PREDICTIVE VALUE OF NEUTROPHIL/LYMPHOCYTE RATIO IN PREDICTING COMPLICATIONS AFTER NON ST ELEVATION MYOCARDIAL INFARCTION

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ABSTRACT

Objective: To determine the predictive value of Neutrophil to lymphocyte ratio in determining complications in patients with non ST elevation myocardial infarction.

Methodology: A Cross sectional study conducted in Cardiology Unit, Hayatabad Medical Complex from August 2011 to February 2012. In a total of 250 patients with non ST elevation MI were enrolled in study. Neutrophil to lymphocyte ratio (NLR) was determined. Those with high NLR were followed over two week period to detect in hospital mortality; Atrial Fibrillation and ST segment Deviation. Association of cellular response with the incidence of post-MI mortality/complications was assessed by multiple logistic regression analyses.

Results: There were 250 patients comprising of 154 (61.60%) males and 96 (38.40%) females. The overall mean age was 51.57 $\pm$12.5 years. The frequency of high neutrophil to lymphocyte ratio was present in 78 (31.20%) patients. The In hospital mortality and atrial fibrillation rate was in 10.26% and 11.54% cases respectively while ST segment deviation was in 57.69% patients.

Conclusion: Patients with Non ST Segment elevation Myocardial Infarction with high Neutrophil to lymphocyte ratio, is a good predictor of In hospital mortality, atrial fibrillation and ST segment deviation. Thus a single CBC analysis may help to identify Non- STEMI patients at risk for mortality and complications..

Key Words: Non ST segment elevation Myocardial Infarction, Neutrophil to lymphocyte ratio, Atrial Fibrillation, In hospital mortality, St segment deviation.

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INTRODUCTION

Coronary artery diseases is a leading cause of death worldwide. Each year 1.3 million people get unstable angina or Non ST Elevation Myocardial Infarction (NSTEMI)[1].

Indo-Pakistani populations have one of the highest risks of coronary artery disease (CAD) in the world. The findings indicate that one in five middle-aged adults in urban Pakistan may have underlying CAD. Moreover women are at greater risk than men[2].

Patient with NSTEMI is at greater risk of cardiac morbidity and mortality especially in first week of presentation with the risk of complete atrioventricular block and new-onset Atrial fibrillation(AF), being highest during the first 2 months after the acute MI (16% event rate)[3].

Sudden cardiac death from ventricular fibrillation during acute myocardial infarction is a leading cause of total and cardiovascular mortality[4].

There are few predictors of short term mortality, new onset AF and ST segment deviation in NSTEMI, of which neutrophil to lymphocyte ratio (NLR) is the strongest. One study showed high NLR (>4.7) in 19.1% patients with NSTEMI with a significant higher in hospital death (8.7%), six month mortality (14.4%) and 4 year (29.8%) mortality as compared to those with low NLR. It also revealed that frequency of new onset AF and ST segment deviation is more, 13% and 39.8% respectively in patient

with higher NLR (>4.7) as compared to low NLR (<3%)[5]. Another study showed that admission NLR is an independent predictor of in-hospital and 6-month mortality in patients with acute coronary syndrome (ACS)[6].

If validated, the finding of an abnormal value for the WBC differential (e.g., N count or N/L ratio) might prompt more aggressive risk factor evaluation and therapy for patients with CAD, similar to the modification of risk assessment and treatment currently recommended for the finding of an elevated high-sensitivity CRP value[7].

METHODOLOGY

After approval from research and ethical committee, all patients who presented to Cardiology Unit, HMC with Non ST Elevation Myocardial Infarction were included in the study. The purpose of the study was explained to the patients. Informed written consent was taken. Demographic characteristics were recorded in the Performa.

All patients were subjected to detailed history and clinical examination. Under strict aseptic conditions, 10cc of oxalate blood was obtained from each patient and was sent to the hematology department of the hospital for determination of Neutrophil to lymphocyte ratio i.e. NLR >4.7 or normal NLR. All heamogram reports were computerized thus avoiding bias. Patients in whom the high NLR was detected, were followed over a period of two weeks to detect in hospital mortality, Atrial Fibrillation and ST segment Deviation. All the patients were managed as per ward protocols under supervision of an expert cardiologist having minimum of five years of experience. All the laboratory investigations were done under supervision of an expert hematologist having minimum of 5 years of experience.

The inclusion criteria was all NSTEMI patients of age 30 years and above of either gender, admitted to cardiology department of HMC. While exclusion criteria was infection or sepsis (excluded by C-reactive protein and blood culture), any type of Hematological disorder diagnosed by medical record or by special smear examination, second NSTEMI and past history of Atrial fibrillation.

Data was analyzed by using a statistical software SPSS version 16.0. Mean ± Standard deviation was calculated for continuous variable like age. Frequency and percentages were calculated for categorical variables like gender, high NLR and its common clinical outcome (in hospital mortality, Atrial Fibrillation and ST segment Deviation). High NLR and its association with post NSTEMI complications were stratified among age and gender to see the effect modifications. All results were presented in the form of tables and graphs.

RESULTS

The total number of patients presenting with non ST segment elevation Myocardial Infarction were 250 . The complications associated with NSTEMI patients with high Neutrophil to lymphocyte ratio were In hospital mortality, atrial fibrillation and ST segment deviation as shown in graph no 1 with ST segment deviation having the highest incidence. Higher age and female gender were predictors of mortality.

There were 154 (61.60%) males and 96 (38.40%) females The mean age of male patients was 54.77years $\pm$11.8 and female patient was 46.43 years $\pm$11.94 with over all mean age of 51.57 $\pm$12.5.

High Neutrophil to lymphocyte ratio was present in 78 (31.2%) patients while the low Neutrophil to lymphocyte ratio was in 172 (68.8%) patients (Table 1).

According to age wise distribution of high Neutrophil to lymphocytes ratio in patients with non ST segment elevation myocardial infarction, maximum patients were in the age group of 61 years and above i.e. 31 (39.74%) patients while minimum number of patients was 7 (8.97%) in the age group of 31 to 40 years age group.

While if age wise distribution of common clinical outcome was seen, the In hospital mortality was maximum in the age group of 60years and above i.e. 4 (5.13%) and nil in the age group of 30 to 40 years age group. The atrial fibrillation was maximum in the age groups of 41 to 50 years and 60 years and above age groups i.e. 3 (3.85%) each. ST segment deviation was observed in 19 (24.36%) patients in the age group 60 years and above. On the other hand only 4 (5.13%) patients from the age group 30 to 40 years were observed to have ST segment deviation (Table 2).

According to gender wise distribution, high Neutrophil to lymphocytes ratio in male patients was 49 (62.82%) and female was 29 (37.18%). The In hospital

Table 1: Frequency of High Neutrophil to Lymphocytes Ration in Patients with non ST Segment Elevation Myocardial Infarction

Neutrophil to Lymphocyte Ratio	Frequency (Percentage)
High	78 (31.20%)
Low	172(68.80%)

Graph 1: Frequency of Common Clinical Outcome in High Neutrophil to Lymphocytes Ratio in Patients with non ST Segment Elevation Myocardial Infarction

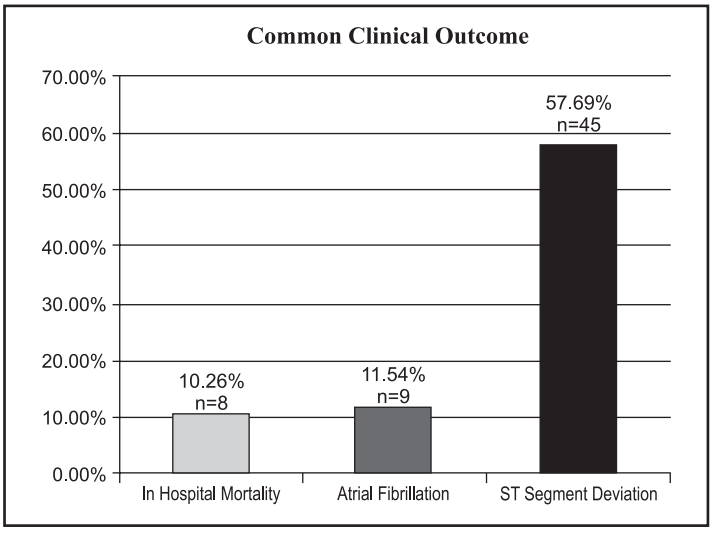

Table 2: Age Wise Distribution of Common Clinical Outcome with High Neutrophil to Lymphocytes Ratio in Patients with ST Segment Elevation Myocardial Infarction

	Common Clinical Outcome		
Age in Years	**In Hospital Mortality**	**Atrial Fibrillation**	**ST Segment Deviation**
30-40	0 (0%)	1 (1.28%)	4 (5.13%)
41-50	3 (3.85%)	3 (3.85%)	9 (11.54%)
51-60	1(1.28%)	2 (2.56%)	13 (16.66%)
60 and Above	4(5.13%)	3 (3.85%)	19 (24.36%)
Total	8(10.26%)	9 (11.54%)	45 (57.69%)

Table 3: Gender Wise Distribution of Common Clinical Outcome with High Neutrophil to Lymphocytes Ratio in Patients with ST Segment Elevation Myocardial Infarction

Common Clinical Outcome of High NLR	Male	Female	Total
In Hospital Mortality	5 (6.41%)	3 (3.85%)	8 (10.25%)
Atrial Fibrillation	6 (7.69%)	3 (3.85%)	9 (11.54%)
ST Segment Deviation	27 (34.61%)	18 (23.08%)	45 (57.69%)

mortality, atrial fibrillation and ST segment deviation were maximum in the male patients; 5 (6.41%), 6 (7.69%) and 27 (34.61%) respectively. The common clinical outcome in female patients were; In hospital mortality 3 (3.85%), Atrial fibrillation 3 (3.85%) and ST segment deviation 18 (23.08%) patients (Table 3).

DISCUSSION

The predictive superiority of NLR in patients with Non ST Segment elevation Myocardial Infarction (NSTEMI) may be due to two factors. Neutrophil are mostly responsible for ongoing active nonspecific inflammation. In contrast Lymphocytes represents regulatory pathway of immune system. In consequence, high NLR reflects two opposite pathways of immune system and therefore more predictive than either parameter alone.

Our study showed a trend of Leukocytosis and ultimately high NLR in patients with Non ST Segment Elevation Myocardial Infarction which also reflects the extent of damaged myocardium and consequently high prevalence of short term complications which included In Hospital Mortality, Atrial Fibrillation and ST Segment Deviation.

Munir et al[8] showed that neutrophil-lymphocyte (N/L) ratio is a better predictor for ACS than leukocyte isolated subtypes. Our results are in agreement with Zazula et al[9], who showed that patients admitted with acute chest pain, presented with significantly increased N/L ratio.

Out of 250 patients in our study, 78 (31.2%) patients showed a high NLR (>4.7).In these patients there was a significant frequency of In Hospital Mortality, which was 10.2%. Munir et al[8] and Azab et al[5] showed in their study a trend to higher mortality (8.7%) in patients with high NLR which is consistent with our results. Tamhani et al[6] investigated relation between admission NLR and Short term mortality in patients with acute coronary syndrome. Their results showed that high NLR is an independent predictor of In Hospital and six month mortality in ACS patients which correlate with our results. Menon et al[10] stated that an elevated white blood cell count at the time of hospital presentation is associated with increased mortality after acute myocardial infarction.

Horne et al[11] stated that total WBC count was found be an independent predictor of death/MI, but greater predictive value was provided by high Neutrophils or low Lymphocytes counts. Optimal risk prediction was given by the NLR, increasing hazard by 2.2-fold. Barron et al[12] also proved that mortality rates were higher in patients with a higher WBC count (0% for WBC count 0 to 53109/L, 4.9% for WBC count 53110 to 103109/L, 3.8% for WBC count 103110 to 153109/L, 10.4% for WBC count >153110/L).

Among patients with high NLR in our study, frequency of Atrial Fibrillation was 11.5% which is favored by previous studies. Azab et al[5] studied the relation of Atrial Fibrillation and high NLR in NSTEMI patients and showed a frequency of 13%, which was statistically significant. Barron et al 12 investigated that frequency of Atrial Fibrillation increases with raising of leukocyte counts (18%, 19%, 20%, 23% and 27% in patients with leukocyte counts of <7500, 7501-9100, 9101-10999,11000-13600 and >13600/mm^3 respectively.

Our study also proved that patients with high NLR has an increased frequency of ST Segment deviation which is also documented by Azab et al[5] also showed significant increase in frequency of ST Segment deviation in patients with high NLR with NSEMI which is consistent with our results.

In this part of the world and especially in Pakistan, where proper facilities are limited and cardiac care centers are usually overburdened, little attention has been given so for to neutrophil to leukocyte ratio among patients of NSTEMI. Additionally there is no local statistics about NLR in our population presenting with NSTEMI and this current study is designed in view to generate local statistics of NLR and its clinical outcome. Also this study will be first of its kind in our local population and based upon results of this study, crucial decisions can be made by consultants in the management of patients with high NLR and higher authorities in opening further areas of research work incorporating NLR in NSTEMI and its association with the common clinical outcome.

The limitation of our study includes selection bias (being an observational study). The study is a small one and was conducted in the hospital which mostly catches patients from a small area of our province (only southern region) and so the results may not be generalized to all population.

CONCLUSION

From the results of our study, it is concluded that High NLR is a good predictor of short term complications like In hospital mortality, Atrial Fibrillation and ST Segment deviation in patients with Non ST Segment elevation Myocardial Infarction. Thus a single CBC analysis may help to identify Non- STEMI patients at risk for mortality and heart failure.

REFERENCES

1. Habib S. Coronary artery disease in women. Pak Heart J 2011;44:18-26.
2. Jaffar TH, Qadri Z, Chaturvedi N. Coronary artery disease epidemic in Pakistan: more electrocardiographic evidence of ischaemia in women than in men. Heart 2008;94:408-13.
3. Narin C, Ozkara A, Soylu A, Ege E, Duzenli A, Sarigul A, et al. The effect of coronary revascularization on new onset complete atrioventricular block due to acute coronary syndrome. Heart Surg Forum 2009;12:E30-4.
4. Bezzina CR, Pazoki R, Bardai A, Marsman RF, de Jong JS, Blom MT, et al. Genome-wide association study identifies a susceptibility locus at 21q21 for ventricular fibrillation in acute myocardial infarction. Nat Genet 2010;42:688-91.
5. Azab B, Zaher M, ,Weiserbs KF, Torbey E, Lacossiere K, Gaddam S, et al. Usefulness of neutrophil to lymphocyte ratio in predicting short and long term mortality after non ST elevation myocardial infarction. Am J Cardiol 2010;106:470-6.
6. Tamhani UU, Aneja S, Montgomery D, Rogers E, Eagle KA, Gurm HS, et al. Association between admission neutrophil to lymphocyte ratio and outcomes in patients with acute coronary syndrome. Am J Cardiol 2008;102:653-7.
7. Waterhouse DF, Cahill RA, Sheehan F, McCreery CJ. Prediction of calculated future cardiovascular disease by monocyte count in an asymptomatic population. Vasc Health Risk Manag 2008;4:177-87.
8. Munir TA, Afzal MN. Assessment of differential leukocyte count in patients with acute coronary syndrome. J Pak Med Assoc 2010;60:548-51.
9. Zazula AD, Precoma-Neto D, Gomes AM, Kruklis H, Barbieri GF, Forte RY, et al. An assessment of neutrophils/lymphocytes ratio in patients suspected of acute coronary

syndrome. Arq Bras Cardiol 2008;90:31-6.

10. Menon V, Lessard D, Yarzebski J, Furman MI, Gore JM, Goldberg RJ. Leukocytosis and adverse hospital outcomes after acute myocardial infarction. Am J Cardiol 2003;92:368-72.

11. Horne BD, Anderson JL, John JM, Weaver A, Bair TL, Jensen KR, et al. Which white blood cell subtypes predict increased cardiovascular risk? J Am Coll Cardiol 2005;45:1638-43.

12. Barron HV, Harr SD, Radford MJ, Wang Y, Krumholz HM. The association between white blood cell count and acute myocardial infarction mortality in patients > or =65 years of age: findings from the cooperative cardiovascular project. J Am Coll Cardiol 2001;38:1654-61.

CONTRIBUTORS

ZAK and MA participated in planning of study, data analaysis and manuscript writing. IA, SAK and YH helped in data managemant. MH supervised the study. All authors contributed significantly to the final manuscript.