Original research article

The Relationship between Leukocyte Count and Left Ventricular Ejection Fraction in Patients with ST-Elevation Myocardial Infarction

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ABSTRACT

Background: ST-Elevation Myocardial Infarction (STEMI) causes significant myocardial damage and increases heart failure risk. Inflammation, reflected by leukocyte count, is considered to play a crucial role in STEMI's pathophysiology, potentially affecting cardiac function. This study aimed to evaluate the relationship between leukocyte count and left ventricular ejection fraction (LVEF) in STEMI patients. **Methods:** A cross-sectional study was conducted from August to September 2024 at RSUD Raden Mattaher Jambi. Data from 80 patient medical records, including leukocyte count at admission and LVEF measured via echocardiography, were analyzed using Fisher's Exact and Spearman's correlation tests. **Results:** Most patients were male (82.5%), with high leukocyte counts (67.5%) and low LVEF (82.5%). The mean age was 57.8 years. Prevalences of hypertension, diabetes, and dyslipidemia were 38.8%, 33.8%, and 47.5%, respectively. Statistical analysis revealed no significant relationship between leukocyte count and LVEF (Fisher's p=0.497; Spearman's p=0.078; r=0.16). **Conclusion:** This study found no significant association between leukocyte count and LVEF in STEMI patients.

Keywords: STEMI; Leukocyte; Ejection fraction

INTRODUCTION

Cardiovascular disease remains the leading cause of death globally. According to the World Health Organization (WHO), in 2019, more than 17 million deaths were attributed to cardiovascular diseases, with three-quarters occurring in low- and middle-income countries. A significant proportion of these deaths result from myocardial infarction, commonly known as a heart attack.[1] The global prevalence of acute myocardial infarction (AMI) is estimated to be around 7.29 million cases. While some studies suggest that the incidence and mortality rates of AMI have decreased over the past few decades, it remains a major global health issue, particularly in developing and underdeveloped regions.[2]

ST-Elevation Myocardial Infarction (STEMI) represents the most severe form of AMI, characterized by transmural myocardial necrosis. Clinically, STEMI is defined by typical ischemic symptoms associated with persistent ST-segment elevation on an electrocardiogram (ECG) and elevated biomarkers of myocardial necrosis. STEMI contributes to approximately 35%–40% of all MI cases.[3] Despite significant advancements in therapeutic interventions, the rates of mortality and recurrent cardiovascular events among STEMI patients remain high. Furthermore, many patients present with complications, such as heart failure, which is a primary clinical syndrome resulting from the heart's inability to pump sufficient blood to meet the body's needs. STEMI is a leading cause of this condition.[4]

The progression of STEMI involves complex mechanisms leading to coronary artery occlusion and myocardial ischemia. The inflammatory response is believed to play a critical role in this pathogenesis. Inflammatory cells and cytokines are markers of myocardial damage and infarct size. Elevated leukocyte counts (leukocytosis) reflect the infiltration of immune cells into the necrotic tissue, occurring as part of the body's response to ischemia and reperfusion injury. Leukocytes contribute to the progression of coronary artery disease through several pathological mechanisms, including promoting proteolytic and oxidative damage to the endothelium, microvascular obstruction, hypercoagulability, and infarct expansion.[5]

In addition, myocardial necrosis and damage caused by STEMI can impair cardiac function. This can be observed through left ventricular function. Left ventricular ejection fraction (LVEF) is a widely available and commonly used indicator of left ventricular function, serving as a marker of myocardial damage and heart failure. Left ventricular dysfunction in the acute phase is known to be a predictor of poor prognosis after MI. As LVEF decreases, the risk of mortality and heart failure increases significantly in STEMI patients. It is estimated that approximately 30%–40% of STEMI patients exhibit reduced LVEF.[6]

Several studies have examined the relationship between leukocytosis and cardiac function in MI patients. A study by Liu et al. (2012) involving MI patients undergoing percutaneous coronary intervention (PCI) demonstrated that leukocyte count had prognostic value in predicting left ventricular remodeling, with a significant correlation between leukocyte count and LVEF. Similarly, a case-control study by Eskandarian et al. (2013) found that leukocytosis was more common in MI patients with systolic dysfunction (LVEF <45%).[7,8]

While previous research has suggested that leukocyte count may be a potential indicator of left ventricular dysfunction in MI patients, further investigation is needed to explore this

relationship's significance and clinical utility in diverse populations. Therefore, this study aims to evaluate the relationship between leukocyte count and left ventricular function, as measured by LVEF, in STEMI patients. The findings of this study may provide valuable insights for clinicians in assessing, screening, and managing STEMI patients.

METHODS

This cross-sectional study was conducted at Raden Mattaher General Hospital, Jambi City. Patient data were obtained by reviewing secondary data from medical records. Baseline characteristics, such as age, gender, smoking status, hypertension, and dyslipidemia, were collected from the medical records. Leukocyte counts were obtained from blood tests performed at hospital admission, while LVEF was obtained from the first echocardiography performed a few days later.

The study sample consisted of all STEMI patients at Raden Mattaher General Hospital from July 2022 to June 2024. STEMI diagnosis was established based on clinical assessment, electrocardiography (ECG) findings, and cardiac biomarker levels. Exclusion criteria included: (a) a history of myocardial infarction or heart failure; (b) prior percutaneous coronary intervention (PCI), coronary artery bypass grafting (CABG), or heart surgery; (c) acute infectious or immunological disorders; (d) malignancy; (e) renal or hepatic failure; and (f) current use of steroids, non-steroidal anti-inflammatory drugs (NSAIDs), or antibiotics.

The hospital's ethics committee approved the study. Data were analyzed using the Statistical Package for Social Sciences (SPSS) software. Univariate analysis was applied to describe patient characteristics. Bivariate analysis to assess the relationship between leukocyte count and LVEF was performed using Fisher's Exact test and Spearman's correlation. Statistical significance was defined as $p<0.05$.

RESULTS

A total of 80 patients were included in the study. **Table 1** presents the distribution of baseline patient characteristics. The mean age of STEMI patients was 57.81 ± 10.31 years, with the majority being male (82.5%). The prevalence of hypertension, diabetes, and dyslipidemia was 38.8%, 33.8%, and 47.5%, respectively. Most patients had uncertain smoking status information (81.3%).

Table 1. Characteristics of patients.

Variable	Mean ± SD or n (%)
Age (years)	57.81 ± 10.31
Gender	
Men	66 (82.5)
Women	14 (17.5)
Smoking	
Yes	6 (7.5)
No	9 (11.3)
No information	65 (81.3)
Hypertension	
Yes	31 (38.8)
No	49 (61.3)
Diabetes Mellitus	
Yes	27 (33.8)
No	53 (66.3)
Dyslipidemia	
Yes	38 (47.5)
No	45 (52.5)
Leukosit (uL)	
≤ 11.000	26 (32.5)
> 11.000	54 (67.5)
LVEF (%)	
< 50%	66 (82.5)
≥ 50%	14 (17.5)

Leukocyte counts were categorized into ≤11,000/uL and >11,000/uL. Leukocytosis was more common in STEMI patients (67.5%). LVEF was divided into two groups: LVEF <50% and ≥50%. Similarly, most STEMI patients had reduced ejection fraction (82.5%).

Table 2. Fisher's Exact analysis between leukocyte count and LVEF.

Variable		LVEF <50%		LVEF ≥50%		P	OR	IK 95%
		n	%	n	%			
Leukosit	>11,000	44	66.7	10	71.4	0.497	1.25	0.35–4.44
	≤11,000	22	33.3	4	28.6			
Total		66	100	14	100			

Table 3. Spearman's correlation analysis between leukocyte count and LVEF.

Variable	LVEF
Leukocyte	$r = 0.16$
	$p = 0.078$

Statistical analysis using Fisher's Exact test demonstrated no significant difference in the incidence of reduced LVEF between STEMI patients with elevated leukocyte counts and those with normal leukocyte counts (p=0.497) (**Table 2**). Additionally, Spearman's correlation analysis showed no significant association between leukocyte count and LVEF in STEMI patients (p=0.078) (**Table 3**).

DISCUSSION

The Characteristic of STEMI patients

The average age of STEMI patients in this study is 58 years. A meta-analysis conducted in the Asia-Pacific region reported an average age of 61.6 years (95% CI 57.9–65.3).[9] In Indonesia, studies conducted in Kupang, Yogyakarta, and Jakarta reported average ages of 56, 57, and 56 years, respectively[10–12]. These findings indicate that STEMI is more commonly observed in older patients. Aging leads to physiological changes in the heart, including a decrease in myocardial reserve capacity, reduced heart rate, and an increase in left ventricular mass. Additionally, older individuals are more likely to have comorbidities and chronic diseases due to prolonged exposure to atherogenic factors. Even with standard therapy, older age is associated with higher mortality, suggesting a worse prognosis for the elderly population.[13]

In this study, the proportion of male patients was higher than that of female patients. Similar findings were observed in a study across 12 European countries, where 6,117 of 8,834 patients were male.[14] In Indonesia, male patients also predominate in STEMI cases, such as in Serang, where 87% of patients were male.[15] A study by Prasetia et al. also found a higher percentage of male patients (82.9%).[11] These data suggest an association between gender and the occurrence of STEMI. Biological and lifestyle factors play a significant role in this association. Key factors such as high cholesterol levels and smoking habits are more commonly observed in men, particularly before the age of 60. Women tend to experience myocardial infarction 9–10 years later than men, primarily due to the protective effects of estrogen before menopause. Furthermore, higher body mass index (BMI) and a history of coronary artery disease are more prevalent in men.[16]

Smoking history was not well-documented in the participants of this study due to a significant number of STEMI patients failing to record their smoking habits. A study by Cenko et al., involving 8,834 patients, reported that 46% of male patients and 29.5% of female patients were smokers.[14] Another study reported that 33.45% of patients were smokers.[13] Smoking contains more than 7,000 harmful substances that contribute to various diseases, including heart disease. These substances trigger hemodynamic changes, endothelial dysfunction, thrombosis, inflammation, lipid disorders, and arrhythmogenesis. Smoking increases the

susceptibility to plaque formation and thrombosis, thus raising the risk of cardiovascular events. It also interacts with human genes, increasing the risk of cardiovascular diseases. Smokers are 3.7 times more likely to suffer from myocardial infarction compared to non-smokers.[17,18]

In this study, the prevalence of hypertension (38.8%), diabetes (33.8%), and dyslipidemia (47.5%) was observed in a significant portion of patients. A similar study by Karim et al. reported prevalences of hypertension (49%), diabetes (34%), and dyslipidemia (35%).[19] Other studies reported slightly different figures, with hypertension at 54%, diabetes at 24%, and dyslipidemia at 58%.[20] Hypertension is associated with atherosclerosis through several mechanisms.[21,22] Hypertension can cause insulin resistance and hyperglycemia, hyperactivity of the sympathetic nervous system, the release of vasoactive factors, and mechanical stress on the heart. Hypertension also directly damages the artery walls, increasing the likelihood of atherosclerotic plaque formation.[23,24] On the other hand, diabetes increases the risk of atheroma formation through metabolic mechanisms such as hyperglycemia, dyslipidemia, and insulin resistance, leading to endothelial and smooth muscle dysfunction, as well as platelet and coagulation dysfunction.[25,26] Elevated levels of proinflammatory cytokines and matrix metalloproteinases contribute to decreased collagen synthesis and increased collagen degradation in the fibrous cap of atherosclerotic plaques.[27] Patients with dyslipidemia are also at higher risk for cardiovascular diseases.[28–30] Lipoproteins contribute to endothelial changes, plaque distribution, atheroma plaque initiation with foam cell formation, and plaque progression. Dyslipidemia increases lipid deposition in arteries, narrowing the vessel lumen and hindering blood flow, which can lead to thromboembolic events such as stroke, transient ischemic attacks, ischemic heart disease, and pulmonary embolism.[31]

Leukocytes and LVEF in STEMI

In recent years, leukocytes have been recognized as indicators of morbidity and mortality risk in patients. As markers of inflammation, leukocytosis can serve as a prognostic indicator in patients without infection. In cardiovascular or cerebrovascular diseases, the severity of leukocytosis correlates with the severity of ischemic damage and patient clinical outcomes. Previous studies have shown that leukocyte count is associated with the degree of coronary artery stenosis and infarct size in patients with AMI.[32,33]

In this study, no significant relationship was found between leukocyte count and left ventricular ejection fraction (LVEF). Previous studies, however, reported different findings. A study by Hussain et al. found a significant result (p=0.001). They evaluated 49 STEMI patients, measuring leukocyte count within the first 24 hours and assessing ejection

fraction. This cohort study showed a moderate inverse correlation (-0.462) between leukocyte count and LVEF, indicating that higher leukocyte counts were associated with lower LVEF.[34] Leukocytosis was also more common in patients with left ventricular dysfunction compared to those without heart failure.[5]

Significant findings were also observed in a study by Jan et al., which investigated the incidence of short-term congestive heart failure after acute myocardial infarction. Two hundred patients with new STEMI and chest pain onset within 12 hours were included. Leukocyte count was measured within 12 hours of hospitalization, and heart failure was assessed within four days. This cross-sectional study found a significant association between leukocyte counts >11,000 and the occurrence of heart failure ($p<0.008$). Neutrophilia was also significantly associated with heart failure ($p<0.016$).[35]

Leukocytes play a crucial role in the inflammatory process, which is the body's response to various diseases. However, inflammation can be a double-edged sword. Inflammation is primarily a protective mechanism against pathogens and tissue injury. Ideally, this response is localized and limited, aimed at eliminating pathogens and damaged cells, followed by the clearance of inflammatory cells and tissue repair, returning to homeostasis. However, prolonged or excessive inflammation leads to chronic inflammation, which is now recognized as a key component of various chronic diseases, including atherosclerosis, arthritis, pulmonary diseases, autoimmune disorders, diabetes, and cancer. The inflammatory response in myocardial infarction is essential for myocardial healing and heart function, involving complement activation, cytokine and chemokine regulation, leukocyte and macrophage recruitment, and fibrosis initiation. However, excessive or prolonged inflammation can cause further myocardial damage.[36]

This is supported by a study by Chia et al., which investigated similar parameters in STEMI patients. They analyzed blood parameters such as leukocyte, neutrophil, lymphocyte count, and the neutrophil-lymphocyte ratio as independent variables, and infarct size and ejection fraction as dependent variables. Notably, dependent variables were measured twice: on hospital admission and 24 hours later. Independent variables were also measured twice: on days 5 and 30. The results differed from those of previous studies. Leukocyte count on hospital admission did not statistically correlate with LVEF on days 5 or 30. However, the relationship became significant when leukocyte count was measured 24 hours later, with a p-value <0.05. The correlation coefficient between leukocytes at 24 hours and LVEF at days 5 and 30 were nearly identical at -0.20 and -0.21, respectively. Although the correlation was weak, it

provided specific insights into the role of leukocyte parameters in the pathogenesis of AMI. This relationship was significantly stronger for leukocyte counts assessed after PCI at 24 hours compared to the initial measurement.[37]

In the early phase of STEMI, inflammatory cells invade the ruptured atherosclerotic plaque, contributing to plaque initiation, progression, and instability in atherosclerotic regions. Neutrophils invade the vessel wall, causing plaque instability by releasing superoxide radicals, cytokines, and proteolytic enzymes. Furthermore, monocytes, which are the first responders, contain large amounts of inflammatory cytokines, including proteases. These inflammatory cytokines contribute to myocardial necrosis.[33] During the maturation phase of tissue repair, if inflammation becomes widespread and prolonged, it can lead to adverse remodeling with scar tissue formation at the injury site, potentially resulting in complications like heart failure and death. This phenomenon is associated with increased left ventricular wall stress after AMI. Consequently, the left ventricle undergoes enlargement as a compensatory mechanism to improve pump function through the Frank-Starling mechanism. Left ventricular dilation further increases myocardial wall stress (Laplace's law), leading to further dilation. This positive feedback loop ultimately causes progressive left ventricular remodeling and, eventually, heart failure.[38]

An increase in leukocyte count is also associated with impaired perfusion in cardiac muscle. In one study, this increase was accompanied by reduced epicardial and myocardial perfusion, as well as increased thromboresistance (slower artery patency and more thrombus formation). Additionally, leukocytes from necrotic tissue are more rigid and less able to traverse microcirculation because they are larger and more rigid than erythrocytes and platelets, making them more prone to causing blockages in small blood vessels. This can lead to microcirculatory defects, exacerbating ischemia and expanding the infarct area.[8] The inflammatory response also regulates repair attempts to replace infarcted areas with connective tissue. Thus, the extent of myocardial necrosis correlates with the level of leukocyte response observed systemically.[37]

Previous research has shown that approximately 40% of STEMI cases experience acute left ventricular systolic dysfunction, and a decrease in LVEF is associated with an increased risk of mortality and heart failure in STEMI patients. Patients with low LVEF who survive longer have a higher risk of hospitalization due to heart failure and mortality from all causes compared to those with normal LVEF.[39] Early injury during STEMI triggers harmful heart remodeling, causing left ventricular dilation and systolic dysfunction, which is associated with an increased risk of heart

failure. Mortality from all causes increases with decreased LVEF.[4]

The change in LVEF after myocardial infarction is a dynamic process that depends on reversible myocardial stunning, irreversible necrosis, and modifications in treatment. Myocardial stunning is a phenomenon in which myocardial contractile function remains impaired but recovers within a few weeks after revascularization. Left ventricular remodeling triggered by irreversible necrosis at the core of the infarct zone affects long-term LVEF recovery. Thus, patients with higher initial LVEF have smaller infarct sizes, lower myocardial ischemia levels, and a higher proportion of myocardial stunning in the infarct zone.[39]

Despite the valuable insights provided by this study, several limitations should be noted. First, the time gap between the blood tests and echocardiographic examination in STEMI patients varied, which may have influenced the results, as the timing of these tests can affect the measurements of leukocyte count and left ventricular ejection fraction (LVEF). Second, both the blood tests and echocardiographic assessments were conducted only once, and repeated measurements could potentially yield different results, providing a more accurate reflection of the dynamic changes post-STEMI. Third, the study only assessed the total leukocyte count, without analyzing the individual types of leukocytes, which could have provided a more detailed understanding of the inflammatory response in STEMI patients. Additionally, many patients were excluded from the study due to the unavailability of echocardiographic data, which may have resulted in a smaller sample size and less comprehensive data. Finally, this study did not control for confounding factors such as age, gender, diabetes, hypertension, and dyslipidemia, which could introduce heterogeneity into the sample and affect the interpretation of the findings. Future studies addressing these limitations with larger, more controlled cohorts and repeated measurements would provide a more robust understanding of the relationship between leukocyte count and LVEF in STEMI patients.

CONCLUSION

This study aimed to evaluate the relationship between leukocyte count and left ventricular ejection fraction (LVEF) in STEMI patients. The results showed no significant correlation between leukocyte count and LVEF, indicating that leukocytosis may not be directly associated with impaired left ventricular function in this cohort. While some previous studies have suggested a connection between elevated leukocyte counts and worse cardiac outcomes, particularly in terms of LVEF and heart failure, our findings did not support this association. This discrepancy could be attributed to the limitations of our study, such as the single-point measurement of leukocyte count and

LVEF, as well as the heterogeneity of the patient population. Despite these findings, it remains clear that inflammation plays a critical role in the pathogenesis of STEMI, and leukocyte count may still serve as a useful marker for monitoring the inflammatory response during the acute phase of myocardial infarction.

RECOMMENDATIONS

Based on the limitations of this study, several recommendations for future research can be made. First, repeated measurements of leukocyte count and LVEF over time, especially in the acute and subacute phases of STEMI, would provide a better understanding of the dynamic relationship between inflammation and cardiac function. Second, additional research controlling for confounding factors such as age, gender, and comorbidities (e.g., diabetes, hypertension, dyslipidemia) would help clarify whether these variables influence the association between leukocytes and LVEF. Furthermore, a larger, more homogenous sample size could increase the statistical power of the study and provide more reliable results. Finally, exploring other inflammatory markers could offer deeper insights into the inflammatory processes affecting left ventricular function in STEMI patients. These efforts would enhance the clinical utility of inflammatory markers in predicting prognosis and improving patient management in STEMI.

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