

## “Association between Neutrophil to Lymphocyte ratio with presence and Severity of Coronary Artery Disease.”

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### Abstract

**Background:** Elevated leucocyte count is marker of inflammation. Atherosclerosis has been increasingly recognised as complex and multifactorial inflammatory disease. Inflammation plays a key role in the initiation, progression and complications of atherosclerosis. So there is need to study relationship between leucocyte count and atherosclerosis. **Objective:** to determine the relation between Neutrophil to lymphocyte ratio and severity of atherosclerosis in coronary arteries. **Material and methods:** prospective observational study, done on 200 patients, presented with angina or angina like symptoms. Evaluated by blood investigations and coronary angiogram. Patient's severity of coronary artery disease was assessed by using Gensini score. **Results:** The study population consisted of 200 consecutive patients undergoing elective CAG. All the members included in study were divided into two groups based on the result of CAG. While 110 cases had abnormal CAG (case), other 90 had the normal CAG (controls). Smoking history has shown a significant higher in cases compared to the normal CAG. The patients with abnormal CAG have shown a significantly higher NLR when compared to the patient with normal CAG ( $p < 0.001$ ). **Conclusions:** There is significant association between severity of coronary artery disease and neutrophils to lymphocyte ratio.

**Keywords:** Neutrophil Lymphocyte ratio, Coronary angiography, Gensini Score.

### I. Introduction

Atherogenesis is an inflammatory process triggered by endothelial injury.<sup>[1]</sup> Effect of this inflammation in Coronary artery disease is well established and plays a role in the initiation and progression of Coronary artery disease.<sup>[2]</sup> Various markers such as high sensitive C reactive protein (hs-CRP), erythrocyte sedimentation rate (ESR), fibrinogen, white blood cell (WBC) count and its subtypes, interleukins<sup>[3]</sup> have been used to assess the severity of inflammation. A new marker to detect inflammation is blood Neutrophil to lymphocyte ratio (NLR). NLR is a cheap and easily usable marker that shows inflammation. Studies showing association of NLR with various malignancies, renal impairment and metabolic syndrome are available in literature.<sup>[4]</sup> The relation between N/L ratio and the presence and severity of CAD has not been extensively studied. In the current study, we sought to investigate the relationship between the leukocyte subtypes and the presence and severity of CAD assessed by Gensini method in patients with suspected CAD.

### II. Materials And Methods

This is a prospective observational study. Evaluated 200 individuals who underwent diagnostic coronary angiography at Tertiary care Hospital Mangalore, between Feb-2016 to May-2016. Indications for CAG were either the presence of typical angina or positive or equivocal results of non-invasive screening tests for myocardial ischemia. Exclusion criteria were the presence of hematologic disorders, known CAD, infectious or inflammatory disease and severe renal or liver disease. Diabetes was defined as fasting glucose levels of more than 126 mg/dl or Glycated Hb of more than 6.5%. Hyperlipidemia was defined as serum total cholesterol concentration more than 200 mg/dl, or serum LDL concentration more than 130 mg/dl. Body mass index (BMI)-calculated as the weight in kilograms divided by the square of the height in meters ( $\text{kg}/\text{m}^2$ ). All patients have given informed consent. Ethical clearance for this study was obtained from Institutional Ethics Committee. Laboratory measurements - blood samples (venous) were collected before the day of coronary angiography for analysis of the following parameters using standard techniques

1. White blood cell, neutrophils and lymphocyte counts, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol. Triglycerides (TG), hemoglobin.
2. NLR was calculated by dividing Neutrophil count to lymphocyte count.
3. The whole blood samples for hematological indices were analyzed on an automated blood cell counter
4. Biochemical parameters were analyzed using automated analyzer.

Coronary angiogram (CAG)- significant coronary artery disease on angiogram defined as stenosis of 50% or greater narrowing of diameter in coronary arteries.

Genisi score used to as a measure of severity of disease :score 1 for 1-25% of narrowing of coronary artery, 2 for 26-50%, 4 for 51-75%, 8 for 76-90%, 32 for more than 90% of occlusion. The above score was multiplied with a factor that (which is numbered according to site of occlusion): eg - for left main coronary artery – score is 5, 2.5 for left anterior and circumflex artery, for mid regional occlusion score is 1.5, for distal left anterior and circumflex artery score is 1.<sup>[5]</sup>

Statistical analysis was performed using the SPSS 23.0 statistical package for windows. Continuous data were expressed as mean ± standard deviation (SD), while the categorical data by percentage. Student t-test used to compare the parametric variables, correlation analysis was performed by the Pearson correlation test.

### III. Results

The study population consisted of 200 consecutive patients undergoing elective CAG. All the members included in study were divided into two groups based on the result of CAG. While 110 cases had abnormal CAG (case), other 90 had the normal CAG (controls). The baseline characteristic has been given in Table 1. Age distribution was similar between the two groups and even female gender was not significantly different. Smoking history has shown a significant higher in cases compared to the normal CAG.

	Case (110)	Control (90)	p-value
Age (years)	601.1 ± 12.2	58.6 ± 10.5	0.126
Female gender	20(20%)	27(27%)	0.261
Systolic blood pressure(mmHg)	140.9 ± 22.0	130 ± 18.2	0.05*
Diastolic blood pressure(mmHg)	88.0 ± 11.8	78.2 ± 12.2	0.001**
Smoking	69(62%)	19(21%)	0.001**
Alcohol use	12(11%)	8(9%)	0.716
GENSINI Score	50.0 ± 31.2	5.9 ± 12.6	<0.001**

\* <0.05 significant

\*\* <0.01 Highly Significant

**Table 1:** Demonstrating the details of mean difference between the cases and controls.

The Laboratory findings are as follows in the table 2. The patients with abnormal CAG has shown a significantly higher NLR when compared to the patient with normal CAG (p < 0.001). In correlation analysis, NLR was significantly correlated with GENSINI score, Table 3.

	Case	Control	p-value
Hemoglobin (g/dL)	14.02 ± 1.6	13.98 ± 1.3	0.354
Leukocyte (cumm)	9.06 ± 2.43	7.01 ± 1.89	0.001**
Neutrophil (cumm)	6.4 ± 2.6	2.5 ± 0.9	<0.001**
Lymphocyte (cumm)	2.0 ± 0.79	2.6 ± 0.89	<0.001**
Platelet (cumm)	246.4 ± 50.0	254.5 ± 60.6	0.243
Neutrophil-lymphocyte ratio (NLR)	3.9 ± 2.7	2.1 ± 1.6	<0.001**
Total Cholesterol (mg/dL)	209.5 ± 50.6	208.4 ± 49.8	0.256
Fasting Glucose (mg/dL)	121.5 ± 42.6	119.2 ± 43.9	0.752
Triglyceride (mg/dL)	180.0 ± 65.0	177.6 ± 60.0	0.557
Low density lipoprotein (mg/dL)	132.6 ± 39.2	126.2 ± 34.6	0.565
High density lipoprotein (mg/dL)	38.2 ± 7.6	46.8 ± 11.6	0.001**

\* <0.05 significant

\*\* <0.01 Highly Significant

**Table 2:** Demonstrating the details of mean difference of parameters between the cases and controls.

	GENSINI SCORE	
	r	P
Neutrophil-Lymphocyte ratio (NLR)	0.442	<0.001**

\* <0.05 significant

\*\* <0.01 Highly Significant

**Table 3:** Demonstrating the correlation of NLR with the severity of coronary artery disease (Gensini score).

#### IV. Discussion

We All know that inflammation play an important role at all the stages of coronary artery disease. Total and differential leukocyte count though very simple and inexpensive test, provides important information. Our study demonstrated that the lymphocyte count is significantly decreased in patients with CAD and the N/L ratio increased in patients with CAD. Both the lymphocyte count and the N/L ratio correlated significantly with the severity of CAD as assessed by Gensini score. Our study results are similar to the results of a number of studies who have proposed that local and systemic inflammation are involved in atherosclerosis and coronary heart disease.<sup>[6]</sup> Muhammed sulaiman et al study showed that high neutrophils and a relatively low lymphocyte count in patients with coronary artery disease.<sup>[7]</sup> Selcuk H et al study showed that elevated N/L Ratio was found to be significantly related to severity of CAD.<sup>[8]</sup> Papa A et al showed that high N/L Ratio has also been associated with increased mortality in clinically stable diagnosed CAD cases. Nunez et al. study showed that N/L ratio as a useful predictor of long-term mortality in patients with ST segment elevation myocardial infarction.<sup>[9]</sup> Ommen, S.R., et al study showed that the relative lymphocyte count has prognostic usefulness in patients with CAD and congestive heart failure.<sup>[10]</sup> The study has some limitations like small sample size, single centre based study and single N/L Ratio reading. High N/L Ratio suggests increased risks of complications so measures can be taken to minimize the complications.

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