

MEAN PLATELET VOLUME AS A PREDICTIVE BIOMARKER FOR RETINOPATHY IN PATIENTS WITH TYPE 2 DIABETES

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ABSTRACT

Objective: To determine the association of mean platelet volume with diabetic retinopathy in our population.

Study Design: Cross sectional study.

Place and Duration of Study: Department of Hematology & Ophthalmology, Combined Military Hospital Lahore, from Jul to Dec 2020.

Methodology: A total of 146 known patients with type 2 diabetes were enrolled in this study. They included 78 patients with diabetic retinopathy (group 1) and 68 without diabetic retinopathy (group 2). Five (5ml) of whole blood was extracted from patients through clean venipuncture in a tube containing EDTA and mean platelet volume was generated through automated haematological analyzer Sysmex KX-21 and HbA1c was generated through automated analyzer Cobas c501.

Result: A total of 146 patients with type 2 diabetes were included in this study. The age of patients ranged from 25-70 years (Mean age: 53.3 ± 0.02 years). Out of 146 patients 66 (45.2%) were males and 80 (54.8%) were females. Among patients with type 2 diabetes 78 (53.4%) has retinopathy while 68 (46.6%) have no retinopathy. A statistically significant difference ($p < 0.005$) was observed in mean platelet volume and platelet distribution width among patients with retinopathy to those without retinopathy.

Conclusion: Mean platelet volume plays a significant role in the determination of retinopathy with type 2 diabetes and helps to monitor progression of disease.

Keywords: Diabetic retinopathy, Mean platelet volume, Platelet distribution width.

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INTRODUCTION

Diabetes mellitus (DM) is a leading cause of macro- and microvascular complications¹. Visual impairment in diabetes mellitus is known as diabetic retinopathy and its underlying pathological mechanism is microangiopathy. Patients with diabetes mellitus are at a high risk to develop diabetic retinopathy which is the most important and common complication with an escalating rate of morbidity². Proliferative diabetic retinopathy is an advanced stage of retinal neovascularization that can lead to complications such as retinal detachment, hemorrhage, and glaucoma³. Retinopathy in patients with type 2 DM has an association with a few genetic and environmental factors. The onset and severity of retinal neovascularization significantly differs among individuals with type 2 DM, due to strong association of diabetic microangiopathy with certain risk and protective factors⁴. Multiple factors associated with the development of diabetic retinopathy (DR) include genetic factors, duration of diabetes, obesity, dyslipidemia, smoking, hypertension, and hyperglycemia refractive index. Impaired insulin action in patients with diabetes may enhance platelet activation resulting

in microvascular (retinopathy) complications⁵.

Platelets play a key role in the maintenance of homeostasis and the function of platelets is correlates with mean platelet volume (MPV)⁶. MPV is used as a marker to indicate the platelet's average size and activity⁷. The larger platelets exhibit a more dense granular structure with increased production of thromboxane A2 and resulting in platelet collagen induced aggregation and hyper-responsiveness to ADP⁸. Structural and functional changes in platelets have been reported in DM possibly due to pathological process. Noticeable increase in MPV has been identified in patients with DM⁹. The large platelets are haemostatically more competent and are a reason for vascular thrombosis. They can lead to myocardial infarction, retinopathy and cardiovascular disease.

Retinopathy is one of the most important complications of diabetes mellitus. Increased MPV is associated with increased risk of vascular complications. The identification of large sized platelets can be done through a routine hematological parameter MPV. The aim was to assess possible association of mean platelet volume with diabetic retinopathy in our population.

METHODOLOGY

It was a cross sectional validation study, carried out in the department of Haematology in liason with

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department of Ophthalmology after taking approval from ethical review board CMH (IRB # 190/2020) Combined Military Hospital Lahore, Pakistan, from July to December 2020.

A sample size of 146 was calculated using frequency of MPV in patients with type 2 diabetes with WHO sample size calculator considering 5% level of significance, and 95% confidence interval. Sampling technique used was non-probability consecutive sampling¹⁰. All adult patients who were diagnosed cases of diabetes as per American Diabetic Association (ADA) irrespective of their gender, socio-economic status, duration of the disease and age above 25 years were included in this study. Patients were divided into two groups based on the presence or absence of retinopathy of any grade diagnosed on fundoscopy. Group I included 50 patients having retinopathy of any grade and group II (control group) had 50 patients without retinopathy. Patients with sepsis (WBC >11 x 10⁹), anemia (Hb<10g/dl), Thrombocytopenia (<150 x 10⁹/l) and those taking antiplatelet drugs were excluded. Five (5ml) blood was extracted from patients through a clean venipuncture in a tube containing EDTA. Hematological parameters including mean platelet volume and platelet count were measured for all patients using automated hematological analyzer Sysmex KX-21 and HbA1C was generated through automated analyzer Cobas c501. Diabetic retinopathy was diagnosed by ophthalmoscopic examination by experts.

Data was analysed using SPSS version 23. Mean and SD were calculated for numerical variables and percentage and frequency for categorical variables. Mean platelet volume (MPV) between group I and group II was compared, considering (p-value ≤0.05) to be statistically significant. Independent sample t-test was applied to determine 95% confidence interval and significant difference between two groups.

RESULTS

A total of 146 patients were included in this study who met the inclusion criteria. The age of patients ranged from 25-70 years (Mean age: 53.3 ± 0.02 years) among those 28 (19.2%) were <40 years and 118 were ranged 40-70 years. Out of 146 patients 66 (45.2%) were males and 80 (54.8%) were females. Among patients with type 2 diabetes 78 (53.4%) has retinopathy while 68 (46.6%) have no retinopathy (figure).

Table showed the comparison of platelet indices in patients with diabetes having retinopathy to those without retinopathy. A statistically significant difference (p-value <0.005) was observed in mean platelet

volume (MPV) among patients with retinopathy to those without while platelet count and platelet distribution width (PDW) has no statistically significant difference (p-value >0.05) among both groups.

Mean platelet count were 229.6 ± 39.1 in group A and 215.0 ± 32.5 in group B. Mean platelet volume were 10.3 ± 1.56 and 7.7 ± 1.01 in patient with retinopathy and without retinopathy respectively. Mean platelet width in group A and B were 9.4 ± 1.4 and 9.1 ± 1.17 respectively.

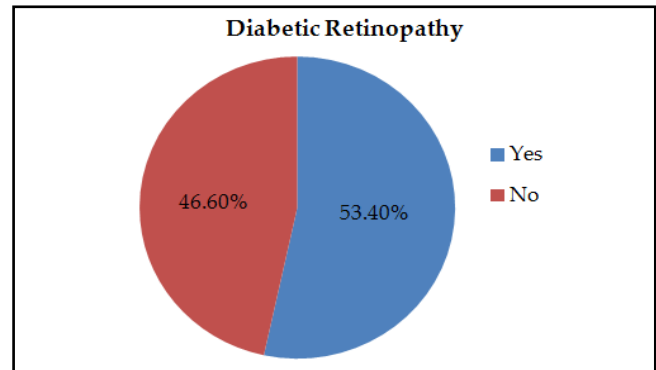


Figure: Percentage of diabetic retinopathy among study population. Among patients with type 2 diabetes 78 (53.4%) has retinopathy while 68 (46.6%) have no retinopathy.

Table: Comparison of platelet indices in patients with diabetes having retinopathy to those without retinopathy.

Parameters	Study Groups		p-value
	Group A (n=78)	Group B (n=68)	
Platelet count (x 10 ⁹ /L)	229.6 ± 39.1	215.0 ± 32.5	0.081
Mean platelet volume (fL)	10.3 ± 1.56	7.7 ± 1.01	0.005
Platelet distribution width (fL)	9.4 ± 1.4	9.1 ± 1.17	0.006

DISCUSSION

DM is one of the most common medical problems in our community, having significant mortality and morbidity. Main clinical feature of this disease is hyperglycemia (raised blood glucose level) due to a defect in insulin secretion or an increase resistance to insulin at cellular level. It is divided into two subtypes. Type 1 or the insulin dependent diabetes mellitus and type 2 the non-insulin dependent diabetes mellitus. Type 2 diabetes is the most common form accounting for around 90-95% of all the diabetic cases worldwide. Patients with diabetes mellitus have an increased risk of developing micro- and macro vascular complications. Retinopathy is one of the most important complications of diabetes mellitus. Mean platelet volume

(MPV) is used as a marker to indicate the size and platelet activity. Increased MPV is associated with increased risk of vascular complications. Large platelets are haemostatically more competent and associated with high thrombotic potential hence place the patient at a higher risk status.

DM is considered a common cause of vascular complications (micro and macro-vascular) which leads to multi organ disease mainly neuropathy, nephropathy, retinopathy and stroke¹¹. The definition of diabetic retinopathy according to American Academy of Ophthalmology is damage to blood vessels in the retina. These blood vessels can swell and leak and sometimes abnormal new blood vessels grow on the retina. There are two main stages of diabetic eye disease. NPDR (non-proliferative diabetic retinopathy) is the early stage of diabetic eye disease. In NPDR, tiny blood vessels leak, making the retina swell. PDR (proliferative diabetic retinopathy) is the advanced stage. It happens when the retina starts growing new blood vessels. This is called neovascularization. These fragile new vessels often bleed into the vitreous. If bleed is significant, it might block vision. Proliferative diabetic retinopathy is very serious, and can steal both central and peripheral (side) vision.

A large group of population with type 2 DM experiences micro and macro-vascular complications to an unavoidable extent. So, modifications in risk factor are required to prevent incessant complications. People with inadequate glycemic control, hypertension and obesity, have a higher prevalence of microvascular complications in diabetics¹². Many studies have demonstrated that high MPV leads to an encounter with conditions such as metabolic syndrome, stroke, and diabetes mellitus. Patients with DM are at greater risk for coronary artery disease and cerebrovascular events than the normal person¹³. A series of studies have shown that increased platelets function or elevated MPV has a strong association with DM.

In patient with diabetes the platelets activation occurs due to high level of prothrombotic components like thromboxane A₂, thromboxane B₂, platelet factor 4, serotonin, and platelet-derived growth factor¹⁴. Mean platelet volume is used as a marker to indicate the size, platelets activity and storage of giant or young platelets that increases the secretion of serotonin and β -thromboglobulin which ultimately enhance the production of thromboxane A₂ and increased susceptibility of aggregation. Papanas *et al*, reported the association of elevation of thromboxane A₂, reduction of pro-

tacyclin level and high MPV with microvascular complications in patients with diabetic retinopathy as compared to normal persons¹¹.

In our study, we determined association of MPV with diabetic retinopathy. MPV was higher in patients with diabetic retinopathy as compared to control group. Buch A and colleagues determined an association between high MPV values and retinopathy indicating increasing activity of the platelets and high incidence of proliferative retinopathy¹⁵. Walinjar *et al*, have also reported that mean platelet volume exhibits a strong and independent relationship with diabetes. They reported substantial relation in cardiovascular complications in diabetes mellitus¹⁶. Ito T and colleagues have described that taurine (an amino acid present in greater amount in platelets) has an essential role to maintain the cell volume through osmoregulation. Its concentration decreases in diabetic condition. The oral administration of taurine overcomes the platelet aggregation to bring back to a normal state. A reduction in taurine level is associated with increased mean platelet volume in diabetic retinopathy¹⁷.

After the onset of DM >60% of the patients develop diabetic retinopathy and blindness over the years. The initial characterization of diabetic retinopathy start with less severe non-proliferative to more severe proliferative retinopathy with vascular occlusions, hemorrhages, cotton wool spots, and increased tendency to form neovascularization¹⁸. Muhiddin *et al*, reported that in all stages of retinopathy in comparison to the control group mean platelet volume was significantly high¹⁹. Van der Meijden *et al*, have described the strong induction of neovascularization is due to vascular endothelial growth factor which is produced by hypoxic condition. The hypoxia in diabetic retinopathy stimulates neovascularization as a repercussion of occlusions and micro-aneurysms²⁰. The growth factors which induce proliferative retinopathy through neovascularization are epidermal growth factor, insulin growth factor-1 and platelet-derived growth factors²¹. Yamashiro *et al*, reported substantially elevated levels of mean platelet volume, specifically in case of proliferative retinopathy where activated platelets liberate growth factors having more contribution in progress to develop complicated disease²². The significantly increased levels of MPV in pro-liferative retinopathy suggest that growth factors released from activated platelets indirectly contribute to disease progression.

This study revealed a positive correlation of the severity of retinopathy with MPV. As the MPV increa-

ses the degree of retinopathy increases from nonproliferative to proliferative and leads to symptoms such as blurred vision or even blindness. A study conducted by Gimeno-orna *et al*, identified that a few cases of the proliferative retinopathy were linked with coronary arteries disorders²³. Tuzcu *et al*, explained the pathophysiology of MPV as a significant marker raised in vascular disease²⁴.

Despite the strong association of MPV with diabetic retinopathy found in the present study, it has some limitations including its relatively small sample size. The difference in MPV between patients with and without retinopathy was close to the significance level. This difference might be found statistically significant in a larger sample size. Useful information about the relationship between MPV and diabetic microvascular complications can be found if findings are augmented with similar studies with large sample size including people from various areas and ethnicities.

CONCLUSION

MPV values were significantly higher in patients with DR as compared to control group. High MPV correlated with severity of DR. In particular, MPV values were statistically significantly higher in patients who developed proliferative DR compared with patients without retinopathy. MPV can be used as an indicator that provides easy access to functional properties and platelet volume parameters. So, it will be very easy in monitoring the severity and progression of the disease.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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