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**ORIGINAL ARTICLE**

# Relationship of Neutrophil to Lymphocytis Ratio with Success of Thrombolysis in Patients of STEMI

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## ABSTRACT

**Objectives:** To determine the frequency of success of thrombolysis using SK in patients of STEMI, To investigate the association of success of thrombolysis with NLR in patients of STEMI.

**Methodology:** A descriptive cross sectional study was carried out at Coronary Care Unit (CCU) of Services Hospital, Lahore. The sample size of 130 patients were enrolled by non-probability consecutive sampling. In this study all male and female patients from 25 to 100 years of age with STEMI who were given SK were included from CCU of Services Hospital, Lahore using non probability consecutive sampling. NLR was calculated. Success of thrombolytic therapy was determined by relief of chest pain & resolution of ≥ 50% ST-elevations (STE) in ECG taken 90 minutes after completion of SK.

**Results:** In this study, there were total 130 cases and out of these 72 (55.38%) were males and 58 (44.62%) were females. High NLR was seen in 43 (33.08%) of the cases. Successful thrombolysis was observed in 99 (76.15%) of the cases. Successful thrombolysis was observed in 29 (67.44%) cases with high NLR and 70 (80.46%) cases with low. There was no significant association of NLR, BMI, smoking, DM and HTN with successful thrombolysis.

**Practical Implication of this Study:** is that in our resource limited country NLR is one of cheapest test to access severity and prognosis so patients with high NLR can be reffered early for intervention even if responded successfully to thrombolysis as complications of STEMI are frequent in high NLR patients as compared to lower NLR.

**Conclusion:** Successful thrombolysis was seen in almost 3/4 cases in acute STEMI. Although a cheaper and readily available prognostic tool, no statistically significant association was found in terms of the admission NLR and the success of thrombolysis. Moreover, there was no significant association in terms of any of the confounders of the study.

**Keywords:** Thrombolysis, Streptokinase (SK), Neutrophil to Lymphocytis Ratio (NLR), ST Segment Elevation MI (STEMI)

## INTRODUCTION

Myocardial infarction (MI) results from rupture of atheromatous plaque and thrombosis in an epicardial vessels leading to imbalance in demand and supply of oxygen to Myocardium.[1]

Pathophisiologically myocardial infarction is irreversible myocardial cell death resulting from ischaemia that is biochemically supported via cardiac enzymes, ECG changes, to detect myocardial injury and necrosis.

The atheromatous plaque starts with thickening of arterial intima without or minimal inflammation of cells and this can be observed shortly after birth. Afterward lipid rich necrotic core surrounded through fibrous tissue is formed. Finally vulnerable plaque consists of necrotic core with thin fiborous cap deficient in smooth muscles and infiltrated with inflammatory cells is found.[2,3]

The mortality rate in myocardial infarction is 30% and half of deaths occur before arrival in the hospital. Other 5% to10% die within 1st year after MI and half are re-hospitalized within 1st year of MI.

The Prognosis of MI depends on extent of infarct, residual left ventricle function whether patient underwent revascularization.

The incidence of Coronary Artery Disease (CAD) related mortality is projected to rise dramatically in developing countries including India, Middle East, Latin America and Sub-Saharan Africa with approximately 80 percent increase from 1990's to 2020's.[4,5]

A significant reperfusion approach is fibrinolysis, particularly, where primary PCI can't be offered within timelines. Benefit of fibrinolytic therapy in patients with STEMI is well established. Largest benefit seen when administered within 12 hours after the symptomatic onset and in patients with highest cardiovascular risk.[6,7]

Atherosclerosis is a multifactorial disease. And there is role of inflammation in formation and developmkent of atherosclerotic plaque. Two inflammatory markers, neutrophil-to-lymphocyte ratio (NLR) and red cell distribution width (RDW) are used to find out risk of mortality plus adverse cardiovascular outcomes in patients having acute myocardial infarction.

In cardiovascular disease, White blood cell count and its subtypes are considered to be classic markers of inflammation. NLR was considered to be a inflammatory marker in cardiac and non-cardiac diseases too. So, it is used as predictor of long term mortality in patients undergoing PCI in STEMI.[8]

As neutrophil and lymphocyte values are readily available in routine blood count analysis, So NLR may be used as cost effective predictor of cardiovascular complications and inflammation.

## MATERIALS AND METHODS

A descriptive cross sectional study was carried out at Coronary Care Unit (CCU) of Services Hospital, Lahore. The sample size of 130 patients was calculated with 8% margin of error and 95% confidence level. All the patients were enrolled by non-probability consecutive sampling. In this study all male and female patients from 25 to 100 years of age with STEMI who were given SK were included from CCU of Services Hospital, Lahore using non probability consecutive sampling. NLR was calculated. Success of thrombolytic therapy was determined by relief of chest pain & resolution of ≥ 50% ST-elevations (STE) in ECG taken 90 minutes after completion of SK. All the data was collected on the predesigned performa. Data was entered and analyzed by using SPSS 25.0. all the quantitative variables were presented by mean+SD and qualitative with frequencies and percentages. Association between success of thrombosis and risk factors were analyzed by using Chi-square test. P-value <0.05 was considered as significant.

**Statistical Technique:** Descriptive Statistics, Chi Square Test

## RESULTS

The study shows that there were total 130 cases and out of these 72 (55.38%) were males and 58 (44.62%) were females. Success of thrombolysis was observed in 99 (76.15%) of the cases (Figure 1).High NLR was seen in 43 (33.08%) and low NLR in 87 (66.92%) of the cases (Figure 2).

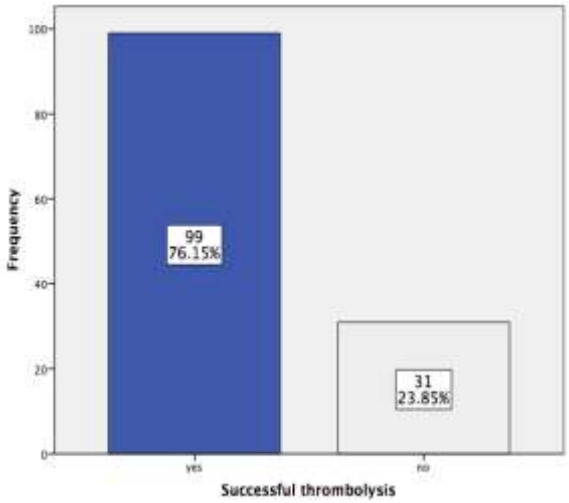


Figure 1: Successful Thrombolysis in Study Subjects

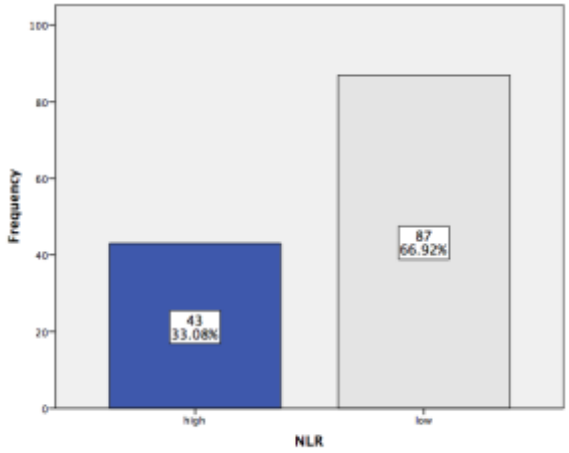


Figure 2: NLR in Study Subjects

From Table 1 it can be observed that mean age of the subjects was 52.49±8.18 years and mean BMI was 24.73±2.93 kg/m$^2$. Mean time since onset of chest pain was 4.71±1.36 hours. Mean NLR was 3.82±0.78 (Table 1).

Table 1: Descriptive Statistics of Risk Factors

| Risk Factors | Minimum | Maximum | Mean | SD |
|---|---|---|---|---|
| Age | 35.0 | 79.0 | 52.49 | 8.18 |
| BMI | 19.4 | 31.2 | 24.74 | 2.93 |
| Time since onset of chest pain (hours) | 1.0 | 8.0 | 4.71 | 1.36 |
| ANC ($10^9$/L) | 6.0 | 14.0 | 10.54 | 1.80 |
| ALC | 2.0 | 7.0 | 2.86 | 0.69 |
| NLR | 2.0 | 5.0 | 3.82 | 0.78 |

It is evident from Table 2 that successful thrombolysis was seen in 55 (76.39%) males and 44 (75.86%) females in their respective groups with p-value = 0.94. Data was stratified for age and successful thrombolysis was seen in 76 (73.79%) cases with age 25-59 years as compared to 23 (85.19%) with age 60-100 years with p-value=0.02 (Table 2). There were 53 (40.77%) smokers and success of thrombolysis was observed in 38 (71.70%). Successful thrombolysis was observed in 29 (67.44%) cases with high NLR and 70 (80.46%) cases with low NLR having p-value = 0.10.There was no significant difference in terms of data stratified for BMI, smoking, DM, HTN and the success of thrombolysis (Table 2).

Table 2: Percentage Distribution of Success of Thrombolysis across Risk Factors

| Factors | Success of Thrombolysis | | $\chi^2$ (p-value) |
|---|---|---|---|
| | Yes | No | |
| Gender | | | |
| Male | 55 (76.39%) | 17 (23.61%) | 0.005 (0.94) |
| Female | 44 (75.86%) | 14 (24.14%) | |
| Age | | | |
| 25-59 | 76 (73.79%) | 27 (26.21%) | 1.53 (0.22) |
| 60-100 | 23 (85.19%) | 4 (14.81%) | |
| BMI | | | 0.013 (0.71) |
| Up to 25 | 57 (75.00%) | 19 (25.00%) | |
| >25 | 42 (77.78%) | 12 (22.22%) | |
| Smoking | | | |
| Yes | 38 (71.70%) | 15 (28.30%) | 0.98 (0.32) |
| No | 61 (79.22%) | 16 (20.78%) | |
| DM | | | |
| Yes | 59 (76.62%) | 18 (23.38%) | 0.02 (0.88) |
| No | 40 (75.47%) | 13 (24.53%) | |
| HTN | | | |
| Yes | 32 (71.11%) | 13 (28.89%) | 0.96 (0.33) |
| No | 67 (78.82%) | 18 (21.18%) | |
| NLR | | | |
| High | 29 (67.44%) | 14 (32.56%) | 2.69 (0.10) |
| Low | 70 (80.46%) | 17 (19.54%) | |

## DISCUSSION

Ischemic heart disease has been leading cause of deaths worldwide for last 15 years with more than 9M deaths in 2016[9] .In Pakistan, leading cause of mortality is IHD as well, claiming 29 percent of total 1.4M deaths in 2016.[10]

Although, the spectrum of IHD ranges from stable angina to ST segment elevation Myocardial infarction, underlying mechanism is mostly atherosclerosis, causing occlusion of the coronary arteries leading to supply & demand mismatch. When the atherosclerotic plaque is disrupted, platelet aggregation occurs at the site of injury & a thrombus is formed which can completely occlude the vessel & deprive myocardium of its blood supply, [11] this is evident on an electrocardiogram (ECG) as an ST segment elevation myocardial infarction. The myocardium can be saved from necrosis, if timely revascularization is done; either with an invasive procedure like primary percutaneous intervention (PCI) or pharmacologically with thrombolytic agents like tissue plasminogen activator (tPA) or streptokinase (SK). Among patients with STEMI,patient,s risk characteristics have an effect on early therapeutic decision[12,13,14].

In this study, successful thrombolysis was observed in 99 (76.15%) out of the 130 cases presented with STEMI. These results were comparable with the findings of the previous studies where the success rate ranges from 50 to 80% of the cases [15] and there are number of factors that are associated with its failure.

According to study done by Saleem et al, out of those 59 patients who received thrombolytic therapy before 12 hrs, 43 (72.8 percent) completely resolved. While those, who received thrombolytic therapy after 12 hrs, none of them completely resolved as per ECG result. These results were almost similar to the present study.[16] This was also supported by study made in Shaikh Zayed Post-graduate Medical Institute Lahore Pakistan, where this efficacy was seen in 73% of the cases and they further described that mortality of patient decrease through giving thrombolytic within 12 hrs.[17]

In another study made by Khaire U et al, they compared early vs late thrombolysis and it was observed that successful thrombolysis which was labelled on the basis of > 50% reduction in ST elevation, where there is beginning of therapy before 6 hrs and was noted in 54% of cases. Whereas only 41 (20.5 Percent) of cases shows improved ST segment > 50% after 6 hrs. of beginning of therapy and overall success rate was noted in 70.5% of cases. [18]

The association between low lymphocyte count and major cardiovascular outcomes has also been shown in several studies[19,20].There is role of neutrophils and lymphocytes in

modulating the inflammation to myo cardial injury[21,22]In the present study Successful thrombolysis was observed in 29 (67.44%) cases with high NLR and 70 (80.46%) cases with low NLR with p = 0.10. The data in the past has shown that higher NLR at time of admission is related to increased morbidity & mortality in patients of acute coronary syndrome (ACS), [23] even in the presence of a normal total leukocyte count (TLC). NLR also tends to be more in STEMI as compared to Non ST elevation ACS (NST-ACS), correlating with the severity of underlying occlusion.

While the significance of NLR in acute coronary syndrome (ACS) is an ongoing area of research, previous studies have seen the relationship of NLR with cardiac biomarkers, [24] spontaneous resolution after MI, complications after thrombolysis, [25] infarct size or coronary re-flow after PCI. Although, PCI is the gold standard for revascularization, however, the expertise is not freely available round the clock in Pakistan & only selected patients can undergo primary PCI. Majority of STEMI patients are managed with intravenous (IV) thrombolytic, mostly SK as it is readily available & is relatively, cost-effective. A significant proportion of patients still require rescue PCI because of the failure of SK to relieve chest pain & resolve ECG changes.

Gul et al further described, more complications had been observed (63.5% vs 25.5%, p-value<0.0001) in high Neutrophil Lymphocyte Ratio (NLR) cluster as compared to those who had low NLR. Incidence of death was found more for patients with high median NLR while median NLR was low for those who were discharged. NLR was found as the significant covariate of mortality (OR=1.131; p-value=0.029). [26]

Several studies show NLR is a prognostic marker in patients with coronary artery disease[27,28,29,30]. study done by Baysal et al determined the association of admission NLR & Red cell distribution width (RDW) with thrombolysis outcome using tPA&Tenectoplase on 102 patients. Their results showed that thrombolysis was successful in 70 (68.63%) and failed in 32 (31.37%) patients which was almost similar to the result of present study showing effective thrombolysis in 76.15% of total cases. The thrombolysis failure group had high NLR (4.2 ±1.7) as compared to thrombolysis successful group (3.2 ± 2.3) with p=0.028 in Baysal's study. High RDW (>14.3fl) was associated with high NLR (4 ± 2.5) & increased rate of thrombolysis failure (51.8%) as compared to low RDW which was associated with a lower NLR (2.8 ± 1.5) & a low thrombolysis failure rate (6.5%) with p= 0.007.[31] Our study showed that 67.44% of the cases with high NLR had successful thrombolysis, as compared to 80.46% of the cases with low NLR.

Pashapour et al in Tabriz, Iran studied the relationship of NLR & PLR using Reteplase as the thrombolytic agent. Insignificant association was found between either NLR or level of response to thrombolytic therapy (OR 1.209 at 95% CI, p = 0.055). Moreover, insignificant association was observed between NLR and ejection fraction. Increased NLR and PLR was observed to linked with an increase in the rate of cardiac complications in STEMI patients (OR 1.198 at 95% CI, p = 0.016). [31]

There were a few limitations to this study as it didn't compare the successful outcome of STEMI with other treatment modalities like other thrombolytic agents like tPA or with primary angioplasty.However risk stratification prior to intervention has great clinical importance to identify patients at high risk and optimize therapeutic management by intervention with PCI[32,33].

However, there were many strengthening points as well, as this study showed good success rate even with a relatively cheaper thrombolytic agent; though complication rates were not studied. It also assessed another cheaper and readily available routine blood marker i.e. NLR to look for its prognostic value in relation to success of thrombolysis. Though there was a higher success rate in patients with a low admission NLR, however it was not found to be statistically significant.

## CONCLUSION

Successful thrombolysis was seen in almost 3/4$^{th}$ cases in acute STEMI treated with Streptokinase and there was no significant difference in terms of any of the confounders of the study. Moreover, although a cheaper and readily available prognostic tool, no statistically significant difference was found in terms of the admission NLR and the success of thrombolysis. However as various studies showed complications of STEMI and high NLR so patients with high NLR should be preferred for further work up and early time for intervention even after successful thrombolysis.

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