Mean Platelet Volume, Immature Platelet Fraction and Beta Thromboglobulin in Acute Coronary Syndrome Patients

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Abstract

Objective: Conventionally troponin and iso-enzymes of creatinine kinase are used for risk stratification and diagnosis of cardiac diseases. Our objective is to compare the levels of mean platelet volume (MPV), immature platelet fraction (IPF) and beta thromboglobulin level (BTL) in healthy individuals and patients of acute coronary syndrome to discover parameters which can be used to design strategies of risk stratification, early diagnosis, timely management and prophylaxis.

Methods: The 170 study participants were divided into two groups, Cases (85) and Controls (85). The required parameters MPV and IPF were evaluated using sysmex XN 1000 where as BTL were assessed using ELISA technique. Mean ± Standard Deviation and Median ± Inter Quartile Range was used for quantitative data. Independent sample t-test was applied to compare mean of normally distributed data. Mann Whitney U test was applied to compare median of non-normal data. P-value ≤0.05 was considered significant.

Results: Mean IPF in cases and control was 8.716±6.2834 (%) and 3.83±1.63% respectively with statistically significant high levels in cases. MPV (fL) in cases was 11.65±1.53 and in controls was 10.74 ± 1.04, with statistically significant higher value in cases. Mean BTL (ng/ml) in cases was also statistically higher i.e. 28.35±17.83 versus 14.28±5.80.

Conclusion: The study concluded that levels of MPV, IPF and BTL were normal among controls while raised levels of IPF and BTL were observed among cases.

Key Words: Mean platelet volume, immature platelet fraction, Beta thromboglobulin, Acute coronary syndrome.

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Introduction

Cardiovascular diseases are major cause of death around the world.[1] Among them, acute coronary syndrome (ACS) is the leading cause of morbidity and mortality. ACS accounts for first presentation of coronary vessel diseases and is a broader term used for describing signs and symptoms of cardiac ischemia.[2] On the basis of signs and symptoms, ECG findings and certain laboratory parameters ACS can be sub-grouped as ST-segment elevation myocardial infarction, non-ST-segment elevation myocardial infarction and unstable angina often necessitating endovascular or open interventions to avoid fatal events like cardiogenic shock causing sudden arrest of cardiac activity further leading to death.[3,4] Amongst today's challenges, the major goal is to design such strategies which can prevent the occurrence of adverse coronary events and identify the individuals who are at greater risk of occurrence of ACS.[5]

Cardiac troponins and iso-enzymes of creatine kinase are routine investigations which are being used for the diagnosis of ACS. Troponin is the most sensitive, specific and reliable cardiac marker and is being currently used as gold standard investigation for the diagnosis and risk stratification in ACS patients. However, it remains undetectable in 40 – 60% of the patients

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who are suffering from ACS. Platelet indices are more reliable and accurate tool, as a new cardiac biomarker, of cardiovascular events and can potentially be used for the risk stratification of cardiovascular diseases.[6] The biological functions of platelets have now been extended far more than the traditional homeostasis and thrombotic events.[6] Platelets are now being considered as a source of inflammatory mediators, which are being guarded by their contact with arterial surfaces. Activated platelets release inflammatory mediators which further leads to platelet adhesion. The atherothrombotic potential of platelets causes release of further mediators which leads to activation of the inflammatory process and propagation of coronary vessel thrombosis predisposing to the thrombotic events.

Platelets vary in properties like size, density, and activity. Variations in these parameters can be associated with the initial triggering factor of ACS. Platelets which are large in size have stronger adhesion potential and aggregating effect than the platelets with smaller size. Increase in volume of platelets is associated with increased prothrombotic potential of atherosclerotic plaque in ACS and is a risk factor for thrombus formation in coronary vessels in patients of AMI.

MPV is a component of CBC and is commonly used as most reliable index for the platelet size identification and the status of its activation. An increase in MPV is associated with various cardiovascular risk factors and comorbidities like DM, hypertension, hypercholesterolemia, and obesity.

The above facts and observations have led to the hypothesis that increased MPV in subjects can be a beneficial tool in risk stratification of cardiovascular effects. As MPV is thought to be a marker of the size of platelets and consequently correlates with the activation status of platelets. The increase MPV in the patients of non-ST elevation ACS does not only indicates a greater risk of non-STEMI but also indicates increased risk of ischemic complications. Several researchers have concluded in various observational studies that in ACS, MPV is highest in subjects with MI than those having stable angina. Therefore, MPV can be useful to estimate extent and severity of coronary vessel diseases.

Amongst circulating platelets, the youngest form is reticulated platelets. They are bigger than senescent platelets and they have the residual RNA that gives reticulated appearance and are hyperactive because they express more GP 1b and GP 2b/3a receptors. Now-a-days, a fast fully automated method is available for the quantification of reticulated platelets via a parameter called IPF, which is ratio of reticulated platelets and total number of platelets. MPV indicates the measure of platelet reactivity and if increased shows worst prognosis.

IPF may be a more sensitive and specific indicator as compared to MPV for measurement of platelet reactivity. It is noticed that in subjects with coronary artery disease (CAD), IPF is increased as compared to normal healthy subjects. The formation of atherosclerotic plaque results in complications like MI and stroke due to the occlusion of thrombotic vessels.[8] Vascular damage repair and the maintenance of narrow capillaries to remain patent is a complex mechanism and platelets act as a key for regulation of the process. Platelets contribute to both the dysfunction of endothelium and rupture of plaque in the process of atherosclerosis.[9]

The platelet interaction with endothelium lining vessels causes excessive activation of platelets which reduces the half-life and increases the turnover of platelets, hence influence the MPV and IPF.[10]

Activation of platelets causes the release of specific proteins. B thromboglobulin is the first platelet- specific protein which is released during the aggregation of platelets. Inflammatory and thrombotic processes both play part in the pathogenesis of development of ACS.[11]

In respect to the above-prescribed issues, platelet activation parameters can be beneficial tools of disease progression before the occurrence of cardiac cell necrosis. Hence the goal of this study was the evaluation of chosen platelet morphological indices MPV, IPF and BTL in patients of ACS compared to controls.[12]

The insight of above-discussed literature, a cross-sectional comparative study was planned which will help understand not only the detailed pathophysiology of ACS but also the risk stratification and to set out prophylactic strategies in high-risk patients to prevent occurrence of ACS.

Methods

It was a cross-sectional comparative study carried out at The Department of Pathology, Postgraduate Medical Institute, Lahore between November 2017 to November 2018. The subjects were selected from Punjab Institute of Cardiology Lahore. Using purposive convenience sampling technique, 85 subjects were selected who

were diagnosed cases of the ACS (Case group) and 85 were normal healthy individuals (Control group), mean age of controls were decided and matched according to the mean age of cases.

Inclusion criteria was based on diagnosis criteria of ACS that is:

Detection of rise of cardiac troponin I levels > 0.04ng/ml and presence of at least one of the following:

- Clinical symptoms of ischemia
- Significant ST-segment T wave changes
- Development of pathological Q waves

Patients with active inflammation, cancer, chronic circulatory insufficiency, severe renal failure, diabetes, past history of ACS or taking antiplatelet or anticoagulant treatment were excluded.

A custom designed performa was used to obtain informed consent and record personal information. Questionnaire was filled for each patient, containing information about collected samples and their results. A 3mL venous blood sample was collected in two separate vacutainers from each patient under aseptic measures. The purple capped vacutainer containing EDTA was used for MPV and IPF and the yellow capped vacutainer containing acid citrate dextrose was used for BTL.

Mean Platelet Volume and Immature Platelet Fraction were performed on blood in EDTA vacutainer, within 3 to 4 hrs of sample collection on Sysmex automated hematology analyzer (XN – 1000). Plasma BTL was detected by using commercially available Elisa's kits according to the manufacturer's instructions. The key variables assessed in our study were:

- Immature Platelet Fraction
- Mean Platelet Volume
- BetaThromboglobulin

Data was entered and analyzed using SPSS version 24. Mean ± standard (S.D) andmedian± inter quartile range (IQR) was used for quantitative data like Age (years), Pulse beat per minute (BPM), systolic and diastolic blood pressure (mmHg), Jugular venous pressure (cm), Cholesterol level (mg/dL), Blood glucose levels (mg/dL), Serum creatinine (mg/dL), Cardiac troponin I (ng/ml), IPF (%), MPVfL (Femtolitre) and Plasma BTL (ng/ml). Independent sample t-test was applied to compare mean of normally distributed data [BP Systolic and diastolic (mmHg), Jugular venous pressure (cm), Cholesterol level (mg/dL), Serum creatinine (mg/dL) and MPVfL (Femtolitre)] in both groups. Mann Whitney U test (denoted by Z in analysis) was applied to compare median of non-normal data such as [Age (years), Pulse beat per minute (BPM), Blood glucose levels (mg/dL), Cardiac tropnin I (ng/ml), IPF (%), Plasma Beta and Thromboglobulin Level (ng/ml)]. P-value≤0.05 was considered as significant.

Results

Demographic and Clinical parameters of studied population:

Distribution of Respondents According to studied parameters:

The mean IPF in cases and control was 8.716 ± 6.2834 (%) and 3.83±1.63% respectively with statistically high levels in cases, p-value < 0.001.

Z-test = 6.58

p-value≤ 0.001 (Significant)

The MPV(fL) in cases was11.65 ± 1.53 and in controls

Table 1: *Demographic and Clinical parameters of studied population:*

	Normal Parameters		Kolmogorov-Smirnov (Z)	p-value	Distribution
	Mean	S.D			
Age (Years)	55.59	10.38	1.67	0.01	Non-Normal
Pulse beat per minute (BPM)	88.47	14.55	1.66	0.01	Non-Normal
BP Systolic (mm Hg)	132.29	13.42	1.10	0.18	Normal
BP Diastolic (mm Hg)	99.93	19.86	1.35	0.052	Normal
Jugular Venous Pressure (cm)	3.51	0.50	4.48	0.00	Normal
Cholesterol level (mg/dl)	234.45	21.48	1.24	0.09	Normal
Blood Glucose levels (mg/dl)	132.52	32.75	2.00	0.00	Normal
Serum Creatinine (mg/dl)	1.10	0.35	1.26	0.08	Normal
Cardiac Troponin (ng/ml)	0.15	0.16	3.48	0.00	Non-Normal
IMMATURE PLATELET FRACTION (%)	6.27	5.19	2.27	0.00	Non-Normal
Mean Platelet Volume (fL)	11.19	1.38	0.99	0.28	Normal
Plasma Beta Thromboglobulin Level (ng/ml)	21.32	14.99	2.97	0.00	Non-Normal

Table 2: *Descriptive statistics of Immature Platelet Fraction (%) beta thromboglobulin and mean platelet volume:*

		Mean	SD	Median	IQR	Minimum	Maximum
Immature Platelet Fraction (%)	**Case**	8.71	6.283	7.50	1.4	31.6	6.8
	Control	3.83	1.63	3.40	1.2	6.8	2.8
	Total	6.27	5.19	5.15	1.2	31.6	4.5
Mean Platelet Volume (fL)	**Case**	11.65	1.53	11.80	8.7	17.0	1.7
	Control	10.74	1.04	10.70	7.0	12.8	1.5
	Total	11.19	1.38	11.20	7.0	17.0	1.5
Beta Thromboglobulin Level (ng/ml)	**Case**	28.35	17.38	28.0	4.0	83.5	22
	Control	14.28	5.80	13.90	3.9	25.0	6.9
	Total	21.318	14.98	14.70	3.9	83.5	15.7

was 10.74±1.04, with statistically higher mean platelet volume in cases as compared to controls, p- value <0.001.

t-test = 4.553

p-value≤0.001 (Significant)

The mean BTL (ng/ml) in cases was also statistically higher as compared to controls i.e. 28.35 ± 17.83 versus 14.28 ± 5.80, p-value < 0.001.

Z-test = 5.73

p-value≤ 0.001(Significant)

Discussion

Age is considered the most important factor that plays a significant role in progression of numerous diseases because most of the diseases are prevalent among elderly people. Present study indicated that majority of the patients in both groups were over 50 years old. The findings of a similar study conducted by Pervin and teammates (2013) were comparable with our study who reported that mainstream of the patients in both groups was more than 40 years old while some of them were upto 40 years old. Our Study indicated that mean age of the cases was 57.04+11.62 years and the mean age of controls was 54.14+9.84 years. The results of a recent study performed by Khalifa and coworkers (2017) highlighted that mean age of the cases was 61.32+7.20 years while the mean age of the controls was 57.40+7.89 years.[13] Another study carried out by Abideen and associates (2017) indicated that mean age of the cases was 50.87±11.02 years while among controls mean age was 47.31±12.09years.[14]

High blood pressure and cholesterol are considerable risk factors associated with ACS. It was found during the study that blood pressure both systolic and diastolic was raised in cases as compared to controls. The mean systolic BP in cases and controls was 137.68 ± 15.621 mmHg and 128.89 ± 18.813 mmHg, while the mean diastolic in cases and control was 86.36 ± 9.716 and 81.39 ± 11.536 mmHg respectively. The findings of a study undertaken by Abdallah and collaborators (2010) showed results similar to our results indicating that mean systolic blood pressure among cases was 132+30 mmHg and among controls 136+30 mmHg while mean diastolic blood pressure among cases was 80+17 mmH g and among controls 79+15mmHg.

During study blood glucose, serum creatinine and cardiac troponin-I were also assessed among cases and controls. Study showed that most of the patients in both groups had normal levels of blood glucose and serum creatinine while raised values of Cardiac Troponin I were seen among majority of the cases but these values were found decreased among most of the controls.

As ACS remains a serious public health problem, so there is need to identify the risk factor to control the disease among population. It has been observed that among patients with ACS the mean platelet volume, IPF and BTLs are raised as compared to normal healthy individuals. During this study when the levels of MPV, IPF and Plasma β-TG were evaluated, study demonstrated that among majority of controls, the levels of mean platelet volume, IPF and BTL were found normal, while in major proportion of cases raised level of MPV, IPF and BTL were observed. Study pointed out that mean IPF among cases was 8.72+6.28 and among controls 3.83+1.63 with statistically significant results showing raised levels among cases. The findings of a study performed by Berny-Lang and fellows (2014) indicated that mean IPF among cases was 5.0 +2.8 and among controls were 4.6+2.7 showing statistically insignificant results.[2] Likewise in our study MPV among cases was 11.65+1.53 and among controls 10.74+1.04 showing statistically significant results.

The results of our study are almost comparable with the study conducted by El- Dosouky and Shehata (2016) who reported that MPV among cases was 13.3+24 and among controls 10.0+0.8 with statistically significant results.[15] Virtually similar results were also obtained from a study undertaken by Abideen and associates (2017) who confirmed that MPV among cases was 10.99+1.34 and among controls 9.21+0.98 with statistically significant results.[13] As far as Plasma β-TG is concerned, study showed a great increase among cases that mean plasma β-TG level among cases was 28.35 + 17.84 ng/mL while among controls it was 14.29 + 5.80 ng/mL showing statistically significant results. The results of another study carried out by Joanna Kaminska (2018) reported that the BTL were significantly higher in patients of ACS as compared to controls.

Conclusion

Current study estimated the levels of MPV, IPF and BTL among patients of ACS and normal healthy individuals. Study concluded that levels of MPV, IPF and BTL were normal among controls while raised level of MPV, IPF and BTL were observed among cases. However, all three parameters had statistically significant difference between the study groups being higher in cases. These results would be useful in early diagnosis of ACS. Increased levels of MPV, IPF and BTL can be used as indicators predisposing to any thrombotic event eventually leading to ACS.

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Conflict of Interest: None

References

1. Morrad B, Eraslan S, Gorenek B. Prevalence and Types of Supraventricular and Ventricular Arrhythmias Developing in Patients with Acute Coronary Syndrome Cardiology & Cardiovascular Medicine Journal. 2017; 2(1).
2. Go AS, Mozaffarian D, Roger VL, et al. Executive summary: heart disease and stroke statistics—2014 update: a report from the American Heart Association. Circulation. 2014;129(3):399-410.
3. Ahmad S, Asghar N, Rauf A. Vein graft patency in post-cabg symptomatic patients: an angiographic study. Journal of University Medical & Dental College. 2015;6(3):38-45.
4. Wang XH, Liu SQ, Wang YL,et al. Correlation of serum high-sensitivity C-reactive protein and interleukin-6 in patients with acute coronary syndrome. Genetics and Molecular Biology. 2014 ;13(2):4260-4266.
5. Arbab-Zadeh A, Nakano M, Virmani R,et al. Acute coronary events. Circulation. 2012;125(9):1147-1156.
6. Patil SK, Karchi SD. A comparative study of platelet indices in acute coronary syndrome. International Journal of Contemporary Medical Research 2017; 4(3): 77-83.
7. Schmoeller D, Picarelli MM, Paz Munhoz T,et al. Mean platelet volume and immature platelet fraction in autoimmune disorders. Frontiers in medicine. 2017;4:146.
8. Hristov M, Weber C. Myocardial infarction and inflammation: lost in the biomarker labyrinth. Circulation Research. 2015;116:781–783.
9. Nording HM, Seizer P, Langer HF. Platelets in inflammation and atherogenesis. Frontiers in immunology. 2015;6:98.
10. Pal R, Bagarhatta R, Gulati S,et al. Mean platelet volume in patients with acute coronary syndromes: a supportive diagnostic predictor. Journal of clinical and diagnostic research: JCDR. 2014;8(8):MC01.
11. Tanindi A, Sahinarslan A, Elbeg S, et al.Relationship between MMP-1, MMP-9, TIMP-1, IL-6 and risk factors, clinical presentation, extent and severity of atherosclerotic coronary artery disease. The open cardiovascular medicine journal. 2011;5:110-116.
12. Kamińska J, Koper OM, Siedlecka-Czykier E, et al. The utility of inflammation and platelet biomarkers in patients with acute coronary syndromes. Saudi Journal of Biological Sciences. 2018;25(7):1263-1271.
13. Khalifa KA, Helwa MA, Mousa AM. Reticulated platelets in acute coronary syndrome patients. Menoufia Medical Journal. 2017;30(3):880-886.
14. Salman F, Usman R, Shakireen N,et al. Platelet indices in newly diagnosed patients of myocardial infarction. Khyber Medical University Journal. 2017;9(2).
15. El-Dosouky II, Shehata IE. Value of the mean platelet volume in evaluation of patients with acute coronary syndrome. Journal of Medical Diagnostic Methods. 2016;5(1):1-5.

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H.A: Data collection

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T.R: Study design, data collection