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FREQUENCY OF IN HOSPITAL MORTALITY IN PATIENTS WITH HIGH NEUTROPHIL/LYMPHOCYTE RATIO PRESENTING WITH ST ELEVATION MYOCARDIAL INFARCTION

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Contribution
JS conceived the idea and designed the study. Data collection and manuscript writing was done by UA, TA, and HA. All the authors contributed equally to the submitted manuscript.

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ABSTRACT

Objective: To determine the frequency of in-hospital mortality in patients with high NLR presenting with STEMI.

Methodology: Consecutive patients with STEMI and high NLR presenting at Cardiology department, Lady Reading Hospital, Peshawar were evaluated for our study. Out of the 236 patients admitted from 1st September 2015 to 28th February 2016, 191 patients qualified for study inclusion. NLR was calculated by dividing the total number of neutrophils over the total number of lymphocytes obtained via a computerized heamogram. A high NLR was defined as value >4.7. In hospital mortality and the effect of various class of patients with or without conventional risk factors was assessed.

Results: The mean high NLR in study population was 6.38±1.28. In-hospital mortality due to cardiac cause was 12% (n=23) which included 8.37% (n=16) males. Statistically significant higher values of mean high NLR were found to be associated with in-hospital mortality and presence of conventional risk factors including hypertension, diabetes, and smoking with the exception of hypercholesterolemia. Among the patients who died, more had adverse events in form of higher Killip class and arrythmias.

Conclusion: High NLR has fair prognostic value in patients presenting with acute STEMI. Raised values correlate well with the presence of conventional risk factors which increase the risk of post MI adverse events and appears additive to conventional risk factors and biomarkers.

Key Words: ST elevation myocardial infarction (STEMI), Neutrophil to lymphocyte ratio (NLR), Total leucocyte count (TLC), Coronary artery disease (CAD), Acute coronary syndrome (ACS)

INTRODUCTION

Cardiovascular disease (CVD) has become an important cause of mortality in most countries.[1] People of Indo-Asian origin have one of the highest susceptibilities to coronary artery disease (CAD) in the world[2] and it is not surprising that CAD is now the leading cause of death in this part of the world.[3]

Leukocytes play a crucial role in the progression of atherosclerosis leading to CAD.[4] An association between increased WBC count, severity of CAD and survival has been described in patients with acute coronary syndrome (ACS).[5] Neutrophils are the most abundant leukocytes in the peripheral blood. Shortly after onset of ischemia, endothelial cells release adhesion molecules that, along with released chemokines, trigger neutrophil release.[6] Increased neutrophil count in peripheral blood is associated with short-term post-MI adverse outcomes and worse angiographic findings.[7] Higher values of leukocyte subtypes and NLR, in patients with ACS, has been associated with adverse clinical outcome and procedural results after percutaneous coronary intervention (PCI).[8,9] NLR has a high value in predicting death and/or MI in high risk patients with CAD.[10]

NLR also predicts the long term mortality in STEMI patients[11], and in patients undergoing PCI.[12] A high NLR is independently associated with higher mortality rates up to 5 years, and appears additive to conventional risk factors and commonly used biomarkers.[13]

The aim of this study is to determine the frequency of in-hospital cardiac mortality in patients with high NLR presenting with STEMI in our set and class of people with or without conventional risk factors. Based on a single inexpensive test we can stratify high-risk patients and offer them more aggressive and timely diagnostic and therapeutic treatment options.

METHODOLOGY

This descriptive cross sectional study was conducted from 1st September 2015 to 28th February 2016 at Cardiology department of Lady Reading Hospital Peshawar on patients admitted with acute STEMI with high NLR including both genders and age between 30-80 years.

Acute STEMI was diagnosed if there was rise and/or fall of cardiac troponin (c-Tn) with at least one value above the 99th percentile upper reference limit along with any symptom of ischemia, ECG changes suggestive of new ischemia, development of pathologic Q waves or imaging evidence of infarction. Patients having clinical evidence of active cancer, severe renal failure, known hematological disorders, active hepatobiliary diseases, active infection, chronic inflammatory diseases and those receiving steroid therapy for autoimmune diseases were excluded.

After admission to the CCU, all patients were subjected to detailed history, followed by complete routine examination. Under strict aseptic conditions, 5cc oxalated blood was obtained from each patient and sent to the hematology department. A computerized heamogram was obtained to minimize bias.

Patient's demographic data including age, gender, smoking status, diabetes status, hypertension status and hypercholesterolemia was noted. In-hospital mortality was defined as death during hospital stay due to cardiac cause within 2 weeks of admission. NLR was calculated by dividing the total number of neutrophils over the total number of lymphocytes. A high NLR was defined as >4.7.[14, 15,16] Hypercholesterolemia was defined as total cholesterol level ≥240mg/dl. Hypertension was defined as systolic blood pressure >140mm Hg and diastolic blood pressure > 90mm Hg or taking antihypertensive medications. Diabetes was defined as HBA1C ≥6.5, a fasting blood glucose >126mg/dl or taking anti-diabetic medications. All the data was recorded on a predesigned proforma and entered in SPSS version [21].

RESULTS

Among study patients, 66.5% (n=127) were males and 33.5% (n=64) were females. Frequency of in-hospital mortality was 12% (n=23) including 69.56% (n=16) males. (Fig 1)

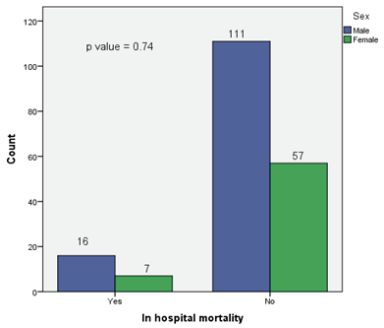


Fig 1: Gender wise distribution of in-hospital mortality

The mean age was 59.61±8.06. Mean high NLR was 6.38±1.28. Mean age in patients who died and those discharged was 68.91±9.43 and 58.32±6.97. Mean high NLR in patients who died was 8.43±1.02 and 6.09±1.03 in those who were discharged. (p-value<0.0001). (Table 1)

Hypertension was present in 47.1% (n=90) of patients. Mean high NLR in hypertensive versus normotensive patients was 6.60 ±1.29 and 6.17±1.23 respectively (p-value 0.02). Diabetes mellitus was present in 29.3% (n=56) patients. Mean high NLR in diabetics versus non-di-

Table 1: Mean high NLR and in-hospital mortality

		In-hospital mortality	
	Total study population	Yes (12%)	No (88%)
Age (mean)	59.61	68.91	58.32
High NLR (mean)	6.38	8.43	6.09
P-value		<0.0001	

abetics was 7.00±1.34 and 6.12±1.16 respectively (p-value <0.0001). Hypercholesterolemia was present in 12.6% (n=24) patients with mean high NLR of 6.61±1.35- compared to patients with normal cholesterol who has a mean high NLR of 6.33±1.26 (p-value 0.29). Smokers were 15.18% (n=29), among who 89.65% (n=26) were males. The mean high NLR in smokers and non-smokers was 6.95±1.83 and 6.27±1.13respectively (p-value 0.009) (Table 2).

Patients were categorized according to Killip classification (Killip 1: No evidence of CHF, Killip 2: Rales, raised JVP, or S3 gallop, Killip 3: Pulmonary edema and Killip 4: Cardiogenic shock). Among non survivors 8.7 % (n=2) were in Killip Class 1, 17.4% (n=4) were in Killip Class 2, 26.1% (n=6) in Killip class 3 and 47.8% (n=11) were in Killip class 4 at presentation. Among the discharged patients 69.6 % (n=117) were in Killip class 1, 23.8 % (n=40) in Killip class 2, 5.4 % (n=9) were in Killip class 3 and 1.2 % (n=2) were in Killip class 4.

The relationship between in-hospital mortality in different Killip class in terms of mean-high NLR is summarized in table 3.

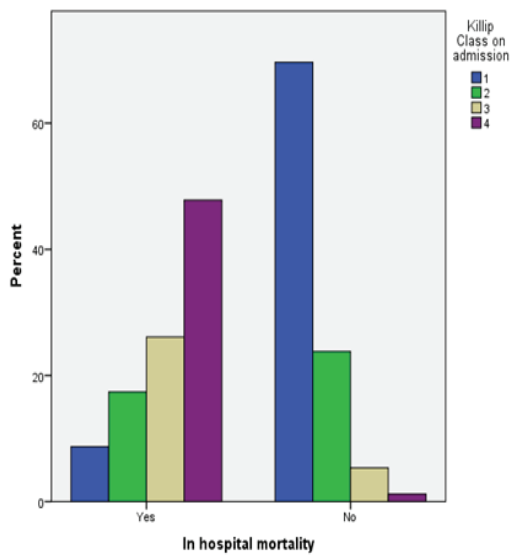
Killip class	In-hospital mortality	
	Yes (mean high-NLR)	No (mean high-NLR)
1	8.06	6.09
2	8.71	6.07
3	9.24	6.35
4	8.98	6.84

Arrythmias were defined as ventricular tachycardia, ventricular fibrillation, atrial fibrillation, atrio-ventricular block and new bundle-branch block during hospitalization. Among the non-survivors, 82.60% (n=19) developed arrythmias. Their mean high-NLR was 8.49. Among the discharged patients 33.92% (n=57), developed arrythmias as well. Their mean high-NLR was 8.14. (p-value = <.00001).

Table 2: Mean high NLR and conventional risk factors

	Hypertension		Diabetes		Hypercholesterolemia		Smoking	
	Yes	No	Yes	No	Yes	No	Yes	No
Mean high NLR	6.60	6.17	7.00	6.12	6.61	6.33	6.95	6.27
p-value	0.02		<0.0001		0.29		0.009	

Fig 2: Killip class and in-hospital mortality



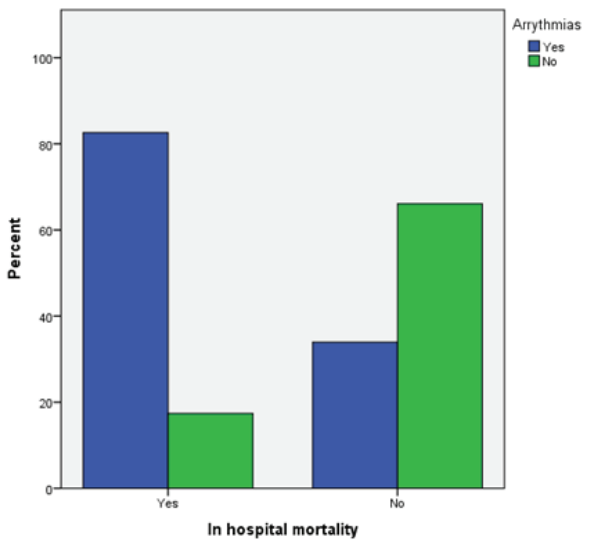


Fig 4: Arrythmias and in-hospital morality

DISCUSSION

Several biomarkers are available to risk stratify STEMI patients.[17-21] Elevated neutrophils have shown to be

associated with worse angiographic outcomes,[22] large infarct size,[23] and short-term prognosis in STEMI patients.[24] Lymphopenia in such patients can be attributed to stress response because of raised cortisol levels[25] and is shown to be an early marker in acute MI.[26]

Leukocyte count, its subtypes and calculating NLR, is a cheap and easily available investigation modality. Elevated NLR incorporates the two WBC subtypes into a single risk factor predictive of CAD burden. The association between cardiovascular mortality and raised TLC and high NLR has been well established.[9, 27-30] In our study, frequency of in-hospital in study population was 12% which is more than 8.70% observed by Jingyu He et al.[29] The reasons include thrombolysis with streptokinase in our patients compared to primary PCI in patients studied by Jingyu He et al.[29], delayed hospital presentation (due to limited resources, late diagnosis, and social issues), and more baseline risk factors in our study population.

Older patients had higher mortality rates as compared to the younger patients which was statistically significant. Older patients more frequently present with a higher inflammatory burden, age-associated diseases and more number of risk factors for CAD.[31]

The mean high NLR in the expired patients was higher compared to the discharged patients. This effect has been observed in studies performed by other investigators.[10, 13, 27, 29, 31, 32] High NLR is associated with increased incidence of adverse cardiovascular events in patients with conventional risk factors for CAD.[33-35] We observed that higher mean NLR values were associated with presence of hypertension, smoking and diabetes and hypercholesterolemia. General population who smokes exhibit low NLR [36, 37,] because smoking causes migration of neutrophils from intravascular compartment to peripheral tissues.[38] But since STEMI is an acute inflammatory process, we assume that effect of smoking is offset giving a picture of high NLR in our study population.

We observed incremental increase in high-NLR with increasing Killip class. In the study by Jingyu He et al, 50.43% patients were in Killip class ≥ 2, having high NLR (> 4.7) on presentation.[29] Increasing Killip class has been associated with higher mortality in STEMI patients39 and its association with high-NLR augments the prognostic value of the later in risk stratifying patients.

More cases of fatal and non-fatal arrythmias were observed in our study patients having higher values of mean NLR consistent with the findings by Ghaffari et al.[40]

NLR is an inexpensive and readily available marker that provides an additional level of risk stratification beyond that provided by conventional risk scores in predicting in-hospital and long-term mortality. Based on their risk profile, patients with high baseline NLR can be managed more aggressively providing them early stress tests, imaging modalities, diagnostic angiography, post MI rehabilitation and in low risk patients, unnecessary diagnostic and treatment modalities can be avoided.

LIMITATION OF STUDY Anemia was not considered in our study, which has significant effects on outcomes of MI. Only short-term outcomes of patients with STEMI and high NLR were studied, whether high NLR has any implication on long-term mortality in our patients remained to be sought out. Based on previous studies the cutoff value for high NLR was taken as >4.7. While in studies performed by others, values higher have been considered. Therefore, a standardized value of NLR that is our population specific is yet to be determined. We did not calculate a repeat NLR value at 24 hours post admission, which may give us even more prognostic information.

CONCLUSION

NLR has fair prognostic value in patients presenting with acute STEMI regarding the adverse clinical outcomes in the form of in-hospital mortality, both short term and long term. Being a cheap and easily available marker, this utility should be utilized to risk stratify patients presenting with STEMI.

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