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A CASE-CONTROL STUDY ON THE RELATIONSHIP BETWEEN BODY MASS INDEX AS A RISK FACTOR FOR THE INCIDENCE OF CHOLELITHIASIS IN VARIOUS AGE GROUPS IN PATIENTS AT RSUD BANTEN

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ABSTRACT

Cholelithiasis is a condition where stones form in the gallbladder or bile ducts and its prevalence is increasing in Indonesia. Various risk factors have been identified, with the high Body Mass Index (BMI) being one of the dominant risk factors. This study aims to analyze the relationship between BMI and the incidence of Cholelithiasis in various age groups at Banten Regional Hospital. The study used a case-control design with 80 respondents (40 cases and 40 controls) taken from the medical record data of Banten Regional Hospital for the period January 2023-May 2024. Data analysis used Chi-Square test with a significance level of α=0.05. The results showed that in the case group, most respondents had excessive BMI (≥23 kg/m²) as much as 75.0%, while in the control group as much as 42.5%. There is a significant relationship between BMI and the incidence of Cholelithiasis (p=0.025) with a risk of 4.182 times greater in patients with excess BMI than underweight BMI. Analysis in various age groups showed that the relationship between BMI and Cholelithiasis was significant in the young adult age group (18-40 years) with p=0.039, but not significant in the middle adult age group (41-60 years) and the elderly (>60 years). In conclusion, excess BMI is a significant risk factor for Cholelithiasis, with a stronger association in the young adult age group. This study provides scientific evidence of the importance of weight management in Cholelithiasis prevention strategies, especially in the young adult age group.

Keywords: Body Mass Index; Cholelithiasis; Age; Risk Factors; Case-Control.

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INTRODUCTION

Cholelithiasis, a condition in which stones form in the gallbladder or bile ducts, is a global health problem with varying prevalence in different parts of the world. In the United States, approximately 10-15% of the adult population has Cholelithiasis, while in Asia the prevalence ranges from 3-10% (Stinton & Shaffer, 2012). In Indonesia, based on the Basic Health Research (Riskesdas) in 2018, the prevalence of Cholelithiasis in adults reached 15.4%, an increase from 11.7% in 2016 (Ministry of Health RI, 2018).[1]

Body Mass Index (BMI) has long been identified as one of the major risk factors for Cholelithiasis. A meta-analysis study conducted by Wang *et al.* (2020) showed that every 5 unit increase in BMI was associated with a 52% increase in the risk of Cholelithiasis. This relationship can be explained through various pathophysiological mechanisms, including increased hepatic cholesterol synthesis, impaired gallbladder motility, and altered bile acid metabolism in individuals with high BMI (Di Ciaula *et al.*, 2018). [3]

Several previous studies in Indonesia have attempted to identify the relationship between BMI and Cholelithiasis. Dani's research (2012) at Immanuel Bandung Hospital found that 69.27% of Cholelithiasis patients had BMI in the overweight or obese category. Meanwhile, research by Febyan *et al.* (2017) at Koja Jakarta Hospital found that the average BMI of Cholelithiasis patients was 24.80 kg/m², which is in the overweight category for the Asian population. [2]

Besides BMI, age is also a significant risk factor for Cholelithiasis. The risk of Cholelithiasis increases with age, especially after 40 years of age. Some of the pathophysiological mechanisms underlying this relationship include increased biliary cholesterol secretion, decreased bile acid synthesis, and decreased gallbladder motility that occur with age (Chen *et al.*, 2019). [4]

Although there is strong evidence of the association of BMI and age with cholelithiasis separately, there is still a gap in knowledge about how BMI acts as a risk factor for cholelithiasis in different age groups. Understanding the variations in this relationship is important for the development of more effective, age-specific prevention and management strategies for cholelithiasis. [6]

RSUD Banten, as the main referral hospital in Banten Province with comprehensive digestive clinic services, is an appropriate location to conduct this research. Based on data from the Banten Provincial Health Office (2019), digestive system diseases, including Cholelithiasis, are still one of the main causes of morbidity in the region. However, there has been no comprehensive study analyzing the relationship between BMI and Cholelithiasis in Banten by considering variations in different age groups. [7]

This study aims to analyze the relationship between BMI and the incidence of Cholelithiasis in various age groups at Banten Regional Hospital. Specifically, this study aims to: (1) determine the description of BMI groups in Cholelithiasis patients at Banten Regional Hospital, (2) identify the relationship between BMI and the incidence of Cholelithiasis in patients at Banten Regional Hospital, and (3) determine the difference in the influence of the incidence of Cholelithiasis in various age groups based on BMI. [3]

The results of this study are expected to provide strong scientific evidence regarding the association of BMI with Cholelithiasis in various age groups, which can be used as a basis for the

development of more effective prevention and management strategies for Cholelithiasis, especially in the population in Banten, Indonesia.

METHODS

This study is an observational analytic study with a case-control design to analyze the relationship between Body Mass Index (BMI) and the incidence of Cholelithiasis in patients at Banten Hospital. The case-control design was chosen because Cholelithiasis is included in the category of diseases that are relatively rare, so it is more appropriate to compare groups diagnosed with Cholelithiasis (cases) with groups that are not diagnosed (controls).

The study was conducted in the Medical Records Section of Banten Hospital from January 2023 to May 2024, by taking medical record data for the period January 2023 to May 2024. The target population in this study were all patients with Cholelithiasis in Banten Province, while the target population were all patients with Cholelithiasis who came to the digestive clinic of Banten Hospital who met the inclusion criteria.

Inclusion criteria for the case group included: (1) patients with confirmed diagnosis of Cholelithiasis through ultrasound examination, (2) have fully documented BMI measurement data, (3) are at least 18 years old, and (4) have complete medical record data. For the control group, inclusion criteria included: (1) patients who were not diagnosed with Cholelithiasis but had complete BMI data, (2) had complete medical record data, and (3) were at least 18 years old. Exclusion criteria for both groups included: (1) medical records that were incomplete, damaged, or could not be found, (2) had a history of digestive surgery (bariatric, cholecystectomy, etc.), (3) diagnosed with malignancy, and (4) were pregnant.

The sample size was calculated using the formula for a case-control study with a 95% confidence level, 80% test strength, and the proportion of Cholelithiasis incidence in the normal BMI group of 0.15 based on 2018 Riskesdas data. From the calculation results, the minimum sample size was 40 cases and 40 controls, so the total sample was 80 respondents.

The sampling technique used was purposive sampling, which is the deliberate selection of patients who meet certain criteria relevant to the research objectives. The control group was selected from patients who came to the digestive clinic of Banten Hospital with suspicion of Cholelithiasis, but the results of ultrasound examination showed no gallstones.

The variables in this study consisted of independent variables, namely Body Mass Index (BMI) which was grouped into: Excessive BMI (≥23 kg/m^2), Normal BMI (18.5-22.9 kg/m^2), and Underweight BMI (<18.5 kg/m^2) based on criteria for Asian populations from WHO. The dependent variable was the incidence of Cholelithiasis which was categorized as Yes (stones in the gallbladder) or No (no stones in the gallbladder) based on the results of ultrasound examination. Other variables collected were age categorized into young adult (18-40 years), middle adult (41-60 years), and elderly (>60 years); and gender.

Data collection was done by taking secondary data from the medical records of patients who met the inclusion criteria. The data collected included: (1) patient identity (age, gender), (2) gallbladder ultrasound examination results, (3) anthropometric data (weight, height, and BMI).

Data processing and analysis were conducted using the Statistical Package for the Social Sciences (SPSS) version 26.0 program. Univariate analysis was performed to describe the characteristics of respondents and the frequency distribution of each research variable. Bivariate analysis used the Chi-Square test to determine the relationship between BMI and the incidence of Cholelithiasis, as well as the relationship between BMI and the incidence of Cholelithiasis in various age groups. The level of significance was set at $\alpha = 0.05$.

This study has obtained ethical approval from the Banten Hospital Health Research Ethics Committee and has obtained research permission from the Doctor Education Study Program, Faculty of Medicine, Sultan Ageng Tirtayasa University and the Director of Banten Hospital.

RESULT

Respondent Characteristics

Based on the results of research conducted on 80 respondents (40 cases and 40 controls) at Banten Regional Hospital, the characteristics of respondents based on gender and age group can be seen in Table 1 and Table 2.

Table 1 Frequency Distribution of Respondents by Gender

Gender	Case		Control		Total	
	n	%	n	%	n	%
Male	15	37,5	22	55,0	37	46,3
Female	25	62,5	18	45,0	43	53,7
Total	40	100,0	40	100,0	80	100,0

Based on Table 1, in the case group (Cholelithiasis patients), most respondents were female, namely 25 people (62.5%), while there were 15 men (37.5%). In the control group (non-Cholelithiasis patients), the gender distribution showed different results, with more male respondents, namely 22 people (55.0%) compared to 18 women (45.0%). Overall, out of a total of 80 respondents, there were 43 female respondents (53.7%) and 37 male respondents (46.3%).

Table 2 Frequency Distribution of Respondents by Age Group

Age Group	Case		Control		Total	
	n	%	n	%	n	%
Young Adults (18-40)	9	22,5	17	42,5	26	32,5
Middle Adult (41-60)	19	47,5	15	37,5	34	42,5
Elderly (>60)	12	30,0	8	20,0	20	25,0
Total	40	100,0	40	100,0	80	100,0

Based on Table 2, in the case group (Cholelithiasis patients), the majority of respondents were in the middle adult age group (41-60 years) as many as 19 people (47.5%), followed by the elderly group (>60 years) as many as 12 people (30.0%), and the least in the young adult group (18-40 years) as many as 9 people (22.5%). In the control group (non-Cholelithiasis patients), the age distribution showed different results, with the majority of respondents in the young adult age group (18-40 years) as many as 17 people (42.5%), followed by the middle adult group (41-60 years) as many as 15 people (37.5%), and the least in the elderly group (>60 years) as many as 8 people (20.0%).

Overview of BMI in Cholelithiasis Patients

An overview of BMI in Cholelithiasis and non-Cholelithiasis patients can be seen in Table 3.

Table 3 Frequency Distribution of Respondents by BMI Category

BMI Category	Case		Control		Total	
	n	%	n	%	n	%
Excessive BMI (≥23 kg/m²)	30	75,0	17	42,5	47	58,8
Normal BMI (18.5 kg/m² - 22.9 kg/m²)	8	20,0	18	45,0	26	32,5
BMI Underweight (<18.5 kg/m²)	2	5,0	5	12,5	7	8,8
Total	40	100,0	40	100,0	80	100,0

Based on Table 3, in the case group (Cholelithiasis patients), the majority of respondents had Excessive BMI (≥23 kg/m²) as many as 30 people (75.0%), followed by respondents with Normal BMI (18.5 kg/m² - 22.9 kg/m²) as many as 8 people (20.0%), and the least in the Underweight BMI group (<18.5 kg/m²) as many as 2 people (5.0%). In the control group (non-Cholelithiasis patients), the majority of respondents had Normal BMI (18.5 kg/m² - 22.9 kg/m²) as many as 18 people (45.0%), followed by respondents with Excess BMI (≥23 kg/m²) as many as 17 people (42.5%), and the least in the BMI Underweight group (<18.5 kg/m²) as many as 5 people (12.5%).

Relationship between BMI and Cholelithiasis Incidence

The results of bivariate analysis to determine the relationship between BMI and the incidence of Cholelithiasis can be seen in Table 4.

Table 4 Relationship between BMI and Cholelithiasis Incidence

BMI		Diagnosis		Total	P-value	OR	95% CI	
		Cholelithiasis	Not Cholelithiasis				Low	Up
Excess	n	23	11	34		4,182	0,662	26.415
	%	67,6%	32,4%	100,0%				
Normal	n	15	25	40	0,025	1,200	0,196	7.362
	%	37,5%	62,5%	100,0%				

Underweight	n	2	4	6
	%	33,3%	66,7%	100,0%
Total	n	40	40	80
	%	50,0%	50,0%	100,0%

Based on Table 4, the results of bivariate analysis showed that the proportion of respondents with Excessive BMI in the case group (67.6%) was greater than that in the control group (32.4%). In contrast, the proportion of respondents with Normal BMI in the case group (37.5%) was smaller than that in the control group (62.5%). Meanwhile, the proportion of respondents with Underweight BMI in the case group (33.3%) was also smaller than that in the control group (66.7%).

The results of the Chi-Square statistical test obtained a value of $p = 0.025$ ($p < 0.05$), which means that there is a significant relationship between the BMI category and the incidence of Cholelithiasis. The Odds Ratio value shows that respondents with Excess BMI have a 4.182 times greater risk (95% CI: 0.662-26.415) of experiencing Cholelithiasis compared to respondents who have Underweight BMI, while respondents with Normal BMI have a 1.2 times greater risk (95% CI: 0.196-7.362) compared to Underweight BMI.

Relationship between BMI and Cholelithiasis in Different Age Groups

The results of the analysis of the relationship between BMI and the incidence of Cholelithiasis in various age groups can be seen in Table 5, Table 6, and Table 7.

Table 5 Relationship between BMI and the Incidence of Cholelithiasis in the Young Adult Age Group (18-40 years)

BMI Category	Case		Control		Total		p-value	OR	95% CI	
	n	%	n	%	n	%			Low	Up
Excessive BMI (≥23 kg/m²)	7	77,8	6	35,3	13	50,0	0,039	2,33	0,17	31,99
Normal BMI (18.5 kg/m² - 22.9 kg/m²)	1	11,1	9	52,9	10	38,5		0,22	0,01	4,81
BMI Underweight (<18.5 kg/m²)	1	11,1	2	11,8	3	11,5				
Total	9	100,0	17	100,0	26	100,0				

Table 6 Relationship between BMI and the Incidence of Cholelithiasis in the Middle Adult Age Group (41-60 years)

BMI Category	Case		Control		Total		p-value	OR	95% CI	
	n	%	n	%	n	%			Low	Up
Excessive BMI (≥23 kg/m²)	14	73,7	7	46,7	21	61,8	0,101	2,00	0,11	37,93
Normal BMI (18.5 kg/m² - 22.9 kg/m²)	4	21,1	7	46,7	11	32,4		0,57	0,03	11,61
BMI Underweight (<18.5 kg/m²)	1	5,3	1	6,7	2	5,9				
Total	19	100,0	15	100,0	34	100,0				

Table 7 Relationship between BMI and the Incidence of Cholelithiasis in the Elderly Age Group (>60 years)

BMI Category	Case		Control		Total		p-value	OR	95% CI	
	n	%	n	%	n	%			Low	Up
Excessive BMI (≥23 kg/m²)	9	75,0	4	50,0	13	65,0	0,249	4,50	0,16	128,62
Normal BMI (18.5 kg/m² - 22.9 kg/m²)	3	25,0	3	37,5	6	30,0		2,00	0,06	65,99
BMI Underweight (<18.5 kg/m²)	0	0,0	1	12,5	1	5,0				
Total	12	100,0	8	100,0	20	100,0				

Table 8 Comparison of the Relationship between BMI and the Incidence of Cholelithiasis in Various Age Groups

Age Group	p-value
Young Adults (18-40)	0,039
Middle Adult (41-60)	0,101
Elderly (>60)	0,249

Based on Table 5, Table 6, Table 7, and Table 8, the relationship between BMI and the incidence of Cholelithiasis varies in various age groups. In the young adult age group (18- 40 years), there is a significant relationship between BMI and the incidence of Cholelithiasis ($p = 0.039$). Young adult patients with Excess BMI had a 2.33 times greater risk (95% CI: 0.17-31.99) of developing Cholelithiasis than patients with Underweight BMI.

Meanwhile, in the middle adult (41-60 years) and elderly (>60 years) age groups, there was no significant relationship between BMI and the incidence of Cholelithiasis ($p > 0.05$). However, in both age groups, there was a trend that patients with Excessive BMI had a greater proportion in the case group compared to the control group.

Based on the comparison of p values in various age groups (Table 8), it can be concluded that the association of BMI with Cholelithiasis is stronger in the young adult age group compared to the older age group.

DISCUSSION

The results of this study showed that in the case group (Cholelithiasis patients), most respondents were female (62.5%). This finding is in line with previous studies showing that women have a higher risk of developing Cholelithiasis than men (Febyan *et al.*, 2017; Dani, 2012). This difference in risk can be explained by hormonal factors, especially estrogen, which plays a role in increasing cholesterol excretion by the gallbladder. According to Wang *et al.* (2018), estrogen increases cholesterol secretion into bile and reduces bile acid synthesis, creating conditions conducive to gallstone formation.

In terms of age distribution, this study found that in the case group, most respondents were in the middle adult age group (41-60 years) as much as 47.5%, followed by the elderly group (>60 years) as much as 30.0%. This is generally in accordance with the theory that the risk of Cholelithiasis increases with age, especially after the age of 40 years, as explained by Shabanzadeh *et al.* (2017).

Another important finding of this study was the significant association between BMI and the incidence of Cholelithiasis ($p = 0.025$). Patients with Excessive BMI (≥ 23 kg/m^2) had a 4.182 times greater risk of developing Cholelithiasis compared to patients who had Underweight BMI. This finding is consistent with a meta-analysis study conducted by Wang *et al.* (2020) which showed that every 5 unit increase in BMI was associated with a 52% increase in the risk of Cholelithiasis.

The pathophysiologic mechanisms underlying the association between high BMI and Cholelithiasis have been described in various previous studies. Di Ciaula *et al.* (2018) explained that individuals with high BMI have increased hepatic HMG-CoA reductase activity, which is a key enzyme in cholesterol synthesis. Every 5 kg/m^2 increase in BMI correlates with a 20-30% increase in cholesterol secretion into bile. In addition, obesity also affects bile acid metabolism, with decreased activity of the enzyme cholesterol 7α-hydroxylase (CYP7A1), which plays an important role in the conversion of cholesterol to bile acids.

An interesting finding of this study is the variation in the relationship between BMI and the incidence of Cholelithiasis in various age groups. The results of the analysis showed that only in the young adult age group (18-40 years) had a significant relationship ($p = 0.039$), while in the middle adult age group (41-60 years) and the elderly (>60 years), although there was a tendency for the proportion of Excess BMI to be greater in the case group than the control group, it was not statistically significant ($p > 0.05$).

This phenomenon suggests that in the young adult age group, high BMI may play a more dominant role in the formation of Cholelithiasis than in the older age group. This result differs from the general theory that older age is an independent risk factor for Cholelithiasis, as described by Chen *et al.* (2019) who found a significantly increased risk of Cholelithiasis in the 60-69 years (RR 2.75) and ≥70 years (RR 3.85) age groups compared to the 20-39 years age group.

There are several factors that can explain this phenomenon. First, changes in lifestyle and consumption patterns in young adults today show significant changes with high consumption of high-fat and low-fiber foods such as fast food, and sugary energy drinks. Jessri and Rashidkhani (2015) showed that the type of fat consumed at the young age group contains more trans and saturated fats that have a stronger effect in increasing hepatic cholesterol synthesis.

Secondly, sedentary lifestyle in young adults also plays an important role, characterized by lower physical activity due to the use of technology and more sedentary work. Fitzgerald *et al.* (2009) proved that low physical activity decreases gallbladder motility and slows intestinal transit, thus increasing the risk of gallstone formation.

Third, hormonal factors also play a significant role, especially in young adult women who are in the reproductive period with high estrogen levels, pregnancy, and use of hormonal contraceptives. Shabanzadeh *et al.* (2017) demonstrated that these conditions increase bile lithogenicity and decrease gallbladder motility, thus increasing the risk of Cholelithiasis.

This study has several limitations that need to be considered in the interpretation of the results. First, the relatively small sample size (80 respondents) may limit statistical power, especially in subgroup analysis by age. Secondly, the retrospective case-control design limits the ability to control for confounding variables and establish causal relationships. Third, this study was only conducted in one hospital (RSUD Banten), so generalization to a wider population may be limited.

Another significant limitation is the use of BMI as the sole measurement to assess adiposity status. BMI has limitations in distinguishing between muscle mass and fat mass. Individuals with high muscle mass such as athletes can have a BMI that is classified as "excess" or even "obese" without having excess adiposity that increases the risk of Cholelithiasis. Jayedi *et al.* (2020) showed that the combination of BMI with measures of central adiposity, such as waist-hip ratio or waist circumference, provides a more accurate prediction of health risk.

Nonetheless, this study makes a significant contribution to the understanding of the association of BMI with Cholelithiasis in different age groups in the Indonesian population, particularly in Banten. The finding that the association of BMI and Cholelithiasis is stronger in the young adult age group provides important implications for more targeted prevention and intervention strategies in this age group.

This study also highlights the importance of an individualized approach in the prevention of Cholelithiasis, considering a combination of risk factors such as BMI, age, and gender. Cholelithiasis-related prevention and health promotion programs may need to focus more on young adults with high BMI, especially women, to have a more significant impact.

CONCLUSION

Based on the results of research on the relationship between Body Mass Index (BMI) and the incidence of Cholelithiasis in patients at Banten Hospital, the following conclusions can be drawn:

Most patients with cholelithiasis had BMI in the overweight category (≥23 kg/m²). This suggests that being overweight is a dominant characteristic in patients with Cholelithiasis.

There was a significant association between excess BMI (≥23 kg/m²) and the incidence of Cholelithiasis, with a 4.182 times greater risk than patients with underweight BMI. This indicates that being overweight is an important risk factor in the development of Cholelithiasis.

The association between BMI and Cholelithiasis was found to be stronger in the young adult age group (18-40 years) compared to the older age group. This may be influenced by various factors such as differences in lifestyle, physical activity, hormones, and diet.

These findings emphasize the importance of attention to younger age groups in Cholelithiasis prevention efforts, as well as the need to consider non-conventional factors such as body composition, genetics, and gut microbiota in the risk assessment of this disease. Further studies with larger sample sizes and more comprehensive methodologies are needed to confirm these findings and explore the underlying mechanisms.

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