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ORIGINAL ARTICLE

The Relationship of Coronary Artery Disease Severity with the Neutrophil to Lymphocyte Ratio in the Patients Undergoing Coronary Angiography

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ABSTRACT

Background: For identification of the coronary artery diseases the neutrophil to lymphocyte ratio is considered as a well-known marker.

Objective: To evaluate the relationship of neutrophil to lymphocyte ratio (NLR) with CAD severity and to determine the reference value of NLR for prediction of the CAD.

Study design: It was a cross-sectional study with statistical approach, Peshawar institute of cardiology and Punjab Institute of cardiology Lahore from May 2021 to October 2021.

Material and Methods: The 132 patients visited the Peshawar institute of Cardiology and Punjab Institute of cardiology Lahore were included in this research. The patients who had undergone the coronary angiography for angina with ischemic ECG changes were selected. SYNTAX score was used to assess the CAD severity. The high, intermediate and low SYNTAX group was created on the basis of results. The BeneSphera analyzer was used to determine the neutrophil and lymphocyte count. The NLR was calculated. The Pearson's correlation test, ANOVA and logistic regression analysis was performed for the statistical analysis.

Results: Out of the 132 patients were selected, the average age range was between 24 years to 85 years. Among them 67 % of the patients were male and 40 % of patients had a low score of SYNTAX. On the other hand, 33 % of the patients had medium syntax scores. The range of the NLR was between 1.1to9.76 (median 2.54 and mean 3.31 ±1.90). The average standard deviations in low SYNTAX group was 57.12 ±12.018. While it was 61.92±12.23 in intermediate SYNTAX group and 63.01±12.54 high SYNTAX group. The dyslipidemia, diabetes mellitus were more commonly observed in the high SYNTAX group. This group also had low lymphocyte count and high neutrophil count.

Conclusion: For the prediction of CAD, the ratio of neutrophils to lymphocytes can be considered. By the calculation of this ratio, it is easy to highlight the correlation between CAD and severity level.

Keywords: Coronary angiography, SYNTAX, neutrophil to lymphocyte ratio (NLR), Cardiovascular diseases (CAD).

INTRODUCTION

Despite the advances in modern therapeutics, the cardiovascular diseases CAD are the major cause of mortality and morbidity around the globe. The role of inflammation in the atherosclerosis can't be ignored. The CAD play significant role in initiation and progression of the atherosclerotic. The reversible episodes of myocardial demands are observed in the patients diagnosed with the stable angina[1-2]. For the treatment of the patients with non-ST-elevation acute coronary syndrome (NSTE-ACS) the evaluation of patient prognosis and knowledge about the validated risk factors is required. The revascularization and prognosis in such patients is highly effected by coronary lesions. The SYNTAX score is indicative of the coronary lesions complexity. The prediction play important role in selection of the best therapeutic methods. There is a close association between the devastating disease i.e CAD and inflammation. The pathophysiological process of the body are highly effected by atherosclerotic. With the increased in the inflammatory status in the CAD patient poor prognosis is observed[3-4].

The previous studies have proved that there is a significant relationship between CAD and inflammatory markers. NLR are the emerging prognostic markers for the chronic stable angina CSA patients. The number of circulating inflammatory cells changes with the acute ischemic changes occur during ACS. It is highly non-invasive method. The extensive studies are conducted on the inflammatory markers[5]. The higher neutrophil to lymphocyte ratio are associated with higher levels of inflammation. The neutrophil indicate the non-specific inflammation and regulatory pathway marker is another name of lymphocytes[6].

It can be routinely used for prediction of coronary disease severity. By dividing the number of neutrophils by number of lymphocytes the neutrophil to lymphocyte ratio can be calculated. The higher NLR are indicative of increased CAD severity. The gold standard for clinical judgment of the CAD is coronary angiography. The quantitative indicator of coronary artery severity is Gensini score[7].

The inflammatory marker i.e white blood and subtypes play significant role in atherogenesis pathogenesis. The worst cardiovascular consequences are associated with the high neutrophil and low lymphocyte blood counts. For the prediction of the cardiovascular events in the asymptomatic patients these marker are highly used.

For prediction of coronary atherosclerotic burden the neutrophil to lymphocyte NLR ratio are assessed. It is easily available method. This method is cost effective and highly used for the prediction of CAD severity. The elevated levels of NLR are associated with increase in long term risk of mortality[8-9].

MATERIAL AND METHODS

It was a cross-sectional study with statistical approach, Peshawar institute of cardiology and Punjab Institute of cardiology Lahore. The 132 patients visited the cardiology department of our institute teaching hospital were selected for the research. The duration of the study was one year from March 2021 to March 2022. The patients who had undergone the coronary angiography for angina with ischemic ECG changes were selected. According to the inclusion criteria the patient of age greater than 20 years were selected. The ethical and review board committee of the hospital approved the study. The sample was calculated from the previous study[10]. The confidence interval was 95%. Its power was 80%. The precision was 10%. The two cardiologist reviewed the coronary angiography film.

The patients diagnosed with obstructive pulmonary disease, chronic liver disease, chronic kidney disease, hematopoietic system disorder, history of using glucocorticoid therapy and acute infection were excluded from the study. SYNTAX score was used

to assess the CAD severity. The high, intermediate and low SYNTAX group was created on the basis of results. The patients with the SYNTAX score less than 22 were included in low SYNTAX group. The patients with the SNTAX score range between 23 to 32 were included in intermediate group and those with SYNTAX score greater than 32 were included in the high SYNTAX group. The BeneSphera analyzer was used to determine the neutrophil and lymphocyte count. The NLR was calculated. The Pearson's correlation test, ANOVA, Chi-square test logistic regression analysis was performed for the statistical analysis. The sensitivity of the NLR was calculated. For comparison of nonparametric variables the Mann-Whitney test was performed. The p value less than 0.05 was considered statistically significant.

RESULTS

The 132 patients were selected for this study, and the average age was from 24 years to 85 years. Among them 67 % of the patients were male and 40 % of patients had a low score of SYNTAX. On the other hand, 33 % of the patients had medium syntax scores. The patients who have CAD had some of the common symptoms of the disease like high blood pressure (57 %), smoking (38 %), diabetes (44 %), and past history of IHD. The older people had more severe symptoms of the disease as compared to the young ones. The level of the white blood cells like neutrophils, eosinophils, and lymphocytes also differ greatly in different groups of different SYNTAX levels. However, no significant increase in white blood cells was observed in the group having an intermediate level of SYNTAX. Some other parameters like serum creatinine, LDL, and left ventricle fractions were not changed in different groups. The basic parameters of different groups are mentioned in the table.

Table 1: Basic parameters of the score of SYNTAX;

Parameters	SYNTAX score 1 to 22 n: 53	SYNTAX Score 22 to 32 n: 44	SYNTAX score More than 32 n: 34	Value of P
Age ± standard deviation	57.12 ± 12.018	61.92 ± 12.23	63.01 ± 12.54	0.06$^{\mu}$
Number of males	34 (63.4)	33 (72.4)	24 (68.2)	0.68*
Diabetic patients	21 (35)	21 (37.8)	21 (55.4)	0.16*
High BP	29 (50.7)	33 (69.8)	21 (54.3)	0.13*
Smokers	21 (34.5)	16 (33.7)	18 (47.8)	0.34*
Alcoholic	11 (20)	11 (24.0)	12 (32.3)	0.43*
History of CAD	2 (4)	1.0 (2.1)	3.0 (7.3)	0.16*
Dyslipidemia patients	6 (11)	5 (12.1)	6 (12)	0.98*
Creatinine level	1.02 ±0.47	1.026 ± 0.32	1.01 ± 0.32	0.92$^{\mu}$
LDL	142.39 ± 38.55	133.86 ±40.73	134.81 ±38.96	0.73$^{\mu}$
LVEF	38.65 ± 15.38	39.45 ± 12.98	38.26 ± 12.01	0.74$^{\mu}$
White blood cells	9688.82 ±3278	9961 ±3283	10252 ± 3134	0.72$^{\mu}$
No. of neutrophils	5860.38	6667.26	7278.42	0.0001*
No. of lymphocytes	2685.23	2363.52	1891	0.0012*
NLR	2.25 ±1.266	3.03 ±1.52	4.734 ±2.061	0.0001μ
Aspirin usage	17 (3.02)	17 (35.7)	16 (42.8)	0.42*
Statin usage	17 (3.02)	17 (35.7)	16 (42.8)	0.52*
Blocker of B	12 (18.9)	12 (23.4)	14 (36.8)	0.06*
ACEIs	6 (12.3)	11 (20)	12 (32.3)	0.026

After the regression analysis, it was predicted that diabetes, high blood pressure, and the other symptoms involved in high blood pressure. These factors are considered markers for the identification of syntax levels. In these parameters, NLR is considered the strongest marker of the CAD initiation. When analysis of white blood cells and their other sub types was done, it was predicted that the AUC (Area under the curve) was high for the NLR. So NLR is considered as a suitable marker because of its high sensitivity and specificity. In the table below all the results are represented.

Table 2: ROC analysis of given characteristics.

Parameters	AUC	CI of 95 %	Value of P
White blood cells	0.529	0.42 – 0.62	0.45
No. of neutrophils	0.789	0.73 – 0.863	More than 0.001
No. of lymphocytes	0.796	0.765 -0.87	More than 0.001
NLR	0.866	0.724 -0.86	More than 0.001

DISCUSSION

This research work emphasizes the importance of NLR for the prediction of CAD. The severity level of the disease can be calculated by the score of SYNTAX. The SYNTAX score can be calculated with the help of different symptoms in patients. The intensity of the symptoms also varies with the age group. The patients who had coronary artery angiography changes have a high score of SYNTAX.[11,12] The severity of the disease, as well as its prediction, can be efficiently done by measuring the level of NLR. The NLR is considered an efficient biomarker for the identification of the disease. This method has high specificity as well as high sensitivity.

In the case of atherogenesis, there is an active process of inflammation along with dysfunction of lipid infiltration. A number of studies have been done to find out the particular biomarker for the identification of the disease. The white blood cells count within the body is considered a biomarker of different cardiovascular diseases but it does not state about the severity of the disease. [12] Apart from white blood cells count, neutrophils and lymphocytes ratio also alter in some cardiovascular diseases[13]. The concentration or average counting of the subtypes varies at different SYNTAX levels. Therefore, the ratio of neutrophils to lymphocytes can be used to calculate the inflammatory processes of coronary artery disease. In case of a high value of the ratio, it is suggested that inflammation of the coronary artery is at advanced stage.

When previous studies were considered, it was suggested that the level of white blood cells did not vary in different disease levels despite the fact that, the total number of white blood cells is much higher in the case of intermediate SYNTAX levels[14]. Therefore, by the following study, it was suggested the following merits for the High SYNTAX level of the disease. For the higher level, there should be higher values of NLR as well as a high value of neutrophils and a low value of lymphocytes. This statement suggested that, the NLR level have a positive correlation with the level of neutrophils and a negative correlation with the level of lymphocytes[15]. All of these changes lead to the higher level of disease as well. Moreover, it can also be predicted that the level of neutrophils and NLR is much higher in the CAD of old age patients and lymphocytes reduced in those patients.

Therefore, NLR is considered as the strongest bio marker of the coronary artery disease. When all the variable parameters

were considered the value of NLR higher than 2.00 predict the coronary artery disease. This method confirmations that for the CAD sensitivity is about 96 % and specificity is 85 %. The sensitivity of the NLR was calculated by the ROC analysis which was higher than 0.8 indicates the higher sensitivity. This study was compared with the other studies narrated in the literature[16]. The comparison with the similar type of studies suggested the similar results that strongly gives validation about this study. However, the study that was performed in the china have cut off value for NLR was 2.03 with AUC value 0.63. Their study suggested the 63 % sensitivity of the NLR for the determination of inflammatory disease. Another study was done by medical staff of Turkey, their results also suggested the sensitivity of NLR for the detection of CAD is 68 %. However, in all the cases, the number of neutrophils were higher and number of lymphocytes were less in severe patients of CAD[17,18].

The limitation of this study is the very small sample size. All of these samples were not so versatile, they all are collected from the patients of a single hospital. All the given population of area was not included in this study. All the details about every patients was not confirmed. Some patients also given arbitrary information about some parameters[19]. The research team did not observe and estimate the particular factors involve in the initiation of the disease. Also the other biomarkers were not compared with the NLR biomarker. There was need to study the risk factors involve in the coronary artery disease, which also play their role in the inflammation of other regions of cardiovascular system[20-21].

CONCLUSION

For the prediction of CAD, the ratio of neutrophils to lymphocytes can be considered. By the calculation of this ratio, it is easy to highlight the correlation between CAD and severity level.

NLR is well-thought-out as a strong marker after this research, it gives the most probable cut-off value for the indication of disease along with severity level. The sensitivity (96 %) and specificity (85 %) of this method are also high.

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