

Original research article**Evaluation of platelet indices and hsCRP to predict microvascular complications among diabetics**

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Abstract

Aim: The aim of the present study was to evaluate platelet indices and hsCRP to predict microvascular complications among diabetics

Methods: A total of 200 participants were enrolled, which included 100 cases and 100 controls. Among both the cases and controls, 60 were male patients and 40 were female patients. All patients with diabetic range sugar were included as cases. The controls were all non-diabetics. Diabetics were further divided into two groups-Group A with HbA1C < 6.5% and Group B with HbA1C values > 6.5%. Platelet indices (MPV, PDW and PLCR) and hsCRP were measured for both cases and controls.

Results: The age group and platelet counts in both groups were comparable. There were a higher percentage of individuals with abdominal obesity among diabetics than among non-diabetics. The platelet indices- MPV (11.45 fL vs. 8.56 fL, $p < 0.0001$), PDW (15.68% vs. 11.43%, $p < 0.0001$), PLCR (46.3% vs. 32.4%, $p < 0.0001$) were higher among cases than controls respectively. Platelet indices- MPV (12.3 fL vs. 10.68 fL, $p < 0.0001$), PDW (16.7% vs. 10.8%, $p < 0.0001$), PLCR (47.4% vs. 45.6%, $p < 0.0001$) were higher among diabetics with complications than diabetics without complications respectively. Furthermore, hsCRP were significantly higher among diabetics than among non-diabetics (4.33mg/L vs. 2.8mg/L, $p < 0.001$).

Conclusion: Our study showed a positive correlation between Diabetes mellitus and platelet activation and reactivity as indicated by increased platelet indices. High HbA1C and diabetic complications which indicate poor glycaemic control are associated with higher platelet indices. One of the important outcomes of our study is the positive correlation between high platelet indices and diabetic complications, indicating role of increased platelet reactivity in the microvascular and macrovascular complications of diabetes mellitus. Furthermore our study has found a positive correlation between hsCRP an inflammatory marker and diabetes mellitus.

Keywords: Platelet indices, hsCRP, microvascular complications, Diabetes mellitus, prothrombotic state

Introduction

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycaemia. In the modern world, the global burden of diabetes worldwide in 2017 was estimated to be 425 million and 82 million in South East Asia. This is expected to rise to 629 million worldwide and 151 million in South East Asia by 2045 ^[1]. Factors resulting in hyperglycaemia include reduced insulin secretion, decreased glucose utilization, and increased glucose production. A number of secondary pathophysiologic changes in multiple organ systems are a result of this metabolic dysregulation ^[2]. At present, the prevalence of diabetes in Indian adults is 8.8% ^[3]. An array of long-term systemic complications occur as a result of hyperglycaemia which can be broadly divided into macrovascular complications (Coronary Artery Disease, Peripheral Arterial Disease, Stroke) and microvascular complications (Diabetic Retinopathy, Diabetic Nephropathy, Diabetic Neuropathy) ^[4]. Persistent hyperglycaemia and insulin resistance are responsible for the prothrombotic state of platelets that persists in DM. Development of vascular complications in DM are largely believed to be a result of increased platelet activity. Hyperglycemia contributes to greater platelet reactivity through direct effects and by promoting glycation of platelet proteins. As insulin inhibits activation of platelets, relative or absolute deficiency of insulin would increase platelet reactivity ^[5].

Average size and activity of the platelets is indicated by mean platelet volume (MPV). Large circulating platelets, reflected by increase in MPV, are younger, more reactive and aggregable. They also contain denser granules, secrete more serotonin and produce more thromboxane A₂ than smaller platelets. Increase in MPV has been documented in patients with metabolic syndrome, stroke and DM. Similarly platelet distribution width (PDW) is an indicator of variation in platelet size which may be a sign of

active platelet release. Platelet large cell ratio (PLCR) is directly related to PDW and MPV [6]. Another parameter associated with increased risk of cardiovascular risk in patients with type 2 DM is hsCRP (high sensitivity C-reactive protein), which is higher in diabetic individuals with microvascular complications [7].

Materials and Methods

A total of 200 participants, including 100 cases and 100 controls, who were age and gender matched, from 10 Jan 2023 to 10 Dec 2023 were included in the study. Among both the cases and controls, 60 were male patients and 40 were female patients. All patients with diabetic range sugar were included as cases. The controls were all non-diabetics. Platelet indices (MPV, PDW and PLCR) and hsCRP were measured for both cases and controls. Diabetics were further divided into two groups-Group A with HbA1C < 6.5% and Group B with HbA1C values > 6.5%.

Individuals with anemia, myeloproliferative disorders, drugs causing bone marrow suppression, thrombocytopenia and pregnancy were excluded from the study.

Results

Majority of the individuals in both case and control groups were in the age group of 40-70 years. The platelet counts in both groups were comparable and identical. Among the diabetic group, 20% were case of diabetic neuropathy with history of neuropathic pain/tingling numbness in lower limbs, 40% cases were cases of diabetic retinopathy as diagnosed by fundus examination using direct ophthalmoscope. BMI was higher among diabetic patients than among non-diabetic patients. There were a higher percentage of individuals with abdominal obesity among diabetics than among non-diabetics (Table 1). The platelet indices were higher among cases than controls (Table 2) and higher among diabetics with complications than diabetics without complications (Table 3). Platelet indices and hsCRP were significantly higher among diabetics than among non-diabetics (Table 1).

Table 1

Baseline characteristics	Cases	Controls	P value
Age (years)	40-70	40-70	
Male gender	60%	60%	
Female gender	40%	40%	
Fasting blood sugar (mean)	140 mg/dl	90 mg/dl	
Post prandial blood sugar	240 mg/dl	130 mg/dl	
History of IHD	50%	12%	<0.0001
History of HTN	43%	15%	<0.0023
Diabetic neuropathy	20%	-	
Diabetic retinopathy	40%	-	
BMI (Mean)	26.2+/-3.5	23.4	<0.001
Waist Hip Ratio	0.95	0.86	<0.0001
hsCRP (mg/L)	4.33	2.8	<0.001

Table 2: Platelet indices among cases and controls

Platelet indices	Cases	Controls	P value
MPV (Mean)	11.45 fL	8.56 fL	<0.0001
PDW	15.68%	11.43%	<0.0001
PLCR	46.3%	32.4%	<0.0001
PCT	0.25%	0.22%	<0.0001

Table 3: Comparison of platelet indices between Diabetics with complications and uncomplicated Diabetes

Platelet indices	Diabetics with complications	Uncomplicated Diabetics	P value
MPV	12.3 fL	10.68 fL	<0.0001
PDW	16.7%	10.8%	<0.0001
PLCR	47.4%	45.6%	<0.0001
PCT	0.27%	0.24%	<0.0001

Table 4: Comparison of platelet parameters between individuals with HbA1C<6.5% and HbA1C>6.5%

Platelet parameters	HbA1C <6.5%	HbA1C >6.5%	P value
MPV	10.49 fL	12.46 fL	<0.0001
PDW	14.78%	18.68%	<0.005
PLCR	42.3%	48.6%	<0.0001
PCT	0.23%	0.27%	< 0.110

Discussion

Development and sustainment of vascular complications in patients with type 2 diabetes mellitus are secondary to increased reactivity and baseline activation of platelets.⁸ Moreover, hyperglycaemia-induced up-regulation of glycoproteins (Ib and IIb/IIIa), and P2Y12 signaling which are key events underlying atherothrombotic risk in Type 1 DM and Type 2 DM.⁹ Increased glucose induces vascular abnormalities by increased formation of advanced glycation end products and activation of protein kinase C^[10].

In our study, the MPV was significantly higher in the diabetic group than the non-diabetic controls (11.45 fL vs. 8.56 fL, $p < 0.0001$), which was similar to the studies done by other researchers. Akinsegun *et al.* showed lower MPV in diabetic cases compared to the controls with no statistical significant difference^[11]. In addition, other platelet indices like PDW was also significantly higher in diabetic subjects compared to controls (15.68% vs. 11.43%, $p < 0.0001$). Studies done by Demirtas *et al.* and Jabeen *et al.* showed significantly higher PDW levels among diabetic cases. The PLCR is a relatively new platelet volume parameter and is generated by only a few machines, with the Sysmex analyser being one of them. Our study concluded that PLCR was significantly higher among diabetics than non-diabetic patients (0.25% vs. 0.22%, $p < 0.0001$)^[12, 13].

In agreement with study done by Kodiate *et al.* and Papanas *et al.* our study showed higher MPV in diabetic patients with micro and macrovascular complications than nondiabetic controls (12.3 fL vs. 10.68 fL, $p < 0.0001$)^[14, 15]. This confirms the role of increased platelet activity in the pathogenesis of vascular complications among diabetics. Furthermore, higher levels of PDW (16.7% vs. 10.8%, $p < 0.0001$) and PLCR (47.4% vs. 45.6%, $p < 0.0001$) were also observed in diabetics with complications in our study which is concordant with the results observed in study done by Mowafy *et al.*^[9].

Conclusion

Development and sustainment of vascular complications in patients with type 2 diabetes mellitus are secondary to increased reactivity and baseline activation of platelets^[8]. Our study showed a positive correlation between Diabetes mellitus and platelet activation and reactivity as indicated by increased platelet indices. High HbA1C and diabetic complications which indicate poor glycaemic control are associated with higher platelet indices. One of the important outcomes of our study is the positive correlation between high platelet indices and diabetic complications, indicating role of increased platelet reactivity in the microvascular and macrovascular complications of diabetes mellitus. Furthermore our study has found a positive correlation between hsCRP an inflammatory marker and diabetes mellitus, indicating a dysregulated inflammatory response which may lead to prothrombotic state.

References

1. Tabish SA. Is diabetes becoming the biggest epidemic of the twenty-first century? *Int. J Health Sci. (Qassim)*. 2007;1:5-8.
2. American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. *Diabetes Care*. 2014;37(1):S81-90.
3. IDF Diabetes Atlas. International Diabetes Federation. IDF Diabetes Atlas. 8th ed. Brussels, Belgium: International Diabetes Federation, 2017.
4. Fowler MJ. Microvascular and macrovascular complications of diabetes. *Clin Diabetes*. 2008;26:77-82.
5. Keating FK, Sobel BE, Schneider DJ. Effects of increased concentrations of glucose on platelet reactivity in healthy subjects and in patients with and without diabetes. *Am J Cardiol*. 2003;92:1362-1365.
6. Kumari Shilpi, Potekar RM. A Study of Platelet Indices in Type 2 Diabetes Mellitus Patients. *Indian J Hematol Blood Transfus*. 2018 Jan-Mar;34(1):115-120.
7. Kang ES, Kim HJ, Ahn CW, Park CW, Cha BS, Lim SK, *et al.* Relationship of Serum High Sensitivity C-Reactive Protein to Metabolic Syndrome and Microvascular Complications in Type 2 Diabetes. *Diabetes Res Clin Pract*. 2005;69(2):151-9.
8. Stratmann B, Tschoepe D. Pathobiology and cell interactions of platelets in diabetes. *Diab Vasc Dis Res*. 2005;2:16-2.
9. Mowafy N, Metwaly E, Hashish B, Bazeed M. A study of the value of some platelet parameters in patients with type 2 diabetes mellitus. *Al-Azhar Assiut Med J*. 2015;13:13-18.
10. Kodiatte TA, Manikyam UK, Rao SB, Jagadish TM, Reddy M, Lingaiah HK. Mean platelet volume in type 2 diabetes mellitus. *J Lab Phys*. 2012;14:5-9.
11. Akinsegun A, Olusola D, Sarah J, Olajumoke O, Adewumi A, Majeed O, *et al.* Mean platelet volume and platelet counts in type 2 Diabetes: mellitus on treatment and non-diabetic mellitus controls in Lagos, Nigeria. *Pan Afr Med J*. 2014;18:1-5.
12. Demirtas L, Degirmenci H, Akbas E, Ozcicek A, Timuroglu A, Gure A, *et al.* Association of hematological indices with diabetes, impaired glucose regulation and microvascular complications of diabetes. *Int. J Clin. Exp. Med*. 2015;8:11420-11427.

13. Jabeen F, Rizvi H, Aziz F, Wasti A. Hyperglycaemic induced variations in hematological indices in type 2 diabetics. *Int. J Adv. Res.* 2013;1:322-334.
14. Kodiatte TA, Manikyam UK, Rao SB, Jagadish TM, Reddy M, Lingaiah HK. Mean platelet volume in type 2 diabetes mellitus. *J Lab Phys.* 2012;14:5-9.
15. 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;15:475-478.