

## Relation of Monocyte Count to Thrombus Burden in ST-Segment Elevation Myocardial Infarction Patients Undergoing Primary Percutaneous Coronary Intervention

Shafiq ur Rehman,<sup>1</sup> Muhammad Faizan,<sup>2</sup> Anam Shakeel,<sup>3</sup> Khawar Naeem Satti,<sup>4</sup> Muhammad Mohsin<sup>5</sup>

### Abstract

**Objective:** To determine the association of monocyte count to thrombus burden in ST-segment elevation myocardial infarction (STEMI) patients undergoing primary percutaneous coronary intervention (P-PCI).

**Method:** This analytical, cross-sectional study was done in the Angiography Department of Rawalpindi Institute of Cardiology, Rawalpindi from October 30, 2020 to April 30, 2021. After taking ethical approval, 180 STEMI patients undergoing P-PCI who presented within 24 hours of symptoms were included using nonprobability convenient sampling. Informed written consent of the patients was obtained. Primary PCI with stenting was done and the thrombolysis in myocardial infarction (TIMI) scale was applied to determine intracoronary thrombus burden. The blood samples of patients were taken to estimate monocyte count. The data was analyzed through the Statistical Package for the Social Sciences (SPSS) version 25.

**Results:** The frequency of thrombus burden was high in 71(39.4%) patients and low in 109(60.6%) patients. The monocyte count showed a significant difference in patients with high thrombus versus low thrombus burden. In low thrombus burden patients, the mean monocyte count was  $0.49 \pm 0.50$  and in high thrombus burden patients, the mean monocyte count was  $0.64 \pm 0.48$ . The results of stratification of thrombus burden with age group showed significant p-value and with others showed non-significant p-value.

**Conclusion:** The monocyte count is a reliable, inexpensive and simple-to-measure predictor of high thrombus burden in coronary arteries in STEMI patients undergoing primary PCI.

**Keywords:** Thrombus burden; Monocyte count; ST-segment elevation myocardial infarction; Primary Percutaneous coronary intervention

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### Introduction

Myocardial infarction (MI) is the most severe form of cardiovascular disease. ST-segment elevation

myocardial infarction (STEMI) contributes to a significant proportion of cardiovascular mortality and morbidity.<sup>1</sup> The prevalence of cardiovascular diseases particularly STEMI is rising continuously mainly in low-and middle-income countries (LMICs). The issue has worsened owing to the large population size in these countries. The World Health Organization has reported that 80% of cardiovascular mortality occurs in LMICs. There is an estimated increase of 3 million cases of STEMI annually in these countries. In addition, STEMI affects young people in LMICs in much larger numbers than in other countries. It is also a cause of significant

1,2,4,5. Department of Cardiology, Rawalpindi Institute of Cardiology, Rawalpindi

3. Department of Gastroenterology, Holy Family Hospital, Rawalpindi

#### Correspondence:

Dr. Shafiq ur Rehman ; Assistant Professor Cardiology, Rawalpindi Institute of Cardiology, Rawalpindi, Email: drshafiq799@gmail.com

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financial burden for these countries leading to an annual loss of around \$3.76 trillion.<sup>2</sup>

The pathogenesis of STEMI involves the formation of a thrombus in coronary arteries resulting from the rupture of atherosclerotic plaque and subsequent decrease in coronary blood supply.<sup>3</sup> Despite the development of numerous pharmacological and invasive therapies, including thrombectomy and glycoprotein IIB/IIIa antagonists, the management of intracoronary thrombi remains challenging.<sup>4</sup> Primary percutaneous coronary intervention (P-PCI), which restores normal blood flow and has better clinical results, is the preferred treatment option.<sup>5</sup> But the occurrence of the phenomenon of slow flow/ no-reflow jeopardizes the advantages of P-PCI.<sup>6</sup> The available data revealed that this phenomenon occurs in 4% to 30% of patients after P-PCI.<sup>7,8</sup> High thrombus burden is the most significant predisposing factor of slow flow/no-reflow and adversely affects the success rate of P-PCI. During the procedure, a thrombus can embolize to the distal territory increasing the infarct size, thus decreasing cardiac function from microvascular obstruction.<sup>9</sup> High thrombus burden is linked to lack of flow, stent thrombosis or coronary artery spasm and worse clinical outcomes such as reinfarction, cardiac rupture, arrhythmia, heart failure, embolization and even death.<sup>10,11</sup>

The treatment of STEMI may benefit from determining the predisposing factors of high thrombus burden. Two factors predicting the thrombus burden in STEMI patients are red cell distribution width (RDW) and bilirubin level.<sup>4,12</sup> Monocytes may play a role in coronary artery disease (CAD) pathogenesis, and a high monocyte count has been linked to an increased risk of MI.<sup>13</sup> It has been revealed that monocytes are involved in thrombus formation and plaque rupture by secreting enzymes that breakdown the extracellular matrix, releasing various pro-coagulant factors and promoting inflammation.<sup>13,14</sup> High monocyte counts are an important indicator of inflammation and therefore high thrombus burden. Literature has reported that monocyte counts independently predict slow reflow/no-reflow following primary PPCI in STEMI patients.<sup>14</sup>

The current study was conducted to detect the frequency of high thrombus burden in STEMI patients undergoing P-PCI in our setup and also assessed the association of various cardiovascular risk factors with thrombus burden in these patients. The study also determined the difference in monocyte counts between patients with high thrombus and low thrombus burden. This will

help us in the risk assessment of the patients with high thrombus burden undergoing P-PCI. Early identification of these patients will help us to improve our practice for better prevention and management of this condition.

## Materials and Methods

This analytical, cross-sectional study was done in the Angiography Department of Rawalpindi Institute of Cardiology, Rawalpindi from October 30, 2020 to April 30, 2021. By using 100% confidence level, 7% margin of error and 34.8% STEMI patients with high thrombus burden, the sample size of 178 patients was calculated which was rounded off to 180 patients.<sup>15</sup>

After taking approval from hospital's ethical committee, all STEMI patients undergoing P-PCI with ages ranging from 18-80 years who presented within 24 hours of symptoms were included using a nonprobability convenient sampling technique. Informed written consent of the patients was obtained for this study. The exclusion criteria were patients with chronic stable or unstable angina, reinfarction or past history of CAD, P-PCI or coronary artery bypass grafting (CABG). All the patients were given aspirin, clopidogrel and unfractionated heparin. Primary PCI with stenting was done using the standard radial approach. The patients received tirofiban (glycoprotein IIb/IIIa receptor inhibitor) based on operator judgement. After ante-grade flow was achieved, the thrombolysis in myocardial infarction (TIMI) scale was applied in all patients to determine intracoronary thrombus burden. The TIMI thrombus grade 0-2 showed low thrombus burden and TIMI grade 3-4 indicated high thrombus burden. Before giving aspirin and clopidogrel, the blood samples of patients were taken in standard ethylenediaminetetraacetic acid (EDTA) containing vacutainers. The reference range for monocyte count was taken as  $285-500 \times 10^9/L$ . All the data including patient demographic profile & risk factors were collected through a pre-designed proforma.

## Statistical Analysis

The data was analyzed through the Statistical Package for the Social Sciences (SPSS) version 25. Quantitative variables such as age and monocyte count were presented as mean and standard deviation (SD). Qualitative variables such as gender, hypertension, obesity, diabetes mellitus, tobacco consumption and thrombus burden were presented as frequency and percentage. Mean monocyte count was compared between high and low thrombus burden by using an independent sample t-test.

Data was stratified for gender, age, diabetes mellitus, hypertension, obesity and tobacco consumption by applying a Pearson Chi-Square test. The significant p-value was  $\leq 0.05$ .

## Results

In this study, 111(61.7%) patients were males and 69 (38.3%) were females. Patients had a mean age of  $61.11 \pm 7.11$  years. The patients of  $<60$  years were 76 (42.2%) and  $\geq 60$  years were 104(57.8%). The mean TIMI score was  $3.28 \pm 1.00$ . Hypertension was present in 108 (60%) patients, 103(57.2%) patients had obesity, 69(38.3%) patients had diabetes mellitus while 74(41.1%) patients had the history of tobacco consumption. The frequency of thrombus burden was high in 71(39.4%) patients and low in 109(60.6%) patients. These results are shown in Table 1.

The monocyte count showed a significant difference

**Table 1:** Various Parameters of the Study Participants

Parameter	Frequency (Percentage)
<b>Gender</b>	
Male	111(61.7%)
Female	69(38.3%)
<b>Age Groups</b>	
< 60 years	76(42.2%)
>60 years	104(57.8%)
<b>Hypertension</b>	
Hypertensive	108(60%)
Nonhypertensive	72(40%)
<b>Obesity</b>	
Obese	103(57.2%)
Nonobese	77(42.8%)
<b>Diabetes mellitus</b>	
Diabetic	69(38.3%)
Nondiabetic	111(61.7%)
<b>Smoking</b>	
Smoker	74(41.1%)
Nonsmoker	106(58.9%)
<b>Thrombus burden</b>	
High	71(39.4%)
Low	109(60.6%)

in high thrombus versus low thrombus burden. In low thrombus burden patients, the mean monocyte count was  $0.49 \pm 0.50$  and in high thrombus burden patients, the mean monocyte count was  $0.64 \pm 0.48$ . (Table 2)

The results of stratification of thrombus burden with age

**Table 2:** Monocyte Count in High Thrombus vs Low Thrombus Burden Patients

Monocyte count	Thrombus Burden	n	Mean	SD	P-Value
	Low	109(60.6%)	0.49	0.50	<b>0.047*</b>
	High	71(39.4%)	0.64	0.48	

\*Statistically significant

group showed significant p-value and with others showed non-significant p-value. These results are tabulated in Table 3.

**Table 3:** Stratification of Thrombus Burden with Various Study Parameters

Parameter	Thrombus Burden			Chi-square statistics	p-value
	Low	High	Total		
<b>Gender</b>					
Male	70(63.1%)	41(36.9%)	111(61.7%)	0.7622	0.382
Female	39(56.5%)	30(43.5%)	69(38.3%)		
Total	109(60.6%)	71(39.4%)	180(100%)		
<b>Age groups</b>					
<60 years	28(36.8%)	48(63.2%)	76(42.2%)	30.967	<b>0.00001*</b>
>60 years	81(77.9%)	23(22.1%)	104(57.8%)		
Total	109(60.6%)	71(39.4%)	180(100%)		
<b>Hypertension</b>					
Hypertensive	67(62%)	41(38%)	108(60%)	0.248	0.618
Nonhypertensive	42(58.3%)	30(41.7%)	72(40%)		
Total	109(60.6%)	71(39.4%)	180(100%)		
<b>Obesity</b>					
Obese	65(63.1%)	38(36.9%)	103(57.2%)	0.656	0.417
Nonobese	44(57.1%)	33(42.9%)	77(42.8%)		
Total	109(60.6%)	71(39.4%)	180(100%)		
<b>Diabetes mellitus</b>					
Diabetic	42(60.9%)	27(39.1%)	69(38.3%)	0.0046	0.945
Non-diabetic	67(60.4%)	44(39.6%)	111(61.7%)		
Total	109(60.6%)	71(39.4%)	180(100%)		
<b>Smoking</b>					
Smoker	48(64.9%)	26(35.1%)	74(41.1%)	0.977	0.322
Non-smoker	61(57.5%)	45(42.5%)	106(58.9%)		
Total	109(60.6%)	71(39.4%)	180(100%)		

\*Statistically significant

## Discussion

Coronary artery thrombosis and atherosclerotic plaque

rupture are the key phenomena involved in the pathogenesis of STEMI. The monocyte count significantly affects the prognosis in STEMI patients undergoing P-PCI. The monocytes, when activated, become macrophages and become deposited in the vessel wall leading to the formation of atherosclerotic plaque.<sup>16,17</sup> The process of atherogenesis and rupture of plaque involves chronic inflammation and oxidative stress. Monocytes have a key role in the inflammatory process.<sup>18,19</sup> Literature has reported that monocyte count is an independent predictor of high thrombus burden.<sup>20,21</sup> High thrombus burden is associated with higher rates of procedural complications during P-PCI, adverse outcomes and cardiovascular deaths.<sup>22</sup>

In our study, patients had a mean age of  $61.11 \pm 7.11$  years and 61.7% were males. Similarly, in a study by Wang et al., patients had an average age of  $62.2 \pm 13.6$  years and 81% were male.<sup>15</sup> The mean age was  $62.6 + 12.8$  years with the majority of male patients (76%) in a study.<sup>20</sup> On the other hand, the mean age of the study participants was  $51.14 \pm 9.02$  years in a study by Soltan et al with 67.4% males.<sup>23</sup> The average patients' age was  $40 \pm 5$  years in another study.<sup>22</sup> Our results showed that 39.4% of the STEMI patients undergoing P-PCI had a high thrombus burden. Similar results were reported by Wang et al. with 34.8% of the STEMI patients undergoing P-PCI having high thrombus burden.<sup>15</sup> Other studies reported a very high frequency of high thrombus burden among patients with STEMI. In a study conducted at KRL Hospital, Islamabad, the frequency of high thrombus burden was 67.4%.<sup>24</sup> In other studies, 56.3% and 50.3% of the STEMI patients undergoing P-PCI had high thrombus burden.<sup>20,23</sup> In a study by Ge et al., 54.9% of the STEMI patients had a high thrombus burden.<sup>22</sup>

In our study, high thrombus burden had no association with the risk factors of diabetes mellitus, hypertension, obesity and tobacco consumption but it was significantly linked to the patient's age. Another study reported no correlation between high thrombus burden and other parameters (age, gender, hypertension, diabetes mellitus, smoking and hyperlipidemia).<sup>15</sup> Separham found no significant association of monocyte count with age, gender and diabetes mellitus.<sup>21</sup> According to Soltan et al., gender and diabetes mellitus were significantly

linked to high thrombus burden.<sup>23</sup> High thrombus burden was significantly associated with hypertension, according to another study.<sup>22</sup> In contrast, in another study, 100% of patients with high thrombus burden were hypertensive & smokers, 98.3% were diabetic and 60% were obese. There was a significant association of these risk factors with high thrombus burden.<sup>24</sup>

Our results showed a significant difference in the mean monocyte count in high thrombus ( $0.64 + 0.48$ ) versus low thrombus burden ( $0.49 + 0.50$ ) patients. Similarly, the mean monocyte count was  $70.27 \pm 3.24$  in high thrombus burden and  $61.89 \pm 5.71$  in low thrombus burden patients with a p-value of 0.0021.<sup>24</sup> Wang et al. reported a statistically higher monocyte count in high thrombus burden patients ( $0.61 \pm 0.29 \times 10^9/L$ ) than in low thrombus burden patients ( $0.53 \pm 0.24 \times 10^9/L$ ).<sup>15</sup> In a study by Arsoy et al., monocyte count to high-density lipoprotein cholesterol ratio (MHR) was measured, with a greater ratio in the high thrombus group (25.4) than the low thrombus group (16) with a significant p-value.<sup>20</sup> Similar results were seen in another study in which MHR was  $.052 \pm 0.019$  and  $0.014 \pm 0.008$  in high thrombus and low thrombus burden groups, respectively., (p-value < 0.001).<sup>23</sup> The mean monocyte count was  $0.81 \pm 0.33$  and  $0.59 \pm 0.28$  in high and low thrombus burden patients, respectively with statistically significant results in a study.<sup>21</sup>

## Conclusion

The monocyte count is a reliable, inexpensive and simple-to-measure predictor of high thrombus burden in coronary arteries in STEMI patients undergoing primary PCI.

## Limitations of the Study

- Our study recruited patients from a single tertiary care hospital. A large multicenter study should be conducted in the future.
- The patients with high thrombus burden were neither followed up for adverse clinical outcomes nor monocyte counts were measured after P-PCI.

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### Authors Contribution

**SR:** Conceptualization of Project

**MF:** Data Collection

**AS:** Literature Search

**KNS:** Statistical Analysis

**MM:** Drafting, Revision

**MM:** Writing of Manuscript