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Original Article

Correlation between Complications associated with Type 2 Diabetes Mellitus and Platelet Indices

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ABSTRACT:

Background: Diabetes mellitus is a disease characterized by either deficiency of insulin or its peripheral resistance resulting in hyperglycaemic and non enzymatic glycation of protein.Several studies have revealed that platelet with increase number and size possibly affecting the platelet distribution width contributing in the pathogenesis of vascular complication. The present study was conducted with the aim to establish the correlation between complications associated with type 2 diabetes mellitus and platelet indices. **Materials and methods:** The present study was conducted on 150 patients in the Department of Medicine in collaboration with Department of Biochemistry and Department of Pathology at GMC Patiala. The study was divided into two groups Group I: without microvascular complications and Group II with microvascular complications, and Group-A (HbA1c ≤ 7%),Group-B(HbA1c>7%). At least two microaneurysms and/or retinal haemorrhage and/or signs of retinal damage were considered as Diabetic Retinopathy. Student t test was applied as a test of significance and p value of less than 0.05 was considered as significant. **Results:** The mean Platelet crit amongst Group I subjects was 0.24±0.67 and amongst Group II subjects was 0.30±0.22. The p value was 0.02. The mean HbA1c in Group A was 6.56% and that in Group B was 9.20% with a mean RBS/FBS of 163.30 mg/dl in Group A and 243.50 mg/dl in Group B. It was also found in our study that mean age of patients of Group A was less i.e. 48.82 years as compared to Group B in which it was 53.58 years. **Conclusion:** All platelet indices (MPV, PDW, Platelet Crit, P-LCR, Platelet Count were significantly increased in patients with nephropathy than in patients without of nephropathy.

Key words: Diabetes, Platelets, Nephropathy.

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INTRODUCTION

Diabetes mellitus is a disease characterized by either deficiency of insulin or its peripheral resistance resulting in hyperglycaemic and non enzymatic glycation of protein.[1] It is associated with acute and chronic complications.The development of long term complications has a close relationship with endothelial dysfunction mainly caused by poor glycaemic control and is leading cause of poor quality of life in this group of individuals.[2] The search for assessment tools to establish and early diagnosis of these complications has been a challenge but in recent year, several studies have highlighted the participation of platelet as one of the coagulation system element involved in the genesis of these events.[3-6] Glycosylated haemoglobin is a useful index of mean glycaemia during preceding 120 days.[7] It is also a predictor of complications as measures reducing HbA1c correspondingly reduce the risk of complications.[8] Platelets are tiny, disc shaped, non nucleated, flattened structure 1-4 μm in diameter. They are derived from cytoplasm of megakaryocytes and are well influenced by patient's general health and nutritional status. (Around 65% of platelets are smooth; disc shaped inert cells whereas the remaining 10- 35% are less clearly defined cells; spherical platelets).[9] The morphological differences that exist in platelets have important implications for measuring platelet size and assessing the functional expressions of platelets.[10] The differences in platelet volume vividly correlates with differences in density, dense body content, enzymatic activity of lactate dehydrogenase, platelet aggregation to adenosine di-phosphate and serotonin uptake and release, supporting the relevance of the Mean Platelet Volume(MPV) as a measure of platelet function.[11] Several studies have revealed that platelets with increased number and size possibly affecting the platelet distribution width contributing in the pathogenesis of vascular complication. Larger platelets are more enzymatically and metabolically active and have higher thrombotic ability as compared to small size platelets.[12] The present study was conducted with the aim to establish the correlation between complications associated with type 2 diabetes mellitus and platelet indices.

MATERIALS ANDMETHODS

The present study was conducted on 150 patients in the Department of Medicine in collaboration with Department of Biochemistry and Department of Pathology at GMC Patiala. Newly diagnosed or on follow-up both males and females between 35 and 60 year with Type-2 DM, visiting outdoor and admitted as indoor patients in the Rajindra Hospital /GMC Patiala during 2016-2017 were included in the study. Patients with uncontrolled hypertension, patients on insulin or other anti platelet drugs were excluded from the study. Patients who had recent clinical evidence of acute recent cardiac, liver and renal dysfunction were also excluded. Clinical and laboratory characteristics of the patients were assessed for platelet indices, microvascular complications and HbA1c values. The study was divided into two groups Group I: without microvascular complications and Group II with microvascular complications, and Group-A (HbA1c≤7%), Group-B (HbA1c>7%). At least two microaneurysms and/or retinal haemorrhage and/or signs of retinal damage were considered as Diabetic Retinopathy. Presence of microalbuminuria or macroalbuminuria was accepted as Nephropathy. Neuropathy was assessed by Neuropathy Disability Score (NDS). Under aseptic conditions venous sample was withdrawn and platelet indices like MPV, PDW, platelet count etc were calculated. HbA1c was computed by chromatography analyser, Erba Mannheim. All the results were arranged in a tabulated form and analysed using SPSS software. The results were expressed as percentage of total. Student t test was applied as a test of significance and p value of less than 0.05 was considered as significant.

RESULTS

The study enrolled a total of 150 subjects, out of which 72 were males and 78 were females.

Table 1 shows the association of Platelet indices within two Groups of controlled and uncontrolled diabetes mellitus which were A and B respectively. The mean HbA1c in Group A was 6.56% and that in Group B was 9.20% with a mean RBS/FBS of 163.30 mg/dl in Group A and 243.50 mg/dl in Group B. It was also found in our study that mean age of patients of Group A was less i.e. 48.82 years as compared to Group B in which it was 53.58 years. The mean values of Platelet Indices MPV, Platelet Crit, PDW were higher in the Group B while the Platelet Count was low in Group B as compared to Group A. Table 2 shows the platelet indices and nephropathy complications based on grouping of complications. The mean Pt Ct amongst Group I subjects was 0.24±0.67 and amongst Group II subjects was 0.30±0.22. The p value was 0.02. The mean MPV amongst Group I subjects was 9.46±1.40 and amongst Group II subjects was 9.92±1.31. The p value was 0.04. The mean PDW amongst Group I subjects was 12.00±3.55 and amongst Group II subjects was 13.72±5.72. The p value was 0.02. In Group II patients with nephropathy all the platelet indices were significantly increased as compared to the Group I without nephropathy. Patients of type 2 diabetes mellitus with nephropathy had a significant p-value of all platelet indices when the two above groups were compared.

As in the Table-3 it was seen that Group 2 with neuropathy showed a significant p-value in relation to the platelet indices, Platelet Crit , PDW and P-LCR as compared to Group I which was not associated with neuropathy. MPV was increased in Group II as compared to Group I but it was not statistically significant. Platelet count was significantly decreased in Group II with neuropathy as compared to Group I and was statistically significant. The mean PCT in Group I and Group II was 2.74±0.85 and 2.48± 0.71 respectively. The mean P-LCR in Group I and Group II was 28.60±6.37 and 31.25±8.18 respectively.

The results in Table 4 showed significant changes in the values of MPV, PLCR in patients Group II with retinopathy as compared to Group1 which was not associated with retinopathy. The mean MPV in Group I was 9.46±1.32 and in group II was 10.09±1.38. The mean PDW in Group I and Group II was 12.33±4.48 and 13.79 ±5.24 respectively. PDW and Platelet Crit did not show any statistically significant change in the two groups though both were increased in associated with retinopathy as compared to Group I but it was not statistically significant as shown by p- values.

Table 1: Demographic and clinical characteristics of groups

	Mean ±SD	
Character	**Group A (Hb-A1C ≤ 7) (N=64)**	**Group B (Hb-A1C > 7) (N=86)**
Age (in yrs)	48.82±8.70	53.05±7.87
Hb-A1C (%)	6.56±0.28	9.19±1.7625
RBS/FBS (mg/dl)	163.30±32.05	243.50±97.39
PtCt (%)	0.23±0.06	0.30±0.20
MPV (fl)	8.72±0.74	10.39±1.29
PDW (fl)	10.32±1.59	14.70±5.48
PCT (10^3)	3.03±0.77	2.36±0.0.71
PLCR (%)	25.96±4.21	32.32±7.78

Table 2: Platelet indices and nephropathy complications based on grouping of complications

Platelet Index	Group I (Without nephropathy) (N=77) Mean±S.D	Group II (With nephropathy) (N=73) Mean±S.D	t-value (p-value)	Sig.
PtCt (%)	0.24±0.67	0.30±0.22	2.322 (0.022)	S
MPV (fl)	9.46±1.40	9.92±1.31	2.038 (0.043)	S
PDW (fl)	12.00±3.55	13.72±5.72	2.217 (0.028)	S
P-LCR (%)	27.76±5.96	31.58±7.91	3.337 (0.001)	S
PCT (10^3)	2.49±0.74	2.78± 0.84	2.444 (0.026)	S

Table 3: Platelet indices and neuropathy complications

Platelet Index	Group I (Without Neuropathy) (N=92) Mean±SD	Group II (With Neuropathy) (N=58) Mean±SD	t-value (p-value)	Sig.
PtCt (%)	0.25±0.74	0.30±0.22	1.992 (0.048)	S
MPV (fl)	9.55±1.34	9.90±1.41	1.541 (0.1250)	NS
PDW (fl)	12.01±3.55	14.16±6.40	2.730 (0.007)	S
P-LCR (%)	28.60±6.37	31.25±8.18	2.211 (0.029)	S
PCT (10^3)	2.74±0.85	2.48± 0.71	1.982 (0.049)	S

Table 4: Platelet indices and retinopathy complications

Platelet Index	Group I (Without Retinopathy) (N=97) Mean±S.D	Group II (With Retinopathy) (N=53) Mean±S.D	t-value (p-value)	Sig.
PtCt (%)	0.25±0.13	0.30±0.20	1.718 (0.088)	NS
MPV (fl)	9.46±1.32	10.09±1.38	2.759 (0.007)	S
PDW (fl)	12.33±4.48	13.79 ±5.24	1.792 (0.075)	NS
P-LCR (%)	28.41±6.38	31.84±8.14	2.839 (0.005)	S
PCT (10^3)	2.68±0.79	2.57±0.83	0.837 (0.404)	NS

DISCUSSION

Diabetes has an insidious development and is often diagnosed due to the presence of microvascular and macrovascular complications.[13] Acute complications of Diabetes Mellitus are Diabetic ketoacidosis and Hyperglycaemic hyperosmolar state. Chronic complications of Diabetes Mellitus affect many organ systems and are responsible for the majority of morbidity and mortality associated with disease. Chronic complications can be divided into vascular and non vascular complications.[14] Diabetic nephropathy is one of the most common complications and is an important cause of renal failure.[15] Microalbuminuria is the earliest clinically detectable stage diabetes induced damage to the kidneys at which appropriate interventions can slow the progression or even reverse nephropathy.[16]

Platelet indices as biomarkers in diabetes have been under study for so many years. The first study investigating MPV effect in patients with diabetes was conducted by Wincour et al[17] in 1994. The study demonstrated that MPV was higher in patients with diabetes. Coban et al[18] later said that MPV was higher in prediabetes and as well as diabetes mellitus.

The basic mechanism in diabetic complications includes the formation of advanced glycation end products, activation of Protein Kinase C and disturbances in polol pathways. As MPV is seen increased in patients of type 2 diabetes mellitus, there is presence of large platelets which are younger, more reactive, aggregable, contain denser granules. They also secrete more serotonin, β-thromboglobulin and thromboxaneA2 than the smaller platelets. All these can produce a procoagulant effect and can cause thrombotic vascular complications. This suggests a relationship between platelet indices and diabetic vascular complications. Thus increased platelet indices like MPV, PDW and PLCR may assume an important role in signaling the development of micro vascular complications in diabetes. In a study conducted by Papanas et al[19] (2004) amongst 416 subjects, MPV is higher in type 2 diabetic patients than in non-diabetic patients. Among type 2 diabetic patients MPV is higher in those who have microvascular complications (retinopathy or microalbuminuria). In our study, the mean PtCt amongst Group I subjects was 0.24±0.67 and amongst Group II subjects was 0.30±0.22. The p value was 0.02. The mean MPV amongst Group I subjects was 9.46±1.40 and amongst Group II subjects was 9.92±1.31. The p value was 0.04. The mean PDW amongst Group I subjects was 12.00±3.55 and amongst Group II subjects was 13.72±5.72. The p value was 0.02. In Group II patients with nephropathy all the platelet indices were significantly increased as compared to the Group I without nephropathy. Patients of type 2 diabetes mellitus with nephropathy had a significant p-value of all platelet indices when the two above groups were compared. In a study conducted by Jindal et al[4] , platelet indices, especially PDW, are different between diabetics and controls as well as between diabetics with and without microvascular complications. Discriminant analysis using PDW and MPV could classify majority of patients with diabetic complications. Platelet indices MPV, PDW and Platelet -Large Cell Ratio were significantly higher in diabetic patients. In our study, platelet Crit , PDW and P-LCR were significantly increased in Group II with neuropathy as compared to Group I which was not associated with neuropathy. MPV was increased in Group II as compared to Group I but it was not statistically significant. Platelet count was significantly decreased in Group II with neuropathy as compared to Group I and was statistically significant. The mean Platelet count in Group I and Group II was 2.74±0.85 and 2.48± 0.71 respectively. The mean P-LCR in Group I and Group II was 28.60±6.37 and 31.25±8.18 respectively. In a study conducted by Kumari and Potekar[20] et al, MPV, PDW and PLCR were significantly higher in diabetics compared to non diabetics. Among the diabetics, MPV, PDW and PLCR were higher in those with complications as compared to those without complications.

CONCLUSION

Platelets play a role in the development of diabetic complications. Platelet hyperactivity and increased platelet activation results from a combination of factors including the effects of insulin, hyperglycemia, hyperlipidemia, endothelial dysfunction, oxidative stress, and inflammatory state in type 2 diabetes. From the above study, we can conclude that all platelet indices (MPV, PDW, Platelet Crit, P-LCR, Platelet Count) were significantly increased in patients with nephropathy than in patients without of nephropathy.

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