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ORIGINAL RESEARCH REPORT

The effect of type 2 diabetes mellitus (T2DM) as a comorbid factor on the morbidity rate and length of hospital stay (LoS) in patients undergoing cholecystectomy

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ABSTRACT

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Materials and Methods: This study used a descriptive analytical design with a retrospective approach. The total sampling technique was employed to determine the number of samples required. A total of 201 cases of gallstone disease were observed at Dr. Ramelan Naval Hospital, Surabaya between June 2019 and September 2020. However, a sample of 146 cases met the inclusion and exclusion criteria. The secondary data were collected from the medical records of the patients. The data were analyzed using SPSS 25 (IBM, US). **Results**: The contingency coefficient test revealed a correlation between diabetes as a comorbid factor and disease incidence (p = 0.019). In addition, the results suggested a correlation between diabetes as a comorbid factor and length of hospital stay (p = 0.034). **Conclusion**: The findings indicated that comorbidities such as diabetes were associated with morbidity rate and length of hospital stay in patients undergoing cholecystectomy.

Background: Cholecystectomy is a gold standard approach for the

treatment of cholelithiasis. The efficacy of this treatment varies

considerably, with morbidity and hospital stay depending on the

country and hospital. Objective: This study aims to determine the

effect of diabetes mellitus as a comorbid factor on morbidity rate and length of stay following cholecystectomy at Dr. Ramelan Naval

Hospital, Surabaya between June 2019 and September 2020.



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Highlights

- 1. Diabetes mellitus as a comorbid factor affects the outcome of patients undergoing cholecystectomy.
- 2. Diabetes mellitus affects the morbidity rate and the length of hospital stay following cholecystectomy.

INTRODUCTION

Cholecystectomy remains a significant treatment option for patients with symptomatic gallstones, with a prevalence of more than 20% in Europe (Gutt et al., 2020), and between 22.6% and 80% in developing countries (Lee et al., 2022). Cholecystectomy is chosen for less postoperative pain, shorter hospital stay, and lower operative morbidity and mortality rates (Kanakala et al., 2011). Morbidity and mortality due to cholecystectomy vary between countries and hospitals, despite the procedure being regarded as having a relatively low risk in terms of major complications (Sandblom et al., 2015). The success of cholecystectomy can be assessed in terms of morbidity, mortality, length of hospital stay (LoS), and quality of life (QoL) of the patient (Lee et al., 2022).

Morbidity is defined as any condition that manifests within 90 days after cholecystectomy (Sahbaz et al., 2017). The most common morbidities associated with cholecystectomy include cardiovascular complications as the leading cause of death, bile duct damage, and pulmonary complications (Syrén et al., 2021). A total of 3,245 complications were recorded among the 6,898 patients involved in a previous study. The mortality and morbidity rates associated with cholecystectomy are directly influenced by factors such as age and history of concomitant common bile duct exploration (CBDE) (De Silva et al., 2022; Fagenson et al., 2021). Other factors include the American Society of Anesthesiologists (ASA) physical status classification, surgical setting, operative approach, the Nassar operative difficulty scale (Wong et al., 2024), acute admission, and comorbidity (Sandblom et al., 2015). In addition, the presence and severity of inflammation, male sex, body weight (overweight or obese), and previous abdominal surgery were identified as risk factors (Kanakala et al., 2011). The mortality rate following surgery for benign conditions range from 0.1% to 0.7% (Sandblom et al., 2015). A study indicated that the postoperative outcome of cholecystectomy was less favorable in patients with severe cholecystectomy than in those with mild or moderate cholecystectomy. Nevertheless, no instances of mortality were recorded (Saito et al., 2017).

Type 2 diabetes mellitus (T2DM) has been associated with the development of gallstones, with a higher prevalence observed in individuals with T2DM than in those without T2DM (Ratheesh et al., 2023). Furthermore, obesity, female sex, ethnicity, high fat/carbohydrate diet, estrogen therapy, and Gilbert's syndrome have been identified as the risk factors for gallstones (Liu et al., 2015). Therefore, comorbidities such as T2DM can influence morbidity and LoS. A study conducted by Teng et at. (2021) found that 1,587 (26.21%) of the patients with cholelithiasis were diagnosed with T2DM and exhibited complications. However, research on the effect of T2DM on the outcome of cholecystectomy remains limited and contradictive (Teng et al., 2021). In fact, diabetes has caused many negative effects on the crucial processes of wound healing and cellular function (Burgess et al., 2021).

Length of stay (LoS) is a measure of the number of days a patient must remain hospitalized. LoS can be determined by calculating the number of days a patient remains in the hospital from admission to discharge (or dead). The average length of stay (ALoS) is calculated by dividing the number of days of inpatient care (alive or dead) in the hospital during a given period by the number of patients (alive or dead) discharged from the hospital for a specified period (Kulkarni and Dongre, 2023; Street et al., 2021). ALoS for patients undergoing cholecystectomy is five days. If the ALoS extends beyond five days, it is considered that the hospital stay is prolonged (Kulkarni and Dongre, 2023; Scala et al., 2021). The global prevalence of diabetes mellitus is estimated to be 170 million cases. A total of 1,587 patients (26.21%) with cholelithiasis exhibited complications due to diabetes. Research has indicated that diabetic patients are more likely to be admitted to the hospital (Teng et al., 2021). If comorbid factors can be identified, avoided, and controlled, it is anticipated that the safety aspect of cholecystectomy will



be enhanced. Moreover, preventing morbidity and prolonged hospital stay following cholecystectomy will reduce healthcare costs.

OBJECTIVE

This study aims to determine the effect of type 2 diabetes mellitus on the morbidity rate and length of stay in patients undergoing cholecystectomy. This study is a preliminary investigation that will contribute to a better understanding of the management of cholelithiasis.

MATERIALS AND METHODS

Study design

This study used a descriptive analytical design with a quantitative approach using data in the form of number and categories which were analyzed and are presented in tables. The inclusion criteria for this study were all cholelithiasis patients who underwent cholecystectomy at Dr. Ramelan Naval Hospital, Surabaya between June 2019 and September 2020. The exclusion criteria for this study were cholelithiasis patients whose medical records were incomplete, patients with a history of abdominal trauma or abdominal surgery, and cholelithiasis patients with biliary system malignancies.

The morbidity rates in this study were observed in patients with renal failure, postoperative infection, surgical complications requiring further surgery, readmission following surgery, heart failure, cardiogenic shock, conversion to open cholecystectomy, post-cholecystectomy syndrome, congestive heart failure, and septic shock.

Data collection

The sample was selected using a non-probability sampling technique, specifically the total sampling method, whereby the entire population was taken as the sample for this study. The sample consisted of patients treated in the operating room at Dr. Ramelan Naval Hospital, Surabaya.

Data analysis

The data were analyzed using SPSS 25 (IBM, US). The contingency coefficient was used to determine the statistical difference between morbidity and treatment duration of cholecystectomy patients. Moreover, the incidence and treatment duration between diabetic and nondiabetic patients were analyzed using the contingency correlation test. The result was considered significant at a p-value of 0.05.

RESULTS

A total of 146 patients with complete medical records were included in this study. Their data were analyzed using both descriptive and analytical techniques. Figures 1 and 2 illustrate the characteristics of the patients according to sex and age.

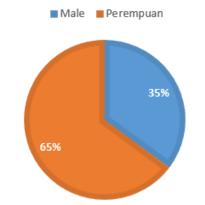


Figure 1. The sex distribution of the patients

As presented in Table 1, the number of cholecystectomy patients who had diabetes and exhibited complications following the procedure was six (26.1%), while 17 (73.9%) did not exhibit complications. In comparison, the number of patients undergoing cholecystectomy who did not have

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diabetes but exhibited complications was 11 (8.9%), while 112 (91.1%) did not exhibit complications. The contingency coefficient correlation revealed a significant difference between diabetes and morbidity in cholecystectomy (r = 0.191; p = 0.019), indicating that the prevalence of morbidity was higher in diabetic patients (26.1%) compared to non-diabetic patients (8.9%). In other words, patients with diabetes mellitus had a 2.93 times higher risk for developing comorbidities during cholecystectomy (95% CI [1.198, 7.100], p = 0.019).

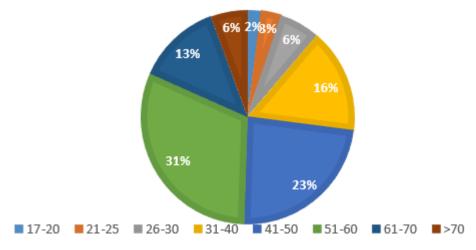


Figure 2. The age distribution of the patients

Table 1. The	distribution of pat	tients with diabete	s mellitus as a con	norbid factor in re	lation to morbidity (n=146)
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Comorbid Factor	Morbidity Rate	Without Morbidity	p-value	r
Diabetes	6	17	0.019 ^a	0.191
	(26.1%)	(73.9%)		
Non-Diabetes	11	112		
	(8.9%)	(91.1%)		

^aContingency coefficient correlation test

As presented in Table 2, the number of diabetic patients who underwent cholecystectomy and were hospitalized for more than five days was 18 (78.3%), while five (21.7%) were hospitalized for five days or less. In comparison, the number of patients who underwent cholecystectomy without comorbidities and were hospitalized for more 5 days were 67 (54.5%), while 56 (45.5%) were hospitalized for five days or less. A significant difference in the length of hospital stay was observed between patients with diabetes and patients without diabetes (p = 0.034), indicating that the prevalence of patients with diabetes who were hospitalized for more than five days (78.4%) was higher than those without diabetes (54.5%). The other words, diabetic patients had a 1.43 higher likelihood of being hospitalized for more than five days (95% CI [1.098, 1.881], p = 0.034).

Table 2. The distribution of patients with diabetes mellitus as a comorbid factor in relation to length of stay (n=146)

Comorbid Factor	Length of Hospital Stay > 5 days	Length of Hospital Stay ≤ 5 days	p-value	r
Diabetes	18	5	0.034 ^a	0.173
	(78.3%)	(21.7%)		
Non-Diabetes	67	56		

^aContingency coefficient correlation test

(54.5%)



(45.5%)

DISCUSSION

T2DM is a risk factor for gallstone development due to its impact on bile salt secretion and gallbladder emptying, which is caused by insulin resistance (Chen et al., 2018). This study found that patients with diabetes had a greater risk of developing other health conditions, with a higher prevalence than patients without diabetes. This finding is consistent with the finding of a study conducted by Lequertier et al. (2021) which indicated that diabetes is an independent risk factor for gallstone diseases, which is associated with mortality, infectious complications, cardiovascular disease, and kidney failure following cholecystectomy (Lequertier et al., 2021). A study by Pagliarulo et al. (2004) also yielded similar results. However, epidemiological evidence yielded contradictory results. Recent findings suggested that cholecystectomy is associate with a higher prevalence of metabolic syndrome (MetS) due to a significant increase in weight within six months of cholecystectomy (Chen et al., 2018). Furthermore, cholecystectomy is known to influence lipid metabolism, resulting in increased serum hepatic triglyceride (TG) concentrations, very-low-density lipoprotein (VLDL)-TG levels, and apolipoprotein B-48 production. However, this evidence was observed in mice (Amigo et al., 2011). Epidemiological data indicated that postoperative patients had a higher risk of developing cardiovascular disease (CVD) (Chavez-Tapia et al., 2012).

Health professional and scientists have proposed that cholecystectomy and T2DM had a mutual relationship, with both conditions affecting one another (Mohammadyari et al., 2023). A study conducted by Fagenson et al (2021) found that postoperative complications were reported to be 2.65 times higher in diabetic patients at 1,139 (6.05%) patients. In addition, Eckert et al. (2023) argued that the potential causes of diabetes-related complicated during cholecystectomy may be attributed to reduced T-cell responses, impaired neutrophil function, and impaired humoral immunity. Consequently, diabetes increases the risk of infection. Infections exacerbated by diabetes can lead to the development of pathologies such as postoperative infections, urinary tract infections, and kidney failure (Eckert et al., 2023).

Patients with diabetes who underwent delayed laparoscopic cholecystectomy were four times more likely to experience a worsening of surgical area infection than patients who immediately received surgical intervention. This indicated that diabetes can exasperate the infection in the surgical area (Bhandari et al., 2017; Tomic et al., 2022). Banday et al. (2020) and Serban et al. (2021) found that diabetes is one of the accompanying pathological factors that cause severe inflammation and increase severe adhesion of anatomical structures in the patient, which can result in complications during conversion to open cholecystectomy (Banday et al., 2020; Serban et al., 2021). This study found that diabetes affects the conversion rate.

In addition, patients with diabetes also experience morbidities in the form of bile acid diarrhea and postcholecystectomy syndrome, although the mechanism by which diabetes affects these morbidities, remains unclear. Post-cholecystectomy syndrome is more likely to result from disruption of bile flow following the removal of the gallbladder as a reservoir (Łącka et al., 2020). One case of a patient with diabetes showed morbidity in the form of shock, likely due to other comorbidities such as hypoalbuminemia and hyponatremia, which were experienced by the patient (Elsamna et al., 2020; Hahn and Gebäck, 2014).

The ALoS following cholecystectomy was 10.91 hours (ranged from one day to four days). Over 25% patients had prolonged hospital stays due to postoperative complications, such as pain, sepsis, and social reasons. One patient was readmitted due to infection (Bazeer et al., 2018). This study found that patients with T2DM had longer hospital stays than patients without T2DM. This finding suggested that diabetes was associated with LoS. Other studies yielded similar results, including a study conducted by Chiang et al. (2021) which demonstrated that diabetes is one of the comorbid factors affecting the length of treatment, with 18 (39.1%) patients having prolonged hospital stays for more than five days. A study using multivariate analysis found 10 independent predictive factors affecting LoS of patients undergoing cholecystectomy, including patients with anticoagulation medication, those with standard-pressure pneumoperitoneum, those with metoclopramide medication, those undergoing abdominal drainage, those with complications, those taking oral analgesic, and those admitted privately. This study did not explicitly identify T2DM as a comorbidity, but it can be classified as a complication (Ko-Iam



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et al., 2017). T2DM is a significant risk factor in the development of infections due to poor glycemic control, which in turn reduces the immune response, including T-cell and neutrophils, and alters the leucocyte function, including migration, phagocytosis, and chemotaxis (Cozma et al., 2022).

The findings of this study are consistent with those of Erum et al. (2023) which found that diabetic patients tend to have prolonged hospital stays (Erum et al., 2023). Burgess et al. (2021) and Wan et al. (2021) identified a biomolecular mechanism by which diabetes interferes with the phosphorylation of endothelial nitric oxide synthase (eNOS), which plays a role in the mobilization of endothelial progenitor cells (*EPCs*). The expression of stromal cell-derived factor alpha 1 α (SDF-1 α), which activates various signaling pathways during stem cell attachment and migration, is also reduced in epithelial cells, diabetic wounds, and myofibroblasts, preventing EPCs from reaching the wound site, thereby inhibiting it following the surgical procedure and leading to prolonged treatment duration (Burgess et al., 2021; Wan et al., 2021). It is recommended that blood sugar levels in diabetic patients be checked prior to surgery, as this may contribute to prolonging the treatment period in diabetic patients.

Limitations

This study has a number of limitations. First, the number of samples was relatively small, with only 146 cases out of 201 gallstone cases that met the inclusion criteria of this study. This number is very low in comparison to existing research and reviews. In addition, this study did not categorize the patients according to the type of cholecystectomy performed, which may have resulted in a bias between morbidity rate and length of stay in patients undergoing open cholecystectomy and laparoscopic cholecystectomy.

CONCLUSION

The findings indicated that comorbidities such as diabetes were associated with morbidity rate and length of hospital stay in patients undergoing cholecystectomy.

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Conflict of Interest

None.

Funding

None.

Ethical Clearance

This study received ethical approval from the Research Ethics Subcommittee of Dr. Ramelan Naval Hospital, Surabaya in October 2020 with a certificate number 38/EC/SKEPKRS/2020.

Author Contribution

AMAA: conceptual and writing the draft; WPM: conceptual; DP: conceptual; RY: conceptual; RPA: data analysis.

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