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PREDICTORS OF NO-REFLOW PHENOMENON AFTER PRIMARY PCI IN ACUTE MYOCARDIAL INFARCTION

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ABSTRACT
Background: The background of the No-reflow phenomenon (NRP) is that it is a serious complication of the primary percutaneous coronary intervention (PCI) performed in patients suffering from acute myocardial infarction (AMI). It refers to failure of the myocardium to receive perfusion despite successful opening of the epicardial coronary artery and there is an increased morbidity and mortality risk. It is believed that inflammatory processes, electrolyte disturbances and haematological parameters may play a role in its occurrence.
Objective: To explore the clinical and laboratory characteristics associated with no-reflow following primary PCI for AMI patients, and to see if the levels of serum magnesium, C-reactive protein (CRP) and white blood cell (WBC) count are associated with one another.
Methods: Retrospective study was carried out with 384 records of AMI patients in Cardiology Department of The Punjab Institute of Cardiology Hospital, Lahore from January 2025 to July 2025. Patients >18 years of age who had a confirmed AMI diagnosis and laboratory tests for WBC, CRP and magnesium were done within 24 hours of admission were included in the study. The sample size was determined according to the formula given by WHO. Association of laboratory parameters and no-reflow was determined by using appropriate statistical program.
Results: There was a correlation between elevated CRP and WBC counts with increased inflammatory burden and increased size of infarct. Low levels of magnesium in the bloodstream were associated with the risk of coronary vasospasm and increased risk of ventricular arrhythmias. High CRP, high WBC and low magnesium were independently associated with no-reflow after primary PCI, with significant increases in risk for no-reflow in patients with all three of these risk factors.
Conclusion: No-reflow is predictable in AMI patients treated with PCI by the use of simple, inexpensive, and readily available tests such as CRP, WBC count, and serum magnesium levels. Early detection of those at risk can inform clinical care and help to implement preventive interventions.

KEYWORDS: No-reflow, Acute myocardial infarction, Primary PCI, C-reactive protein, White blood cells, Serum magnesium, Inflammation, Prognosis

1. INTRODUCTION

Acute myocardial infarction (AMI) is a major cardiovascular emergency in the world that is associated with significant morbidity and mortality [1]. It is caused by abrupt blockage of a coronary artery which is usually caused by rupture of an atherosclerotic plaque with subsequent thrombosis. This stoppage causes an ischemic crisis of the myocardium, and if severe, permanent necrosis of the heart muscle [2]. AMI is a complex disease composed of four components: atherosclerosis, thrombosis, endothelial dysfunction, oxidative stress and inflammation.
Inflammation is an important contributor to AMI, and affects plaque formation, rupture and subsequent myocardial injury [3]. C-reactive protein (CRP), which is an acute-phase protein that is produced by the liver in response to proinflammatory cytokines, especially interleukin-6 (IL-6), is well-known to be a marker of systemic in Flammarion [4]. A higher CRP level following myocardial injury has been correlated with larger myocardial injury, reperfusion failure, further myocardial events, heart failure and mortality. Its prognosis value is not just for risk stratification but also to learn about the inflammatory burden of AMI patients [5].
Another easily obtained measure of inflammation is the number of white blood cells (WBCs). Myocardial necrosis stimulates the immune system, and this is one of the causes of leukocytosis in AMI [6]. As the amount of WBC increases, the infarct size also increases, there is a greater likelihood of impaired reperfusion, and complications are more likely to be present including a risk of the no-reflow phenomenon (NRP), which is a lack of reperfusion

after successful epicardial coronary artery recanalization [7]. As a part of WBC, neutrophils may worsen myocardial damage via release of enzymes and ROS .

Electrolyte disturbances (magnesium imbalance) are another important factor affecting AMI outcome [11]. Magnesium plays a critical role in myocardial contractility, vascular tone, membrane stability and regulation of ion channels [8]. Hypomagnesemia is a frequently seen electrolyte disturbance that occurs in the first 24–48 hours after AMI and can cause arrhythmias, ventricular tachycardia, coronary vasospasm and sudden cardiac death [9]. Importance of serum magnesium in early complications after MI, as seen in the acute phase, which is associated with a decrease in serum magnesium due to intracellular shifts and lipolysis [10].

The no-reflow phenomenon has been associated with poorer outcome and with a higher likelihood of death, larger infarct size and is a critical complication of primary percutaneous coronary intervention (PCI) [11]. Clinically, there is an interest in finding predictive markers for NRP, as this will help to direct preventative measures and better manage patients . Although previous studies have evaluated the role of CRP, WBC or magnesium alone, few studies evaluate the joint predictive role of these parameters [12]. The objective of this work is to find the correlation of NRP in AMI patients undergoing primary PCI with serum magnesium, CRP and WBC in this regard.

Objective

To detect the factors that predict the occurrence of no reflow in acute myocardial infarction (AMI) patients who had primary PCI. In particular, it analyses the correlation of serum Magnesium levels, CRP and WBC with the incidence of no-reflow. The results will help to achieve early risk stratification, plan preventative measures and enhance clinical outcomes after PCI.

METHODOLOGY

The study was done in 384 adult patients (>19 years) with confirmed AMI undergoing primary PCI at The Punjab Institute of Cardiology Hospital, Lahore in a retrospective observational study from January 2025 to July 2025. Tests of serum magnesium, C-reactive protein (CRP) and white blood cell (WBC) counts within 24 hours of admission were required for inclusion. Chronic inflammatory disorders patients, prior PCI within 6 months, as well as incomplete laboratory data, were excluded. Laboratory data was obtained from the hospital's records from automated chemistry and hematology analyzers. Sample size was determined by the formula provided by the World Health Organization (WHO) in a prevalence study. Logistic regression and chi-square tests were used to determine the association between magnesium, CRP, WBC and the presence of no-reflow phenomenon. P-values < 0.05 were considered as statistically significant.

Inclusion Criteria

The adult patients were those >18 years at the time of AMI diagnosis and who received primary percutaneous coronary intervention (PCI). Laboratory data for serum magnesium, C-reactive protein (CRP) and white blood cell (WBC) counts were available for only patients admitted to the hospital in the first 24 hours. Both males and females, and all AMI types were included.

Exclusion Criteria

Patients were excluded from chronic inflammatory and hematologic disorders, patients with chronic kidney disease and patients with PCI every 6 months. Laboratory or clinical data were so incomplete or were missing that cases were also excluded. Patients with known electrolyte abnormalities not associated with AMI and magnesium supplementation prior to admission were excluded to prevent confounding of the analysis of predictors for the no-reflow phenomenon.

Data Collection

Patients' hospital medical records and laboratory data base were used as sources for retrospective data collection. A structured data collection form was used to obtain demographic data, clinical history, angiographic data and laboratory findings. Automated chemistry analyzers were used to determine the serum magnesium levels, automated immunoassay analyzers were used to determine the CRP levels, and automated hematology analyzers were used to determine the WBC levels. All testing were done within 24 hours of admission of patient. Entries were double entered and cross-referenced with source data to ensure data quality. No-reflow was reported after primary PCI according to angiographic TIMI flow grades (≤ II being defined as no-reflow). Data were inputted into SPSS and analysed statistically. Correlation between magnesium, CRP, WBC and no-reflow incidence were evaluated by logistic regression and chi-square test and the significance value was $p < 0.05$.

Data Analysis

We used SPSS version 384 for analysis of data. Continuous variables, such as serum magnesium, CRP, and WBC counts, were expressed as mean ± SD, and categorical variables, such as gender and no-reflow were expressed as frequencies and percentages. Logistic regression analysis was used to determine associations between laboratory parameters and no reflow incidence. Chi-square tests were used to compare categorical groups. The Pearson correlation coefficient was used to assess the correlations between magnesium, CRP and WBC levels. A p value of < 0.05 was considered statistically significant. The results were analyzed to determine the predictive value for the no-reflow phenomenon and their clinical relevance for early risk stratification.

RESULTS

There were 384 patients who were subjected to AMI analysis – of these 210 were male and 174 were female. The mean age was 54.3 ± 10.6 years. Sixty-eight (17.7%) patients were in no reflow. Patients with no-reflow had significantly higher CRP levels (mean 32.5 ± 10.8 mg/L) and WBC counts (14.8 ± 3.2 $\times 10^3/\mu L$) compared to those with normal reperfusion (CRP 18.2 ± 7.5 mg/L, WBC 10.9 ± 2.5 $\times 10^3/\mu L$; $p < 0.001$). Serum magnesium was lower in the no-reflow group (1.62 ± 0.18 mmol/L vs. 1.88 ± 0.15 mmol/L; $p < 0.001$). High CRP, elevated WBC and low magnesium were independent predictors of no-reflow post primary PCI by logistic regression analysis.

Table 1. Demographic Characteristics of AMI Patients (n = 384)

Variable	Category	Frequency (n)	Percentage (%)
Gender	Male	210	54.7
	Female	174	45.3
Age (years)	18–40	38	9.9
	41–50	76	19.8
	51–60	112	29.2
	61–70	98	25.5
	>70	60	15.6

As seen in Table 1, majority of the AMI patients were males (54.7%) and majority were aged between 51 – 60 years. This is consistent with the world-wide epidemiology of AMI men are affected more often than women and the middle-aged more often than the elderly.

Table 2. Laboratory Parameters by No-Reflow Status

Parameter	No-Reflow (n=68)	Normal Flow (n=316)	p-value
CRP (mg/L)	32.5 ± 10.8	18.2 ± 7.5	<0.001
WBC ($\times 10^3/\mu L$)	14.8 ± 3.2	10.9 ± 2.5	<0.001
Serum Mg (mmol/L)	1.62 ± 0.18	1.88 ± 0.15	<0.001

No-reflow patients had significantly higher levels of inflammatory markers (CRP, WBC) and lower magnesium when compared to normal coronary reperfusion, suggesting these to be potential predictors of no-reflow.

Table 3. Comorbidities and Risk Factors

Risk Factor	No-Reflow (n=68)	Normal Flow (n=316)	p-value
Hypertension	40 (58.8%)	138 (43.7%)	0.03
Diabetes Mellitus	22 (32.4%)	84 (26.6%)	0.35
Smoking	30 (44.1%)	102 (32.3%)	0.07
Previous MI	10 (14.7%)	28 (8.9%)	0.12

Without reflow patients were significantly more likely to have hypertension. Trends for other risk factors (diabetes, smoking and previous MI) were not statistically significant.

Table 4. Angiographic Characteristics

Characteristic	No-Reflow (n=68)	Normal Flow (n=316)	p-value
Single-vessel disease	28 (41.2%)	160 (50.6%)	0.18
Multi-vessel disease	40 (58.8%)	156 (49.4%)	0.18
LAD involvement	42 (61.8%)	190 (60.1%)	0.78
RCA involvement	22 (32.4%)	90 (28.5%)	0.51
Culprit lesion thrombus grade ≥3	46 (67.6%)	108 (34.2%)	<0.001

A high grade of thrombus burden (grade ≥3) was a significant factor associated with no-reflow, which supports the contribution of this parameter to impaired myocardial perfusion as a procedural factor and as a pathophysiological factor.

Table 5. Logistic Regression Analysis of No-Reflow Predictors

Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
CRP (per mg/L)	1.08	1.05–1.11	<0.001
WBC (per ×10³/μL)	1.22	1.12–1.33	<0.001
Serum Mg (per mmol/L)	0.12	0.05–0.28	<0.001
Hypertension	1.89	1.05–3.39	0.03
Thrombus Grade ≥3	3.44	1.91–6.18	<0.001

The multivariate logistic regression analysis indicates that increase in CRP, increase in WBC, decrease in Mg2+, hypertension and increase in thrombus grade are independent risk factors for no-reflow. The protective effect is due to Magnesium, and the risk factors are CRP, WBC and thrombus burden.

DISCUSSION

In the present study, the predictor(s) of the no-reflow phenomenon (NRP) in 384 patients with acute myocardial infarction (AMI) undergoing primary percutaneous coronary intervention (PCI) were assessed [13]. The overall rate of no reflow did not differ significantly from the previously published range of 10% to 30% based on patient or procedural characteristics and was 17.7% in our cohort [14]. Our results indicate that inflammatory markers, electrolyte abnormalities and thrombus burden are independent predictors of NRP.

Elevated C-reactive protein (CRP) and white blood cell (WBC) count were shown to be significant contributors to no-reflow, as inflammation was [15]. Patients who developed NRP exhibited mean CRP levels of 32.5 ± 10.8 mg/L and WBC counts of 14.8 ± 3.2 ×10³/μL, compared to 18.2 ± 7.5 mg/L and 10.9 ± 2.5 ×10³/μL in patients with normal reperfusion ($p < 0.001$). These results confirm the hypothesis that systemic inflammation contributes to microvascular obstruction by inducing endothelial dysfunction and activate neutrophils and the formation of microthrombi [16]. Increased CRP has been associated with greater infarct size and impaired cardiac perfusion and poor cardiovascular outcome previously in AMI patients undergoing PCI, underscoring its value as a prognostic indicator in these patients. Likewise, leukocytosis is a sign of an activated inflammatory response which can worsen ischemic damage and worsen no-reflow.

In addition, low serum magnesium level was an independent predictor of NRP. No-reflow patients had significantly lower magnesium levels compared with patients with normal reperfusion (1.62 ± 0.18 mmol/L vs. 1.88 ± 0.15 mmol/L, $p < 0.001$) [17]. Magnesium is one of the most important intracellular cations that have anti-arrhythmic, vasodilatory and stabilising effects on myocardial membranes, and is known to help to regulate vascular tone. In the acute stage of AMI, hypomagnesemia may also result in coronary vasospasm, arrhythmia, and microvascular perfusion defects, as found in previous studies on the protection in the setting of myocardial reperfusion [18].

High thrombus burden (grade ≥3) was highly associated with no-reflow (OR 3.44, $p < 0.001$). This is consistent with the finding that after successful epicardial recanalization, the larger the intracoronary thrombus, the greater the distal embolization and microvascular obstruction, which will result in reduced myocardial perfusion. Pre-existent endothelial dysfunction, as represented by hypertension, was also a major predictor, which implies that endothelial dysfunction can worsen the damage of the microvasculature.

All the above factors suggest a multifactorial pathophysiology of NRP: inflammation, electrolyte disturbance, and a thrombus burden. Raised CRP and WBC levels are due to systemic inflammation and local inflammation activation, which can be exacerbated by low magnesium that results in microvascular constriction & poor reperfusion [19]. These laboratory parameters can be identified before PCI and impact treatment decisions, these include intracoronary vasodilators, magnesium supplementation and optimized antithrombotic therapy, when the risk of NRP is high.

This study has some limitations, such as its retrospective design and the use of a single-centre data set that may not be generalizable. Also, the magnesium, CRP and WBC changes over time beyond 24 hours were not evaluated. Further studies with serial biomarker monitoring are recommended in the future to further clarify causal relationships and improve the risk prediction model.

Finally, our results confirm that CRP, plasma WBC, plasma magnesium, hypertension and thrombus burden are independent risk factors for no-reflow following primary PCI. The identification of these prognostic factors early can help suggest prophylactic measures, optimize myocardial reperfusion and minimize bad outcomes in the AMI patient [20].

CONCLUSION

The no-reflow phenomenon continues to be an important complication of primary PCI during AMI which has a negative impact on patient outcomes. In this study, high levels of C-reactive protein, high white blood cell count, low serum magnesium, hypertension and high thrombus burden were all independent risk factors for no-reflow. Targeted interventions like vasodilators, magnesium supplementation or optimised anti-thrombotic therapy can then be used to manage these laboratory and clinical parameters, which can be done early to stratify risk. Identification of high-risk patients before PCI may lead to better myocardial perfusion and less complication, as well as better recovery after PCI. Further multicentre prospective studies are warranted to confirm these results, and to develop predictive tools for clinical use.

REFERENCES

[1] Abdelbasit, M. S., Abdelaziz, M., Saqr, A. A. H., & Samy, M. (2025). Clinical and Technical Predictors of No-reflow during Primary Percutaneous Coronary Intervention of Patients with Acute Myocardial Infarction. *Zagazig University Medical Journal*, *31*(7), 2824-2831.

[2] Ahmed, A. Y., Almeleigy, N. A., Ammar, S. M., & Elsheikh, K. A. E. (2024). Predictive value of systemic immune-inflammatory index in predicting No-reflow phenomenon in patients with ST-segment elevation myocardial infarction after primary PCI. *Int J Cardiol Sci*, *6*, 105-113.

[3] Bamarinejad, F., Kermani-Alghoraishi, M., Soleimani, A., Roohafza, H., Yazdekhasti, S., Azarm, M., Bamarinejad, A., & Sadeghi, M. (2024). Clinical, laboratory, and procedural predictors of slow flow/no reflow phenomenon after emergency percutaneous coronary interventions in ST-elevated myocardial infarction. *The Egyptian Heart Journal*, *76*(1), 146.

[4] Deng, L., Zhao, X., Su, X., Zhou, M., Huang, D., & Zeng, X. (2022). Machine learning to predict no reflow and in-hospital mortality in patients with ST-segment elevation myocardial infarction that underwent primary percutaneous coronary intervention. *BMC Medical Informatics and Decision Making*, *22*(1), 109.

[5] Ebrahimi, R., Rahmani, M., Fallahtafti, P., Ghaseminejad-Raeini, A., Azarboo, A., Jalali, A., & Mehrani, M. (2024). Predicting the no-reflow phenomenon in ST-elevation myocardial infarction patients undergoing primary percutaneous coronary intervention: a systematic review of clinical prediction models. *Therapeutic Advances in Cardiovascular Disease*, *18*, 17539447241290438.

[6] Elrayes, M., Youssif, A., & Youssef, M. M. A. (2022). Predictors of No-Reflow Phenomenon after Percutaneous Coronary Intervention in ST-Segment Elevation Myocardial Infarction Patients. *Zagazig University Medical Journal*, *28*(6), 1205-1213.

[7] Gad, M. M., Elmaghawry, L. M., Alfathi, M. A., & Elsanan, M. (2022). Predictors and Outcomes of No Reflow Phenomenon Post-Primary Coronary Intervention in Young Patient. *The Egyptian Journal of Hospital Medicine*, *89*(1), 5003-5008.

[8] Jafari Afshar, E., Gholami, N., Samimisedeh, P., Mozafarybazargany, M., Tayebi, A., Memari, A., Yazdani, S., & Rastad, H. (2024). Utility of electrocardiogram to predict the occurrence of the no-reflow phenomenon in patients undergoing primary percutaneous coronary intervention (PPCI): a systematic review and meta-analysis. *Frontiers in Cardiovascular Medicine*, *10*, 1295964.

[9] Khalfallah, M., Allaithy, A., & Maria, D. A. (2022). Impact of the total ischemia time on no-reflow phenomenon in patients with ST elevation myocardial infarction undergoing primary percutaneous coronary intervention. *Anatolian journal of cardiology*, *26*(5), 382.

[10] Khalfallah, M., Maria, D. A., & Allaithy, A. (2022). Impact of stress hyperglycemia on no-reflow phenomenon in patients with ST elevation myocardial infarction undergoing primary percutaneous coronary intervention. *Global Heart*, *17*(1), 23.

[11] Li, X., Yu, C., Lei, L., Liu, X., Chen, Y., Wang, Y., Qiu, S., & Xiu, J. (2024). Association of pre-PCI blood pressure and no-reflow in patients with acute ST-elevation coronary infarction. *Global Heart*, *19*(1), 28.

[12] Ma, J., Wang, M., Wu, P., Ma, X., Chen, D., Jia, S., & Yan, N. (2024). Predictive effect of triglyceride-glucose index on No-Reflow Phenomenon in patients with type 2 diabetes mellitus and acute myocardial infarction undergoing primary percutaneous coronary intervention. *Diabetology & Metabolic Syndrome*, *16*(1), 67.

[13] PANTEA-ROȘAN, L. R., ȚICA, O., ȚICA, O. A., POPESCU, M. I., BOGDAN, I., BUZLE, A., MOISI, M. I., & PANTEA, V. A. (2025). Mortality predictors in patients with ST-segment elevation myocardial infarction presenting no-reflow phenomenon after primary PCI: experience of a tertiary center. *ROM. J. INTERN. MED*, *63*(4), 265-276.

[14] Ruíz-Avalos, J. A., Bazán-Rodríguez, L., Espinoza-Escobar, G., Martínez-Villa, F. A., & Ornelas-Aguirre, J. M. (2022). Predictors in no-reflow phenomenon in acute myocardial infarction with ST-segment elevation. *Archivos de cardiologia de Mexico*, *92*(4), 461-468.

[15] Sökmen, E., & Ateş, M. S. (2025). Usefulness of platelet mass index in the prediction of angiographic no-reflow in patients with acute ST-segment elevation myocardial infarction. *BMC Cardiovascular Disorders*, *25*(1), 376.

[16] Sun, Y., Ren, J., Li, L., Wang, C., & Yao, H. (2023). RDW as A predictor for No-Reflow phenomenon in DM patients with ST-Segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. *Journal of Clinical Medicine*, *12*(3), 807.

[17] Toprak, K., Toprak, İ. H., Acar, O., & Ermiş, M. F. (2024). The predictive value of the HALP score for no-reflow phenomenon and short-term mortality in patients with ST-elevation myocardial infarction. *Postgraduate Medicine*, *136*(2), 169-179.
[18] Wang, L., Huang, S., Zhou, Q., Dou, L., & Lin, D. (2024). The predictive value of laboratory parameters for no-reflow phenomenon in patients with ST-elevation myocardial infarction following primary percutaneous coronary intervention: A meta-analysis. *Clinical Cardiology*, *47*(2), e24238.
[19] Yu, Y., Wu, Y., Wu, X., Wang, J., & Wang, C. (2022). Risk factors for no-reflow in patients with ST-elevation myocardial infarction who underwent percutaneous coronary intervention: a case-control study. *Cardiology Research and Practice*, *2022*(1), 3482518.
[20] Zhang, X.-T., Lin, Z.-R., Zhang, L., Zhao, Z.-W., & Chen, L.-L. (2022). MELD-XI score predict no-reflow phenomenon and short-term mortality in patient with ST-segment elevation myocardial infarction undergoing primary percutaneous coronary intervention. *BMC Cardiovascular Disorders*, *22*(1), 113.