesis.

Conclusion

There is no association between obesity and hypercholesterolemia with gall stone type in cholelithiasis patients.

Author Contribution

Heru Sutanto Koerniawan was responsible for generating the study concept, data gathering, as well as interpreted the results. Ida Bagus Dharma Putra and Ketut Putu

Yasa were responsible as supervisors in this study

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