

Diagnosis and Prognosis of Cardiovascular Disease by Inflammatory Markers (Neutrophil Lymphocyte Ratio and Platelet Lymphocyte Ratio)

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Abstract:- Cardiovascular disease (CVD) defined as class of diseases that involve the heart or blood vessels. CVD is a term for several linked pathologies, commonly defined as coronary heart disease (CHD), cerebrovascular disease, peripheral arterial disease, rheumatic and congenital heart diseases and venous thromboembolism. Cardiovascular diseases are most popular common chronic disease. The total white blood cell count (WBC) and its subtypes, neutrophil to lymphocyte (N/L) ratio, can be used as an indicator of systemic inflammation. The N/L ratio has been demonstrated to have the greatest predictive power of death, cardiac disease and other complications. Elevated N/L ratio is an independent predictor of long-term inflammation can be measured by using a variety of biochemical and hematological markers. Although many specific biomarkers have been identified, most of which are time consuming and expensive. Recent evidence indicated that the ratio of sub types of blood cells have a significant prognostic value for cardiovascular disease. This study to evaluate Neutrophil-Lymphocyte ratio and platelet lymphocyte ratio among Sudanese cardiovascular disease patients. This study included 100 CVD patients and 100 controls without CVD. The NLR and the PLR were calculated as the ratio of neutrophil count to lymphocyte count and as the ratio of platelet count to lymphocyte count, respectively. ANOVA test was used in bivariate analysis to assess the factors affecting NLR and PLR. NLR was significantly higher in CVD patients when compared to controls (5.6 ± 3.3 vs. 1.7 ± 0.8 ; $P = 0.000$). Also CVD patients showed significantly higher value of PLR when compared to control group (162.3 ± 83.2 vs. 98.4 ± 28.1 ; $P = 0.000$). Moreover, both parameters (NLR & PLR) were significantly high in males CVD patients and non-STEMI CVD subtype ($P < 0.05$). In this study, NLR and PLR, simple inflammatory marker, can be used as an auxiliary parameter for predicting the diagnosis of CVD. And also, they can provide an additional level of risk stratification in patients with CVD.

Keyword:- Cardiovascular Disease, Platelet Lymphocyte Ratio And Neutrophil-Lymphocyte Ratio.

I. INTRODUCTION

Cardiovascular disease comprised of coronary artery diseases (such as angina and myocardial infarction)¹, heart failure, stroke, hypertensive heart disease and rheumatic heart disease ,

International CVD accounts for 31% of mortality and the majority of this in the form of coronary heart disease and cerebrovascular accident². CVD is becoming the main cause of morbidity and mortality in the world³. CVD often accompany with leukocytosis and it is thought to be associated with short term morbidity and mortality. The neutrophil –lymphocyte ratio represent the balance between neutrophil and lymphocyte levels in the body and indicators of systemic inflammation⁴. Several clinical trials have reported the association between increased absolute neutrophil count (ANC) in peripheral blood and short-term post-MI adverse outcomes and worse angiographic findings also the value of monocyte count in predicting heart failure following MI. NLR may also reflect the myocardial remodeling responses after reperfusion injury⁴. In a study that investigated the relation between changes in CBC parameters and inflammation, a large increase in neutrophil counts and a pronounced decrease in monocyte and lymphocyte counts were observed⁵; the PLR has been presented as a potential indicator to detect excess thrombotic activity and inflammation in oncologic and cardiac disorders^{6 and 7}. Risk Factor of cardiovascular diseases may be some of these or all : Genetics may be due to Multiple single nucleotide polymorphisms (SNP) have been found to be associated with cardiovascular disease in genetic association studies, but usually their individual influence is tiny, and genetic denoting to cardiovascular disease are poorly studied⁸, Age is the most crucial risk factor in occurring cardiovascular or heart diseases, with approximately a tripling of risk with each decade of life⁹ And Gender (Women develop heart disease more than men , also The reason for this difference among genders is not fully understood. Sex hormones are likely to be involved in the relative protection from cardiovascular disease noted in women before menopause¹⁰. Recent evidence indicated that the ratio of sub types of blood cells have a significant prognostic value for cardiovascular disease. Elevated levels of neutrophil lymphocyte ratio (NLR) were also found associated with poor survival of patients undergoing coronary artery bypass graft¹¹ Systemic inflammation can

be measured by using a variety of biochemical and hematological markers^{12and 13}. platelet to lymphocyte ratio (PLR), seemed to be a potential indicator in CVD prognosis. Recently, the prognostic importance of PLR has been investigated by several studies⁴.

II. MATERIALS AND METHODS

This study is cross-sectional study, designed to measure the NLR\PLR as a markers for systemic inflammation in CVD patients. Samples were collected randomly from patients in Sudan Centre for Heart Care and Almoalim Medical City at Khartoum state, during the period from August-December 2018. CBC (Sysmex XP-300) were performed for laboratory investigation, also questionnaire was conducted in this study. Hundred samples from patients diagnosed with cardiovascular diseases (regarding of age, gender and type of disease and exclude Patients who are diabetic, renal disease patients and diseases other than cardiovascular diseases) and other 100 samples from normal healthy individuals were used as control. NLR was calculated as the ratio of neutrophil count to lymphocyte count, and PLR was calculated as the ratio of platelet count to lymphocyte count.

III. RESULTS

The study population consisted of 100 patients as with CVD as case group and 100 individuals without CVD as control group. The majority of the case group 52(52%) found in age group more than 60 years, and the majority of control group 45(45%) found in age group from 40-60 years (P= 0.000)

In the gender of the study population, the majority of the case group 65 (65%) were males while near to one-half (51%) of control group were females (P= 0.016). Concerning the types of CVD among the case group, 70(70%) had STEMI, 15(15%) had non-STEMI and also 15(15%) had unstable angina.

Regarding to the NLR, the case group showed significantly higher value of NLR when compared to control group (5.6±3.3 vs. 1.7±0.8; P= 0.000) (figure 2)

Likewise, the case group showed significantly higher value of PLR when compared to control group (162.3±83.2 vs. 98.4±28.1; P= 0.000) (figure 3)

As illustrated in table 3, the age of the CVD patient showed insignificant association with both NLR (P= 0.729) and PLR (0.40) The correlation between NLR and PLR with the gender of CVD patients showed that, NLR was significant higher in male (6.7±4.7) than female (3.9±2.4), the difference was statistically significant (P= 0.008). Also PLR was significant higher in male (182.5±62.2) than female (156.6±67.4), and the difference was statistically significant (P= 0.013) (table 4).

Concerning to the correlation between NLR and PLR with the type of CVD patients, the highest value of NLR was found in non-STEMI patients (6.8±5.9) and lowest value in the patients with unstable angina (2.9±1.8), the correlation was statistically significant (P= 0.003). Similarly, the highest value of PLR was found in non-STEMI patients (219.0±126.1) and lowest value in the patients with unstable angina (147.3±68.3), the correlation was statistically significant (P= 0.007) (table 5).

In the comparison of CBC findings among the study groups, the mean value of hemoglobin for case group was 10.6 g/dl ± 1.6 and control group was 14.4 mg/dl ± 2.5 (P= 0.000). The mean value of PCV for case group was 32.4% ± 5.3 and 40.3 % ± 1.8 for control group, (P= 0.000). The mean value of WBCs count for case group was 8.9x10³/μL ± 1.8 and 5.4x10³/μL ± 1.0 for control group, and the difference was statically significant (P= 0.000). The mean value of platelets count for case group was 316x10³/μL ± 92.2 and 286x10³/μL ± 50.4 for control group, (P= 0.000). The mean value of neutrophil count for case group was 6.8x10³/μL ± 1.5 and 2.7x10³/μL ± 0.9 for control group, (P= 0.000). The mean value of lymphocyte count for case group was 1.8x10³/μL ± 0.8 and 2.0x10³/μL ± 0.5 for control group, (P= 0.001) (table 6).

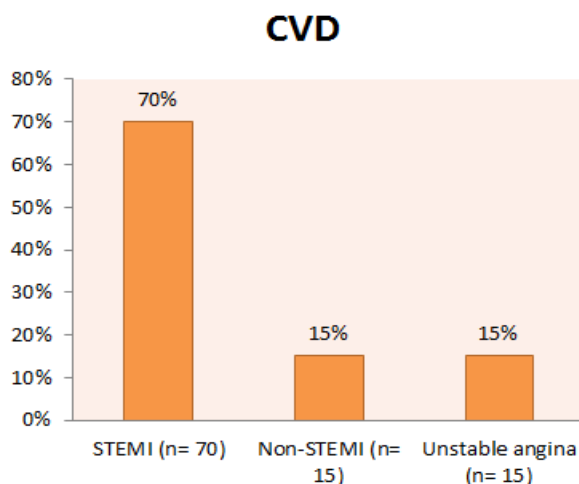


Fig 1:- The types of CVD among case group (N= 100)

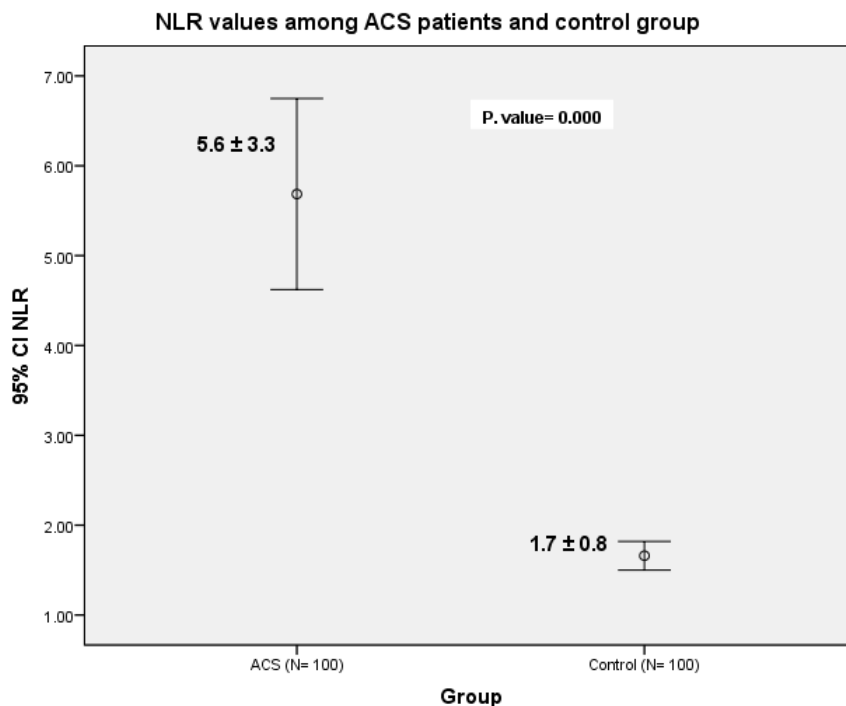


Fig 2:- The comparison of NLR values among the case and control groups

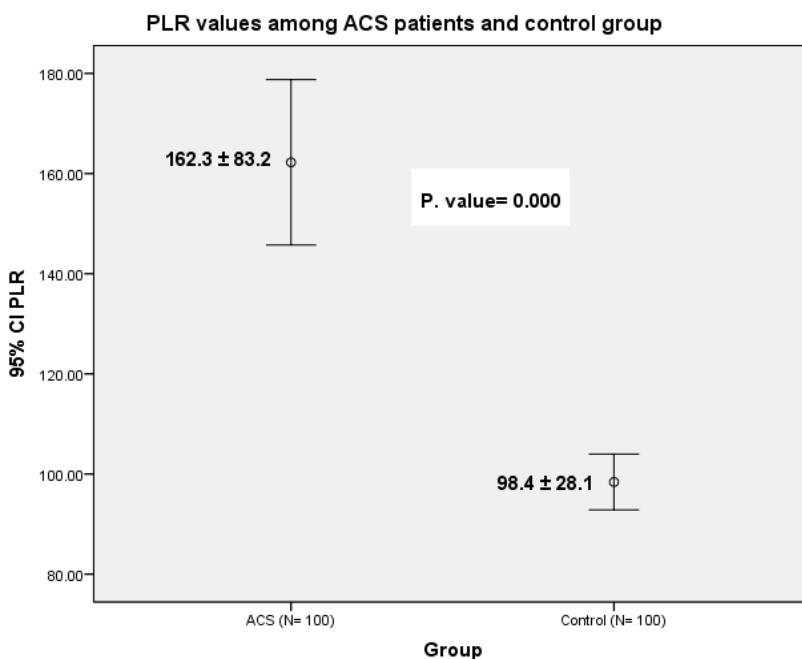


Fig 3:- The comparison of PLR values among the case and control groups

	Age (Years)			P. value
	<40	40-60	>60	
NLR	5.2±1.2	5.4±4.4	6.5±5.6	0.729
PLR	129.7±58.5	136.3±65.4	141.7±94.6	0.40

Table 3: The mean ± SD of NLR and PLR regarding the age of the case group (N= 100)

	Gender		P. value
	Male	Female	
NLR	6.7±4.7	3.9±2.4	0.008*
PLR	182.5±62.2	156.6±67.4	0.013*

Table 4: The mean ± SD of NLR and PLR regarding the gender of the case group (N= 100)

	CVD types			P. value
	STEMI	Non-STEMI	Unstable angina	
NLR	3.0±0.9	6.8±5.9	2.9±1.8	0.003*
PLR	175.0±73.1	219.0±126.1	147.3±68.3	0.007*

Table 5: The mean of NLR and PLR regarding the CVD types among the case group (N= 100)

CBC	Group		P. value
	CVD (N= 100) Mean (SD)	Control (N= 100) Mean (SD)	
Hemoglobin (g/dl)	10.6(1.6)	14.4(2.5)	0.000*
PCV (%)	32.4(5.3)	40.3(1.8)	0.000*
WBCs (10 ³ /μL)	8.9(1.9)	5.4(1.0)	0.000*
Platelets (10 ³ /μL)	316(92.2)	286(50.4)	0.000*
Neut. (10 ³ /μL)	6.8(1.5)	2.7(0.9)	0.000*
Lymph. (10 ³ /μL)	1.8(0.8)	2.0(0.5)	0.001*

Table 6: The comparison of CBC findings among the case and control groups

IV. DISCUSSION

The study showed that, NLR was significantly higher among CVD patients than in normal individuals. There were significant reduction in lymphocytes and elevation in neutrophils among CVD patients ($p < 0.05$), consequently, these was reflected in the NLR was significantly difference. Our findings go in same line with several studies^{14 and 15}.

PLR has been proposed to be a pro-thrombotic and inflammatory marker (Wang, *et al.*, 2013). In the present study, PLR was significantly higher among CVD patients than in normal individuals. There were significant reduction in lymphocytes and elevation in platelets count among CVD patients ($p < 0.05$), these was reflected in the PLR was significantly difference. Our findings consistence with many of literatures^{16,17, 18 and 19}.

The present results show that there were a significant increase in platelet counts among CVD group in contrast to normal individuals. Increased platelet counts and platelet activation have an important role in thrombus formation and the progression of atherosclerosis. The change of platelets count responding to abnormal vessel walls, can result in arterial thrombosis. Furthermore, increased platelets counts have been demonstrated to promote inflammation and lead to a more aggressive course of active atherosclerosis^{20and21}. A previous study has determined that higher baseline platelet counts may be associated with CVD events²². Moreover, reported that, Platelet activation is also significantly associated with platelet counts²³, The current results in agreement with Li. *et al* (2014) who mentioned that Inappropriate platelet activation is an important pathogenic component of thrombosis at the site of vascular injury and leads to CVD mainly ACS.

The present study demonstrated that, the lymphocytes count was significantly reduced in CVD patients when compared to normal participants. A low blood lymphocyte count has been shown to be related with worse cardiovascular consequences in patients with CAD and chronic heart failure. This can be justified by in cases of sustained inflammation, lymphocyte counts decrease due to increased lymphocyte apoptosis. The present data in accordance with previous studies have demonstrated that relative and absolute lymphocyte concentrations are lower in patients who suffered from CVD^{24 and 25}.

Although the difference was not significant ($P > 0.05$) the older CVD patients tended to have the highest value of NLR and PLR. The result is disagreement with who reported that patients with higher NLRs were significantly older ($P = 0.001$) and tended to have a lower frequency of previous cardiovascular disease²⁶.

V. CONCLUSION

The present study concluded that, the NLR and the PLR of CVD patients were higher than those of the normal individuals. Moreover, both parameters (NLR and PLR) were significantly high in male non-STEMI CVD subtypes.

Neutrophil-lymphocyte ratio (NLR), a new addition to the long list of markers, is an inexpensive, easy to obtain, widely available marker of inflammation, which can aid in the risk stratification of patients with various cardiovascular diseases in addition to the traditionally used markers.

NLR and PLR, is a simple indicator, can initially introduced into clinical practice to improve the diagnosis and prognosis of CVD.

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