PLATELET AGGREGATION AND CLOTTING TIME IN TYPE II DIABETIC MALES

Background: Diabetes mellitus is a heterogeneous disorder that affects cellular metabolism in variety of ways and coagulation indices are reported to be adversely affected. Insulin resistance is a marked pathophysiology of Type II diabetes causing abnormalities in the microvascular and macrovascular circulations. The entire coagulation cascade is dysfunctional in such condition. Platelets may assume an important role in atherosclerosis in diabetes. Prothrombin time (PT) and activated partial thromboplastin time (APTT) are haematological indices that give an idea about the coagulation status of patients. Hence the present study is undertaken to see the effect of diabetes on platelet aggregation and coagulation parameters like PT and APTT.

Aims & Objective: To study platelet aggregation and clotting time (PT, APTT) in type II diabetic males.

Materials and Methods: The present study included 30 type II diabetic males and 30 normal male subjects. Platelet aggregation was studied by O Brein J R method using ADP reagent. Clotting time (prothrombin time, activated partial thromboplastin time) was estimated by using coagulometer.

Results: ADP induced platelet aggregation was significantly higher while PT and APTT were significantly lower in diabetic group compared with control group (p<0.05) by applying unpaired 't' test.

Conclusion: Our study showed increased platelet agreeability and decreased PT, APTT in type II diabetic males. So, type II diabetic patients are more prone to diseases such as coronary artery disease, cerebrovascular disease and peripheral vascular disease.

Key Words: Diabetes Mellitus; Platelet Aggregation; Prothrombin Time (PT); Activated Partial Thromboplastin Time (APTT); Insulin

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INTRODUCTION

The global prevalence of diabetes mellitus has been estimated at 347 million individuals and is rapidly increasing. Diabetes mellitus is commonly associated with both microvascular and macrovascular complications. Patients with type 2 diabetes mellitus have a two- to four-fold increase in the risk of coronary artery disease which accounts for 60% of their deaths. Hyperglycemia, a well-defined risk factor for accelerated atherosclerosis and vascular disease, may cause vessel damage.[1-3]

Evidences for abnormal platelet functions in diabetes mellitus have been shown as: altered platelet functions, increased aggregation of platelet that leads to acceleration of atherogenesis.[1-3] Platelets in type 2 diabetic individuals adhere to vascular endothelium and aggregate more readily than those in healthy people.[4]

The prothrombin time (PT) and the activated partial thromboplastin time (APTT) are global coagulation tests used to assess the coagulation system in a clinical setting.[5-8] Prothrombin time is a laboratory screening test used to detect disorders involving the activity of the factors I, II, V, VII, and X of the extrinsic and common pathways . Activated partial thromboplastin time is used to screen for abnormalities of the intrinsic and common clotting systems and to monitor the anticoagulant effect of circulating heparin. It measures the activities of factors I, II, V, VIII, IX–XI, and XII of the intrinsic and common pathways.[5] Shortened clotting times could, therefore, be the expression of a hypercoagulable state.[8]

Hence present study is undertaken to see the effect of type 2 diabetes on platelet aggregation, prothrombin time and activated partial thromboplastin time.

MATERIALS AND METHODS

The present study was conducted in 30 type 2 diabetic males aged between 40-60 years suffering from diabetes for more than 5 years. Age matched males not suffering from diabetes mellitus and any other systemic diseases were selected as controls. Patients suffering from type 1 diabetes hypertension, cancer, cardiac and respiratory diseases and those on anticoagulant therapy were excluded.

The study was conducted after permission from the institutional ethical committee. Written consent of cases and controls were taken. 9 ml of fasting blood sample was taken and mixed with 1 ml of 3.8% of trisodium citrate in test tube. It was then centrifuged at rate of 1300 rpm for 15 min. 2 ml of platelet rich plasma from above sample was taken in test tube and kept in a preset colorimeter. The absorbance reading was noted. After that 0.1 ml ADP solution was added and then mixed. Now the absorbance was noted again at the end of 20 seconds. Change in absorbance at the end of 20 seconds was taken as change in platelet agreeability (O Brein J R method). The optical density difference was compared between cases and controls. Platelet poor plasma was taken for estimation of prothrombin time and activated partial thromboplastin time with the help of coagulometer.

Statistical analysis was done by applying unpaired 't' test using Graph pad prism 5 software.

RESULTS

Table 1 shows comparison of basic parameters between diabetics and non-diabetics and the difference was not significant (p value >0.05). Table 2 shows the comparison of coagulation parameters in cases and controls. Platelet aggregation was more in diabetics, so the optical density difference was higher in them as compared to controls. The difference was very highly significant (p<0.0001). Also significant difference was noted in PT and APTT showing a lower value in diabetics than controls (p<0.05).

Table-1: Comparison of basic parameters between cases and controls

Parameter	Mean ± SD		p value	Significance
	Cases (n=30)	Controls (n=30)		
Age (yrs)	52.17 ± 0.8698	51.70 ± 1.137	0.7456	NS
Weight (kg)	62.93 ± 1.989	63.53 ± 1.666	0.8179	NS
Height (cm)	160.7 ± 1.214	159.7 ± 1.273	0.5848	NS
BMI (kg/m²)	24.25 ± 0.5506	24.81 ± 0.5767	0.4905	NS

Table-2: Comparison of some coagulation parameters between cases and controls

Parameter	Mean ± SD		p value	Significance
	Cases (n=30)	Controls (n=30)		
Platelet aggregation (ODD)	0.062 ± 0.004	0.027 ± 0.002	<0.0001	VHS
PT (sec)	10.43 ± 0.3380	11.37 ± 0.2467	0.0296	significant
APTT (sec)	28.40 ± 0.7799	30.73 ± 0.6485	0.0250	significant

ODD: Optical Density Difference; VHS: Very Highly Significant

DISCUSSION

Our study shows shortened PT, APTT in type II diabetic males. PT is an indicator of extrinsic and common pathway while APTT indicates defects in intrinsic and common pathway. This may account for abnormalities in coagulation haemostasis. Platelet dysfunction and abnormalities in coagulation cascade can accelerate atherogenesis in diabetic patients. Insulin resistance (IR) is a uniform finding in type 2 diabetes, as are abnormalities in the microvascular and macrovascular circulations.[4]

Metabolic disturbances that commonly occur in patients with IR are atherogenic dyslipidemia, hypertension, glucose intolerance, and a prothrombotic state.[1] The prothrombotic state is characterized by increased fibrinogen levels, increased plasminogen activator inhibitor (PAI)-1 , and different abnormalities in platelet function.[4] Hyperglycemia may cause vessel damage through at least three apparently unrelated pathway: advanced glycation end product (AGE) formation, activation of protein kinase C (PKC) and sorbitol accumulation by way of polyol pathway.[2]

Patients with type II diabetes have increased populations of platelets that express activation-dependent adhesion molecules, such as activated GpIIb-IIIa, lysosomal Gp53, thrombospondin, and Pselectin.[1] Among diabetic individuals, increased platelet agreeability and adhesiveness are due to the following: (1) Reduced membrane fluidity; (2) Altered Ca2+ and Mg2+ homeostasis; (3) Increased arachidonic acid metabolism; (4) Increased TXA2 synthesis; (5) Decreased prostacyclin production; (6) Decreased NO production; (7) Decreased antioxidant levels; (8) Increased expression of activation-dependent adhesion molecules (e.g., GpIIb-IIIa, P-selectin). Platelets from patients with type II diabetes exhibit enhanced platelet aggregation activity early in the disease course that may precede the development of Cardiovascular disease.[1]

Fibrinogen levels may also be elevated in diabetes, and this would contribute to fibrin clot formation and platelet aggregation.[6] Fibrinolytic activity has been reported to be low in type 2 diabetes. This is thought to be due to high levels of plasminogen activator inhibitor -1, which inhibit the formation of fibrinolytic plasmin from plasminogen.[1] These anomalies account for hypersensitivity of platelets to aggregants and hyposensitivity to antiaggregants and are thought to contribute to enhanced atherosclerosis via increased platelet activity at sites of vessel injury.

An elevated level of prothrombin has also been associated with thrombosis, and elevated levels of prothrombin lead

to increased thrombin generation in an in vitro model of hemostasis. Thus, it seems likely that elevated prothrombin levels could contribute both to thrombotic risk and to a shortening of the PT and APTT.[6]

In patients with diabetes mellitus, abnormalities in coagulation haemostasis, platelets dysfunction and reduced activity of fibrinolytic system can collectively accelerate atherogenesis in diabetic patients. Our findings of decreased PT, APTT matches with that of D.L Sauls et al, while decreased APTT matches with that of Ying Zhao et al and Wolfgang Korte et al.

CONCLUSION

Our study shows shortened PT, APTT and increased platelet agreeability in diabetic mellitus patients that makes them more prone to cardiovascular, cerebro-vascular and peripheral vascular diseases. Therefore, hypercoagulable state management may have a preventive value in subsequent vascular complications in patients with diabetes mellitus.

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