



Investigating the Relationship Between the Monocyte Percentage and Monocyte-Lymphocyte Ratio with the Type, Duration, and Complications of Cholecystectomy: A Cross-sectional Study

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Abstract

Background: Cholecystectomy is a common surgical procedure performed to remove the gallbladder. It plays an essential role in treating various biliary diseases, especially gallstones and gallbladder inflammation (cholecystitis). It is of great importance to investigate factors that affect surgical results and predict related complications.

Materials and Methods: At the beginning of the study, following approval by the ethics committee, clinical records of patients were collected from Bandar Abbas Shahid Mohammadi Hospital. Supplemental data were gathered via telephone contact with patients or their families when necessary. The collected data were analyzed using SPSS software and appropriate statistical methods.

Results: A total of 189 cholecystectomy patients (72.6% female, 91.6% laparoscopic procedures) who underwent surgery at Shahid Mohammadi Hospital, Bandar Abbas, between 2022 and 2023 were enrolled in this study. Their monocyte and lymphocyte percentages, monocyte-to-lymphocyte ratio (MLR), and other related clinical information were collected. The MLR was significantly higher in patients with underlying disease ($P < 0.05$). It was also significantly higher in patients who underwent laparotomy, those hospitalized in the intensive care unit (ICU) after surgery, and those who developed surgical site infections. In patients who had postoperative bleeding, both the monocyte percentage and the MLR were significantly higher. Additionally, the percentage of lymphocytes was elevated in these patients.

Conclusion: The findings suggest that the MLR may serve as a valuable biomarker for identifying patients at higher risk of postoperative complications following cholecystectomy.

Keywords: Cholecystectomy, Infection, Bleeding, Biomarker

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Introduction

Gallbladder disease is a common condition in the United States and a major digestive system issue worldwide (1, 2), with gallstones being one of the most prevalent. Gallstones (cholelithiasis) affect 10-20% of the adult population, and their prevalence in the US increased by 6.5% (from 7.4 to 13.9%) between 1988-1994 and March 2020 (3). Approximately, 750 000 cholecystectomy procedures (gallbladder removal) for treating gallstones are performed annually in the US, with a total cost being around \$6.5 billion (2). Although gallstones are not associated with high mortality (4), their complications and links to gallbladder, pancreatic, and colorectal cancers have been well documented. According to the National Institutes of

Health, about 3,000 people die from gallstones each year in the US (2). Risk factors for gallbladder disease include gender, race, age, obesity, dyslipidemia, oral contraceptive use, diabetes mellitus, and alcohol abuse (5-7), which can vary by global region (8). High-calorie and high-fat diets are additional lifestyle-related factors that contribute to gallstones' prevalence (9).

Several surgical methods are used to treat cholelithiasis, ranging from conventional open surgery to modern laparoscopic techniques (10). Laparoscopic cholecystectomy has largely replaced open surgery for the management of cholelithiasis due to its inherent benefits. Today, laparoscopic gallbladder surgery is considered the gold standard method for treating gallstones and is

expected to eventually replace open techniques entirely (10-12). Several factors influence surgical decisions and help predict postoperative complications. These include white blood cell count (WBC), body mass index (BMI), and gallbladder wall thickness (13). Other identified predictors are male gender, duration of preoperative symptoms, and serum levels of alkaline phosphatase, amylase, and C-reactive protein (CRP) (14). Surgical duration is also a key predictor of post-cholecystectomy complications (15). Additional contributing factors include older age, male gender, cholecystitis (with or without stones), and the surgeon's experience. A high BMI and male gender have also been linked to specific surgical challenges (16).

Inflammation, which is present in both cholelithiasis and acute cholecystitis (inflammation of the gallbladder), poses a significant risk during surgery. It can complicate anatomical identification, thereby increasing the likelihood of bleeding or bile duct injury (17). Elevated levels of CRP, procalcitonin, and leukocytes are commonly observed in these conditions and can support the decision to proceed with surgery (18).

Monocytes represent another inflammatory marker that has been less frequently studied in previous research. A study in Turkey examined the relationship between the monocyte-to-lymphocyte ratio (MLR) and intraoperative adhesions in cholecystectomy (19, 20). The results indicated that higher MLR values were associated with an increased rate of intraoperative adhesions (18). Monocytes also play a critical role in regulating immune responses, particularly through interaction with lymphocytes. Both types of cells become highly activated in response to infection, and monocyte-lymphocyte interactions can improve the immune response. Several studies have established that a rise in MLR can affect prolonged hospitalization and an increased likelihood of the risk of open surgery (21). Furthermore, increased preoperative MLR has also been associated with reduced postoperative survival in patients with gallbladder cancer (22).

This study investigates the relationship between monocyte inflammatory factors (monocyte percentage and MLR) and surgical outcomes, including type of operation, duration, and complications, in patients at Bandar Abbas Medical Center. The goal was to evaluate the predictive value of these factors to improve surgical decision-making and patient outcomes.

Materials and Methods

This study employed a census sampling method, encompassing all patients undergoing surgery at Shahid Mohammadi Hospital, Bandar Abbas, between 2022 and 2023 who met the inclusion criteria. Consequently, the study sample was identical to the study population.

Inclusion criteria comprised patients with complete clinical records, including age, gender, marital status,

education level, medical history, type and duration of surgery, postoperative intensive care unit (ICU) admission, postoperative recovery status, and monocyte count. Exclusion criteria included patients with incomplete clinical records, as well as a history of diabetes, cancer, concurrent inflammatory diseases, or hypertension.

Data were collected via the hospital's Health Information System (HIS) and supplemented by demographic data (e.g., age, gender, marital status, education level, and underlying conditions) collected via telephone contact with patients or, if required, their families. Clinical information (i.e., monocyte percentage, MLR, surgical procedure, surgical duration, ICU admission status, and operating room time) was obtained from patients' clinical records.

Data were analyzed using SPSS software. Descriptive statistics (i.e., mean, variance, and standard deviation) were calculated. Inferential statistics, including independent samples t-tests, Pearson correlation coefficients, one-way ANOVA, and linear or multivariate logistic regression, where appropriate, were used to examine relationships between monocyte levels, MLR, and relevant clinical variables. Non-parametric alternatives, including the Mann-Whitney U test, Spearman's rank correlation coefficient, and Kruskal-Wallis test, were employed when data did not meet normality assumptions. Normality was assessed using the Kolmogorov-Smirnov test. A significance level of $P < 0.05$ was considered statistically significant. The study specifically assessed the impact of surgical type, duration, postoperative ICU admission, postoperative biological function, and the need for reoperation on monocyte percentage and MLR.

Results

Demographic Data

The study population consisted of 189 patients diagnosed with cholecystitis who underwent cholecystectomy. The majority (72.6%) were female, while 27.4% were male.

According to Table 1, the mean monocyte percentage for men patients was 8.34 (SD = 2.741), while for women patients, it was 8.45 (SD = 2.766). The mean lymphocyte percentage for men and women was 15.314, with a standard deviation of 2.5978 for men and 2.4535 for women. The mean MLR for men and women was 0.53920

Table 1. Relationship Between Gender and Monocyte/Lymphocyte Percentages and MLR

	Sex	Mean \pm SD	P Value
Monocyte percentage	Male	2.74 \pm 8.34	0.85
	Female	2.76 \pm 8.45	
Lymphocyte percentage	Male	2.59 \pm 15.31	0.73
	Female	2.45 \pm 15.34	
MLR	Male	0.15 \pm 0.54	0.76
	Female	0.21 \pm 0.55	

Note. MLR: Monocyte-to-lymphocyte ratio; SD: Standard deviation.

and 0.55539, respectively. Statistical analysis showed no significant differences between genders in the percentages of monocytes and lymphocytes or their numbers ($P > 0.05$).

According to Table 2, there was no significant relationship between education level and monocyte percentage, lymphocyte percentage, and MLR, and the difference between them was not significant ($P > 0.05$).

Comorbidity With Other Diseases

Among the 189 patients, 76.3% had no history of underlying diseases (e.g., cardiovascular, renal, vascular disease, diabetes, or hypertension), whereas 24.7% reported having at least one condition. According to Table 3, there was no statistically significant relationship

Table 2. The Relationship Between Education Level and Monocyte/Lymphocyte Percentages and MLR

	Educational Level	Mean \pm SD	P Value
Monocyte percentage	Illiterate	2.52 \pm 8.35	0.17
	Under diploma	5.0 \pm 9.0	
	Diploma	2.77 \pm 8.19	
	Bachelor's Degree	3.13 \pm 8.0	
Lymphocyte percentage	Illiterate	2.66 \pm 15.58	0.22
	Under diploma	0.25 \pm 12.80	
	Diploma	2.28 \pm 8.85	
	Bachelor's Degree	2.60 \pm 15.96	
MLR	Illiterate	0.10 \pm 0.53	0.58
	Under diploma	0.16 \pm 0.57	
	Diploma	0.21 \pm 0.55	
	Bachelor's Degree	0.13 \pm 0.54	

Note. MLR: Monocyte-to-lymphocyte ratio; SD: Standard deviation.

Table 3. The Relationship Between Underlying Disease and the Monocytes/Lymphocytes Percentages and MLR

	Underlying Disease	Mean \pm SD	P Value
Monocyte percentage	Male	2.98 \pm 9.06	0.09
	Female	2.62 \pm 8.14	
Lymphocyte percentage	Male	3.05 \pm 15.17	0.99
	Female	2.37 \pm 15.29	
MLR	Male	0.23 \pm 0.59	0.007
	Female	0.14 \pm 0.52	

Note. MLR: Monocyte-to-lymphocyte ratio; SD: Standard deviation.

Table 4. Relationship Between Surgery Type, Postoperative Complications, and Monocyte/Lymphocyte Percentages and MLR

	Surgery Type	Mean \pm SD	P Value	Surgical Site Infection	Mean \pm SD	P Value	Postoperative Bleeding	Mean \pm SD	P Value
Monocyte percentage	Laparoscopy	2.58 \pm 8.14	0.001	Yes	2.25 \pm 9.00	0.11	Yes	3.66 \pm 12.00	0.001
	Laparotomy	2.59 \pm 9.06		No	2.80 \pm 8.27		No	2.52 \pm 8.15	
Lymphocyte percentage	Laparoscopy	2.58 \pm 15.40	0.12	Yes	3.29 \pm 15.03	0.47	Yes	2.91 \pm 16.09	0.45
	Laparotomy	2.53 \pm 15.22		No	2.41 \pm 15.36		No	2.53 \pm 15.26	
MLR	Laparoscopy	0.17 \pm 0.53	0.001	Yes	0.60 \pm 0.13	0.001	Yes	0.211 \pm 0.74	0.001
	Laparotomy	0.05 \pm 0.68		No	0.17 \pm 0.53		No	0.16 \pm 0.53	

Note. MLR: Monocyte-to-lymphocyte ratio; SD: Standard deviation.

between the presence of underlying diseases and the percentages of monocytes or lymphocytes ($P > 0.05$). However, the MLR was significantly higher in patients with underlying diseases compared to those without such diseases ($P < 0.05$).

Surgery Type and Postoperative Complications

According to Table 4, the monocyte percentage was significantly higher in patients who underwent laparotomy ($P < 0.05$). Although the lymphocyte percentages were significantly higher in patients who underwent laparoscopy, this difference was not statistically significant ($P > 0.05$). The MLR was also significantly higher in patients who underwent laparotomy ($P < 0.05$). Additionally, the monocyte percentage was higher and the lymphocyte percentage was lower in patients with surgical site infection, but these differences were not significant ($P > 0.05$). However, MLR was significantly elevated in patients with surgical site infections ($P < 0.05$). Similarly, both monocyte percentage and MLR were significantly higher in patients with postoperative bleeding ($P < 0.05$), whereas lymphocyte percentage was also higher in these patients, but this difference was not statistically significant ($P > 0.05$).

Intensive Care Unit Admission

As illustrated in Table 5, the percentages of monocytes and the MLR were significantly higher in patients who were admitted to the ICU after surgery ($P < 0.05$). The percentage of lymphocytes was also higher in ICU-

Table 5. Relationship Between Postoperative ICU Admission and Monocyte/Lymphocyte Percentages and MLR

	Postoperative Hospitalization in ICU	Mean \pm SD	P Value
Monocyte percentage	Yes	2.92 \pm 9.94	0.01
	No	2.67 \pm 8.20	
Lymphocyte percentage	Yes	3.23 \pm 16.48	0.08
	No	2.45 \pm 15.19	
MLR	Yes	0.09 \pm 0.59	0.005
	No	0.17 \pm 0.53	

Note. ICU: Intensive care unit; MLR: Monocyte-to-lymphocyte ratio; SD: Standard deviation.

admitted patients, but this increase was not statistically significant ($P > 0.05$).

Discussion

Gender Differences

The present descriptive cross-sectional study involved 381 patients diagnosed with cholecystitis who underwent cholecystectomy. The findings demonstrated that male patients had a higher monocyte percentage, lymphocyte percentage, and MLR; however, these differences were not statistically significant. Similarly to the present study, Lipman et al found that male gender, elevated WBC counts ($WBC > 12000 \times 10^3/\mu L$), low albumin levels (albumin < 3.4 mg/dL), diabetes, and other factors influenced the surgical outcomes of cholecystectomy (23). Although MLR was higher in men, the difference was not statistically significant, which is consistent with our findings. Lipman et al identified male gender, elevated WBC counts, low albumin levels, diabetes, and other factors as influencing surgical outcomes of cholecystectomy (23). Furthermore, Kama et al reported that male gender, prior operative interventions, and acute cholecystitis were significant predictor variables for surgical outcomes in patients undergoing cholecystectomy (24). The results of this study suggest that cholecystectomy may affect the immune system similarly in both genders. However, other factors, such as fluctuations in immune cell numbers, particularly monocytes and lymphocytes, are also noteworthy, as they may reflect the body's immune response to surgery. Nevertheless, the absence of significant differences between men and women in this study suggests that cholecystectomy has a comparable impact on both genders.

Educational Level

It was also noted that other clinical characteristics such as percentage of lymphocytes, monocytes, or MLR were higher in patients with higher education levels, although these differences were not statistically significant compared to other groups. In their study, Baky and Donoghue pointed out that patient education before surgery can enhance their understanding of surgical procedures, risks, and the phases of healing. This awareness may help decrease anxiety and improve patient cooperation during the postoperative phases. Unfortunately, the study does not differentiate the effects of education level. However, logically and in retrospect, patients with higher education may be more capable of comprehending preoperative training and information (25). Similar findings were reported by de Aguilar-Nascimento et al (26) and Toğaç and Yılmaz (27).

Comorbidity With Other Diseases

In this study, similar to those conducted by Tarabay et al and Gul et al, the percentage of monocytes and the MLR in

individuals with cholecystitis was higher than that in other patients (28, 29). Chronic diseases such as cardiovascular, renal, and vascular conditions can influence the immune system, often leading to alterations in lymphocyte and monocyte counts. Interestingly, an increase in monocyte count along with abnormal lymphocyte distribution is also observed in chronic inflammatory conditions caused by comorbid diseases. Higher levels of inflammation are characteristic of diabetes and hypertension, which can cause alterations in the immune profile, particularly in the number and function of lymphocytes and monocytes. It becomes evident that hypertension can change monocyte levels. Hence, in simplified terms, an increase in monocytes in hypertensive patients may be considered an inflammatory marker. According to some previous research, people with high levels of monocytes are prone to cardiovascular diseases. Most chronic complications, such as those seen in type 2 diabetic patients, affect the normal functioning of lymphocytes. This dysfunction may result in a lowered ability to fight off infections, and hence, an increased incidence of disease (30).

Surgical Method

Sista et al and Gomatos et al, in a study similar to ours, based their observation on the fact that after laparoscopic or laparotomy surgery, the mean percentage of lymphocytes might be higher in the laparoscopic group due to better immune response and less surgical stress. Conversely, there is some evidence that the proportion of monocytes may be higher in patients undergoing laparotomy. This could be attributed to the higher levels of inflammation experienced as a result of open surgery to date, which in turn leads to higher levels of immune system activity. These observations indicate that the surgical method may play a role in changing the cell makeup of an immune response rather dramatically. Laparoscopy, which is less invasive, may lead to an improved immune response compared with laparotomy, and is hence used in clinical research to enhance patients' clinical outcomes. (31, 32).

Surgical Site Infection

This study also reveals that the percentage of monocytes was higher, and the percentage of lymphocytes was lower, in patients with surgical site infections. Of particular interest, surgical site infections are among the most frequent complications observed following surgeries and cause severe complications and costly treatments. Monocytes play a role in regulating immune responses and support this function through interactions with lymphocytes. Lymphocytes are divided into two main categories: T cells and B cells. T lymphocytes help eliminate infected cells, while B lymphocytes help with the production of antibodies. Both types of cells become highly activated in response to infections, and when monocytes interact with them, the immune response can be enhanced.

Studies have demonstrated that through cytokine synthesis and expression of the surface receptors, monocytes can stimulate lymphocytes. For instance, monocytes can produce cytokines like interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF- α), which help stimulate T and B lymphocytes. As mentioned above, antibodies are produced by B cells, which originate from stem cells in the bone marrow. After activation, B cells develop into plasma cells, which release antibodies to help fight against infections. Meanwhile, myeloid progenitors give rise to macrophages and dendritic cells, which are involved in innate immune defense and antigen presentation. These cells capture, surround, and digest pathogens, and also produce cytokines and chemotactic agents that attract other immune cells. Such multiplex interactions between monocytes and lymphocytes can decrease post-operation-related infections. It is crucial to address these infections and understand the roles of monocytes and lymphocytes in their development and control.

Postoperative Bleeding

In this study, similar to findings of Kar and Atay (33) and Wang et al (34), the percentage of monocytes and the MLR were significantly higher in patients experiencing postoperative bleeding. However, the higher levels of lymphocytes in patients with postoperative bleeding were not statistically significant. Postoperative bleeding remains one of the common surgical complications and can result in severe postoperative complications, including prolonged hospital stays. Therefore, the role of monocytes and lymphocytes as inflammatory and immune cells in inflammation and wound healing is essential. Immune cells such as monocytes and lymphocytes serve as key markers in the inflammatory process and wound repair. Since monocytes are involved in tissue remodeling and the regulation of bleeding following surgery, elevated monocyte levels may reflect a severe inflammatory response and an increased tendency to bleed. The WBC profile in patients also needs careful monitoring; if the MLR tends to be high in most cases, it may indicate an underlying chronic inflammation, which in turn may increase the risk of postoperative bleeding. Furthermore, a low lymphocyte count can also decrease the body's capacity to control infection and inflammation, further predisposing the patient to postoperative bleeding.

Intensive Care Unit Outcomes

In line with our study, Khomusi et al observed that the percentage of monocytes and the MLR were significantly higher in patients who were hospitalized in the ICU after surgery (35). However, unlike in our study, their ICU patients had a higher percentage of lymphocytes. In general, the percentage of lymphocytes in ICU patients was decreased, which may be attributed to poor

immunocompetence, which may result from extreme stress, infection, or inflammation. The higher percentage of monocytes in ICU patients is likely due to increased immune system activity and inflammation. This increase can be attributed to inflammation and can also be viewed as a sign of significant inflammation. Overall, alterations in simplified ratios such as the neutrophil-to-lymphocyte ratio (NLR), along with changes in lymphocyte and monocyte levels, can be useful in assessing the severity of pathology and the clinical condition of ICU patients. Such data may assist in predicting readmission probabilities, hospital stay duration, and patient care required. Lymphocytes and Monocytes were also suggested by Prabhu et al to be further explored regarding their need for ICU admission (36). In general, an increase in monocyte levels and a decrease in lymphocyte percentage indicate complications in the disease status. In other words, patients requiring ICU care often present with higher monocyte counts and lower lymphocyte levels. These changes may act as biomarkers for predicting the potential for complications and assessing disease severity.

Conclusion

The findings of the study indicate that there were no significant differences in the percentages of monocytes and lymphocytes between men and women, as well as based on the level of education. In patients with underlying diseases, the MLR was higher. Moreover, in patients who underwent laparotomy, the percentage of monocytes and MLR increased significantly. In patients who were hospitalized in the ICU, the percentage of monocytes and the MLR were also higher. In patients with surgical site infection, the MLR increased significantly, while the differences in the percentages of monocytes and lymphocytes were not significant. Additionally, in patients with postoperative bleeding, the percentage of monocytes and the MLR increased significantly, whereas the opposite is true for fluctuations in the percentage of lymphocytes.

This study encountered limitations in documenting patient information. It is recommended that the effects of other inflammatory factors such as interleukins also be investigated in future studies.

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Authors' Contribution

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Competing Interests

The authors declare no conflict of interests.

Consent for Publication

Consent for publication was obtained from all participants.

Data Availability Statement

The data sets used during the current study are available from the corresponding author upon reasonable request.

Ethical Approval

The study was approved by the Research Council and Ethics Committee of Hormozgan University of Medical Sciences (IR.HUMS.REC.1403.058).

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