

Utility of Platelet Indices in Assessing the Risk of Coronary Artery Disease in Patients of Diabetes Mellitus

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Abstract

Background: Platelet volume indices (PVI) such as mean platelet volume (MPV), platelet distribution width (PDW) and platelet large cell ratio (P-LCR), are the indicators of increased platelet activity which may play a role in development of vascular complications in diabetic patients. This study was performed to evaluate and compare the platelet volume indices such as MPV, PDW, P-LCR in patients of type 2 diabetes mellitus (DM) with and without manifested coronary artery disease in order to identify their usefulness in determining the risk for development of coronary complications.

Methods: Analytical cross-sectional study included 150 patients of which 100 patients were diagnosed as type 2 DM and 50 apparently healthy controls. The study cases were divided into two groups based on presence or absence of coronary artery disease. Group A included 50 cases of type 2 DM without manifested coronary artery disease and group B included 50 cases of type 2 DM with manifested coronary artery disease. PVI was obtained using automated cell counter.

Results: MPV, PDW, P-LCR were significantly higher in diabetics as compared to controls subjects ($P < 0.001$ for all). However, no statistically significant difference was found between diabetics with and without manifested coronary artery disease.

Conclusions: The study showed higher PVI in diabetic subjects when compared to control subjects, but no difference between patients with and without manifested coronary artery disease suggesting that various other factors might be associated with the pathogenesis of CAD in patients of DM.

Introduction

Diabetes mellitus (DM) is a pandemic disease and most challenging problem in today's world.^[1] It is considered as a "prothrombotic state" owing to sustained hyperglycemia, dyslipidemia and insulin resistance causing endothelial and pericyte injury. Altered platelet morphology have been observed in diabetes in the form of enhanced platelet activity.^[2] Patients with type 2 DM have increased risk of developing cardiovascular disease (CVD). Moreover, CVD is one of the major cause of mortality in diabetic patients. Platelet activation plays an important role in the initiation and progress of atherothrombosis.^[3] Larger platelets contain denser granules and are metabolically and enzymatically more active and produce more thromboxane A₂.^[4, 5] Hence, MPV and PDW might help in assessing thrombotic risk whereas, P-LCR can give the measure for proportion of larger platelets.

In the present study we assessed the platelet indices in patients of diabetes mellitus with and without CAD and compared it with normal controls in order to identify its association in pathogenesis of CAD.

Subjects And Methods

Present study was analytical cross-sectional study. A total of 150 subject were included out of which study cases having DM (n=100) and control subjects (n=50) from July 2018 to May 2019. All the

consecutive cases of T2DM who came to our hospital were included in the study. Patients having history suggestive of inflammatory conditions such as rheumatoid arthritis were excluded from the study.

The study cases were divided into two groups based on absence or presence of coronary artery disease as group A and B respectively. Group A included 50 cases of T2DM without manifested CAD and group B included 50 cases of T2DM with manifested CAD. Controls included 50 apparently healthy individuals without history of diabetes mellitus or coronary artery disease. Diabetics were diagnosed based on American Diabetes Association criteria of random blood glucose levels ≥ 200 mg/dl. (ref) Control subjects had a blood glucose levels of ≤ 110 mg/dl. Diabetic subjects with manifested CAD included complications like acute myocardial infarction, history of chest pain associated with shortness of breath, palpitations, nausea, vomiting or diagnosed by any one of the following ECG/ ECHO/serum markers CK MB/ Troponin T/ NT proBNP. Detailed clinical history was taken from both cases and control subjects and complete clinical evaluation was done.

Venous blood samples were collected in EDTA and were analyzed using automated analyser (Sysmex KX-21, NY, USA)

Values of HbA1c, Random blood glucose, NT proBNP were performed on D-10 hemoglobin testing system by Bio Rad, TransAsia (ERBA) EM 360 fully automated by Agappe diagnostics and COBAS e 411 fully automated by Roche diagnostics, Mannheim, Germany respectively.

The parameters which were obtained were analyzed using IBM SPSS 23.0 (ARMONK, NY, USA). Statistical test such as Student t test, Mann Whitney U test were used for finding the significant difference between two groups. Kruskal Wallis Test was used for finding significant difference between cases and controls. P value of < 0.05 was taken to be statistically significant.^[6, 7]

Results

Mean random blood glucose of group A was 189.94 ± 104.15 mg/dl, group B was 179.18 ± 70.95 mg/dl and control group was 93.54 ± 11.64 mg/dl which was statistically significant (p value < 0.001 , Student-t Test, Table 1)

Comparison of HbA1c between cases and control which was statistically significant (p value < 0.001 , Student-t Test) is shown in Table 1.

It was observed that the mean of NT-proBNP was higher in group B when compared to group A with p value < 0.05 as shown in Table 2.

Hypertension was seen in 22 out of 50 patients in group A and 39 out of 50 patients in group B. There was significant association p value < 0.05 between hypertension and presence of coronary artery disease in patients with diabetes mellitus as shown in Table 3.

The mean age of group A was 50.36 years (± 10.5 years), compared to group B which was 58.64 years (± 9.08 years). Platelet count and platelet volume indices were compared between cases (group A and group B) and controls.

Mean platelet count of the control group ($298.08 \pm 56.34 \times 10^3 / \mu\text{l}$) was higher as compared to group A ($240.40 \pm 106.25 \times 10^3 / \mu\text{l}$, p value < 0.001) and group B ($256.28 \pm 98.47 \times 10^3 / \mu\text{l}$, p value < 0.003) which was statistically significant. However, the difference between mean among group A and group B was statistically insignificant with p value of 0.255. [Table 4]

The platelet indices including MPV, PDW and P-LCR also showed significant statistical difference between cases and controls p value < 0.001 , but there was no statistically significant difference between group A and group B respectively. [Table 4]

Discussion

In our study, we found that the platelet count was decreased in the diabetic subjects compared to controls, however no statistical significance was observed in diabetes with and without coronary artery disease.

In the present study, there was a significant difference in the platelet indices compared between cases and control but no significant difference of indices between diabetes with and without complications.

MPV is a parameter to assess the platelet size, and is an indicator of platelet reactivity. It has been seen that the larger platelets are more reactive than the smaller platelets. [8, 9]

In our study, MPV was significantly higher in diabetic subjects when compared to controls. Similar results were seen in other studies conducted by Shilpi et al and Pujani et al. [10, 11] MPV was not significant between group A and group B results of which were similar to studies conducted by Jindal S et al [12] and Shilpi et al [11] but in discordance with other studies done by Kodiatte et al [8] which showed higher MPV in diabetic patients with complications.

In the present study, the platelet distribution width (PDW) was significantly higher in diabetics subjects when compared to controls, similar results was seen with the study conducted by Dindar et al. [13]

The difference between PDW of group A and group B was insignificant which was similar to studies conducted by Dubey I et al and Shilpi K et al, but in discordance with other studies. [1, 10, 11, 14]

In addition, P-LCR was also found to be higher in diabetics when compared to control subjects similar to other studies. [1, 12] However, in the present study the difference of P-LCR between group A and group B was insignificant which was in accordance with other studies but in discordance with some studies. [2, 8-10, 12, 15]

The discordance which was seen in our study may be due to the fact that the patients with coronary complications (group B) were on antiplatelet therapy.

B-type natriuretic peptide (BNP), cardiac hormone, and its N- terminal fragment (NT-proBNP) are synthesized and secreted from the ventricular myocardium. These markers are seen to be elevated in patients of acute coronary syndromes due to ventricular dysfunction.

In our study, NT-proBNP was found to be statistically significant in diabetic patients with coronary artery disease.

Cardiovascular disease is the most common cause of morbidity and mortality in adults. The major risk factors include arterial hypertension and diabetes. In the present study, we found a significant correlation between hypertension and presence of coronary artery disease in patients with diabetes mellitus.

Diabetes and hypertension often occur together as they share some common risk factors such as obesity and insulin resistance. The presence of hypertension in diabetic patients increases the risk for coronary artery disease.

Limitations of the study

The study had obvious limitations which was a small sample size and also was not multifactorial which would help in comparing the platelet volume indices and other pathological and clinical parameters such as lipid profile, homocysteine, obesity, BMI, smoking etc.

Conclusion

In conclusion, the results of present study have shown that the platelet count and the platelet volume indices such as Mean platelet volume, Platelet distribution width, Platelet large cell ratio were found to be altered in patient of diabetes mellitus when compared to normal healthy controls. The study also indicated that the platelet volume indices were not different between the patients of diabetes mellitus with and without manifested coronary artery disease.

We found significant association between hypertension and manifested coronary artery disease in diabetic subjects, suggesting that various other factors might be associated with pathogenesis of coronary artery disease in patients of diabetes mellitus.

We suggest that a larger study should be conducted to identify the role of platelet indices various in the pathogenesis of coronary complication in patients of diabetes mellitus keeping in mind the multiple co variables in pathogenesis of DM and CAD.

Declarations

- **Ethics approval and consent to participate:** The study was approved by the Ethical committee of our institute. Written informed consent was taken from the participants before participating in the study.
- **Consent for publication:** Written informed consent was taken from the participants for the publication of this study
- **Availability of data and materials:** Not applicable
- **Competing interests:** None declared
- **Funding:** No funding was received for this study.
- **Authors' contributions:** AK and SKY done Data collection and drafted the manuscript. SS and HVS conceptualized and designed the study and done Data analysis and interpretation. NS made critical revisions in the article. Final approval of the article was given by all the authors.
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- **Authors' information (optional) Compliance with Ethical Standards:** Not applicable

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Tables

Table 1: Comparison between Random blood glucose and HbA1c (Student t- test)

| Parameters | Group A | Group B | Controls | P value (Group A vs Control) | P value (Group B vs Control) | P value (Group A vs Group B) |
|-------------|-------------------|------------------|-----------------|---------------------------------|---------------------------------|---------------------------------|
| RBS (mg/dl) | 189.94 (± 104.15) | 179.18 (± 70.95) | 93.54 (± 11.64) | < 0.001 | < 0.001 | 0.547 |
| HbA1c (%) | 8.00 (± 2.75) | 7.83 (± 2.36) | 4.26 (± 0.31) | < 0.001 | < 0.001 | 0.733 |

Table 2: Comparison of NT- proBNP (pg/ml) among studied cases (Mann Whitney U test)

| | Group A | Group B | P value |
|-----------|-----------------|-------------------|---------|
| NT-proBNP | 35.22 (± 22.06) | 1155.7 (± 777.56) | < 0.05 |

Table 3: Distribution of Hypertension among the studied cases (Chi square test)

| | Hypertension (Present) | Hypertension (Absent) | Total |
|---------|------------------------|-----------------------|-------|
| Group A | 22 | 28 | 50 |
| Group B | 39 | 11 | 50 |
| Total | 61 | 39 | 100 |

Table 4: Comparison of platelet count and platelet indices in cases and controls (Student t test)

| Parameters | Group A | Group B | Controls | P value (Group A vs Control) | P value (Group B vs Control) | P value (Group A vs Group B) |
|--|------------------------|-----------------------|-----------------------|------------------------------|------------------------------|------------------------------|
| Platelet count (X 10 ³ / μ l) | 240.40 (\pm 106.25) | 256.28 (\pm 98.47) | 298.08 (\pm 56.34) | < 0.001 | < 0.003 | 0.225 |
| MPV (fl) | 11.96 (\pm 1.22) | 11.81 (\pm 1.18) | 9.73 (\pm 0.6) | < 0.001 | < 0.001 | 0.525 |
| PDW (fl) | 16.16 (\pm 3.25) | 16.36 (\pm 3.66) | 11.00 (\pm 0.73) | < 0.001 | < 0.001 | 0.771 |
| P-LCR (%) | 38.92 (\pm 7.61) | 38.48 (\pm 8.12) | 24.80 (\pm 2.14) | < 0.001 | < 0.001 | 0.547 |