Evaluation of the relationship between monocyte to HDL ratio with STEMI, STEMI severity, thrombosis, and early repolarization

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Abstract---Introduction Due to the relationship between high maximum heart rate (MHR) values and the severity of coronary atherosclerosis and cardiac events, as well as standard features and clinical outcomes of early repolarization significant and myocardial infarction with ST-segment elevation, this study investigated the relationship between monocyte to HDL ratio and STEMI, STEMI severity, Thrombosis, and early repolarization were performed. Method This cross-sectional prospective observational study was performed on STEMI patients referred to Imam Khomeini Hospital in Ahvaz in 1399. In this study, STEMI patients and individuals with referred early repolarization patterns are evaluated during the first 12 hours after the onset of pain and used for statistical analysis of SPSS software version 22. Results: In this study, 36 patients have studied with a mean age of 61.6±14.4; 23 patients were male, and the rest were female. The ratio of monocytes to HDL in STEMI patients varied based on the age and sex of the patients. The mean MHR in STEMI patients

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Based on PCI need was 16.4±2.9 in patients in need and 20.5±2.1 in patients who were candidates for CABG. The ratio of monocytes to HDL in STEMI patients varied based on the occurrence and severity of thrombosis. The mean MHR was 18.1±3.2 in STEMI patients and 9.2±2.2 in Early repolarization patients. The ratio of monocytes to HDL in STEMI patients varied based on vessel score. The percentage of monocytes to HDL in STEMI patients went based on the severity of LV dysfunction and stroke severity. Conclusion The present study showed a significant relationship between the ratio of monocytes to HDL with STEMI, STEMI severity, thrombosis, and its severity. This study also indicates that the mean MHR rate in STEMI and premature repolarization patients are significantly different.

Keywords---Early repolarization, STEMI, MHR, monocyte.

Introduction

Atherosclerotic cardiovascular disease is coronary artery disease’s most common underlying cause, including ischemic heart disease (IHD) and cerebrovascular disease (1-3). Ischemic heart disease and stroke are the leading and third leading causes of death globally, accounting for 84.5% of cardiovascular deaths and 28.2% of all-cause deaths worldwide (4). A side effect of many medicines could lead to heart problems (5). Endothelial cells, Leukocytes, and intima smooth muscle are the main components of atherosclerotic plaque formation (6). As atherosclerosis and cardiovascular disease progress, inflammation plays an important role, and atherosclerotic plaque rupture is the primary cause of acute myocardial infarction with increasing ST segment (7-8). In contrast, high-density lipoprotein cholesterol (HDL-C) has anti-inflammatory and antioxidant properties and anti-thrombotic effects (9, 10). HDL cholesterol protects endothelial cells against inflammation and oxidative stress by preventing the uptake of monocytes into the arterial wall by controlling the activation of monocytes and the proliferation of monocyte progenitor cells (11-12). The association of high monocyte counts and low HDL-C with inflammation and oxidative stress has led to testing a new marker called the monocyte-to-density lipoprotein ratio (MHR) in cardiovascular disease. Indeed, MHR may predict the number of monocytes and HDL-C levels in predicting short-term and long-term cardiovascular outcomes. Recently, MHR was reported as a new marker for significant adverse effects in heart disease (13). Inflammation and accumulation of lipids are the two prominent symptoms of atherosclerosis as a chronic disease (14). Monocytes make up about one-fifth of the peripheral blood mononuclear cells (12) and are essential immune system cells that play a unique role during the inflammatory response (16). They are divided into three subtypes based on the expression of lipopolysaccharide receptor (CD14) and FCγ-III receptor with low affinity at their surface: classical monocytes, which make up approximately 90%, middle monocytes, and nonclassical monocytes (17). It has been shown that high-density lipoprotein (HDL), as an anti-atherosclerotic agent, can inhibit the expression of tissue factors in monocytes by inhibiting p38 activation and the inhibition of phosphoinositide 3-kinase (18). According to density, HDL particles are divided into two main subgroups: HDL2, the less dense, fat-rich form, and HDL3, the
thicker, more protein-rich paper (19). Several biological activities resulting from these heterogeneous particles have been identified, including reverse cholesterol transport and antioxidant, anti-inflammatory, anti-apoptotic, anti-thrombotic, and anti-atherosclerotic effects (20, 21). It also prevents the uptake of monocytes into the arterial wall by reducing their F-actin content, reducing the expression of CD11b on monocytes and endothelial adhesion molecules, thereby preventing monocytes from adhering to the endothelium. And thus controls the monocyte (22). In clinical studies, small HDL was associated with the presence and severity of atherosclerotic disease. Conversely, large HDL was negatively correlated with the presence of CAD (coronary artery disease), disease severity, and progression (23). These observations hypothesize that monocytes and HDL-C have apparent functions in the Progression or inhibition of atherosclerosis. Monocytes play a crucial role in causing atherosclerosis, and there is growing evidence to support the use of white blood cell counts as predictors of future coronary events. MHR is a practical, cost-effective, and highly predictive indicator of CVD (cardiovascular diseases).

**Materials and Methods:**

This study aimed to investigate the relationship between monocyte to HDL ratio with STEMI (ST-Elevation Myocardial Infarction), STEMI severity, thrombosis, and early repolarization, and identify an accurate, inexpensive and available marker to assess and predict thrombosis and STEMI severity and thus help manage patients. STEMI. This prospective cross-sectional observational study was performed on STEMI patients referred during the first 12 hours after the onset of pain to Imam Khomeini Hospital in Ahvaz in 1399. Inclusion criteria included age over 18 years, patient consent to participate in the study, referral in the first 12 hours after the onset of chest pain, and exclusion criteria also included thrombolytic therapy during the last 24 hours, any infectious and systemic inflammatory diseases. History of hematologic disease including anemia (*12 g/dL for females, *13 g/dL for males), malignancy, renal or hepatic insufficiency, cardiovascular disease, recent infarction, and a history of blood transfusion in the previous three months. STEMI diagnosis is based on chest pain for more than 30 minutes, an increase or decrease in cardiac biomarkers, an increase in the ST segment > 0.1 mV on at least two consecutive electrocardiogram leads, or a new LBBB pattern. ERP detection is performed if notch or slur is observed on the lower slope of the R wave, J peak ≥ 0.1 mV in 2 consecutive leads and STE ≥ 1 mm at the junction between the end of the QRS and the beginning of the ST (J point) segment in at least two consecutive leads Becomes. Hypertension is defined as systolic blood pressure ≥ 140 mm Hg and diastolic blood pressure ≤ 90 mm Hg in repeated measurements using any antihypertensive drug. Diabetes mellitus is defined as fasting plasma glucose > 126 mg/dL or < 200 mg/dL in any size or use of anti-diabetic medications. The presence or absence of PCI (Percutaneous Coronary Intervention), echocardiographic results, and coronary angiography are also evaluated and recorded. All STEMI patients undergo elective coronary angiography. Culprit lesions can be treated with stents and balloon angioplasty if needed. Coronary angiograms are digitally recorded for quantitative analysis. Digital angiograms are analyzed by two experienced cardiologists who do not know the study data. The presence and grade of thrombosis are determined by using grade thrombolysis (thrombolysis in myocardial infarction) (24): Patients are
divided into two groups, low thrombotic load (grades 0 to 3) and high thrombotic burden (grades 4 and 5), based on the severity of thrombosis. The SYNTAX score is determined based on the number of lesions and their functional complexity and is used to determine the severity of coronary artery disease in STEMI patients (25, 26). Each lesion with a diameter of 1.5 mm and stenosis of ≥ 50% is assessed using an online SS calculator (www.syntaxscore.com), and the SYNTAX Score (SS) is calculated. Based on the mean of SYNTAX1, patients are divided into three groups: low intensity (0-22), (mean value 23-32), and high power (> 32) (27). The ratio of monocytes to HDL is also calculated using the measured parameters, and its relationship with STEMI, STEMI severity, thrombosis, and early repolarization is investigated. They were used for statistical analysis of SPSS software version 22. In quantitative variables, mean and median will describe the data center, and standard deviation and amplitude will tell data to scatter. In qualitative variables, frequency and percentage will describe the data. The Kolmogorov-Smirnov test checks the normality of the data and Q-Q diagram, and the Leven test contains the homogeneity of variances. To analyze the data univariately, we will use the T-Test (Mann-Whitney nonparametric test), ANOVA (or Kruskal-Wallis nonparametric test), Chi-square test (or Fisher’s exact test), and Pearson correlation coefficient (or Spearman). . Linear and logistic regression are used to analyze the data in a multivariate manner. The significance level in tests is considered 0.05.

Results:

In this study, a total of 36 patients were studied. The minimum age of patients was 38, the maximum was 90 years, and the mean age of patients was 61.6±14.4. Regarding gender, 23 patients were male, and 13 were female. According to the independent t-test, the ratio of monocytes to HDL in STEMI patients varied based on the age and sex of the patients. However, this difference was insignificant (P-value 0.4 and 0.3, respectively). The mean MHR was 18.4±2.8 years for men and 17.5±4 years for women. First, the normality of MHR data distribution was evaluated and confirmed by the Kolmogorov-Smirnov test to determine parametric or nonparametric tests (0.2). Based on PCI requirements, the mean MHR in STEMI patients was 16.4±2.9 in patients in need and 20.5±2.1 in candidates for CABG (coronary artery bypass grafting) (P-value = 0.00). One-way analysis of variance showed that the ratio of monocytes to HDL in patients STEMI varies according to the occurrence and severity of thrombosis, which is a significant difference (Table 1). The mean MHR in STEMI patients was 18.1±3.2, and in Early repolarization, patients were 9.2±2.2 (P-value = 0.00). A one-way analysis of variance showed that the ratio of monocytes to HDL varied by vessel score in STEMI patients (P = 0.00). One-way variance analysis showed that the proportion of monocytes to HDL in STEMI patients varies based on the severity of LV dysfunction (Table 2). An independent t-test revealed that the percentage of monocytes to HDL in STEMI patients varies based on RV dysfunction. The ratio of monocytes to HDL in STEMI patients varies based on the presence of the underlying disease. One-way variance analysis showed that the percentage of monocytes to HDL in STEMI patients varies based on the stroke severity.
Monocytosis is an independent risk marker for cardiovascular disease, and high monocyte counts are associated with plaque progression during the acute phase of myocardial infarction. As a result, monocytes have been identified as an independent marker for STEMI progression (28-29). The monocyte to HDL ratio is a new marker that indicates proatherogenic and antiestrogenic balance, and high MHR values are associated with the severity of coronary atherosclerosis and cardiac events (30, 31). Therefore, this study investigated the relationship between monocyte to HDL ratio with STEMI, STEMI severity, thrombosis, and early repolarization. Kanbay and colleagues first reported a monocyte-to-HDL ratio as an independent prognostic marker for cardiovascular events in chronic kidney disease (32). This study shows that the ratio of monocytes to HDL in STEMI patients based on vessels score is significantly different. Also, the ratio of monocytes to HDL in STEMI patients differed based on the severity of LV and RV dysfunction. It was also shown that the ratio of monocytes to HDL in STEMI patients differed based on the occurrence and severity of thrombosis. Arısoy, in 2017 showed that the ratio of monocytes to HDL in the high thrombosis group was significantly higher than in the low thrombosis group. In studies, the ratio of monocytes to HDL in STEMI patients differed based on the occurrence and severity of thrombosis. Arısoy, in 2017 showed that the ratio of monocytes to HDL in the high thrombosis group was significantly higher than in the low thrombosis group. In studies, the ratio of monocytes to HDL was an independent predictor of high thrombosis load. As a result, the monocyte to HDL ratio is an independent predictor of high thrombosis load in STEMI patients undergoing primary PCI (33). Another study showed that the ratio of monocytes to HDL could predict the severity of coronary artery disease in STEMI patients treated with primary PCI (26). Our study shows that the mean MHR in STEMI patients requiring PCI was significantly lower than in CABG candidates. In contrast to our research by Villanueva in 2020, which aimed to evaluate the ratio of monocytes to HDL as a predictor of mortality and significant cardiovascular side effects in patients with STEMI under primary PCI, showed that the ratio of monocytes to HDL was high at the time of hospitalization. STEMI under primary PCI is associated with in-hospital mortality and significant cardiovascular side effects (34). Another study in China in 2019 showed that the ratio of monocytes to HDL is an independent predictor of mortality with any cause and MACE in CAD patients under PCI (35). This difference in the results of our study with the study stated was probably due to the smaller sample size or the severity of the clogged arteries that made the patient a candidate for CABG. Evidence has shown that HDL cholesterol has anti-inflammatory, antioxidant, and anti-thrombotic effects. In addition, lower HDL and LDL levels have been reported as independent predictors of mortality in acute coronary syndromes and other clinical diseases (36). A significant association exists between an increase in the number of monocytes and the presence of atherosclerosis and its complications. In addition, we know that the inhibitory effect on monocyte activation can be attenuated in the presence of low serum HDL cholesterol levels. Therefore, it can be argued that an increase in MHR may predict adverse cardiovascular events in STEMI patients. Wang also showed a linear and positive correlation between monocyte to HDL ratio and the risk of ischemic stroke in a large population in China in 2019. They stated that the MHR marker indicates a high atherosclerotic load and has a better predictive value for stroke than conventional risk factors (37). Sercelik in Turkey in 2018 showed that the ratio of monocytes to HDL (MHR) was the only independent predictor of STEMI (38). This study and similar studies show that MHR is a practical, cost-effective, and highly
predictive indicator of CVD. Simple MHR calculation in clinical practice is one of the advantages of using this index to predict disease. It is cheaper to evaluate than other inflammatory markers, such as interleukin (IL) -1, IL-6, tumor necrosis factor-α, monocyte-1, and serum amyloid A. It can be said that different studies have one thing in common: the increase in MHR level is associated with poor cardiovascular outcomes. It is a sign of more severe disease and possible Progression. MHR, on the other hand, is associated with inflammation and is closely related to CRP in predicting monocyte and HDL cholesterol measurements separately. Therefore, we suggest that MHR and its positive correlation with CRP are markers of systemic inflammation and predict atherosclerotic development. Progression and predictor of clinical outcome in CVD associated with inflammatory conditions. Whether this index has predictive value and can be affected by various fat-modifying treatments is also questionable.

Conclusion

The present study showed a significant relationship between the ratio of monocytes to HDL with STEMI, STEMI severity, thrombosis, and its severity. This study also indicates that the mean MHR rate in STEMI and premature repolarization patients are significantly different. Because MHR is a cheap and accessible diagnostic test routine laboratory test among our STEMI patients, we can consider its value in predicting cardiovascular outcomes.

Limitations

Our research, like other research, has limitations. First, the sample size of patients was relatively small. More extensive studies with larger sample sizes are needed to diagnose better the causal relationship between MHR and myocardial infarction and related factors. It was also a cross-sectional, single-focus study that may lead to biased results.

Recommendation

To further support our conclusion, multicenter, multiethnic, and large-scale clinical trials are needed. Therefore, we recommend conducting prospective studies with larger sample sizes to evaluate whether there is an association between MHR admission and cardiovascular outcomes. Future research should identify MHR-specific cut-offs that could increase the risk of cardiovascular events. Another possible tool is to monitor the effectiveness of the response to treatment at the MHR level.

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Conflicts of Interest:

The authors declare that they have no conflicts of interest.

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**Table 1:** Monocyte to HDL ratio in STEMI patients based on the occurrence and severity of thrombosis

<table>
<thead>
<tr>
<th>Severity of thrombosis</th>
<th>Case number</th>
<th>average ± SD</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Low</td>
<td>17</td>
<td>16.8±3.8</td>
<td></td>
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<tr>
<td>Moderate</td>
<td>13</td>
<td>18.9±2.5</td>
<td>0.07</td>
</tr>
<tr>
<td>high</td>
<td>6</td>
<td>19.9±1.7</td>
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</tbody>
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**Table 2:** Monocyte to HDL ratio in STEMI patients based on the severity of LV dysfunction

<table>
<thead>
<tr>
<th>Severity of LV dysfunction</th>
<th>Case number</th>
<th>average ± SD</th>
<th>minimum</th>
<th>maximum</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>5</td>
<td>12.8±0.9</td>
<td>11.50</td>
<td>14.00</td>
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</tr>
<tr>
<td>Moderate</td>
<td>14</td>
<td>16.6±1.8</td>
<td>13.80</td>
<td>19.90</td>
<td>0.00</td>
</tr>
<tr>
<td>high</td>
<td>17</td>
<td>20.28±1.5</td>
<td>18.00</td>
<td>24.40</td>
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