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Comparison of Preangiography Haemogram-Derived Inflammatory Indices (HDII) Between Non-ST-Elevation Acute Coronary Syndrome (NSTE-ACS) and Chronic Coronary Syndrome (CCS) Patients

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Abstract *- This study aimed to compare the preangiography Haemogram-Derived Inflammatory Indices (HDII), such as neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), and mean platelet volume (MPV) between patients with Non-ST-Elevation Acute Coronary Syndrome (NSTE-ACS) and Chronic Coronary Syndrome (CCS) undergoing Percutaneous Coronary Intervention (PCI), and investigate the correlation of above-mentioned Indices with clinical and angiographic risks evaluated by the GRACE (Global Registry of Acute Coronary Events. Version 2) admission-6-month mortality and the SYNTAX risk scores for patients with ACS.* ***Methods.*** *All essential laboratory tests and Haemogram-Derived Inflammatory Indices (HDII) calculations were performed during the first hour of admission, before percutaneous coronary intervention (PCI) in 100 patients with Non-ST-Elevation Acute Coronary Syndrome (NSTE-ACS) and 91 patients with Chronic Coronary Syndrome (CCS). The clinical and angiographic risks were assessed by the GRACE and SYNTAX scores, respectively, in the group of patients with NSTE-ACS.* ***Results.*** *Neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), and platelet-to-lymphocyte ratio (PLR) were significantly higher in patients with Non-ST-Elevation Acute Coronary Syndrome (9.79 ± 6.33 vs 2.61 ± 1.39, 0.80 ± 0.58 vs 0.36 ± 0.19, and 262.2 ± 166.2 vs 141.0 ± 66.8, respectively. p<0.0001). The GRACE risk score was 1.4-times higher in the group with a high NLR quantile (7.050±0.1929 95% CI [6.667 to 7.433]) compared to those with low NLR (4.985±0.1708 95% CI [4.646 to 5.324], p<0.0001). The SYNTAX score was 1.6-times higher in the group with a high NLR quantile (1.414±0.0934 95% CI [1.229 to 1.600] vs 0.884±0.0541 95% CI [0.776 to 0.991], p<0.0001).* ***Conclusions.*** *According to the results of the present study, elevated periprocedural Haemogram-Derived Inflammatory Indices (HDII) indicate a more intense inflammatory and prothrombotic state in patients with Non-ST-Elevation Acute Coronary Syndrome (NSTE-ACS) compared to patients with Chronic Coronary Syndrome (CCS), but only neutrophil-to-lymphocyte ratio (NLR) is positively and significantly correlated with clinical and angiographic risks measured by GRACE and SYNTAX tools, respectively.*

Keywords *- Chronic Coronary Syndrome (CCS); GRACE risk score; Haemogram-Derived Inflammatory Indices (HDII); Mean platelet volume (MPV); Monocyte-to-lymphocyte ratio (MLR); Neutrophil-to-lymphocyte ratio (NLR); Non-ST-Elevation Acute Coronary Syndrome (NSTE-ACS); Platelet-to-lymphocyte ratio (PLR); SYNTAX risk score.*

I. INTRODUCTION

Cardiovascular diseases (CVDs) have remained the world's biggest killer, responsible for 32% of all global deaths.[1] The role of inflammatory markers in the pathogenesis of cardiovascular diseases has been studied extensively in the last decade.[2-21]

There has been a recent focus on inexpensive and easily accessible Haemogram-Derived Inflammatory Indices (neutrophil-to-lymphocyte ratio [NLR], monocyte-to-lymphocyte ratio [MLR], platelet-to-lymphocyte ratio [PLR], and mean platelet volume [MPV]) as a strong predictor of cardiovascular risk.[2,22-29]

A. Neutrophil-to-lymphocyte ratio (NLR)

NLR is a ratio of neutrophils (Ns), which are responsible for active nonspecific inflammation and lymphocytes (Ls), which are markers of general health and physiological stress (in case of lymphopenia).[30] So, NLR integrates different immune pathways and is more predictive than either parameter alone.[2]

Elevated NLR as a marker of underlying acute inflammation indicates thrombus formation in case of myocardial infarction.[31,32] The highest NLR tercile has a high specificity for Acute Coronary Syndrome (ACS) compared with the lowest NLR tercile and is associated with poor outcomes.[31,33] According Tamhane et al., in ACS patients with high NLR compared with those with low NLR was reported significantly higher in-hospital mortality (8.5 vs 1.8%; p=0.013) and 6-month mortality rates (11.5 vs 2.5%; p<0.001).[34]

Recent studies indicate that NLR is an independent predictor of long-term mortality in CAD after percutaneous coronary intervention (PCI).[35] According to Poludasu et al., during median follow-up to 3.6 years in patients undergoing PCI, the mortality rate was significantly higher (31%) in the group with preprocedural NLR ≥3.5 compared with the group of periprocedural NLR<3.5 (p<0.001).[36]

Elevated NLR is an independent predictor of mortality in stable coronary artery disease (CAD), as well as its development and progression.[28,29,37-39] During the 3-year follow-up period, high NLR was associated with significantly

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increased cardiac death and nonfatal myocardial infarction in patients with stable CAD.[29]

Among the patients with CAD requiring repeat coronary angiography the progression rate of atherosclerosis was significantly higher in patients with high NLR compared with the nonprogressive group (56 vs 39%; p = 0.03).[37]

B. Monocyte-to-lymphocyte ratio (MLR)

Atherosclerosis is a chronic inflammatory process characterized by the infiltration of immune cells, including monocyte, neutrophils, and lymphocyte.40 Accumulation of monocytes in the arterial wall leads to the formation and progression of atherosclerosis by secretion of proinflammatory cytokines, matrix metalloproteinases, reactive oxidative species, and amplification of the inflammation process.[41] Monocyte-to-lymphocyte ratio (MLR), a widely used marker for the prognosis of tuberculosis, oncologic and autoimmune diseases, has attracted attention for its application to cardiovascular disease.[14]

High monocytes and low lymphocytes, as a hallmark of chronic inflammation, were confirmed to be independent risk indicators of cardiovascular diseases.[42] Hanhua et al., reported that monocyte-to-lymphocyte ratio (MLR) was an independent risk factor of CAD (OR: 3.94, 95% CI 1.20 to 12.95) and a predictor of the lesion severity (OR: 2.05, 95% CI:1.15 to 3.66).[9]

Feng-Hua Song et al., studied a correlation between the monocyte-to-lymphocyte ratio and long-term prognosis in patients with coronary artery disease (CAD) after percutaneous coronary intervention (PCI).[12] High MLR group was associated with significantly increased all-cause mortality (ACM) [HR=1.366, 95% CI 1.366-3.650, p=0.001] and cardiac mortality (CM) [HR=2.379, 95% CI 1.611 to 3,511, p<0.001] compared to the low MLR group. High MLR was also highly associated with major adverse cardiovascular events (MACEs) [HR=1.227, 95% CI 1.003 to 1.500, p=0.047] in patients with CAD undergoing PCI.[12]

Based on the results investigation of relationship of MLR with the clinical outcomes in non-ST-elevation myocardial infarction (NSTEMI) patients, had been shown that MLR was an independent predictor for in-hospital MACE [aOR=2.891, 95% CI 1.265 to 8.354, p=0.026] and long-term MACE [aHR=1.793, 95% CI 1.169 to 2.515, p=0.012]. MLR had been better performance to reflect the severity of the coronary lesion and MACE prediction than NLR.[14] In contrast to these results, Zeyuan Fan et al., concluded that elevated MLR and NLR were independent predictors of long-term MACE in patients with NSTEMI. The authors recommended both of them as better predictors of long-term MACE.[15]

C. Platelet-to-lymphocyte ratio (PLR)

Platelets as sources of proinflammatory and prothrombotic factors play a crucial role in the pathophysiology of ACS.[43,44] Platelet-to-lymphocyte ratio (PLR), a recently emerged potential inflammatory biomarker, is significantly associated with atherosclerotic coronary artery disease (CAD).[20] PLR is a novel inflammatory marker and an important prognostic factor of cardiovascular diseases.[19,45-49] In the study conducted by Oylumlu et al., in 538 patients with the acute coronary syndrome (ACS), a high level of PLR was an independent predictor of 5-year mortality [OR=1.005, 95% CI 1.001 to 1.008), p=0.004].[19]

PLR is associated with the severity of coronary artery disease (CAD) and major adverse cardiovascular events (MACE).[20] According to Xue-Ting et al., PLR was an independent risk factor of in-hospital MACEs [OR=1.012, 95% CI 1.006 to 1.018), p<0.001] and severe CAD assessed by the Gensini score [OR=1.004, 95% CI 1.002 to 1.009), p=0.042].[20]

A meta-analysis of ten studies involving 8932 patients with Acute Coronary Syndrome (ACS) demonstrated that elevated PLR levels had a significantly higher risk of in-hospital MACE [RR=2.24, 95% CI 1.81 to 2.77] and long-term adverse outcomes [RR=2.32, 95% CI 1.64 to 3.28].[21]

The study conducted by Asoğlu et al., has shown that elevated PLR is associated with angiographic no-reflow (NR) in patients with None-ST Segment Elevation Acute Myocardial Infarction (NSTEMI) undergoing Primary Coronary Intervention (PCI).[50] The PLR was significantly higher in NR than in patients with normal reflow [108.6 (14.6-511.3) vs. 91.7 (17.2-225.3), p=0.01]. Also, there was a positive and strong correlation between platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR) (r = 0.68, p< 0.001).[50]

D. Mean platelet volume (MPV)

The platelets are key players in atherothrombosis and unstable coronary syndromes through the expression of large numbers of mediators.[17,51-52] Platelets are heterogeneous in size and density, so Mean Platelet Volume (MPV) is commonly used as a potential marker of platelet reactivity. The large platelets have greater prothrombotic potential, therefore elevated MPV is associated with increased thromboxane synthesis, expression of adhesion molecules, and platelet aggregation.[54-56]

Elevated Mean Platelet Volume (MPV) widely observed in patients with hypertension, dyslipidemia, diabetes mellitus, obesity, and smoking marker for the prognosis of tuberculosis, oncologic and autoimmune diseases, has attracted more and more attention as a novel biomarker of cardiovascular diseases.[57-61]

A systematic review and meta-analysis of 16 cross-sectional studies involving 2809 patients with acute myocardial infarction (AMI) concluded that elevated MPV is associated with AMI [mean difference 0.92 fL, 95% CI 0.67 to 1.16), p<0.001], postinfarction mortality [11.5% vs. 7.1%, OR=1.65, 95% CI 1.12 to 2.52), P=0.012], and restenosis following coronary intervention [mean difference 0.98 fL, 95% CI 0.74 to 1.21), p<0.001].[17]

According to *Slavka et al.*, there is a strong relationship between elevated MPV and death due to ischemic heart disease. The risk of mortality increased from 1.2 (8.71 to 9.60 fL category) to 1.8 in the highest category of MPV (≥11.01 fL).[18]

This study aimed to (i) compare the preangiography Haemogram-Derived Inflammatory Indices (HDII), such as

neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), and mean platelet volume (MPV) between patients with non-ST-elevation Acute Coronary Syndrome (NSTE-ACS) and Chronic Coronary Syndrome (CCS) undergoing Percutaneous Coronary Intervention (PCI), and (ii) investigate the correlation of HDII with clinical and angiographic risk evaluated by the GRACE (Global Registry of Acute Coronary Events. Version 2) admission-6-month mortality and the SYNTAX risk scores for patients with the acute coronary syndrome.

II. Materials and Methods

A. Study patients

The study sample consisted of 191 patients who were divided into two groups: Group 1: 100 patients with non-ST-elevation Acute Coronary Syndrome (NSTE-ASC) and Group 2: 91 patients with Chronic Coronary Syndrome (CCS) admitted to the coronary care unit (CCU) of LTD Clinic-LJ (Kutaisi, Georgia) between April 2018 and June 2019, and underwent successful primary percutaneous coronary intervention (PCI). In patients with Chronic Coronary Syndrome (CCS) invasive coronary angiography with revascularization was performed in case of high clinical likelihood of obstructive coronary artery disease (OCAD) and severe symptoms refractory to optimal medical treatment, or typical angina at a low level of exercise and clinical prediction of high-risk of events, or left ventricular dysfunction suggestive of CAD.

Patients with a history of coronary revascularization, or with hemodynamically compromised severe myocardial infarction; those recovering from cardiopulmonary arrest, decompensated heart failure; and those with valvular heart disease, cardiomyopathy, severe supraventricular/ventricular arrhythmias (including atrial fibrillation) and conductivity disturbances, end-stage renal disease (ESRD), chronic inflammatory conditions, active cancer, type 1 diabetes mellitus (DM) or decompensated type 2 diabetes mellitus (DM); pregnancy; those on hormone replacement therapy (HRT) or oral contraceptive assumption were excluded from the study. No corrections or changes had been made in the ongoing pharmacotherapy of patients.

The study was approved by the ethics committee (EC) of Tbilisi State Medical University (TSMU) and the local EC of LTD Clinic-LJ and written informed consent was provided by each study participant.

B. The measurements

All essential laboratory tests were performed during the first hour of admission, before percutaneous coronary intervention (PCI). Total hemogram and differential leukocyte counts were measured by an automated hematology analyzer (BK-6310 5-Part Auto Hematology Analyzer. BIOBASE. China).

The admission-6-month mortality for patients with acute coronary syndrome was evaluated by the GRACE (Global Registry of Acute Coronary Events) ACS Risk and Mortality Calculator (version 2.0) with the following score interpretation (Table 1).[62-65]

TABLE 1. GRACE ACS risk and mortality score interpretation

GRACE score range	Mortality Risk
0-87	0-2%
88-128	3-10%
129-149	10-20%
150-173	20-30%
174-182	40%
183-190	50%
191-199	60%
200-207	70%
208-218	80%
219-284	90%
≥ 285	99%

The complexity of coronary artery disease was determined by the SYNTAX score - angiographic grading tool with the following variables: dominance, number of lesions, segments involved per lesion and presence of chronic total occlusions, trifurcation, bifurcation, aorto-ostial lesion, tortuosity, calcification, and presence of thrombus, diffuse disease and/or lesion of small vessels. According to these variables, a separate angiographic risk score was calculated for each lesion.[66]

C. Statistical analysis

The data were analyzed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). To compare periprocedural Haemogram-Derived Inflammatory Indices (HDII) between two groups, nonparametric tests for independent samples were used. Descriptive statistics, variable frequency analysis, independent-samples T-test, and linear and quantile regression analysis were also used. A statistical significance was taken as a 2-tailed $p<0.05$.

III. Results

A. Study population characteristics

There was no statistically significant difference between the study population characteristics, such as age, male gender, BMI, hypertension, dyslipidemia, ongoing smoking, type 2 DM, and medications, such as beta-blockers, calcium channel blockers, ACEIs or ARBs, and statins. Nitrate consumption was much higher ($p<0.0001$) in patients with Chronic Coronary Syndrome (Table 2).

B. Periprocedural Haemogram-Derived Inflammatory Indices (HDII)

The enrolled patients' periprocedural Haemgram-Derived Inflammatory Indices (HDII) measured in the comparator groups were as follows: neutrophil-to-lymphocyte ratio (NLR): 9.74 ± 6.36 in patients with Non-ST Elevation Acute Coronary Syndrome (Group 1: NSTE-ACS) and 2.61 ± 1.39 ($p<0.0001$) in patients with Chronic Coronary Syndrome (Group 2: CCS). Monocyte-to-lymphocyte ratio (MLR) in Group 1 and Group 2 were 0.80 ± 0.58 and 0.36 ± 0.19, respectively ($p<0.0001$). Platelet-to-lymphocyte ratio (PLR) was 262.2 ± 166.2 in patients with NSTE-ACS and 141.0 ± 66.82 in patients with CCS ($p<0.0001$). Mean platelet volume

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(MPV) was 9.52 ± 1.16 fL in Group 1 and 9.48 ± 1.20 fL in Group 2 with p=0.822 (Table 3).

TABLE 2. Characteristics of the study population

	Group 1 (Patients with ACS) n=100 (Mean ± SD)	Group 2 (Patients with CCS) n=91 (Mean ± SD)	P-value
Age (years)	51.8 ± 0.78	49.1 ± 1.02	0.236
Male gender, n (%)	74 (74)	52 (57)	0.874
BMI	27.76 ± 0.35	27.81 ± 0.36	0.924
Hypertension, n (%)	51 (51)	41 (45)	0.413
Dyslipidemia, n (%)	62 (62)	56 (61.5)	0.948
Smoking, n (%)	52 (52)	45 (49.5)	0.726
Type 2 DM, n (%)	44 (44)	38 (41.8)	0.755
BB, n (%)	31 (31)	27 (29.7)	0.842
CCB, n (%)	36 (36)	28 (30.8)	0.446
ACEIs/ARBs, n (%)	42 (42)	38 (41.8)	0.973
Statins, n (%)	42 (42)	45 (49.5)	0.238
Nitrates, n (%)	22 (22)	42 (46.2)	<0.0001*
Neutrophils, $x10^9$/L	9.56 ± 2.50	4.51 ± 1.47	<0.0001*
Monocytes, $x10^9$/L	0.83 ± 0.43	0.64 ± 0.21	<0.0001*
Lymphocytes, $x10^9$/L	1.28 ± 0.43	2.03 ± 0.85	<0.0001*
Platelets, $x10^9$/L	267.4 ± 101.5	249.3 ± 79.1	0.407

* Statistically significant difference; BMI: body mass index; BB: beta-blockers; CCB: calcium channel blockers; ACSEIs: angiotensin-converting enzyme inhibitors; ARBs: angiotensin receptor blockers.

TABLE 3. Periprocedural Haemogram-Derived Inflammatory Indices (HDII) in patients with Non-ST Elevation Acute Coronary Syndrome (NSTE-ACS) and Chronic Coronary Syndrome (CCS) [Mean ± SD)

	Group 1 Patients with Non-ST Elevation Acute Coronary Syndrome (NSTE-ACS)	Group 2 Patients with Chronic Coronary Syndrome (CCS)	p-value
NLR	9.79 ± 6.33	2.61 ± 1.39	<0.0001
MLR	0.80 ± 0.58	0.36 ± 0.19	<0.0001
PLR	262.2 ± 166.2	141.0 ± 66.8	<0.0001
MPV	9.52 ± 1.16	9.48 ± 1.20	0.941

NLR: Neutrophil-to-lymphocyte ratio; MLR: Monocyte-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; MPV: Mean platelet volume.

Linear regression and Pearson bivariate correlation analysis were performed in the group of patients with Non-ST Elevation Acute Coronary Syndrome (NSTE-ACS) between GRACE (Global Registry of Acute Coronary Events) ACS Risk and Mortality scores, and different periprocedural Haemogram-Derived Inflammatory Indices (HDII), such as neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), and mean platelet volume (MPV, fL), using Z-scores and Standardized Coefficients Beta (Table 4).

The same analysis was conducted with SYNTAX scores and the above-mentioned periprocedural Haemogram-Derived Indices (Table 5).

TABLE 4. Coefficients of Linear Regression and Pearson Bivariate Correlation analysis of Haemogram-Derived Inflammatory Indices (HDII) and GRACE score in patients with Non-ST Elevation Acute Coronary Syndrome (NSTE-ACS) [a]

Model	Unstandardized B / Standardized Coefficients Beta	Coefficients Std. Error	Sig.	Zero-order correlation
(Constant)	1.531E-16	0.037	1.000	
Zscore(NLR)	0.902 / 0.902	0.058	0.000*	0.930
Zscore(MLR)	0.083 / 0.083	0.044	0.063	0.571
Zscore(PLR)	-0.023 / -0.023	0.055	0.671	0.645
Zscore(MPV)	0.018 / 0.466	0.039	0.642	-0.02

*Statistically significant difference; a Dependent Variable: Zscore(GRACE); Zscore(NLR): Zscore of neutrophil-to-lymphocyte ratio; Zscore(MLR): Zscore of monocyte-to-lymphocyte ratio; Zscore(PLR): Zscore of platelet-to-lymphocyte ratio; Zscore(MPV): Zscore of mean platelet volume.

TABLE 5. Coefficients of Linear Regression and Pearson Bivariate Correlation analysis of Haemogram-Derived Inflammatory Indices (HDII) and SYNTAX score in patients with Non-ST Elevation Acute Coronary Syndrome (NSTE-ACS) [a]

Model	Unstandardized B / Standardized Coefficients Beta	Coefficients Std. Error	Sig.	Zero-order correlation
(Constant)	*6.483E-16*	*0.054*	*1.000*	
Zscore(NLR)	*0.704 / 0.704*	*0.086*	*0.000**	*0.835*
Zscore(MLR)	*0.177 / 0.177*	*0.065*	*0.008*	*0.584*
Zscore(PLR)	*-0.002 / -0.002*	*0.081*	*0.985*	*0.588*
Zscore(MPV)	*0.016 / 0.016*	*0.058*	*0.787*	*-0.015*

*Statistically significant difference; a Dependent Variable: Zscore(SYNTAX); Zscore(NLR): Zscore of neutrophil-to-lymphocyte ratio; Zscore(MLR): Zscore of monocyte-to-lymphocyte ratio; Zscore(PLR): Zscore of platelet-to-lymphocyte ratio; Zscore(MPV): Zscore of mean platelet volume.

The quantile regression analysis was performed in the group of patients with Non-ST Elevation Acute Coronary Syndrome (NSTE-ACS). The results of the analysis of the predictive relation between different quartiles of neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), mean platelet volume (MPV), and GRACE (Global Registry of Acute Coronary Events) and SYNTAX scores are shown in Tables 6 and 7, respectively.

IV. Discussion

Inflammation is a crucial player in the pathogenesis of cardiovascular disease. The role of inexpensive and easily accessible Haemogram-Derived Inflammatory Indices (HDII), such as neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), and mean platelet volume (MPV) has been studied extensively in the past decades.

The neutrophil-to-lymphocyte ratio (NLR) is the most studied inflammatory marker, as a strong cardiovascular risk predictor, in patients with Acute Coronary Syndrome (ACS). The prognostic role of rest markers [monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), and mean

The neutrophil-to-lymphocyte ratio (NLR) is the most studied inflammatory marker, as a strong cardiovascular risk predictor, in patients with Acute Coronary Syndrome (ACS). The prognostic role of rest markers (monocyte-to-lymphocyte ratio [MLR][9-15,27], platelet-to-lymphocyte ratio [PLR][7,8,17-21], and mean platelet volume [MPV] [45-61]), which have attracted

platelet volume (MPV)[7]], which have attracted attention for their application to cardiovascular disease, remain uncertain.

TABLE 6. The regression analysis of predictive relation between different quartiles of Haemogram-Derived Inflammatory Indices (HDII) and GRACE score in the group of patients with Non-ST Elevation Acute Coronary Syndrome (NSTE-ACS) [a,b]

Quantile=0.25				**95% CI**	
Parameter	**Coefficient**	**Std. Error**	**Sig**	**Lower Bound**	**Upper Bound**
(Intercept)	71.655	6.2737	0.000*	59.200	84.110
NLR	4.985	0.1708	0.000*	4.646	5.324
MLR	3.670	1.4173	0.011*	0.856	6.483
PLR	0.077	0.0062	0.226	-0.005	0.020
MPV	1.202	0.6239	0.057	-0.036	2.441
Quantile=0.50					
(Intercept)	75.787	6.9600	0.000*	61.970	89.605
NLR	6.171	0.1895	0.000*	5.795	6.547
MLR	1.576	1.5724	0.319	-1.545	4.698
PLR	-0.002	0.0068	0.796	-0.015	0.012
MPV	0.620	0.6921	0.373	-0.754	1.994
Quantile=0.75					
(Intercept)	84.245	7.0870	0.000*	70.175	98.314
NLR	7.050	0.1929	0.000*	6.667	7.433
MLR	-0.482	1.6011	0.764	-3.661	2.696
PLR	-0.008	0.0069	0.233	-0.022	0.005
MPV	-0.335	0.7047	0.636	-1.734	1.064

*Statistically significant difference; a Dependent Variable: GRACE; b Model: (Intercept). NLR, MLR, PLR, MPV; NLR: neutrophil-to-lymphocyte ratio; MLR: monocyte-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; MPV: mean platelet volume; CI: Confidence Interval.

TABLE 7. The regression analysis of predictive relation between different quartiles of Haemogram-Derived Inflammatory Indices (HDII) and SYNTAX score in the group of patients with Non-ST Elevation Acute Coronary Syndrome (NSTE-ACS) [a,b]

Quantile=0.25				**95% CI**	
Parameter	**Coefficient**	**Std. Error**	**Sig**	**Lower Bound**	**Upper Bound**
(Intercept)	0.930	1.9856	0.641	-3.012	4.872
NLR	0.884	0.0541	0.000*	0.776	0.991
MLR	2.120	0.4486	0.000*	1.230	3.011
PLR	0.000	0.0019	0.905	-0.004	0.004
MPV	0.351	0.1976	0.079	-0.041	0.743
Quantile=0.50					
(Intercept)	5.749	4.0527	0.159	-2.297	13.795
NLR	1.313	0.1103	0.000*	1.094	1.532
MLR	1.388	0.9156	0.133	-0.430	3.205
PLR	-0.005	0.0040	0.231	-0.013	0.003
MPV	-0.172	0.4030	0.671	-0.972	0.628
Quantile=0.75					
(Intercept)	1.429	3.4318	0.678	-5.384	8.242
NLR	1.414	0.0934	0.000*	1.229	1.600
MLR	0.739	0.7753	0.343	-0.800	2.278
PLR	0.003	0.0034	0.346	-0.003	0.010
MPV	0.274	0.3413	0.424	-0.404	0.951

*Statistically significant difference; a Dependent Variable: SYNTAX; b Model: (Intercept). NLR, MLR, PLR, MPV; NLR: neutrophil-to-lymphocyte ratio; MLR: monocyte-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; MPV: mean platelet volume; CI: Confidence Interval.

We aimed to (i) compare the periprocedural Haemogram-Derived Inflammatory Indices (HDII), such as neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), and mean platelet volume (MPV) between patients with non-ST-elevation Acute Coronary Syndrome (NSTE-ACS) and Chronic Coronary Syndrome (CCS) undergoing Percutaneous Coronary Intervention (PCI), and (ii) to investigate the correlation of above-mentioned Haemogram-Derived Inflammatory Indices (HDII) with the GRACE (Global Registry of Acute Coronary Events. Version 2) admission-6-month mortality and SYNTAX scores for patients with the acute coronary syndrome.

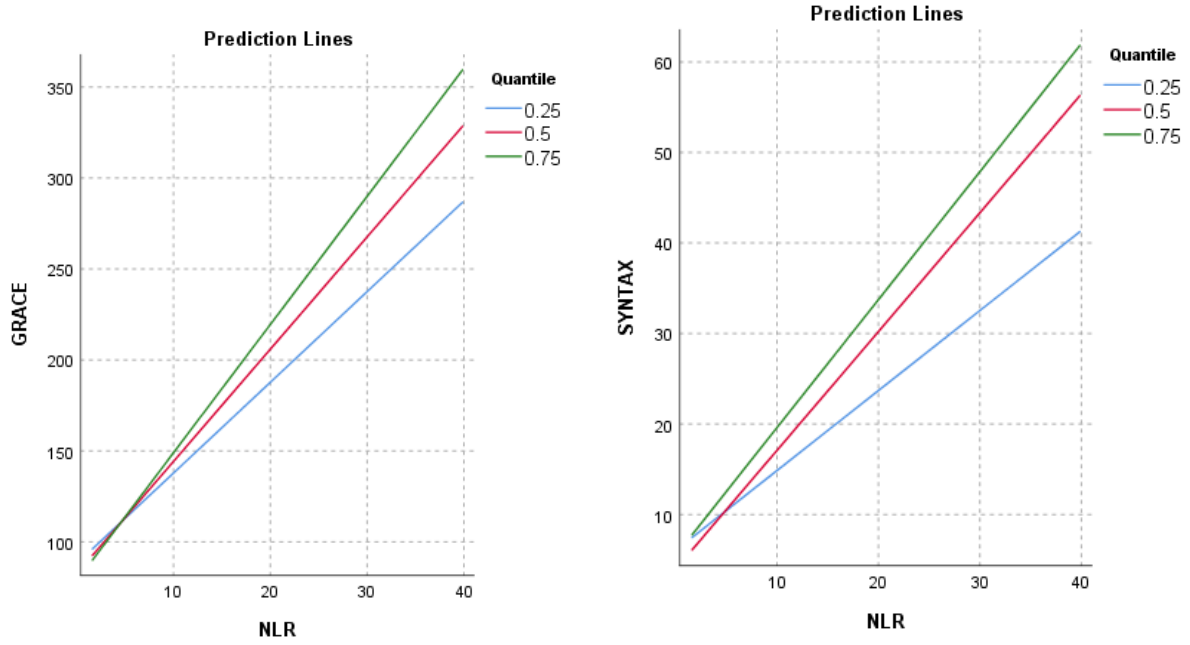
A total of 191 patients (100 patients with NSTE-ACS in Group 1, and 91 patients with CCS in Group 2) undergoing percutaneous coronary intervention (PCI) were included in the study. There were no statistically significant differences between the study population characteristics, except for nitrates consumption, which was much higher ($p<0.0001$) in patients with Chronic Coronary Syndrome. There were statistically significant differences in the absolute count of neutrophils, monocytes, and lymphocytes between the two groups: neutrophils and monocytes were much higher in patients with Non-ST-Elevation Acute Coronary Syndrome, and lymphocytes in patients with Chronic Coronary Syndrome (Table 2). Consequently, all calculated Haemogram-Derived Indices, such as neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), and platelet-to-lymphocyte ratio (PLR), were significantly higher in patients with Non-ST-Elevation Acute Coronary Syndrome (NSTE-ACS), except mean platelet volume (MPV).

Above mentioned data partially coincide with the results of several studies that consider neutrophil-to-lymphocyte ratio (NLR),[2-6,13,15,25,29-31,33-36,38] monocyte-to-lymphocyte ratio (MLR),[9-15,27] platelet-to-lymphocyte ratio (PLR), and mean platelet volume (MPV)[7,8,17-21,45-61] as an independent risk factor for acute coronary events.

In patients with NSTE-ACS the clinical and angiographic risks were assessed by the GRACE and SYNTAX scores, respectively. The linear regression analysis indicated that only neutrophil-to-lymphocyte ratio (NLR) was significantly and positively correlated with clinical and angiographic risks of patients with NSTE-ACS. The standardized B coefficient for neutrophil-to-lymphocyte ratio (NLR) were 0.902 ($p<0.0001$) and 0.704 ($p<0.0001$) regarding clinical (measured by GRACE score) and angiographic (measured by SYNTAX score) risks, respectively.

There was a strong predictive correlation between quantiles of neutrophil-to-lymphocyte ratio (NLR) and risk scores, measured by GRACE and SYNTAX tools (Figure 1).

The GRACE risk score was 1.4-times higher in the group with a high NLR quantile (7.050±0.1929 95% CI 6.667 to 7.433) compared to those with low NLR (4.985 ± 0.1708 95% CI 4.646 to 5.324, $p<0.0001$). Similarly, the SYNTAX score was 1.6-times higher in the group with a high NLR quantile (1.414 ± 0.0934 95% CI 1.229 to 1.600 vs 0.884 ± 0.0541 95% CI 0.776 to 0.991, $p<0.0001$).



a b

a. Predictive correlation between 0.25, 0.50 and 0.75 quantiles of neutrophil-to-lymphocyte ratio (NLR) and GRACE risk score; b. Predictive correlation between 0.25, 0.50 and 0.75 quantiles of neutrophil-to-lymphocyte ratio (NLR) and SYNTAX risk score.

Fig. 1. Predictive correlation between different quantiles of neutrophil-to-lymphocyte ratio (NLR) and GRACE (a) and SYNTAX (b) risk scores

V. CONCLUSIONS

According to the results of the present study elevated periprocedural Haemogram-Derived Inflammatory Indices (HDII), such as neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), and platelet-to-lymphocyte ratio (PLR) indicate a high inflammatory and prothrombotic state in patients with Non-ST-Elevation Acute Coronary Syndrome (NSTE-ACS), but only neutrophil-to-lymphocyte ratio (NLR) is positively and significantly correlated with clinical and angiographic risks measured by GRACE and SYNTAX tools, respectively.

STUDY LIMITATIONS

The present study has two major limitations: (i) the small study population from a single center, and (ii) restriction with only Haemogram-Derived Inflammatory Indices (HDII) without evaluation of other inflammatory markers such as C reactive protein (CRP), tumor necrosis factor-alpha (TNF-a), interleukin-6 (IL-6), etc.

CONFLICTS OF INTEREST

No conflicts of interest.

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