

To Study Red Cell Indices and Platelet Indices in Acute Coronary Syndrome

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ABSTRACT

Introduction: Platelets play a key role in the development and progression of cardiovascular disease. Patient with deranged red cell indices and platelet volume indices can be easily identified during routine hematological analysis and could benefit from preventive measures. Current research aimed to study severity and extent of myocardial injury in patients of Acute coronary syndrome based on echo cardiography and its correlation with red cell indices and platelet indices and to record the correlation of red cell indices and platelet indices with mortality in patients of Acute coronary syndrome.

Material and Methods: A total of 137 patients admitted in medicine intensive care unit were included. All the records were recorded by using structured schedule (Case Report Form) and entered in Microsoft Excel Sheet. Platelet indices and red cell indices were measured in all patients. Global registry of acute coronary events (GRACE) score was used for assessment of the risk of death. Extent of myocardial injury was assessed by left ventricular systolic dysfunction on basis of 2D ECHO.

Results: Blood indices –MPV (10.34 ±1.28), PLCR (38.79 ±10.49) were found to be significantly higher (P<0.0001) in STEMI patient as compared with NSTEMI (MPV 9.52 ±1.13, PLCR33.15 ±8.83) and UA (MPV9.21 ±1.09 PLCR 30.92±7.82). RDW (56.05± 15.16) was significantly higher (p<0.05) in moderately reduced ejection fraction as compared with mildly reduced (RDW50.37±6.63) and normal (RDW50.24±6.63). MPV (10.67±1.13) PDW (16.23±0.59) PLCR (39.66±9.67) were significantly higher (P<0.001, P<0.001 P<0.016 respectively) in high risk mortality group as compared to moderate (MPV10.1±1.23, PDW 15.91±0.44 PLCR36.78±10.37) and low risk group (MPV9.45±1.21 PDW15.89±0.45 PLCR33.11±9.31).

Conclusions: MPV, PDW and PLCR may be considered prognostic markers for acute coronary syndrome. RDW can be used to assess severity of myocardial injury.

Keywords: Acute Myocardial Infarction, Coronary Artery Disease, Red Cell Indices, Platelet Indices, Grace Score, Ejection Fraction.

factors include cigarette smoking, abnormal lipid profiles, high blood pressure, diabetes, abdominal obesity, stress, lack of fruits and vegetables, and lack of daily exercise³. ACS, a common complication of coronary heart disease, is associated with more than 2.5 million hospitalizations worldwide each year⁴. Between 9% and 19% of patients die in the first 6 months after being diagnosed, with about one-half of deaths occurring within 30 days⁵. While significant advances are being made in managing patients, the burden of coronary heart disease has increased as a result of longer life expectancies and the survival rates of individuals with ACS⁶. Therefore, morbidity and mortality caused by ACS are likely to remain significant and to have substantial medical and productivity costs as well as effects on quality of life. While in-hospital mortality rates are higher in older patients, mortality rates in younger age groups aren't declining as fast as in older age groups, and in some cases, they're even rising⁷.

In recent study Red Blood cell distribution width was significantly related with major cardiac adverse events (MACE) in patients with heart failure even after the adjustment of hematocrit values⁸. This parameter is routinely reported as part of the complete blood count (CBC), but its use is generally restricted to the differential diagnosis of anemia⁹. Platelets have a major role in the pathogenesis of acute coronary syndrome (ACS), where plaque rupture is followed by platelet activation and thrombus formation¹⁰. That's why anti-platelet therapy like aspirin and clopidogrel are used to prevent platelet activity. Electronic cell counters have made it possible to measure platelet volume indices (PVI), specifically mean platelet volume (MPV), and platelet distribution width (PDW). This is a simple and cost-effective method of identifying these larger platelets.

Current research aimed to study severity and extent of myocardial injury in patients of Acute coronary syndrome based on echo cardiography and its correlation with red cell indices and platelet indices and to record the correlation of red cell indices and platelet indices with mortality in patients of Acute coronary syndrome.

INTRODUCTION

Acute coronary syndrome (ACS) - which includes ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), and unstable angina - is an umbrella term for life-threatening situations that occur when the blood supply to the heart is blocked due to destabilization of a previously stable atherosclerotic plaque so that part of the heart muscle is unable to function properly or dies¹. ACS can also manifest as sudden cardiac arrest due to ischemia-induced tachyarrhythmias². Risk

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MATERIAL AND METHODS

A single centre prospective cross sectional study was conducted in all patients with newly diagnosed acute myocardial infarction admitted in ICCU, Department of Medicine at Netaji Subhash Chandra Bose Medical College Jabalpur. A detailed history and systemic examination was carried out in every patient. In each case diagnosis was confirmed by ECG and CPK-MB. Total 137 patients with Acute coronary syndrome were enrolled in study who satisfied all the inclusion and exclusion criteria. Sampling was done in 137 patients with newly diagnosed Acute coronary syndrome patients. Under aseptic conditions venous blood samples was drawn at time of admission and was analyzed 120 minutes after venipuncture. Blood was analyzed for following parameters

Red cell indices: Mean corpuscular volume (MCV), Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular hemoglobin concentration (MCHC), Red Blood cell distribution width (RDW)

Platelet Indices: Plateletcrit (PCT), Mean platelet volume (MPV), Platelet distribution width (PDW), Platelet large cell ratio (PLCR)

Out of 137 patients 2D ECHO could be done in 107 patients. Written consent was obtained from all patients participating in study.

Study Duration: This study was conducted for a period of eighteen months from March 2016 to August 2017.

Laboratory methods

After a thorough clinical examination and history taking, the procedure was explained to the subjects. Patients were adequately hydrated before blood collection. 3ml of venous blood was collected from each subject. Complete blood count was estimated by Mindray (3 part) Automated Blood cell counter. 2D ECHO was done with the help of HD 7 PHILIPS MAKE to access myocardial damage in patients with ACS. 2D ECHO was done in 107 no. of cases. GRACE score was used to predict in hospital mortality in patients with ACS.

Criteria for selection of patient

Inclusion criteria: -

Patient included in study are patients, who are established cases of AMI on the basis of detailed history and electrocardiographic criteria with markers including CPK-MB level who gave consent for study.

Exclusion criteria

- Previously diagnosed cases of acute coronary syndrome
- Primary hematological disease involving red blood cells and platelets
- Patients of chronic kidney disease, chronic liver disease, chronic obstructive pulmonary disease, cerebrovascular accident
- Referred patient who were thrombolysed or given loading dose of antiplatelet.

STATISTICAL ANALYSIS

Data was entered in excel and analysed with recent available software. Result were presented in Mean \pm SD. The significance of difference between two proportion was indicated by the ANOVA statistic. Difference were considered to be significant if ($P < 0.05$)

RESULTS

Out of 137 patient 79 (57.65%) cases were at age group of 50-69 yrs. No significant correlation was found between age and incidence of acute coronary syndrome.

In our study male prevalence of Acute coronary syndrome was higher in male (62%) as compared to females (38%). However, this difference is not statically significant.

Majority of cases i.e. 40 cases with GRACE score 1-3% and >3% belong to STEMI group subjects. Majority of cases i.e. 31 cases with GRACE score <1% were from UA group subjects. Majority of cases i.e. 27 cases with GRACE score 1-3% were from STEMI group. Majority of cases i.e. 13 cases with GRACE score >3% were from STEMI group subjects. Statically showed significant correlation (chi square 30.81, $P < 0.05$)

Out of all ACS patients Mean values of RDW and MCHC

Red cell indices	Ejection fraction						P value
	Normal		Mildly reduced		Mod reduced		
	Mean	SD	Mean	SD	Mean	SD	
MCV	94.57	11.59	91.96	9.51	95.02	13.2	0.46
MCH	26.52	2.89	25.74	3.44	26.51	3.72	0.47
MCHC	28.47	2.99	28.15	2.36	28.67	1.97	0.76
RDW	50.24	6.63	50.37	6.63	56.05	15.16	0.05

Table-1: Correlation between red cell indices and ejection fraction

Red cell indices	Grace score						P value
	<1%		1-3%		>3%		
	Mean	SD	Mean	SD	Mean	SD	
MCV	93.68	11.47	92.02	9.4	91.49	8.41	0.59
MCH	26.71	3.15	25.84	2.77	25.66	3.63	0.22
MCHC	28.78	2.43	28.46	2.29	28.17	3.14	0.57
RDW	51.01	8.87	49.94	6.56	50.47	3.41	0.76

Table-2: Correlation between red cell indices and grace score

Platelet indices	Grace score						P value
	<1%		1-3%		>3%		
	Mean	SD	Mean	SD	Mean	SD	
MPV	9.45	1.21	10.1	1.23	10.67	1.13	<0.0001
PDW	15.89	0.45	15.91	0.44	16.23	0.59	0.02
PCT	2.53	0.8	2.6	0.66	2.28	0.92	0.33
PLCR	33.11	9.31	36.78	10.37	39.66	9.67	0.01

Table-3: Correlation between platelet indices and grace score

Platelet Indices	Ejection fraction						P value
	Normal		Mildly reduced		Mod reduced		
	Mean	SD	Mean	SD	Mean	SD	
MPV	9.66	1.42	9.6	1.13	10.05	1.24	0.52
PDW	15.95	0.49	15.93	0.46	15.83	0.65	0.71
PCT	2.68	0.75	2.67	0.88	2.2	0.37	0.10
PLCR	34.77	10.81	33.09	8.78	37.74	10.29	0.31

Table-4: Correlation between platelet indices and ejection fraction

was highest in STEMI group patients while Mean values of MCH and MCV was highest in NSTEMI patients. This was statically insignificant ($P < 0.05$).

Mean of RDW (56.05 ± 15.16) in moderately reduced ejection fraction was significantly increased as compared to normal (50.24 ± 6.63) and mildly (50.37 ± 6.63) reduced ejection fraction ($F 2.998, P < 0.05$). There is increase in mean values of MCV, MCHC in moderately reduced ejection fraction as compared with mildly reduced and normal ejection fraction study group but there was no statically significance ($P > 0.05$). Mean of MCH was highest in normal ejection fraction study group as compared with mildly and moderately reduced ejection fraction. There was no statically significance. ($P > 0.05$) [Table-1].

Mean values of all red cell indices values was highest in GRACE score <1% study group as compared to >1% study group and GRACE score 1-3% STUDY group. There was no statically significant association ($P > 0.05$) [Table-2].

Mean values of MPV and PLCR was highest in mod reduced ejection fraction as compared to mildly reduced and normal ejection fraction study group. This is statically insignificant. ($P > 0.05$). Mean of PDW and PCT was highest in normal ejection fraction study group. This was statically insignificant ($P > 0.05$) [Table-4]

Mean values of MPV, PDW and PLCR was highest in GRACE score >3% study group as compared to 1-3% study group and <1% GRACE score study group ($F 9.159, F 4.027, F 4.0264$ respectively, $P < 0.05$) A statically significant association. Mean values of PCT was highest in GRACE score 1-3% study group as compared to >3% study group and <1% study group. Statically insignificant association ($P > 0.05$) [Table-3]

DISCUSSION

At the present time, it is well know that atherosclerosis is chronic inflammatory disease and varied causative cytokines such as TNF- α , IL-1 β and IL-6 are released in its process^{11,12} These increased inflammatory cytokines in blood stream may have a suppressing effect on erythropoietin (Epo) and hemoglobin synthesis that this situation causes chronic

inflammatory anemia. Previous studies have demonstrated that inflammatory cytokines could modulate erythropoiesis through two pathways first, by inhibition of Epo gene transcription at the kidneys and liver; and second, by suppression of erythroid cell maturation at the bone marrow. The inflammatory cytokine modulation on bone marrow erythroid progenitors desensitizes the cells to Epo, which blocks its anti apoptotic and promaturation effects^{13,14,15} Therefore, decrease in Epo release causes fewer mature or immature red blood cells production and release into circulation

In our study we found that high RDW is associated with reduced ejection fraction which is statically significant. RDW can be used to assess severity and outcome in patients of acute myocardial infraction on their initial presentation Konstantinos Sotiropoulos, Patrick Yerly, Pierre Monney, Antoine Garnier, et al. carried a prospective registry of consecutive patients (n= 408) hospitalized for AHF at their tertiary centre. Patients presenting with AHF at the Emergency Wards were included when hospitalized for heart failure. Patients with acute coronary syndrome, or cardiogenic shock in need of intensive care were not included. Overall 19.9% of all patients presented with high RDW, 65% of these patients had a transthoracic echocardiography during hospitalization; 63.4% of these presented a LVEF <50%¹⁶ which is in agreement of our study.

Mean values of red cell indices was highest in GRACE score <1% study group as compared to >1% study group and GRACE score 1-3% study group but there was no statically significant association. RDW may be used as an independent predictor of all-cause long-term mortality in NSTEMI/STEMI patients. Although our study was inconclusive similar studies were carried by Na Zhao, Lan Mi, et al, who studied the correlations between GRACE risk score and RDW. Their study showed that both the GRACE scoring system and RDW testing have an individual predictive value for cardiovascular events in ACS patients. Moreover, these measures are independently and positively related to each other. Combining the 2 approaches resulted in higher

predictive value for long-term cardiovascular events in ACS patients¹⁷.

Platelet activation is the key step of pathogenesis of acute coronary syndrome. Activated platelets are larger in size, which can be measured by mean platelet volume (MPV). Larger platelets are more adhesive and tend to aggregate more as they more dense granules. They are metabolically and enzymatically more active than small platelets and produce more thromboxane A₂^{18,19} Increased platelet volume will increase the tendency for coronary thrombus formation in Acute Coronary Syndrome patients. The activated platelet is the major biological risk factor for pathogenesis of Acute Coronary Syndrome, so inhibition of this process could play an important role in prevention of Acute Coronary Syndrome. In present study Mean values of both MPV and PLCR was insignificantly higher in moderately reduced study group as compared with mildly reduced and normal study group but Shuichi Fujita, Yoshihiro Takeda et al found that when the data from there study were assessed in tertiles, the prevalence of LVSD seemed to increase according to the MPV or PDW tertile. When analysis was performed by entering all of the variables, they found that, MPV and PDW have a significant association with LVEF²⁰.

In present study Mean values of MPV, PDW and PLCR was significantly higher in GRACE score >3% study group as compared with GRACE score 1-3% and GRACE score <1% which is in agreement with similar study by Zhao-Fei Wan, Dong Zhou, et al. which concluded that MPV is positively associated with the GRACE risk score and it may complement the scoring system in predicting CVD events in patients with ACS²¹.

The diagnostic criteria of Acute Coronary Syndrome are clinical presentation, biochemical markers of acute ischemic injury, and electrocardiographic findings. The present cardiac markers are not sufficiently sensitive at an early stage of Acute Coronary Syndrome. That's why an early and reliable marker is needed for accurate diagnosis of Acute Coronary Syndrome when patients will attend in cardiac emergency department. Platelet parameters especially MPV could be an important and reliable markers in early detection of Acute Coronary Syndrome when other markers are not available. This could lower the morbidity and mortality rates

CONCLUSION

There is a high demand for a reliable, accessible, noninvasive, and hematological prognostic marker in ACS, which would identify patients of high cardiovascular risk in secondary prevention and tailor the therapy to their needs. Many of the indices presented here reflect the complex pathophysiology of ACS. The inflammatory processes play a key role in the development of atherosclerosis, destabilisation of atherosclerotic plaques and formation of clots on the plaque surface. The significance of MPV, and RDW in the prognosis of ACS has been indicated in many studies as it has been shown above.

Among Red cell indices, RDW was found to be significantly higher in moderately reduced ejection as compared to mildly

reduced and normal ejection fraction.

RDW may be considered as an alternate for quick assessment of myocardial damage where 2D ECHO facilities are unavailable. Also MPV, PLCR and PDW may be used as prognostic indicator for morbidity and mortality in cases of myocardial infarction.

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