Total Neutrophil Count and Neutrophil/Lymphocyte Ratio in Predicting In-Hospital Mortality and Complications after St Segment Elevation Myocardial Infarction

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ABSTRACT

Background: It is suggested that neutrophil infiltrate the infarcted zone. These cause leukocytes mediated hypercoagulable state by causing platelet activation and aggregation into the microcirculation. Thus, causing no reflow and increase the infarcted area. Among complete blood count white blood cell count, neutrophil count and neutrophil/lymphocyte ratio has been proposed to predict the mortality and outcome in coronary artery disease. **Objective:** Efficacy of total Neutrophil Count and Neutrophil/Lymphocyte Ratio in Predicting In-Hospital Mortality and complications after St Segment Elevation Myocardial Infarction. **Study Design:** Cross sectional observational study. **Settings:** Coronary care unit, Ibn-Siena Hospital, Multan Pakistan. **Duration:** September 2021 to October 2021. **Methods:** 159 patients with ST segment elevation myocardial infarction. It's a cross sectional observational study conducted in the Coronary care unit, Ibn-Siena Hospital, Multan Pakistan after taking approval from ethical committee. Sampling Technique was nonprobability, consecutive sampling. Patients of both genders presented to coronary care unit with acute ST segment elevation myocardial infarction will be included. Numerical variables were presented by mean ±SD. Chi square test was used for categorical variables. Student t test was used for numerical data. A p value of <0.05 was considered significant. **Results:** Neutrophil/lymphocyte ratio has a significant relation with in-hospital mortality and complication like arrhythmias, pericarditis and total white blood count was significantly associated with cardiogenic shock. Binary regression analysis revealed that Neutrophil lymphocyte ratio is an independent predictor of mortality (OR 1.535, CI 0.967-2.434 and p value of 0.049). **Conclusion:** Patients with STEMI with high white blood cell count and neutrophil lymphocytes ratio are at increased risk of in hospital death.

Keywords: Neutrophil, Neutrophil / Lymphocyte ratio, ST segment elevation myocardial infarction, Complications.

INTRODUCTION

Ischemic heart disease is the leading cause of death worldwide. A large proportion of people die in the same year in which they experience a cardiac event like ST segment elevation myocardial infarction (STEMI), unstable angina or acute coronary syndrome (ACS). Coronary heart disease cause almost one out of five deaths and around 600000 deaths per year in the United States.[1,2]

Pakistan is among the countries where the prevalence of coronary heart disease is high. Around 30-40% deaths in Pakistan are because of coronary artery disease. Pakistani population have high prevalence of risk factors for coronary artery disease.[2,3]

Major cause of cardiovascular disease is atherosclerosis. Inflammation plays an important role in the formation and progression of atherosclerotic patch and its role has been established in many studies.[4,5]

It is suggested that neutrophil infiltrate the infarcted zone. This cause leukocyte mediated hypercoagulable state by causing platelet activation and aggregation into the microcirculation. Thus, causing no reflow and increase the infarcted area.[4,6,7] It is thought to be due to increased inflammatory response mediated neutrophils through the secretion of inflammatory mediators like myeloperoxidase, elastase, oxygen free radicals and arachidonic acid derivatives.[8]

The role of inflammatory markers has been described in cardiovascular diseases. Among them are C-reactive protein, interlukin-6 and high erythrocyte sedimentation rate.[7]

Among complete blood count white blood cell count, neutrophil count and neutrophil/lymphocyte ratio has been proposed to predict the mortality and outcome in coronary artery disease.[4,5,6,7]

In several studies neutrophil/lymphocyte ratio has been studied as a predictor short term and long-term mortality and post myocardial infarction complications.[5,6,7,9,10]

Ghaffari *et al* showed 3.7% and 43.6% in hospital mortality and post myocardial infarction complication. They showed that high age (p 0.04), female gender (p 0.002), low ejection fraction (p < 0.oo1) and high absolute neutrophil count (p 0.04) as a predictor of mortality. While high white cell count (p < 0.03) and high neutrophil/lymphocyte ratio (p 0.01) was predictor of failure and tachyarrhythmia during first day of admission. They noted that patients with neutrophil count >9.68× 10^9 cell/mm^3 at the time of admission have high rate of ventricular tachycardia/ventricular fibrillation (VT/VF) (13.6%, p <0.001) and pulmonary edema (8.6%, p 0.03) during the first 24 hours compared to those with white cell count less than this.[5]

He J *et al* measured neutrophil/lymphocyte ratio at admission, 24, 72 hours and at time of discharge and took average of these. They described that average neutrophil/lymphocyte ratio predicts all-cause mortality more accurately than absolute neutrophil count (p <0.001). They divided the neutrophil/lymphocyte ratio into three groups according to value of neutrophil/lymphocyte ratio. They observed that higher the neutrophil/lymphocyte ratio higher the predictive value for in hospital mortality, long term mortality and post myocardial infarction complication like heart failure, arrhythmias, and recurrent myocardial infarction.[6]

Han YC *et al*. noted 7.1% and 11.3% major cardiac events (MACE which include all cause death, non-fatal myocardial infarction and ischemic stroke) during hospital and at 12 months respectively. When it was analyzed in neutrophil/lymphocyte ratio subgroups with low, medium and high neutrophil/lymphocyte ratio MACE were 3.7%, 11.1% and 19.1% respectively with p value of <0.001at 12 months. In hospital MACE was 2.8%, 5.6% and 12.7% with p value of 0.001, death 1.9%, 5.6% and 12.7% with p value of 0.003.[7]

Coronary artery disease is a leading cause of mortality and morbidity in Pakistan like other low resource countries. The purpose of the current study is to identify patient with coronary artery disease at high risk of death and complication by using simple, inexpensive and readily available test. This will help us in risk stratification and early more extensive treatment methods to reduce mortality and morbidity of high-risk patients. It will also help in improving the quality of life of patients.

METHODS

It's a cross sectional observational study conducted in the Coronary care unit, Ibn-Siena Hospital, Multan Pakistan after taking approval from ethical committee. Sampling Technique was nonprobability, consecutive sampling. Patients of both genders presented to coronary care unit with acute ST segment elevation myocardial infarction was included and patients having active or chronic inflammatory disease, active malignancy, haematological proliferative disorder, autoimmune disease, acute infection, patients receiving steroid therapy were excluded.

Data was collected of 159 patients who meet the inclusion criteria was collected. Patient's demographic details was noted. Detailed history and written informed consent were taken from every patient. All the patients had a complete blood examination at presentation and 24 hours. Patient's outcome i.e., in hospital mortality and post myocardial complication like heart failure, arrhythmias, recurrent myocardial infarction, length of hospital stay, cardiogenic shock and pericarditis was noted and recorded into proforma. All the labs were acquired from the same laboratory and all the assessments was done by a single consultant to eliminate bias. Confounding variables was controlled by exclusion.

All the collected data was entered into SPSS version 20. Numerical variables were presented by mean ±SD. Categorical variables like hospital mortality and post myocardial complication like heart failure, arrhythmias, recurrent myocardial infarction, length of hospital stay, cardiogenic shock and pericarditis was presented by frequency and percentage. Chi square test was used for categorical variables. Student t test was used for numerical data. Binary logistic regression analysis was done for prediction of mortality. A p value of <0.05 was considered significant.

RESULTS

A total of 159 patients fulfilling the inclusion criteria were included in the study. In this 129 were males and only 30 participants were females. The majority of patients were from age group 61-70 years as shown in the table 1 and different parameters of patients are shown in table 2.

Table 1: Age groups

Age Groups	Frequency	Percentage
31-40	8	5.0
41-50	34	21.4
51-60	46	28.9
61-70	50	31.4
71-80	14	8.8
81-90	7	4.5
Total	159	100

Table 2: Frequency of different parameters in study population

Parameter	Positive cases / Negative cases	Percentage
Hypertension	33/126	20.8/79.2
Diabetes	69/90	43.4/56.6
Hyperlipidemia	5/154	3.1/96.9
Smoking	67/92	42.1/57.9
History of CABG	2/157	1.3/98.7
Family history of IHD	12/147	7.5/92.5
Hypertension	88/71	55.3/44.7
Pericarditis	5/154	3.1/96.9
Atrial fibrillation	6/153	3.8/96.2
Cardiogenic shock	22/137	13.8/86.2
VT/VF	16/43	10/90
Patient outcome	5/154	3.1/96.9

Electrocardiographic findings in the study population: Inferior wall Myocardial infarction was noted in most patients followed by anterior wall myocardial infarction. Development of ventricular arrhythmias during first 24 hours and after 24 hours was observed in 8(5%) each, while atrial fibrillation was developed in 6(3.6%) and complete heart block was noted in 7(4.40%).

Outcome of the patients: Mean hospital stay was 3.1±4.2 which range from 1 to 7 days. During hospital stay 5(3.14%) patients died while 154 patients were discharged. Post myocardial infarction complications were as follow: cardiogenic shock in 22(13.8%), pericarditis in 5(3.1%) VSD in 3(1.88%).

Post Myocardial infarction Mortality: In mortality group, patients were generally females with p value of 0.015. Mean age in the survivor and non-survivor was 59±11.2 and 63.43±15 respectively which was statistically significant. Mean heart rate, left ventricular ejection fraction and Complete blood count parameters are shown in the table below. Binary regression analysis revealed that Neutrophil lymphocyte ratio is an independent predictor of mortality (OR 1.535, CI 0.967-2.434 and p value of 0.049)

Table 3: Post myocardial infarction (STEMI) mortality analysis between groups.

	Survivors (n=154)	Non-survivors (n=5)	P value
Age	59 ± 11.2	63.43 ± 15	0.03
Hypertension	143 ± 13	147 ± 23	0.02
Heart Rate	83.84 ± 18.19	71.80 ± 21.83	0.72
Left Ventricular ejection Fraction	40 ± 12	31 ± 11	0.001
White Blood Cell Count	14188.9 ± 8273.7	14600 ± 4454.77	0.912
Absolute Neutrophil Count	10393.2 ± 4762.2	12138 ± 3960.92	0.047
Lymphocyte count	2520.16 ± 1392.14	1766.39 ± 398.8	0.073
Neutrophil lymphocyte ratio	2.74 ± 0.99	4.10 ± 2.4	0.012

In the study frequency of different complication after STEMI and complete blood counts were compared between two groups and it was noted that in patients with atrial fibrillation and VT/VF after 24 hours there was no statistical difference between two groups while patient who developed VT/VF with 24 hours of STEMI has significantly different between two groups with regard to WBC, absolute Neutrophil count and Neutrophil lymphocyte ratio (NLR) except lymphocyte count. Neutrophil lymphocyte ratio was significantly high in patients with pericarditis and WBC count was significantly high in patients with cardiogenic shock as shown in table 4.

Table 4: Post STEMI complications analysis

Complications	Parameters	Cases With	Cases without	P value
VT/VF with 24 hours	WBC	11862.50 ± 1460.85	14321.68 ± 8574.82	0.001
	ANC	9049.88 ± 1475.67	10465.08 ± 4922.44	0.034
	Lymphocytes	2060.0 ± 942.85	2537.84 ± 1414.98	0.06
	NLR	2.75 ± 0.463	2.78 ± 1.13	0.002
VT/VF after 24 hours	WBC	14400.00 ± 2722.394	14321.68 ± 8574.825	0.35
	ANC	11542.50 ± 3090.85	10465.08 ± 4922.44	0.42
	Lymphocytes	2193.25 ± 990.76	2537.84 ± 1414.98	0.27
	NLR	2.88 ± 0.253	2.78 ± 1.14	0.031
Atrial Fibrillation	WBC	14683.33 ± 4667.08	14183.01 ± 8288.99	0.84
	ANC	11790.17 ± 4220.28	10395.46 ± 4762.67	0.24
	Lymphocytes	2114.17 ± 682.08	2511.45 ± 1397.06	0.08
	NLR	2.83 ± 0.40	2.79 ± 1.09	0.36
Pericarditis	WBC	514460.0 ± 4664.54	14193.51 ± 8270.94	0.95
	ANC	11437.00 ± 3513.67	10415.98 ± 4778.54	0.24
	Lymphocytes	2476.00 ± 1780.41	2497.12 ± 1370.14	0.77
	NLR	5.08 ± 3.30	2.71 ± 0,86	0.000
Cardiogenic shock	WBC	15686.36 ± 5782.92	13963.50 ± 8486.72	0.045
	ANC	12333.86 ± 5398.27	10145.26 ± 4574.01	0.28
	Lymphocytes	2622.95 ± 1022.99	2476.20 ± 1428.50	0.43
	NLR	2.68 ± 0.646	2.80 ± 1.13	0.41

DISCUSSION

In this modern era, because of more sedentary lifestyle and changes in the diet has led to increase in the incidence of STEMI. STEMI has higher mortality and morbidity. So early detection of high-risk patients may help to reduce the mortality and morbidity.[11,12] After the occurrence of myocardial infarction, neutrophils infiltrate the damaged zone and increase the injury by producing oxidative stress. As a result of stress there is increase in the catecholamine that will lead to apoptosis of the lymphocytes and inhibit further development of the lymphocytes resulting in lymphopenia and will end with more damage.[13,14] Lymphocytes has the ability to suppress the inflammatory response, so decreased level of lymphocytes in the STEMI patients will result in adverse effect outcome.[15]

In the present study, complete blood count and neutrophil lymphocytes ratio was evaluated with respect to in hospital mortality and adverse outcome. The studies have shown that the raised neutrophil count and neutrophil lymphocytes ratio is associated with raised in hospital mortality[5] when the two groups were compared the survivor and the non-survivor, the significant difference was observed with respect to neutrophil count and neutrophil lymphocytes ratio. A study conducted Avanzas *et al* has shown that high neutrophil count is related with high infarcted zone.[4] Another study also shown that high absolute neutrophil count was related with high mortality rate.[16] Which is also observed in the present study. Another study has shown that raised white blood count is related with raised short term and long-term mortality.[17]

Neutrophil lymphocytes ratio is a simple inexpensive measure that studies have shown that it can predict mortality and morbidity in patients with cardiovascular diseases.[18] Previously it was widely used for diagnostic purpose in many diseases like autoimmune diseases, solid tumors and infectious diseases.[19] In current study neutrophil lymphocytes ratio was high in patients with post myocardial death which is in agreement with previous studies. So neutrophil lymphocytes ratio is helpful in assessing the risk of increased mortality at the time of admission and also long-term mortality.[20] It is also established in the studies that neutrophil lymphocytes ratio is an independent predictor of mortality in patients with acute coronary syndrome.[21] and have positive correlation with mortality and post myocardial complications.[22]

In the present study, post STEMI complications like development of arrhythmias: VT/VF, atrial fibrillation, pericarditis and cardiogenic shock. In current study it was noted that development of VT/VF within first 24 hours was significantly associated with neutrophil lymphocytes ratio, total white blood count and absolute neutrophil count and VT/VF after 24 hours was only significantly associated with neutrophil lymphocytes ratio. Sedat *et al* also showed that neutrophil lymphocytes ratio is significantly high in patients with post myocardial complications.[22] Ghaffari *et al* study also confirmed the findings of the current study.[5] Guoli *et al* showed that neutrophil lymphocytes ratio is independent predictor of mortality and is better than other white blood count parameters.[11] Another study by Punit Gupta noted cardiogenic shock, heart failure, arrhythmias are

significantly more in patients with high neutrophil lymphocytes ratio.[12]

CONCLUSION

It can be concluded from the study that neutrophil lymphocytes ratio and other white blood cell parameters are relatively inexpensive and easily available predictors of in hospital mortality and post myocardial infarction complications in patients with STEMI. As it can be observed that patients with STEMI with high white blood cell count and neutrophil lymphocytes ratio are at increased risk of in-hospital death. So early detection of patient with the help neutrophil lymphocytes ratio can help in stratification of patients and their management which will result in reduction of mortality and morbidity.

LIMITATIONS

It was single center study and has small sample size. Long term mortality was not evaluated which may be needed for more comprehensive assessment of relationship. Other inflammatory mediators were not used.

SUGGESTIONS / RECOMMENDATIONS

Patients who present with STEMI and have high WBC count should be observed closely for the development of post-MI complications and if develop early management help to reduce mortality/morbidity.

CONFLICT OF INTEREST / DISCLOSURE

Non to declare.

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