

# Diagnostic importance of platelet parameters in patients with acute coronary syndrome admitted to a tertiary care hospital in southwest region, Saudi Arabia

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**Objective:** Identifying risk factors for acute coronary syndrome (ACS) is important for both diagnostic and prognostic purposes. Abnormal platelet parameters, mainly platelet count (PC), mean platelet volume (MPV) and platelet distribution width (PDW) are thought to be among these risk factors. In this study, the associations between PC, MPV and PDW and ACS were investigated in patients admitted to the tertiary care hospital in the south west region of Saudi Arabia.

**Materials and methods:** A retrospective cohort of 212 patients with the diagnosis of ACS admitted to Aseer Central Hospital during the period extending from February 1, 2008 to October 31, 2008 were included. The control group consisted of 49 matched subjects who were admitted for chest pain investigation and subsequently found to be non-cardiac chest pain after performing relevant investigations. Blood samples were taken at the time of admission for platelet parameters. Statistical analysis was made using SPSS software and *P*-values were considered significant if  $<0.05$ .

**Results:** A total of 212 patients with acute coronary syndrome (80 patients with MI and 132 patients with UA) and 49 matched controls were studied. The PC was not statistically different among the three groups ( $283.3 \pm 94.8 \times 10^9 L^{-1}$  for MI cases,  $262 \pm 60.8 \times 10^9 L^{-1}$  for UA cases and  $275.8 \pm 58.9 \times 10^9 L^{-1}$  for controls). The MPV was significantly larger in MI cases compared to controls ( $8.99 \pm 1.5$  fl vs.  $8.38 \pm 0.51$  fl, respectively,  $P < 0.009$ ), similarly, the MPV was significantly larger in UA cases compared to controls ( $9.23 \pm 1.19$  fl vs.  $8.38 \pm 0.51$  fl, respectively,  $P < 0.001$ ). The PDW was significantly higher in MI cases compared to controls ( $15.88 \pm 1.5$  fl vs.  $11.96 \pm 1.8$  fl, respectively,  $P < 0.001$ ), similarly, the PDW as also significantly larger in UA cases compared to controls ( $18.1 \pm 1.8$  fl vs.  $11.96 \pm 1.8$  fl, respectively,  $P < 0.019$ ).

**Conclusion:** Platelet parameters mainly MPV and PDW are readily available and relatively simple and inexpensive laboratory tests which we detected to be significantly raised in patients who have suffered an acute coronary syndrome compared with controls.

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Acute coronary syndrome (ACS) is the most prevalent cardiac disorder, affecting over 12 millions in the United States. Each year, it is estimated that one million individuals in the United States suffer a coronary event [20].

Despite improvement in primary prevention and treatment [12], acute coronary syndrome remains the chief cause of death in the United States and most developed countries [15]. Almost half of all victims of myocardial infarction die before they reach the hospital [9].

ACS includes myocardial infarction and unstable angina. Diagnosing ACS is still a challenge despite the remarkable improvement in the diagnostic modalities and physicians continue to admit a large number of patients with chest pain who proved to be non-cardiac patients after thorough investigations [14].

Platelets have a major role in the pathogenesis of ACS, where plaque rupture is followed by platelet activation and thrombus formation leading to coronary artery occlusion [4,5,24]. Anti-platelet agents have a cardinal role in the management of patients with ACS. They interrupt the pathologic cascade of thrombosis. Therefore, acetyl salicylic acid, thienopyridine and glycoprotein 2b/3a inhibitors, which all inhibit the platelet function, are used in the treatment of ACS patients [18].

Platelets vary in size and activity [7,19].

When platelets are activated they become larger in size, which can be measured by both larger mean platelet volume (MPV) and platelet distribution width (PDW). Larger platelets are more adhesive and tend to aggregate more than smaller ones [22]. This increase in platelet volume will increase the tendency for coronary thrombus formation in ACS patients [6].

The Aseer region (population of 12,00,000) is located in the southwest of Saudi Arabia covering an area of more than 80,000 km<sup>2</sup>. The region extends from the high mountains of Sarawat (with an altitude of 3200 m above the sea level) to the Red Sea. Health services delivery in Aseer region is provided by a network of 244 primary health care centers, 16 referral hospitals and one tertiary hospital, Aseer Central Hospital (ACH). ACH, with 500 beds, is run by the Ministry of Health and the College of Medicine of King Khalid University, Abha.

The aim of this study was to investigate whether there is an association between platelet parameters (mainly PC, MPV and PDW) and ACS in patients admitted to the tertiary care hospital in southwest region of Saudi Arabia.

## Materials and methods

### Study population

A retrospective cohort of 212 consecutive patients admitted to Aseer Central Hospital CCU with the diagnosis of ACS during the period extending from February 1, 2008 to October 31, 2008 were included. Diagnosis of the different types of ACS was based on the American College of Cardiology clinical data standards [1].

Exclusion criteria include: patients with severe hepatic impairment, renal impairment (three cases), patients with documented malignancy, or on anti-inflammatory (five cases), anti-coagulants (two cases) or anti-platelet therapy (four cases).

Patients on acetyl salicylic acid were not excluded as it does not interfere with platelet parameters measured [11].

The control group consisted of 49 age and sex matched subjects who were admitted with chest pain for investigation and found to be non-cardiac chest pain after thorough investigations including a normal coronary angiography, which was performed for all of them.

### Clinical data and hematologic parameters collections

All patients underwent a standard 12 lead ECG examination which was interpreted by an expert cardiologist regarding the standard ischemic ECG changes.

Diagnosis of ACS was confirmed with typical symptoms, ECG changes, laboratory tests and/or coronary angiography which was performed on 130 patients (61%).

Aliquots of 2 ml blood were collected in dipotassium EDTA tubes from all the patients on admission by a clean puncture. The sample was run within 2 h of venepuncture using the Sysmex K-4500 automated cell counter (TOA Electronics, Koebe, Japan), then different platelet parameters were measured including PC, MPV and PDW.

### Statistical analysis and ethics

Data were analyzed using SPSS software package. Frequency, percentage, mean, standard deviation and median were used to present the data. For contingency tables Chi square test was used. The student *t*-test was used to assess whether the means of two groups are statistically different from each other. The chosen level of significance was 5%. Approval of the local medical-ethics committee was obtained prior to the study.

## Results

### Clinical characteristics of the study population

A total of 212 patients with ACS [80 patients with myocardial infarction (MI) and 132 patients with unstable angina (US)] and 49 sex and age matched control cases were included.

The mean age of the ACS patients was  $56.59 \pm 13.6$  years and male gender constituted 77.4% (164) of them. No statistically significant difference was detected between the two groups regarding the age or the gender distribution.

Coronary risk factors were more prevalent among ACS cases compared to controls (Table 1).

### Platelet parameters

There was no statistically significant difference in PC between MI cases and controls ( $283.3 \pm 94.8 \times 10^9 L^{-1}$  vs.  $275.8 \pm 58.9 \times 10^9 L^{-1}$ , respectively,  $P = 0.66$ ), or between the UA cases and controls ( $262 \pm 60.8 \times 10^9 L^{-1}$  vs.  $275.8 \pm 58.9 \times 10^9 L^{-1}$ , respectively,  $P = 0.22$ ).

The MPV was significantly larger in MI cases compared to controls ( $8.99 \pm 1.5$  fl vs.  $8.38 \pm 0.51$  fl, respectively,  $P < 0.009$ ), similarly, the MPV was significantly larger in UA cases compared to controls ( $9.23 \pm 1.19$  fl vs.  $8.38 \pm 0.51$  fl, respectively,  $P < 0.001$ ).

The PDW was also significantly higher in MI cases compared to controls ( $15.88 \pm 1.5$  fl vs.  $11.96 \pm 1.8$  fl, respectively,  $P < 0.001$ ), similarly, the PDW was significantly larger in UA cases compared to controls ( $18.1 \pm 18$  fl vs.  $11.96 \pm 1.8$  fl, respectively,  $P < 0.019$ ) (Tables 2 and 3).

## Discussion

Acute coronary syndrome (ACS) is a multi-factorial disorder, where many endogenous and

Table 1. Clinical characteristics of the study population.

Variable	Controls (49)	ACS (212)	P*
Age: (mean $\pm$ SD) years	$58.93 \pm 12.03$	$56.59 \pm 13.630$	0.647
Gender: Male: No (%)	39 (79.6%)	164 (77.4%)	0.465
<i>Coronary risk factors distribution</i>			
Family History of IHD: No (%)	7 (14.3%)	80 (37.7%)	0.001
DM: No (%)	15 (30.6%)	124 (58.5%)	0.001
Hyperlipidemia: No (%)	8 (16.3%)	88 (41.5%)	0.001
Hypertension: No (%)	23 (46.9%)	117 (55.2%)	0.215
Smoking: No (%)	7 (14.3%)	76 (35.8%)	0.004

Table 2. Comparison of platelet parameter values in patients with MI and controls.

Platelet parameter	MI	Controls	P-value
Platelet count ( $\times 10^9 L^{-1}$ )	$283.3 \pm 99.8$	$275.81 \pm 58.9$	0.66
Mean platelet volume (FL)	$8.99 \pm 1.5$	$8.38 \pm 0.51$	0.009
Platelet distribution width (FL)	$15.88 \pm 1.5$	$11.96 \pm 1.8$	0.001

Table 3. Comparison of platelet parameter values in patients with UA and controls.

Platelet parameter	UA	Controls	P-value
Platelet count ( $\times 10^9 L^{-1}$ )	$262 \pm 60.8$	$275.81 \pm 58.9$	0.22
Mean platelet volume (FL)	$9.23 \pm 1.19$	$8.38 \pm 0.51$	0.001
Platelet distribution width (FL)	$18.1 \pm 18$	$11.96 \pm 1.8$	0.019

exogenous risk factors such as smoking, diabetes, hypertension and hyperlipidemia increase its risk [25]. Nevertheless, these risk factors account only partially for all cases of ACS [2]. Therefore, other possible risk factors need to be identified in order to help in predicting ACS.

Generalized platelet activation occurs during the acute coronary event, where the increase rate of platelet consumption at the site of atherosclerotic plaque rupture leads to the release of large size platelets from the bone marrow.

This activation process results in signaling pathways that induce platelets to change their shape (metamorphosis) and size [16] and become more active in secreting thromboxane A2 and ADP into the circulation. Larger platelets are more adhesive and tend to aggregate more than smaller ones [22] that contain more secretory granules and mitochondria and are known to be more active than smaller platelets [17].

The release of thromboxane A2 and ADP stimulates the neighboring platelets, causing them to become activated and in turn secrete additional thromboxane A2 and ADP.

Activated large size platelets not only secrete thromboxane A2 and ADP but also directly bind to the circulating coagulation protein fibrinogen, via the abundant platelet integrin, glycoprotein (GP) IIb/IIIa [23,3].

The platelet–fibrinogen–platelet connection initiates the process of platelet aggregation [8] and thus, leads to coronary thrombus formation and ACS.

These findings led to the hypothesis that larger platelets as determined by their volumes, MPV, may be useful markers in patients with ACS.

In this study we examined the relationship between platelet parameters mainly PC, MPV and PDW and the occurrence of ACS in patients from the southwest region of Saudi Arabia. We found that patients with ACS (both MI and US) tend to have significantly larger MPV and PDW (which both reflect the platelet volume) than the control group. While no statistically significant difference was detected regarding the PC between the three groups.

Recently Lippi et al. have demonstrated in a large scale study that MPV at admission is higher in ACS compared to those with chest pain of non-cardiac origin [13].

Likewise, similar observations were made by other investigators, where MPV was found to be higher in patients with ACS compared to healthy controls [10,21].

In our cohort we did not detect a statistically significant difference regarding the PC among the three groups, similar observation was found by other investigators in a larger scale study [13]. While other studies although, smaller in sample size, reported the PC to be lower while MPV to be higher in ACS patients compared to the controls [10,21].

This discrepancy in findings regarding the PC level and agreement on findings regarding the platelet volume parameters among different studies in ACS patients might indicate that the platelet volume indices rather than the platelet count are more important in determining the risk of developing ACS.

## Conclusion

We concluded that platelet volume parameters mainly MPV and PDW are readily available, relatively inexpensive and useful markers which we detected to be significantly raised in the patients admitted with ACS to the tertiary care hospital in the southwest region of Saudi Arabia compared to the controls. And thus should be utilized with other investigational tools to screen patients presenting to the emergency room with chest pain who are suspected to have ACS.

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