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"Association of Neutrophil to Lymphocyte Ratio and Heart Failure In Patients with Acute St- Elevation Myocardial Infarction at Tertairy Care Centre"

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ABSTRACT
Introduction- Ischemic heart disease (IHD) is a condition in which there is an inadequate supply of blood and oxygen to the myocardium.Inflammation is a component of various disorders of the human body triggered by varying etiologies. Myocardial infarction is not an exception to this. Though the triggering event is an occlusion of the coronary artery, various studies have proved an inflammatory component in the pathogenesis. Neutrophil lymphocyte ratio (NLR) is one among the markers for ongoing systemic inflammatory response.
Objective and methods-
This study investigates the association between the neutrophil-to-lymphocyte ratio (NLR) and heart failure in patients with acute ST-elevation myocardial infarction (STEMI) at a tertiary care centre. The study employs a case-control design, involving 100 patients admitted with acute STEMI, with 50 cases developing heart failure and 50 controls without heart failure admitted in AJ institute of medical sciences and research centre.
Results - NLR, calculated from complete blood counts taken on admission, is compared between groups to determine its potential as a marker for heart failure risk. Statistical analysis shows that elevated NLR is significantly associated with heart failure, supporting its role in risk stratification for STEMI patients.
Conclusion-An elevated on admission NLR >3.5 is associated with development of heart failure in patients with acute STEMI. An elevated on admission NLR will help for additional risk stratification of the patient so that these patients can be put under intensive surveillance for subsequent development of heart failure or other complications of acute STEMI.
Keywords- STEMI, MI , NLR.

I. INTRODUCTION

Cardiovascular disease (CVD) has emerged as the single most important cause of death worldwide especially in the previous decade. CVD accounts for 20% of all deaths in the South East Asia Region (SEAR). CHD was the leading cause of mortality in 2010-responsible for 10.6% of total reported fatalities, or 1.8 million deaths, and more than half of CVD mortality[1]

Incidence of HF among patients hospitalized for an AMI varies widely among earlier studies, reaching up to 50%[2].Acute myocardial infarction (AMI) is a common cardiac ailment in hospitalized patients in industrialized countries. In the USA, there is a significant decrease in the incidence of acute STEMI[3].

Raised levels of inflammation are related with a poor prognosis in CAD. Inflammation plays a vital role in the development of heart failure. Inflammatory stimuli result in release of the inflammatory cytokines TNF alpha, IL -6, AND CRP, also some proteolytic enzymes. These proinflammatory cytokines have destructive effects on the myocardium, resulting in impaired LV performance and HF. Prior studies in this field have demonstrated that elevated levels of pro inflammatory cytokines may result in myocardial remodelling and cardiac arrhythmias.[4-6]

Lymphocytes play an important role in healing by modulating mononuclear cell phenotypes and activating the tissue inhibitor of metalloproteinase – 1 expression. Lymphopenia is more common in stressful conditions due to hypothalamo- pitutary – adrenal axis. The activation of this axis leads to cortisol production and increased cortisol results in decrease in the relative lymphocyte levels. Lymphopenia is an independent prognostic factor and is also associated with decreased survival in heart failure patients[4]

Myocardial infarction is not an exception to this. Though the triggering event is an occlusion of the coronary artery, various studies have proved an inflammatory component in the pathogenesis. Neutrophil lymphocyte ratio (NLR) is one among the markers for ongoing systemic inflammatory response. In our study we aim to see whether there is an association between elevated on admission

NLR and occurrence of heart failure in patients with ST- elevation myocardial infarction (STEMI).[7] This is a case control study design with patients having acute STEMI and developing heart failure taken as the test group and those without heart failure taken as the control group. The number of patients with an elevated NLR (>3.5) is recorded in each group and statistical analysis is used to look for any statistically significant difference between the two groups. This will help us for additional risk stratification of the patients with acute STEMI.

AIMS & OBJECTIVES

To investigate the association between admission NLR and heart failure in acute ST elevation myocardial infarction admitted in AJ institute of medical sciences and research centre, Mangalore.

DETAILS OF THE STUDY

Study design:- Case control study, a secondary data analysis of case sheets over 6 months
Study period:-6 months
Study area:- AJ institute of medical sciences and research centre
Study population:- Patients with acute ST elevation myocardial infarction with and without heart failure
Ethical clearance:- Ethical committee clearance was obtained.
Consent:- Informed consent obtained from all subjects. Patient confidentiality maintained.

SAMPLE SIZE:-

Case control study, a secondary data analysis of case sheets over 6 months. 100 cases of acute STEMI (50 with heart failure and 50 without heart failure) were considered to identify the association between elevated NLR and heart failure in acute STEMI at 95% confidence interval and when the percentage of acute STEMI without heart failure with elevated NLR is 46% and the difference between the two is 30%

INCLUSION CRITERIA:- All patients with acute ST elevation myocardial infarction with and without heart failure.

EXCLUSION CRITERIA:-

¬ Clinical evidence of active infection
¬ End stage liver disease
¬ End stage kidney disease
¬Hematological diseases
¬ Systemic autoimmune diseases
¬ Malignancies
¬ Acute Non-STEMI

METHODOLOGY: In this study a secondary data analysis of case sheets was done. On admission NLR (normal NLR is 1.8-3.5) was calculated from complete blood count taken within one hour of admission in patients with and without heart failure getting admitted to the intensive coronary care unit with acute ST- elevation myocardial infarction taking a sample size of 50 in each group. ST elevation MI is defined as > 0.2mV in V2 – V3, > 0.1 mV in all other leads. A comparison of NLR was made between those with and without heart failure. This study will help us to know the association of NLR and occurrence of heart failure in those with acute ST elevation myocardial infarction. This will help us for additional risk stratification of the patients with acute STEMI. 100 cases of acute STEMI (50 with heart failure and 50 without heart failure) are required to identify the association between elevated NLR and heart failure in acute STEMI at 95% confidence interval and when the percentage of acute STEMI without heart failure with elevated NLR is 46% and the difference between the two is 30%.

DATA ANALYSIS: Data was collected using predesigned proforma. The study population consisted of 100 hospitalised patients admitted to the intensive coronary care unit with acute STEMI, with both males and females included in the study. A complete blood count was done within one hour of admission in the study population and the total neutrophil and lymphocyte count was taken for data analysis. A neutrophil to lymphocyte ratio was calculated. Those patients with STEMI progressing to heart failure based on echocardiography criteria were the test (cases) group. The NLR of the test group was compared with the control group without heart failure.

STATISTICS: The collected data were analysed with IBM.SPSS statistics software 23.0 Version. To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To find the significance in categorical data Chi-Square test was used. In the above statistical tools the probability value 0.05 is considered as significant level

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II. RESULTS

AGE (YEARS)	FEQUENCY	PERCENTAGE %
30-39	8	8
40-49	28	28
50-59	60	60
>60	4	4

Table-1

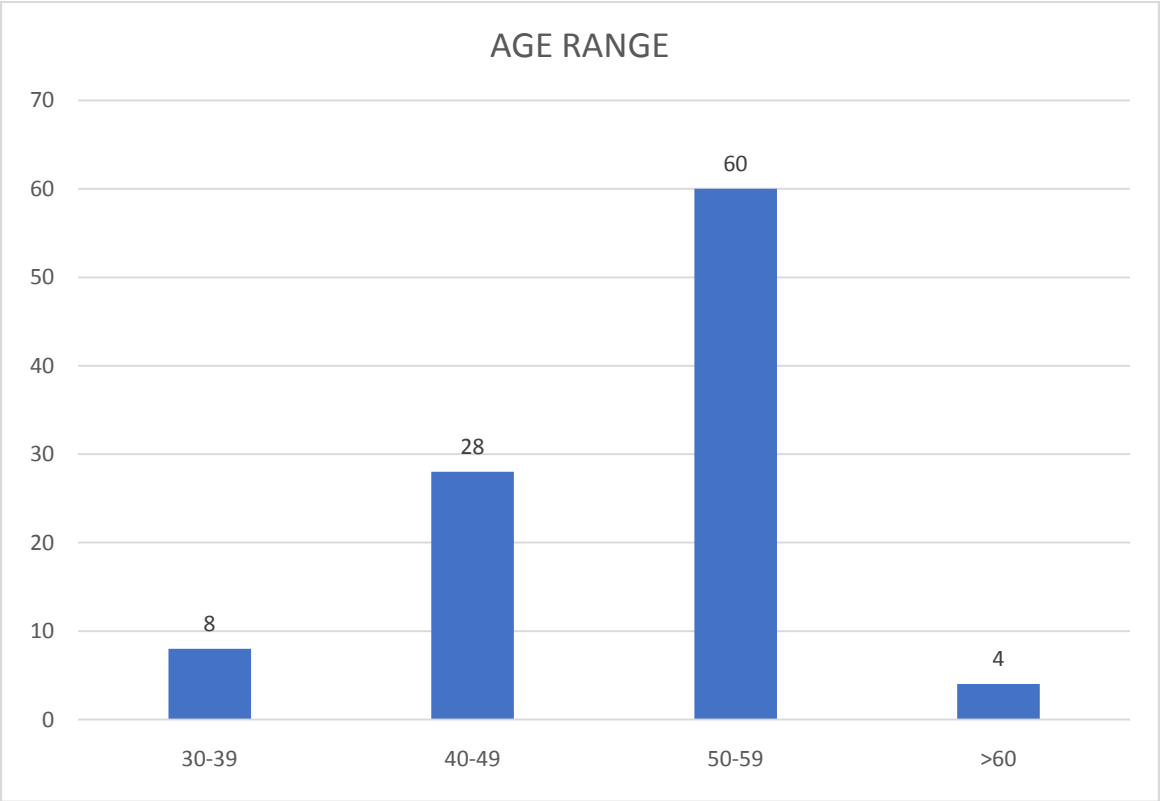

Fig-1

In our study the minimum age of the sample was 32 years and the maximum age was 70 years. From the above table it is seen that the majority of the patients belong to50-59 years rangei.e 60% (N=60). The mean age of the affected study sample was 55 years with a standard deviation of 3.6 years.(table-1, fig-1)

SEX	FREQUENCY	PERCENTAGE
FEMALE	25	25%
MALE	75	75%

Table-1

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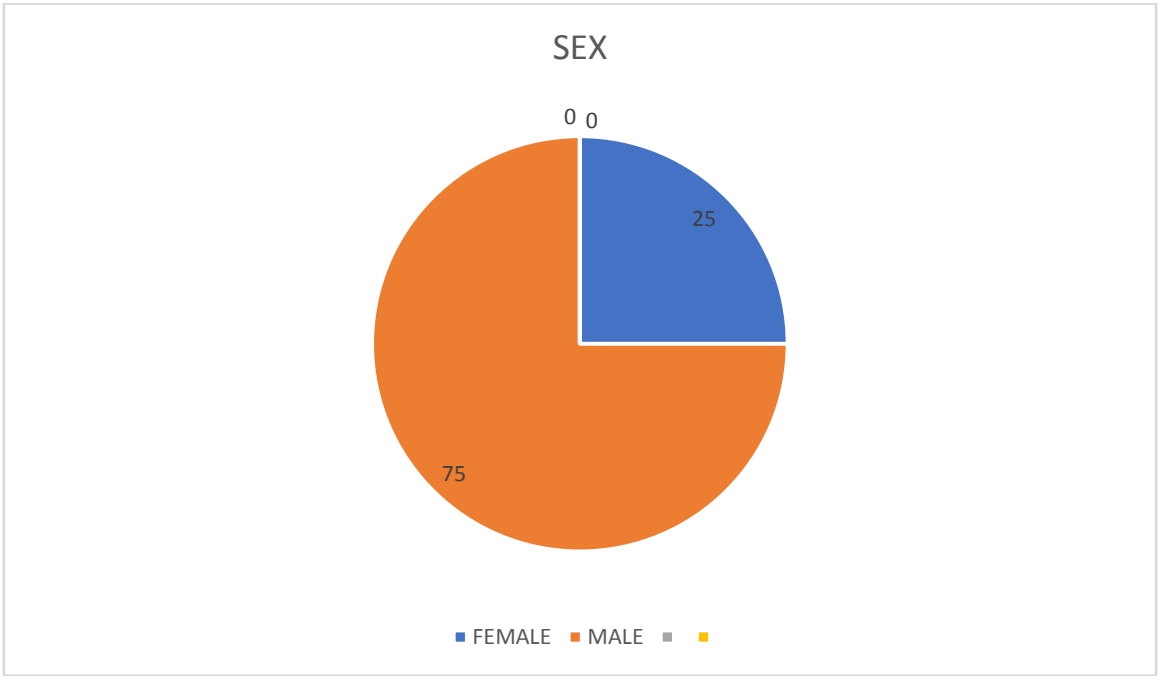

Fig-2

Out of 100 study sample 25% were female and 75% were males. More than two third of cases were males. From our sample it is clear that acute STEMI is much more common in males as compared to females. (table-2, fig-2)

GROUPS		N	MEAN	P VALUE
AGE	CASES	50	53.65	0.081
	CONTROLS	50	51.20	
TOTAL COUNT	CASES	50	8106.4	0.020
	CONTROLS	50	7551.5	
NEUTROPHIL COUNT	CASES	50	5873.0	0.0005
	CONTROLS	50	5019.8	
LYMPHOCYTE COUNT	CASES	50	1673.4	0.117
	CONTROL	50	1803.3	
NEUTROPHIL / LYMPHOCYTE RATIO				
CASES		50	3.62	0.0005
	CONTROL	50	2.87	
EJECTION FRACTION	CASES	50	37	0.0005
	CONTROL	50	61.2	

Table-3

Analysis of group statistics of the distribution of all variables between the groups is depicted in the above table-3 .It is evident from the above table that the P value for the age distribution

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between the two groups is not statistically significant. The distribution of the total count value between the two groups is significant as the P value is 0.020. The lymphocyte count between the two groups is not statistically significant as the P value is 0.117. The neutrophil count in cases was 5873 and in controls was 5019.8,between the two groups is statistically highly significant as the P value is 0.0005. Similarly as evidenced by the distribution of NLR values between the two groups(i.e cases with NLR of 3.617 and controls 2.868) in the previous table there is a highly statistically significant difference between the two groups with elevated NLR seen in patients developing or presenting with heart failure as compared to the control group.

As is part of any comparative statistical analysis it is mandatory to ensure comparability between the two groups by assessing the categorical data for significance between the two groups. This is done by the Chi-Square test. (table-4,5 fig :3-9)

Table-4

Variables	Cases	Control
Total count	**8106.4**	**75551.5**
Neutrophil count	**5873.0**	**5019.8**
Lymphocyte count	**1673.4**	**1803.3**
Ejection fraction %	**37**	**61.2**
Neutrophil / lymphocyte ratio	**3.62**	**2.87**

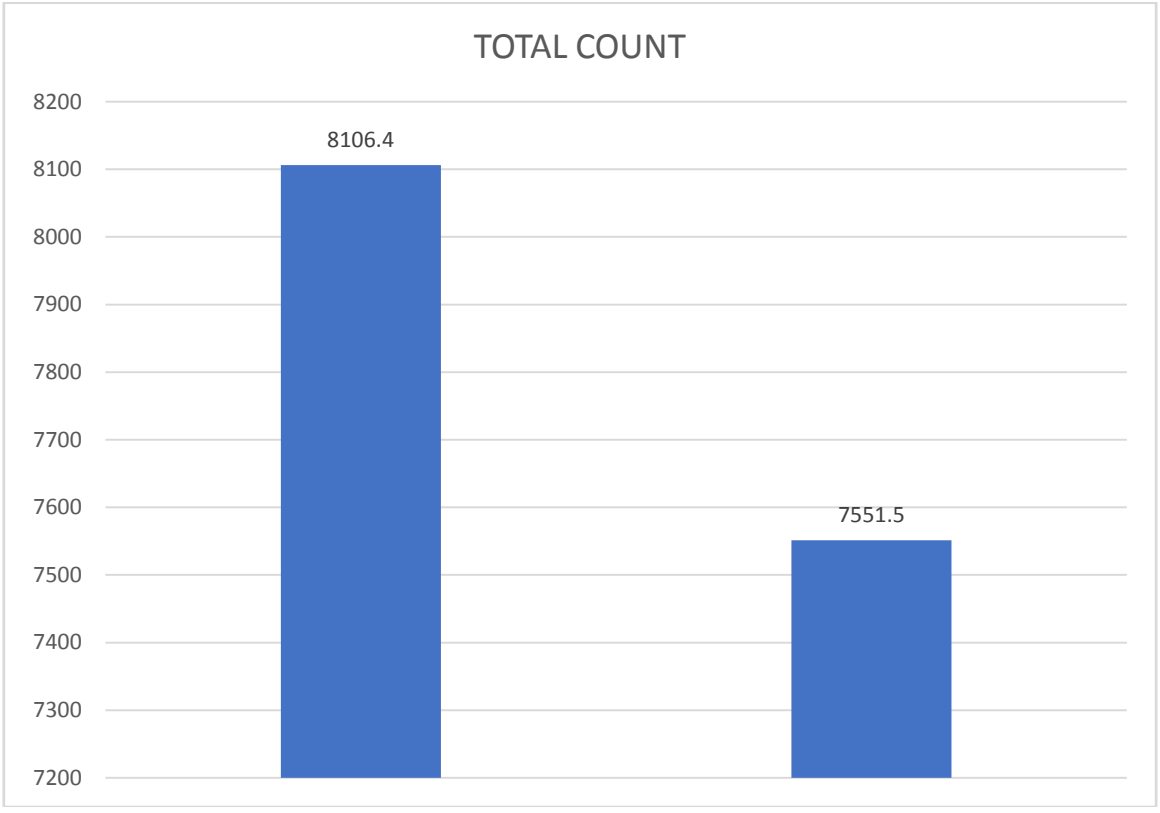

Fig-3

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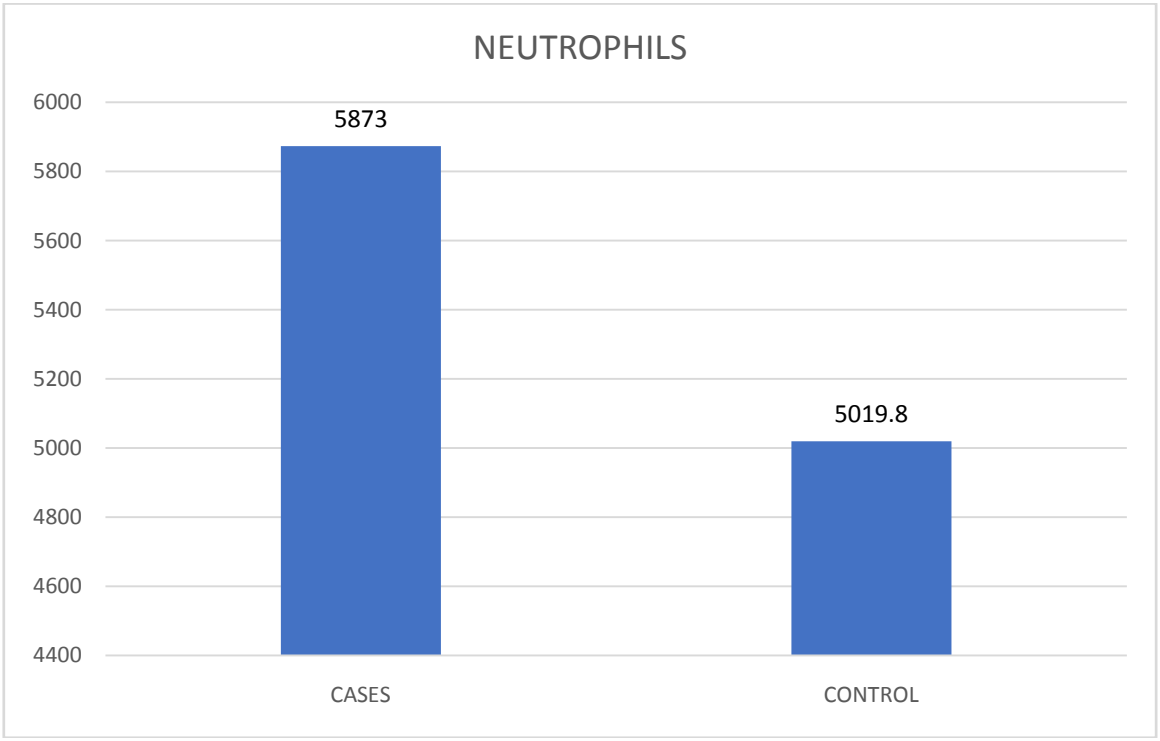

Fig-4

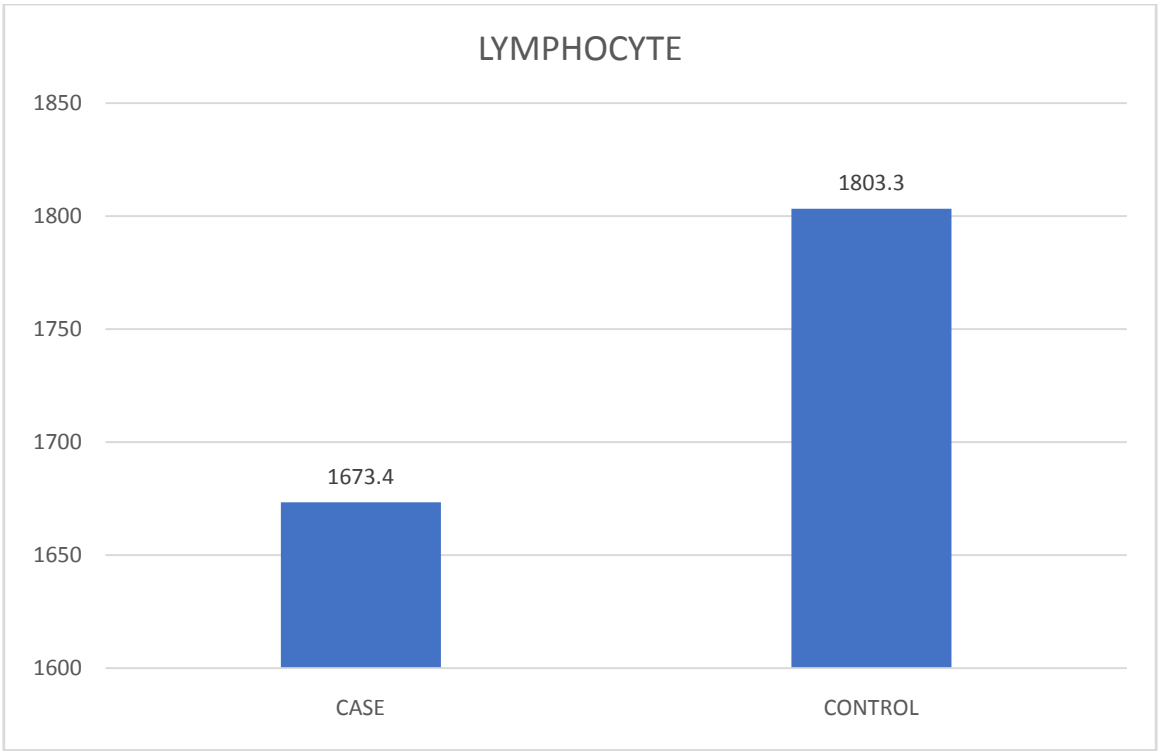

Fig-5

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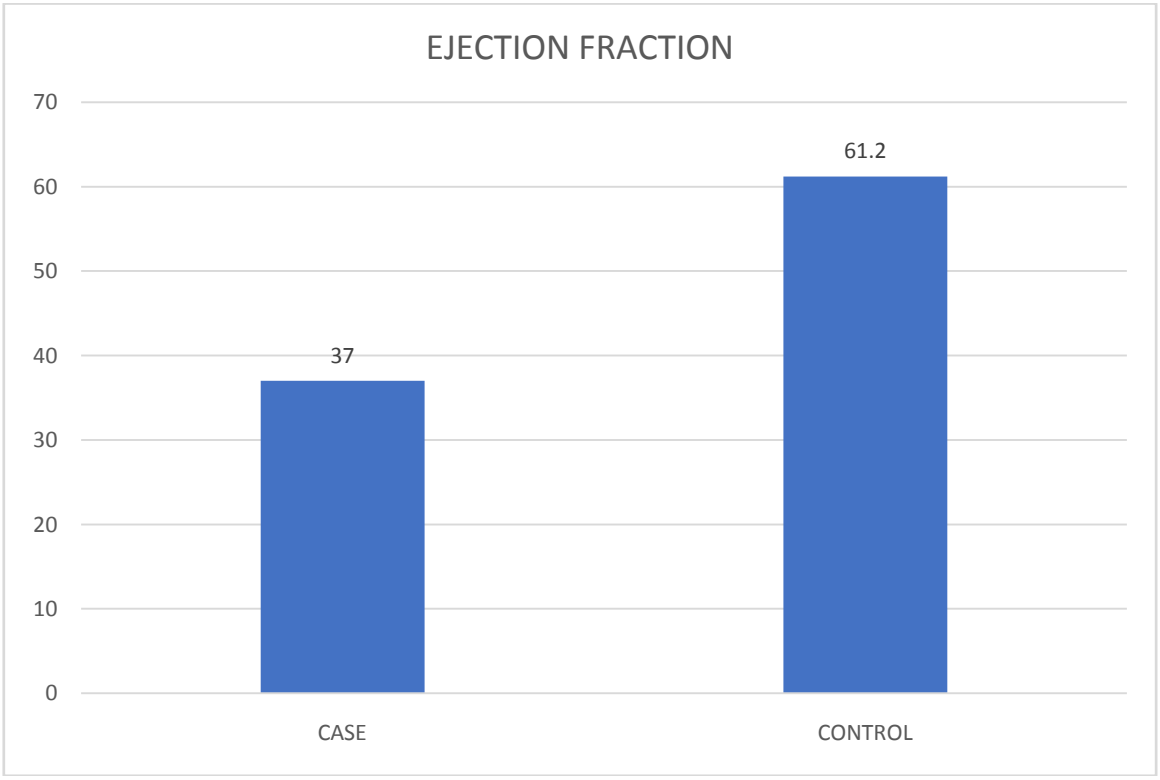

Fig-6

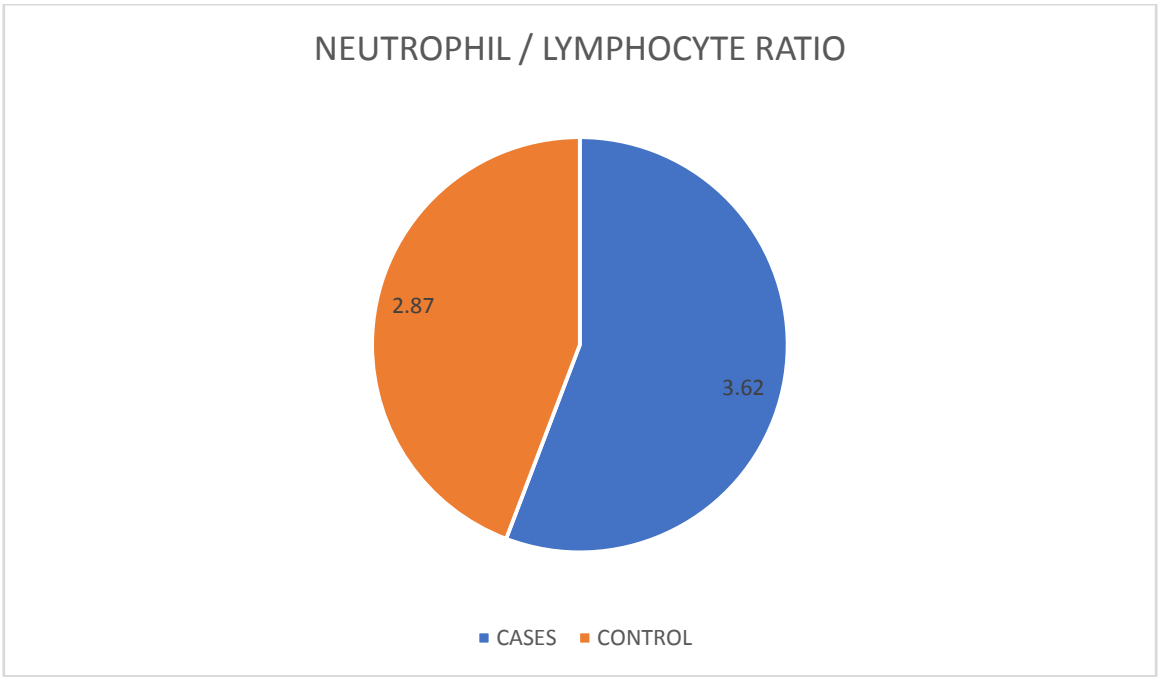

Fig-7

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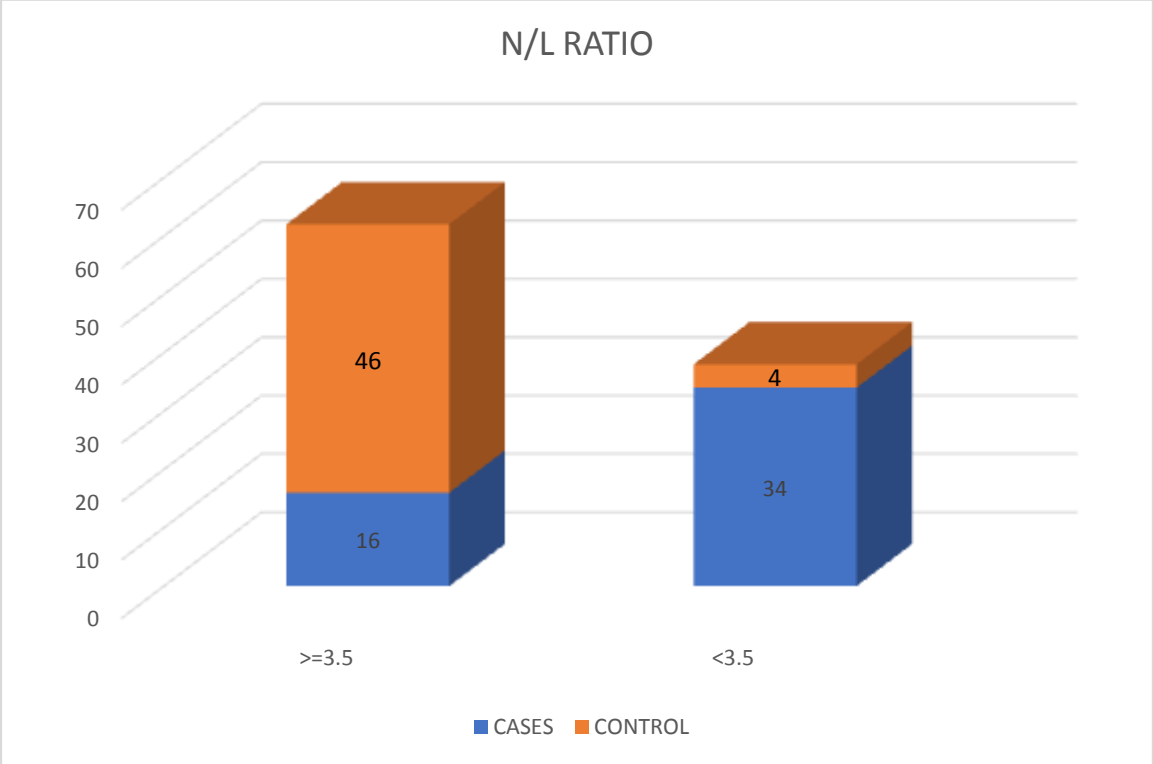

Fig-9

N/L RATIO		N	PERCENTAGE %	PEARSON CHI SQUARE TEST
≥3.5	CASES	16	32	
	CONTROL	46	92	
TOTAL		62		0.0005(HIGHLY SIGNIFICANT)
<3.5	CASES	34	68	
	CONTROL	4	8	
TOTAL		38		

Table-5

III. DISCUSSION

Complete blood count is a cheap, routine and practical laboratory test that gives us important information about the patient's formed blood components. Routine complete blood counts may be useful in diagnosis and prognosis of many diseases. NLR is measured by dividing the number of neutrophils by the number of lymphocytes. NLR is an indicator of systemic inflammation. Inflammation plays a significant role in the body's combat against various noxious insults and is important in the development and progression of various diseases. Even when the total WBC count is in the normal range, NLR has been demonstrated to play a predictive role in the prognosis of chronic and acute inflammatory processes

Several inflammatory biomarkers such as C-reactive protein, lipoprotein-associated phospholipase A2, neutrophil lymphocyte ratio and platelet lymphocyte ratio have been identified as important for risk stratification after AMI

An analysis of the group statistics between the two groups reveals that the mean age of the patients among the cases is 53.65+/- 6.43. The mean age of the patients among the control group is 51.2+/- 6.59. A 60 statistical analysis of the distribution of various age ranges between the two groups was also almost similar ensuring comparability between the two groups. A Pearsons Chi-Square test to assess the significance of age distribution between the two groups in the age category did not achieve statistical significance. (P value 0.170). The gender distribution between the two groups was also similar with 27.3% females in the test and 29.1% females in the control group. The males constituted 72.7% in the test group and 70.9% in the control group which was comparable with study conducted by Sharma et al.[8]

The ejection fraction of the patients in the two groups is significant. The mean EF is 37+/- 7.16 in the test group with heart failure. The mean EF is 61+/-4.28 in the control group without heart failure. The unpaired t-test showed a highly significant difference with a P value of 0.0005. The mean neutrophil count of the cases was 5873 with a standard deviation of 1029. The mean neutrophil count of the control group was 5019.8 Similarly the mean lymphocyte count of the test group was 1673.38. The mean lymphocyte count of the control group was 1803.25. The mean neutrophil to lymphocyte ratio in the control group was 2.868.This falls well within the normal range of NLR among the controls. The mean NLR of the test group was 3.617. The mean NLR of the test group i.e., for patients with acute STEMI and heart failure falls outside the normal range with majority of the patients having an elevated NLR. Our aim is to assess whether this is statistically significant between the two groups

The NLR distribution between the two groups is highly statistically significant with a P value of 0.0005 which showed similar results in the study by Sharma et al with $p < 0.05$[8]. This shows that neutrophils play an important role in the inflammatory process in the pathogenesis and subsequent development of heart failure in patients with acute STEMI. It is also seen that patients with an elevated NLR>3.5 are at risk of developing heart failure comparable with study by Karaca G et al [9]. We have also done a Pearsons Chi-Square test on categorical data by dividing patients with NLR /= 3.5 between the cases and controls. This achieved high statistical significance with a P value of 0.0005.

IV. CONCLUSIONS

The following important conclusions can be drawn from this study 1. There is a statistically significant difference in the neutrophil count between those patients developing heart failure as compared to those without heart failure in patients with acute STEMI. 2. An elevated on admission NLR >3.5 is associated with development of heart failure in patients with acute STEMI. 3. An elevated on admission NLR will help for additional risk stratification of the patient so that these patients can be put under intensive surveillance for subsequent development of heart failure or other complications of acute STEMI. Thus NLR, which is easy to assess and inexpensive, may be a novel biomarker for assessing inflammation and identifying high risk for heart failure in acute ST elevation MI. NLR was inversely correlated with EF. 4. Inflammation with altered yet not clearly elucidated immune response underlies development of complications in patients with acute STEMI. 5. The role of low dose aspirin in addition to having antiplatelet action probably does have some anti-inflammatory activity accounting for its beneficial effect in patients with acute coronary syndrome 64 6. NLR, which is easy to assess and inexpensive, may be a novel biomarker for assessing inflammation and identifying high risk for heart failure in acute ST elevation MI. 7. NLR was inversely correlated with EF and is an independent predictor of heart failure in acute STEMI

V. LIMITATIONS

As is evident from our discussion in the literature review this study may not be applicable to patients with acute STEMI having heart failure with preserved ejection fraction as we have not included these cases. Similarly we have not included patients with acute NSTEMI. Further studies on the relevance of elevated NLR are warranted in both the above groups.

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