

Study of hematological parameters in patients with diabetic retinopathy

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Abstract

Background: Diabetic Retinopathy (DR) is the major cause of blindness among the working population and is the most common microvascular complication of diabetes. Diabetes Mellitus (DM) is a complex disease characterized by chronic hyperglycemia, metabolic abnormalities, and long-term macro- and micro-vascular complications involving the blood vessels, eyes, kidneys, and nerves. The majority of morbidity and mortality associated with diabetes are due to hyperglycemia leading to diabetic complications. Larger platelets contain denser granules which are metabolically and enzymatically more active and have higher thrombotic potential. Mean Platelet Volume (MPV) indicates the activity and average size of platelets and increase in MPV is linked to increased thrombotic potential. Several studies have shown relation between platelet parameters like Platelet count and MPV with presence of vascular complications. **Objectives:** To study the hematological parameters in patients with diabetic retinopathy and to evaluate the association of platelet parameters with glycemic control and vascular complications in patients with diabetic retinopathy. **Materials and Methods:** This was a case control study carried out for 18 months in a tertiary care hospital in patients with diabetic retinopathy. **Results and Discussion:** Patients with DR had low normal hemoglobin level of 13.5 (+/- 1.1) gm/dl. The Red cell Distribution Width was increased in patients with DR (15.4). The ESR in patients with DR was increased. The platelet count had a positive correlation with fasting blood sugar, postprandial blood sugar and HbA_{1C} in patients with DR. **Conclusion:** For identification of vascular complications in patients with Type 2 diabetes, platelet parameters can be used only as an accessory tool but not as a single reliable marker. It is recommended that hematological parameters should be analyzed along with glycemic index and fundus examination to look for retinal changes to rule out impending microvascular complication of diabetes mainly diabetic retinopathy.

Key Words: Diabetes mellitus, Diabetic Retinopathy, Mean Platelet Volume and Platelet count.

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INTRODUCTION

Diabetic Retinopathy (DR) is the major cause of blindness and is the most common microvascular complication of diabetes¹. Diabetes Mellitus (DM) has been considered as a global pandemic². The development of Type 2 DM is caused by interaction between genetic

and environmental factors³. The vascular complications of DM causes increased morbidity and mortality⁴. The injurious effects of hyperglycemia are categorized as macrovascular complications (stroke, peripheral arterial disease and coronary artery disease) and microvascular complications (diabetic neuropathy, nephropathy and retinopathy)⁵. The main reason behind Type 2 DM is impaired insulin secretion and insulin resistance⁶. There is a non-enzymatic interaction between the primary amino group of a protein and the carbonyl group of the reducing sugar in recurrent hyperglycemia. This interaction leads to the formation of compounds that are known as Advanced Glycation End products (AGEs). The molecules linked to AGEs leads to the formation of Reactive Oxygen Species (ROS), which increases oxidative stress. AGEs reduce the bioavailability and activity of endothelium-derived nitric oxide; and thus prevent nitric oxide (NO) release⁷. In long-standing cases

of DM, there is alteration in platelet functions and abnormal interactions between the vascular endothelium and platelets which is found to be an important contributing factor to the complications of DM. Platelets play an important role in the genesis of vascular complications of DM as there is hyperactivity of platelets in the early stage of this disease⁸. Before thrombopoiesis there appear changes in the density, size and reactivity of the platelets. Large platelets are younger and are hyperactive. These larger platelets hold more dense granules and are more thrombogenic. Increased fibrinogen binding, aggregation and thromboxane production indicates hyper-reactivity of platelets in DM⁹.

MATERIALS AND METHODS

This was a case-control study carried out for a period of 18 months (November 2015 to May 2017) among 54 individuals, comprising of 27 patients with diabetic retinopathy and 27 normal individuals. This study comprised of studying the hematological parameters in patients with diabetic retinopathy attending the Diabetic clinic and Ophthalmology clinic (for cases) and Master Health check-up clinic (for controls) after obtaining ethical committee clearance. This study included all patients with diabetic retinopathy and control samples were taken from healthy people. Patients with type-1 diabetes, patients with anemia, thrombocytopenia or on antiplatelet drugs were excluded from the study. Pregnant women as well as patients with debilitating diseases were also excluded from the study.

Data entry and analysis: The data was entered in Microsoft Excel and analyzed using EpiData analysis version V.2.2.2.186 and Stata 12 software. The continuous variables such as age, duration of illness, hematological parameters (Hemoglobin, PCV, RBC, MCV, MCH, MCHC, Platelet count, MPV, ESR at one hour and WBC count) and blood glucose parameters were expressed as Mean (SD) or median (IQR). The categorical variables such as gender, number of cases and controls, and presence of complications were expressed as percentage. The association between continuous variables such as age, duration of illness, hematological parameters (Hemoglobin, PCV, RBC, MCV, MCH, MCHC, Platelet count, MPV, ESR at one hour and white cell count) and blood glucose parameters with diabetic status of the participants (Diabetic or Non-diabetic) were identified using unpaired t test or Mann Whitney U test. The association between categorical variables and diabetic status of the participants were identified using chi-square test. The correlation between patient parameters (duration of illness, age, FBS, PPBS and RBS) and platelet parameters (Platelet count) was

identified using Pearson correlation. The p value of <0.05 was considered as statistically significant.

RESULTS

Table 1: Comparison of Hematological Parameters among the study participants

Haematological parameters in Mean (SD)	Diabetic	Non diabetic	p value*
Haemoglobin (gms/dl)	13.5 (1.1)	14.3 (1.2)	0.013
PCV(%)	38.8 (3.8)	41.5 (3.2)	0.007
RBC (In millions /cumm)	4. 2 (0.5)	4.6 (0.4)	0.005
MCV(fl)	89.1 (5.5)	89.5 (5.7)	0.791
MCH(pg)	30.2 (2.2)	30.8 (2.1)	0.341
MCHC(gms/dl)	33.8 (1.0)	34.4 (1.1)	0.056
RDW	15.4	-	NA
ESR (mm/hour)	25.0 (12.0-44.0)	10.0 (8.0-18.0)	0.001#
Total leukocyte count (cells/cu.mm)	9603.7 (3188.9)	6974.1 (1519.8)	<0.001
Differential count – neutrophils (%)	61.6 (9.1)	55.3 (9.3)	0.016
Differential count – eosinophils (%)	3.6 (3.6)	6.9 (7.2)	0.036
Differential count – lymphocytes (%)	29.1 (7.4)	30.8 (7.0)	0.367
Differential count – monocytes (%)	6.1 (2.7)	7.1 (2.9)	0.166

*unpaired t test # Mann Whitney U test

Table 2: Distribution of platelet parameters of study participants

Platelet parameters	Diabetic	Non diabetic	p value*
Platelet count (lakhs/cu.mm)	3.016296 (0.855562)	2.885926 (0.686161)	0.539
MPV (fl)	8.2 (0.7)	8.0 (0.6)	0.421

*unpaired t test

Table 3: Correlation between platelet count and diabetic patient parameters

Platelet parameters	Patient's comparative parameter	Pearson correlation coefficient - r	p value
Platelet count	Duration of drug intake	-0.50	0.008
Platelet count	Fasting blood sugar	+0.07	0.730
Platelet count	Post prandial blood sugar	+0.04	0.858
Platelet count	HbA1C	+0.02	0.923
Platelet count	Age	-0.46	0.016
Platelet count	MPV	-0.21	0.282

Table 4: Correlation between platelet count and non-diabetic patient parameters

Platelet parameters	Patient's comparative parameter	Pearson correlation coefficient - r	p value
Platelet count	Fasting blood sugar	-0.23	0.244
Platelet count	Post prandial blood sugar	-0.15	0.464
Platelet count	Random blood sugar	+0.17	0.402
Platelet count	Age	-0.43	0.027
Platelet count	MPV	-0.36	0.065

Table 5: Correlation between MPV and diabetic patient parameters

Platelet parameters	Patient's comparative parameter	Pearson correlation coefficient - r	p value
MPV	Fasting blood sugar	-0.20	0.325
MPV	Post prandial blood sugar	-0.14	0.475
MPV	HbA1C	-0.21	0.286
MPV	Duration of drug intake	+0.17	0.398
MPV	Age	+0.30	0.124

Table 6: Correlation between MPV and non-diabetic patient parameters

Platelet parameters	Patient's comparative parameter	Pearson correlation coefficient - r	p value
MPV	Fasting blood sugar	+0.16	0.425
MPV	Post prandial blood sugar	+0.02	0.928
MPV	Random blood sugar	-0.07	0.741
MPV	Age	+0.09	0.668

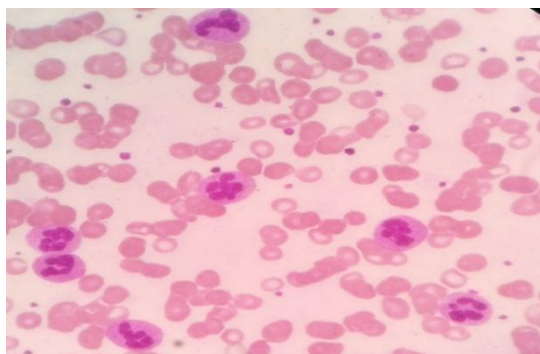


Figure 1: Peripheral smear study of a patient with diabetic retinopathy showing neutrophilia in oil immersion field

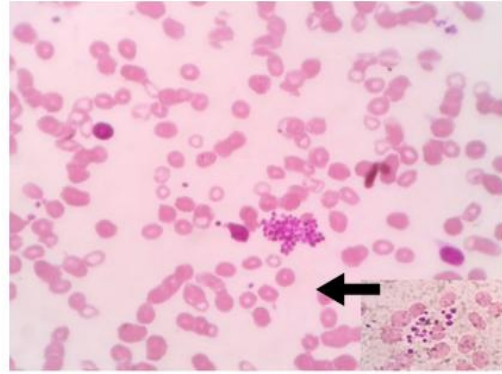


Figure 2: Peripheral smear study of a patient with diabetic retinopathy showing platelet clusters in oil immersion field

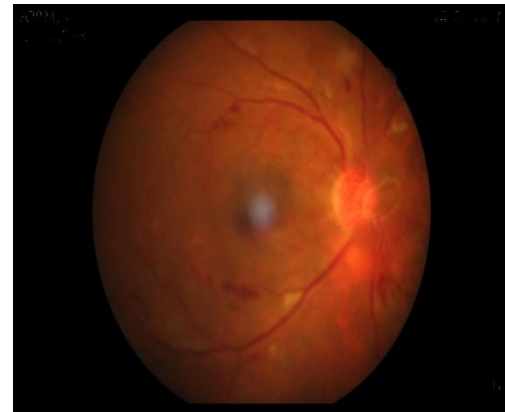


Figure 3: Fundus examination of a patient showing Proliferative Diabetic Retinopathy with neovascularization of optic disc

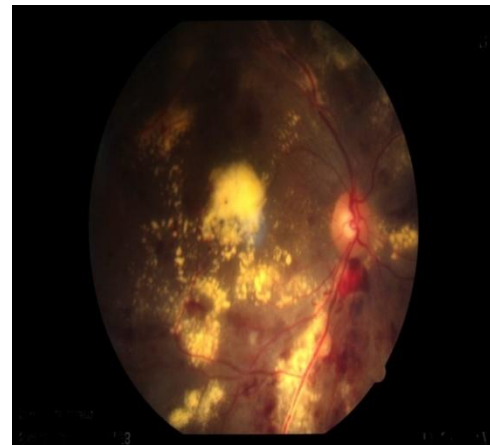


Figure 4: Fundus examination of a patient showing very severe Non-Proliferative Diabetic Retinopathy



Figure 5: Fundus examination of a patient with showing Non-Proliferative Diabetic Retinopathy with exudates

DISCUSSION

Among the 27 patients with DR, 22 were male and 5 were female; and among the 27 normal individuals included in the study, 16 were male and 11 were female. The mean age of patients with DR was 41.5 years and normal individuals was 57.2 years (p value <0.001). Symptoms like blurring of vision, double vision and eye pain were found to be the commonest symptoms in this study. The mean duration of diabetes among the patients with DR was found to be 8 years. The patients with DR had a low normal hemoglobin level of 13.5 (\pm 1.1) gm/dl and hematocrit was reduced to 38.80 (\pm 3.8) %. The RBC count in patients with DR was 4.2 (\pm 0.5) millions/cu.mm, which also showed low normal value. The RDW (Red cell Distribution Width) was 15.4 in the patients with DR which appears to be increased. The ESR value in patients with DR was found to be increased i.e., 25 mm at 1 hour with a p value of 0.001. But hematological parameters like MCV, MCH and MCHC levels were found to be similar in patients with DR and normal individuals. The platelet parameters like platelet count and MPV were found to be similar in the patients with DR and the normal individuals. The Total leukocyte count was also near higher normal level among the patients with DR, with a mean value of 9603/cu.mm. The Differential leukocyte count in patients with DR showed mild neutrophilic preponderance. The mean HbA_{1C} values which indicates the glycemic control in patients with DR was found to be 7.5. The platelet count had a positive correlation with fasting blood sugar, postprandial blood sugar and HbA_{1C} in patients with DR. The MPV (Mean Platelet Volume) did not show any positive correlation with the glycemic parameters. The mean HbA_{1C} level was 7.5 \pm 1.1 which indicates poor glycemic control among the patients with DR. The renal parameters and lipid profile parameters did not show much variation among the patients with DR and normal individuals.

CONCLUSION

The hemoglobin and hematocrit values were found to decrease in patients with DR indicating that they are more prone to anemia. The elevated total leukocyte count with neutrophilia indicated that these patients are likely to have secondary infections. The glycemic control was found to have positive correlation only with platelet count and not with MPV, which may be due to the regular treatment. Patients who had good glycemic control were found to have normal platelet parameters in this study. Therefore, for identification of vascular complications in patients with Type 2 diabetes, platelet parameters can be used only as an accessory tool but not as a single reliable marker. In depth studies are required to know the correlation between HbA_{1C} and MPV. It is recommended that the hematological parameters should be analyzed along with glycemic index and fundus examination to look for retinal changes to rule out impending microvascular complication of diabetes mainly Diabetic Retinopathy.

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