# **ORIGINAL ARTICLE**

# Mean Neutrophils to Lymphocytes Ratio in Patients with Coronary Artery Ectasia

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#### ABSTRACT

Background: The Neutrophil to Lymphocyte (N/L) ratio has appeared as a novel marker of inflammation for cardiac as well as vascular diseases. Atherosclerosis and inflammatory markers shows a major role in the etiology as well as pathogenesis of coronary artery ectasia (CAE).

Objective: This study objective was to know about the mean neutrophils to lymphocytes ratio (NLR) in patients who are known to have Coronary artery ectasia (CAE).

Study Design: This study was a Cross Sectional Study.

Methodology: Total 60 patients with diagnosis of CAE presenting in cardiac emergency or cardiac OPD and admitted in CCU were enrolled. Coronary angiogram was performed to look for evidence of coronary artery ectasia. A blood sample of 5ml was taken and sent to hospital laboratory to find NLR ratio as per operational definition. All collected data was entered and evaluated in SPSS v23.0. It was stratified for gender, age, BMI, DM (200mg/dl) and HTN (>160/90mmHg) to address effect modifiers. Post stratified, t-test was used to rule out these effect modifiers by taking p-value ≤0.05 as significant.

Results: In this study, 60 patients who had Coronary artery ectasia (CAE) fulfilling selection criteria were included from Department of Cardiology, Gulab Devi Hospital, Lahore. In these patients, 37(61.7%) were males and 23(38.3%) were females. Mean age of the patients were 40.5±14.8 years with 18 and 70 as minimum and maximum ages. Mean NLR of the patients were 2.4±1.2 with 0.72 and 4.98 as minimum and maximum values.

Conclusion: Elevated Neutrophil to Lymphocyte ratio (NLR) plays a significant role in the pathogenesis of inflammation in patients with coronary artery ectasia (CAE).

Key Words: Coronary artery ectasia, Neutrophils to Lymphocytes ratio.

## INTRODUCTION

Coronary artery ectasia (CAE) describes as dilatation of arterial segment to a width of minimum 1.5 times of the nearby normal coronary artery lumen<sup>1</sup>. Ectasia denotes to diffusely dilated coronary artery whereas as coronary aneurysm is a focal dilatation of arterial lumen<sup>1</sup>. CAE can be found in up to 5% patients on angiography and 0.22% to 1.4% on autopsy<sup>2</sup>. 50% cases of CAE are due to atherosclerosis, whereas 20-30% are considered congenital in origin.<sup>3</sup> In the coronary tree most commonly involved vessel is the right coronary artery (40- 61%) then comes the left anterior descending artery (15-32%) and left circumflex artery (15-23%).4 In 75% of cases, ectasia is seen in only one coronary artery.<sup>3</sup> Sluggish or turbulent blood flow is produced due to ectasia, which lead to increased incidence of exertional chest pain and MI, irrespective of the severity of simultaneous coronary arterial stenotic disease.<sup>2</sup> Repeated formation and dissemination of micro emboli or thrombotic occlusion of segments distal to the ectasia is the main reason behind these symptoms.<sup>5</sup> Sluggish blood flow in coronary vasculature can also lead to the similar Symptoms.<sup>6</sup> CAE can be divided in four sets: Set 1 shows diffuse ectasia of 2 or 3 vessels, Set 2 shows diffuse ectatic involvement of one vessel and discrete ectasia in another, Set 3 is when only one vessel has diffuse ectasia, and Set 4 shows only one vessel localized or segmental ectasia.<sup>7</sup> Main diagnostic modality for the determination of coronary artery ectasia is coronary angiogram.8 Neutrophils to lymphocytes ratio (NLR) is a simple factor to assess the inflammatory status of a subject with no trouble and is proved useful in the stratification of MACE.9 The neutrophils to lymphocytes (NLR) ratio has recently appeared as a novel marker of inflammation for cardiac as well as vascular diseases<sup>10</sup>. It is calculated from peripheral blood sample by dividing the number of neutrophils by number of lymphocytes.<sup>11</sup> NLR independently predicts the outcome in stable coronary artery disease, and it also predicts short and long-term mortality in patients who are diagnosed acute coronary syndrome.<sup>12</sup> Neutrophil to lymphocyte

ratio (NLR) has revealed to have the highest predictive power for poor outcomes in diagnosed patients or those at high risk for coronary artery disease.<sup>13</sup> The normal value of NLR in adults with good health is between 0.78-3.53.9 There has been a consistent relationship between coronary artery ectasia and neutrophils to lymphocytes ratio. Previous studies showed that 17 Patients with angiographically proven CAE had significantly raised NLR when compared to the those with normal coronary arteries.<sup>14</sup> The prevalence of CAE is reported to be 5% in various angiographic studies and its prevalence is reported to be in between 0.22% and 1.4% in various autopsy series.<sup>15,16</sup> The key objective of this study was to know about the mean neutrophils to lymphocytes ratio (NLR) in patients who are diagnosed with Coronary artery ectasia (CAE).

#### MATERIALS AND METHODS

Design and Setting: This cross sectional study was done in department of Cardiology, Gulab Devi Hospital, Lahore.

Sampling Selection: Using non probability purposive sampling a calculated sample of 60 cases diagnosed with coronary ectasia (arterial segment dilatation to a diameter of minimum 1.5 times of the nearby normal coronary artery assessed angiographically) with age 18-70 irrespective of the gender were enrolled. Patients having history of previous MI, any acute infection, patients with obstructive coronary artery disease on Coronary Angiography and diagnosed case of malignancy were excluded.

Methodology: Patients with diagnosis of CAE presenting in cardiac emergency or Cardiac OPD were admitted in CCU. Written informed consent was taken. Every patient's proforma was filled included in the study mentioning patient socio-demographic profile. Coronary angiogram was performed to look for evidence of coronary artery ectasia (as per operational definition). A blood sample of 5ml was taken and sent to hospital laboratory to find NLR ratio (calculated from peripheral blood smear, used as marker of inflammation)

Statistical Analysis: All data which was collected, was entered and evaluated in SPSS v23.0. Mean±S.D was calculated for quantitative data for example age, BMI and NLR. Frequency (%) was calculated for categorical data like gender. Data were stratified for age, gender, BMI, DM (200mg/dl) and HTN (>160/90mmHg) to address effect modifiers. Post stratified, t-test was applied to exclude these effect modifiers by taking p-value ≤0.05 as significant.

## RESULTS

In this study, 60 patients who had Coronary artery ectasia (CAE) fulfilling selection criteria were included. Among these patients, 37(61.7%) were males and 23(38.3%) were females. 11(18.3%) were between 18-30 age group, while 23(38.3%), 26(43.3%) were between 31-45 and >45 age groups respectively. Mean age of the patients were 40.5±14.8 years with 18 and 70 as minimum and maximum ages. 15(25%) patients had normal weight, while 28(46.7%) and 17(28.3%) were overweight and obese respectively. Among these patients, 25(41.7%) were diabetic and 28(46.7%) were hypertensive. Mean NLR of the patients was 2.4±1.2 with 0.72 and 4.98 as minimum and maximum values. Mean NLR among male was 2.3±1.2 and 2.4±1.2 among females, which is not statistically significant (p=0.841). Mean NLR among diabetic was 3.1±1.1 and 1.9±1.1 among non-diabetics, which is statistically significant (p=0.00001). Mean NLR among hypertensive was 2.6±1.4 and 2.2±1.1 among non-hypertensive, which is not significant statistically (p=0.208). Mean NLR among 18-30 years' age group was 2.0±1.2, 2.3±1.1 among 31-45 years' age group and 2.5±1.3 among >45 years' age group, which is not significant statistically (p=0.504). 68 Mean NLR among normal BMI was 1.0±0.3, 2.3±0.9 among over-weight and 3.7±0.7 among obese, which is statistically significant (p=0.00001)

Table-1: Frequency distribution of age groups

Age groups	Frequency (N=60)	Percent
18-30 years	11	18.3
31-45 years	23	38.3
>45 years	26	43.3

Table-2: Stratification of NLR with respect to age groups

Lymphocytes 11-2.05±1.23 Ratio 31-45 years 23 2.38±1.12 0.504		Age groups	n	Mean±SD	p-value
Ratio 31-45 years 23 2.38±1.12 0.504		18-30 years	11	2.05±1.23	
Kallo 45 vis and 00 0 50 4 07		31-45 years	23	2.38±1.12	0.504
>45 years 26 2.58±1.37		>45 years	26	2.58±1.37	

Table-3: Stratification of NLR with respect to gender

Neutrophils to	Gender	n	Mean±SD	p-value
Lymphocytes	Male	37	2.38±1.27	0.841
Ratio	Female	23	2.38±1.27	0.041

# DISCUSSION

Even after advancements in cardiology, it still remains unclear that what causes that much luminal dilatation in CAE. Though, some markers of inflammation such as interleukin 6, C - reactive protein (CRP), matrix metalloproteinase, tumor necrosis factor Alpha, and some risk factors of atherosclerosis such as smoking, diabetes and advanced age may be possibly have association with the CAE<sup>17-19</sup>. In coronary angiographic studies 1.5% to 5% of patients were reported to have CAE<sup>20</sup>. Patients diagnosed CAE can experience angina pectoris even without CAD. Moreover, it is observed in some studies that the rate of acute coronary events through thrombus, vasospasm or dissection is greater in those diagnosed with isolated CAE than in those who have normal coronary angiograms. Additionally, it is stated in several studies that 29% to 39% of patients who are diagnosed with isolated ectasia had a past event of angina pectoris or myocardial infarction, and rise in mortality has been reported in patients with CAE comparable to the patients with CAD<sup>15,21</sup>. Prior data have revealed a strong link between peripheral white blood cells counts and the risk of adverse cardiac as well as vascular events in both patients with

diagnosed CAD and those without such disease at baseline<sup>22,23</sup>. A marker of inflammation, the NLR ratio, can predict cardiac mortality independently<sup>24.</sup> For the purpose of cardiac risk stratification in patients with CAD, neutrophil-lymphocyte ratio may be useful prediction of severe atherosclerosis 25. It is proposed that inflammation has a pivotal role in development of coronary artery ectasia. Though very simple and inexpensive test (Total and differential white blood cells count), gives significant information. Elevated N/L Ratio was found in the diseased group. Our results match to the results of a numerous studies who proposed that local and systemic inflammation play role in development of and coronary artery  $ectasia^{26,27}$ . Researchers have found a high neutrophil and a relatively low lymphocyte count patients with coronary artery ectasia<sup>28,29</sup>. Furthermore, the elevated N/L Ratio was knows to be considerably related to severity of CAE<sup>30</sup>. Raised N/L Ratio has also been linked with increased mortality in clinicallyatherosclerosis stable diagnosed CAE cases<sup>31</sup>. Koushki and his colleagues found in their studies that statins can lower down N/L ratio, may be because of its anti- inflammatory effects.<sup>32</sup>. Kalaycıoğlu enrolled 405 patients who were diagnosed with isolated CAE, obstructive CAD and insignificant CAD (controls) showed same results that patients with diagnosed isolated CAE had remarkably higher NLR as compared to the patients who are having obstructive CAD and control groups<sup>10</sup>. Zhao separated patients in 3 sets: patients with diagnosed CAE, those patients who are newly diagnosed coronary artery disease (CAD), and those patients who are having normal coronary angiogram (Control Group)<sup>33</sup>. The NLR was remarkably higher in patients in both sets of CAE and CAD groups when compared to those in the control group<sup>33</sup>. Mean NLR in patients who are diagnosed with CAE found in a study was as 2.36 ±1.1616 while another study stated mean NLR in CAE cases was 2.2 ± 0.61<sup>34.</sup>

#### CONCLUSION

Elevated Neutrophil to Lymphocyte ratio (NLR) plays a significant role in the pathogenesis of inflammation in patients with coronary artery ectasia (CAE).

Limitations of study: This study was performed in a single center. Large scale studies are required before a firm final conclusion is achieved.

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