

# **Platelet indices as indicator of diabetic nephropathy among patients attending a tertiary care centre in South-India**

## **Abstract**

**Introduction:** Diabetes mellitus, a chronic metabolic disease affects various organs of the body on a long-term basis. Studies have been conducted on different aspects of the disease, to understand its complications and to detect them earlier to avoid irreversible damage like nephropathy.

**Aim:** The study aims at comparing platelet indices like Plateletcrit (PCT), Platelet Distribution Width (PDW) and Mean Platelet Volume (MPV), with serum creatinine among diabetes, prediabetes patients and non-diabetes controls, to understand the association of the platelet indices and creatinine, an indicator of renal damage.

**Materials and methods:** The cross-sectional study conducted over a period of three months involved 30 non-diabetic controls with normal HbA1c, 30 diabetics and 30 prediabetic subjects, of age group 18-35 years. The groups were classified based on their HbA1c concentration. The blood samples were analyzed for parameters PCT, PDW, MPV, creatinine and HbA1c by their respective methods. The study will guide in understanding the role of platelets in pathogenesis of diabetic nephropathy.

**Results:** Platelet indices like Plateletcrit (PCT), Platelet Distribution Width (PDW) and Mean Platelet Volume (MPV) were found to be increased in diabetics and 30 prediabetic subjects than the non-diabetics. The Platelet indices were also correlating with the serum creatinine levels of the three study groups.

**Conclusion:** There is a positive association between the Platelet indices and creatinine, in patients with pre-diabetes and diabetes who have the risk of progression to diabetic

nephropathy. Hence, the Platelet indices shall be included as early and cost-effective biomarkers of diabetic nephropathy.

**Keywords:** Plateletcrit (PCT), Platelet Distribution Width (PDW) and Mean Platelet Volume (MPV), Creatinine, Diabetic nephropathy.

## **Introduction**

Diabetes mellitus, a non-communicable metabolic disease is multifactorial in origin, with both intrinsic or genetic and extrinsic contributors. Insulin insufficiency and insulin resistance are major intrinsic factors. Life style majorly contributes as an extrinsic factor.

In 2015, about 415 million diabetics were estimated worldwide, reports International Diabetes Federation (IDF) [1].The prevalence of diabetes was 14.4% in urban and 7.4% in rural areas of Tamil Nadu, reports a study conducted by ICMR-INDIAB during the year 2008 to 2010 [2].

Diabetes further leads to various chronic complications based on microangiopathy and macroangiopathy.Increased platelet activity is being reported in the occurrence of vascular complications of the disease [3].Platelets can cause thrombosis and inflammation. [4,5].

Alterations in the platelet parameters were found to be associated with diseases affecting vascular endothelium like diabetes mellitus [6,7]. The hyperactive platelets in patients with diabetes mellitus is responsible in activating the prothrombotic factors. Further, a decrease in fibrinolysis increases the risk of thrombosis in these individuals.

The hyper-reactive platelets in individuals with diabetes are responsible for an increase in activation of factors of prothrombosis and a decrease in fibrinolysis resulting in thrombosis [8-10]. The status of hyperglycaemia observed in diabetes mellitus leads to decreased reduced nitric oxide synthesis from the endothelium leading to a disturbance in anti-aggregation mechanism homeostasis [11].Hence, the present study was intended to

understand the pathogenetic mechanism responsible for the haemostatic alterations in diabetes mellitus.

## **Materials and methods**

The study was held in Sree Balaji Medical College and Hospital in the department of biochemistry for a duration of three months. This was a cross-sectional study which included 30 pre-diabetics and diabetics between 18-35 years of age attending out-patient divisions of General Medicine, as Group-B and Group-C. Group-B included patients with HbA1c 5.7 – 6.4 % and Group-C included patients with HbA1c  $\geq$  6.5 %. Both the study groups included 66% of women and 34% men. Group-A were controls with normal HbA1c ( $<$  5.7 %) concentration, with equal number of men and women (50% each). All the Group-C participants were on treatment for Type-2 Diabetes mellitus.

Inclusion criteria: Clinically diagnosed Patients with pre-diabetics and diabetics, both male and female within the age group of 28 - 35 years

Exclusion criteria: Patients with clinical conditions like Anaemia and those on medications that might affect the platelet concentrations were excluded from the study.

Serum samples from the study group and the control group were drawn after getting informed and written consent, under strict aseptic conditions. The collected samples of all the groups (A, B and C) were analysed for PCT, PDW, MPV, creatinine and HbA1c.

The haematology parameters was analysed in fully automated haematology analyser BC 6800 Mindray, creatinine was analysed in fully automated Biochemistry analyser – BS 480 Mindray and HbA1c in fully automated Biochemistry analyser – BS 390 Mindray by their respective methods [Table 1].

### **Table 1: Parameters with their methods of estimation.**

<b>Parameter</b>	<b>Method</b>
Plateletcrit (PCT) in %	Electrical impedance
Platelet Distribution Width (PDW) in %	Electrical impedance
Mean Platelet Volume (MPV) in fL	Electrical impedance
Creatinine in mg/dl	Sarcosine
HbA1c in %	Immunturbidimetry

The means and standard deviations (SD) of all the parameters were calculated in Group-A, Group-B and Group-C. Statistical analysis was performed with the Statistical Package for the Social Sciences (SPSS) version 17 software. Analysis of variance (ANOVA) was used to find the statistical significance and correlation of Plateletcrit (PCT), Platelet Distribution Width (PDW) and Mean Platelet Volume (MPV) and Creatinine in the various groups (non-diabetics, pre-diabetics and diabetics).  $P \leq 0.05$  was considered significant.

## **Results**

It was observed that the mean and SD of HbA1c was  $5.142 \pm 0.177$  in control Group-A, whereas they were  $6.0 \pm 0.282$  and  $9.091 \pm 2.021$  among the subjects. [Table 2] The HbA1c levels in Group-B and Group-C indicates prediabetes and diabetes respectively.

The parameters PCT, PDW, MPV and creatinine were assessed in all three groups. Pre-diabetic and diabetic subjects had significantly increased levels of PCT, PDW and MPV when compared with control subjects, but there is no significant difference between pre-diabetic and diabetic subjects [Table 2]. The creatinine concentration of all the three groups were within the normal ranges but, its mean and SD were found to be having a slight increase in Group-B and Group-C when compared to Group-A [Table 2].

**Table 2: Comparison among the three groups (A,B and C) by using ANOVA.**

<b>Parameters</b>	<b>Group –A (Mean and SD)</b>	<b>Group –B (Mean and SD)</b>	<b>Group –C (Mean and SD)</b>	<b>P value</b>
HbA1C(%)	5.142 ± 0.177	6.0 ± 0.282	9.091 ± 2.021	< 0.0001**
Creatinine (mg/dl)	0.690 ± 0.129	0.780 ± 0.193	0.795 ± 0.092	0.02*
PCT (%)	0.194 ± 0.041	0.244 ± 0.025	0.247 ± 0.084	0.03*
PDW(%)	15.485 ± 0.389	15.780 ± 0.622	15.983 ± 0.369	0.002**
MPV (fl)	8.340 ± 0.630	9.300 ± 0.600	9.250 ± 1.267	0.01*

PCT - Plateletcrit , PDW- Platelet Distribution Width, MPV - Mean Platelet Volume

The values are statistically significant based on the 'P' value.\*P-value < 0.05, \*\*P-value < 0.01.

The results obtained clearly show increased PCT, PDW, MPV to a greater extent in Group C (Diabetes mellitus patients), lesser extent in Group B (Pre-diabetes mellitus patients) when compared to Group-A (Non-diabetes) healthy controls, with high significance of  $p < 0.01$  [Table 2].

### **Discussion**

The current study showed a gradual increase of PCT, PDW, MPV in an increasing order in the Groups – A, B and C. The values were also found to be statistically significant with a P-value of < 0.05 for the parameters Creatinine, PCT and MPV. P-value was calculated to be < 0.01 for PDW when compared among the three groups.

According to a study, patients with poor glycaemic control were found to have significant higher platelet indices than those with controlled blood glucose levels. A positive and statistically significant correlation was found between the platelet indices, HbA1c and diabetic complications. The platelet indices were the highest among diabetic nephropathy patients [12]. This was in accordance to the current study.

There were different studies conducted which showed a significant difference of the platelet indices like PCT, PDW, MPV when compared between with and without complications of diabetes mellitus [13-16]. PCT, PDW, MPV were significantly higher in diabetic individuals than those in controls. The increase was more significant with microvascular complications than those without the same. A positive association was evident between platelet dysfunction with HbA1C and nephropathy [17]. These studies were further in support of the current study.

The platelet indices were altered and significantly associated with HbA1c levels in diabetics and microvascular complications, demonstrated a study [18].

HbA1c, MPV and PDW were highly significant and increased in patients with diabetes mellitus when compared to the controls ( $P < 0.05$ ), reports a study conducted in Karachi [19]. These studies were in direct correlation with the current study.

A study conducted in North-east India reports significantly higher platelet indices among diabetics when compared to non-diabetics. It was also found that the platelet indices were increased among patients with HbA1C  $> 7\%$  [20]. The current study was conducted in South-India with a similar study outcome.

### **Conclusion**

The study concludes with an increase in platelet indices (PCT, PDW, MPV) among the patients with diabetes mellitus compared to those with pre-diabetic range of HbA1c and controls. There was a significant association between the parameter for diagnosing and monitoring the glucose control in diabetes mellitus (HbA1c), the platelet indices (PCT, PDW, MPV) and the renal marker, creatinine. Hence, the platelet indices shall be considered as early, accessible and cheaper markers of microvascular complications of diabetes mellitus including diabetic nephropathy.

## **Ethical standards**

The study involved human participants following the ethical standards of the tertiary health care institution where the study was conducted.

## **Limitations of the study**

The study population shall be enlarged as it was relatively less.

## **References**

1. International Diabetes Federation. IDF Diabetes Atlas 7th edition. 2015; IDF;13.
2. Pradeepa R, Anjana RM, Joshi SR, Bhansali A, Deepa M, Joshi PP, et al. Prevalence of generalized & abdominal obesity in urban & rural India - the ICMR-INDIAB study (Phase-I) [ICMR-INDIAB-3]. Indian J Med Res 2015; 142: 139-50.
3. Shi Y, Hu FB. The global implications of diabetes and cancer. Lancet 2014; 383:1947-8.
4. Kaplan ZS, Jackson SP. The role of platelets in atherothrombosis. Hematology Am Soc Hematol Educ Program. 2011; 2011:51-61.
5. Jindal S, Gupta S, Gupta R, Kakkar A, Singh HV, Gupta K, et al. Platelet indices in diabetes mellitus: indicators of diabetic microvascular complications. Hematology 2011; 16:86-9.
6. Zaccardi F, Rocca B, Pitocco D, Tanese L, Rizzi A, Ghirlanda G. Platelet mean volume, distribution width, and count in type 2 diabetes, impaired fasting glucose, and metabolic syndrome: A meta-analysis. Diabetes Metab Res Rev. 2015;31(4):402–410.

7. Aypak C, Türedi O, Bircan MA, Yüce A. Could mean platelet volume among complete blood count parameters be a surrogate marker of metabolic syndrome in pre-pubertal children? *Platelets*. 2014;25(6):393–398.
8. Picard, F.; Adjedj, J.; Varenne, O. Diabetes Mellitus, a prothrombotic disease. *Ann. Cardiol. Angeiol*. 2017, 66, 385–392.
9. Sobczak, A.I.S.; Blindauer, C.A.; Stewart, A.J. Changes in Plasma Free Fatty Acids Associated with Type-2 Diabetes. *Nutrients* 2019, 11, 2022.
10. Kaur, R.; Kaur, M.; Singh, J. Endothelial dysfunction and platelet hyperactivity in type 2 diabetes mellitus: Molecular insights and therapeutic strategies. *Cardiovasc. Diabetol*. 2018, 17, 121.
11. Sobczak AIS, Stewart AJ. Coagulatory Defects in Type-1 and Type-2 Diabetes. *Int J Mol Sci*. 2019;20(24):6345.
12. Dwivedi T, Davangeri R. Variation of Platelet Indices among Patients with Diabetes Mellitus Attending Tertiary Care Hospital. *J Clin Diagn Res*, 2018, Nov, Vol-12(11): EC22-EC26.
13. Jindal S, Gupta S, Gupta R, Kakkar A, Singh HV, Gupta K, et al. Platelet indices in diabetes mellitus: indicators of diabetes microvascular complications. *Hematology*. 2011;16(2):86-89.
14. Papanas N, Symeonidis G, Maltezos E, Mavridis G, Karavageli E, Vosnakidis T, et al. Mean platelet volume in patients with type 2 diabetes mellitus. *Platelets*. 2004;15(8):475-78.
15. Ates, O, Kiki I', Bilen H, Keles, M, Koçer I', Kulaçoğ lu DN, Baykal O. Association of Mean Platelet Volume with the Degree of Retinopathy in Patients with Diabetes Mellitus. *Eur J Gen Med* 2009; 6(2):99-102.

16. Ayhan TE, Arıca S, İlhan N, Daglıoğlu M, Coskun M, İlhan O, et al. Relationship between mean platelet volume and retinopathy in patients with type 2 diabetes mellitus. *Graefes Arch Clin Exp Ophthalmol*. 2014;252 (2):237-40.
17. Walinjkar RS, Khadse S, Kumar S, Bawankule S, Acharya S. Platelet Indices as a Predictor of Microvascular Complications in Type 2 Diabetes. *Indian J Endocr Metab* 2019; 23:206-10.
18. Demirtas L, Degirmenci H, Akbas EM, Ozcicek A, Timuroglu A, Gurel A, Ozcicek F. Association of hematological indices with diabetes, impaired glucose regulation and microvascular complications of diabetes. *Int J Clin Exp Med*. 2015;8(7) 11420-11427.
19. Jabeen F, Fawwad A, Rizvi HA, Alvi F. Role of platelet indices, glycemic control and hs-CRP in pathogenesis of vascular complications in type-2 diabetic patients. *Pak J Med Sci*. 2013;29(1):152-156.
20. Bhattacharjee, Datta A, Debbarma R.K., Das S.K. Platelet indices in diabetics and influence of glycemic control – a hospital based study in North-East India. *Int J Med Res Rev* 2016;4(12):2186-2192.