



COMPARISON OF PROTHROMBIN TIME AND ACTIVATED PARTIAL THROMBOPLASTIN TIME BETWEEN PATIENTS WITH DIABETES MELLITUS AND DIABETICS WITH HYPERTENSION

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ABSTRACT

Uncontrolled Diabetes Mellitus Causes both microangiopathy leading to diabetic nephropathy & retinopathy and macroangiopathy leading to coronary heart diseases & also diabetic neuropathy. Hypertension itself is characterized by arteriosclerosis. To assess the coagulation status, we measured PT & APTT in these cases. A 52 Known Type II diabetic patients with hypertension, 32 known Type II Diabetes Mellitus patients & 30 controls were included in the study. Both PT & APTT were measured on CA-50 Sysmex Coagulation Analyzer. The FBS & PPBS were estimated on Humastar-300 complete Auto analyzer. BMI was calculated for all the subjects. The PT was prolonged in Group B ($14.86538 + 0.12290$) than controls ($13.83333 + 0.08419$), $p = 0.0000001$ and Group A ($13.40 + 1.29$), $p = 0.0000001$. The APTT was prolonged in Group B ($34.53846 + 0.27933$) than controls ($30.13333 + 0.32424$) $p = 0.0000001$ and Group A ($30.81 + 2.40$), $p = 0.0000001$ respectively. The FBS was increased in cases than controls ($p = 0.0000001$). The PPBS was also increased in cases than controls ($p = 0.0000001$). The BMI for Group A ($26.55 + 3.2$) Group B ($26.9615 + 2.6515$) and for controls ($25.05 + 2.7268$). This study showed Prolonged PT and APTT in diabetes mellitus with hypertension. Abnormal PT & APTT are the indications of altered activity or absence or decreased levels of clotting factors of intrinsic & extrinsic coagulation pathways respectively. The BMI value indicates that cases are overweight. PT & APTT should be checked in such cases prior to any surgery.

KEYWORDS : Procoagulant, Prothrombin Time (PT), Activated Partial Thromboplastin Time (APTT), Tissue Factor, Fibrinolysis.



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INTRODUCTION

Uncontrolled Diabetes mellitus causes both microangiopathy leading to Diabetic nephropathy, retinopathy and macroangiopathy leading to coronary heart disease and also Diabetic neuropathy⁽⁹⁾. Hypertension substantially increases the risk of both microvascular and macrovascular complications including stroke, Coronary artery disease and peripheral vascular disease, retinopathy, nephropathy and possibly neuropathy⁽⁷⁾. Macrovascular disorders such as atherosclerosis are a recognized major cause of morbidity in the diabetic population, and are implicated in the circulatory disturbances that are seen in diabetes⁽¹¹⁾. The circulatory disturbances are further compounded by alteration in platelet count and activity, coagulopathy, fibrinolytic aberration, haemorrhological factors, and changes in endothelial metabolism. Thrombotic myocardial infarction may be secondary to complicated or ruptured atherosclerotic plaques with further exposure of procoagulant proteins that initiate blood coagulation or due to contact between blood and damaged endothelium. The purpose of the study is to assay some of the Haemostatic factors (PT & APTT) in patients with Type II Diabetes Mellitus (or) NIDDM and correlate the results with Diabetic patients with Hypertension & controls.

MATERIALS AND METHODS

The present study was carried out at ASRAM Medical College and Teaching Hospital at Eluru, in Andhra Pradesh. 32 known Type II Diabetes Mellitus patients as Group A, 52 known Type II Diabetes Mellitus patients with Hypertension as Group B of both sexes, 30 healthy age and sex matched controls were included in the study. After obtaining ethical committee consent and patient consent, closed in the interview was done to the patients. 35-70 years, Type II diabetic with hypertension, Type II Diabetic patients were included in the study. Vitamin-K deficiency,

Pregnancy, Valve replacement was excluded in the study. During questioner, both patient history and Family history was collected. For the Fasting Blood Sugar (FBS) sample, both the patients and controls were instructed to fast for 8-12 hours. During Fasting hours, the patients were allowed to take only water and any other type of food was not allowed. A Fasting venous blood was collected under aseptic condition, by doing vein puncture. The blood was collected in both plain and citrated tubes. A 1.8 ml. of 3.2 % of citrate was used as an Anticoagulant. The citrated blood was centrifuged at 1500 rpm for 10 minutes and plasma was separated immediately. The plasma was used for the estimation of Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) respectively. PT and APTT were measured in plasma on Sysmex 50 coagulation Analyzer immediately. PT was estimated by Liquiplastin Thromboplastin reagent using TULIP Diagnostics Private Limited kits. Similarly APTT was estimated by Liquicelin-E Cephaloplastin reagent using Elagic Acid as an activator using TULIP Diagnostics Private Limited kits. The plain tube blood was allowed to clot for 30 minutes. Serum was separated by centrifuging at 1500 rpm for 10 minutes. The serum was immediately estimated for Fasting Blood Sugar (FBS). After giving, an oral Glucose load of 75 grams of Glucose, Post Prandial Blood Sugar (PPBS) was estimated after 2 hours in serum. The serum Glucose was estimated by G.O.D.-P.O.D. method on Huma star 300 complete Auto analyzer, using Human kits.

RESULTS

The results obtained in this study were from a total of 114 subjects. These 114 subjects have been divided into controls containing (n = 30), Group – A containing (n = 32) and Group-B containing (n = 52). The results are shown in Table-1, Table -2 and Table-3.

Table-1
Comparison of serum FBS , PPBS , BMI , PT ,APTT between Controls & Group A

Groups	FBS	PPBS	BMI	PT	APTT
Controls Mean \pm SD	85.8 \pm 10.94	124.8 \pm 10.45	25.05 \pm 2.72	13.83 \pm 0.46	30.13 \pm 1.77
Group A Mean \pm SD	155.62 \pm 50.01	235.59 \pm 61.9	26.55 \pm 3.23	13.40 \pm 1.29	30.81 \pm 2.40
t – value	42.49	55.11	3.5	-9.680	7.555
p – value	0.001**	0.001**	0.001**	0.5	0.001**
Inference	Highly significant	Highly significant	Highly significant	Not significant	Highly significant

Table 1 shown the Serum levels of FBS, PPBS , APTT and calculated BMI were significantly increased and there was no significant change in PT levels in controls and Group-A

Table -2
Comparison of serum FBS , PPBS , BMI , PT ,APTT between Controls & Group B

Groups	FBS	PPBS	BMI	PT	APTT
Controls Mean \pm SD	85.8 \pm 10.94	124.8 \pm 10.45	25.05 \pm 2.72	13.83 \pm 0.46	30.13 \pm 1.77
Group B Mean \pm SD	198.557 \pm 73.7	268.25 \pm 67.82	26.94 \pm 2.67	14.84 \pm 0.84	34.53 \pm 2.0
t – value	1.631	22.403	6	11.854	19.52
p – value	0.2	0.001**	0.001**	0.001**	0.001**
Inference	Not significant	Highly significant	Highly significant	Highly significant	Highly significant

Table 2 shown the Serum levels of PPBS , PT ,APTT and calculated BMI were significantly increased and there was in FBS levels and not significant in controls and Group-B

Table – 3
Comparison of serum FBS , PPBS , BMI , PT ,APTT between Group A & Group B

Groups	FBS	PPBS	BMI	PT	APTT
Group A Mean \pm SD	155.62 \pm 50.01	235.59 \pm 61.9	26.55 \pm 3.23	13.40 \pm 1.29	30.81 \pm 2.40
Group B Mean \pm SD	198.557 \pm 73.7	268.25 \pm 67.82	26.94 \pm 2.67	14.84 \pm 0.84	34.53 \pm 2.0
t – value	5.963	0.8125	1.229	16.22	15.70
p – value	0.001**	0.4	0.2	0.001**	0.001**
Inference	Highly significant	Not significant	Not significant	Highly significant	Highly significant

Table 3 shown the Serum levels of FBS, PT ,APTT were significantly increased and PPBS levels were increased and are not significant and there was no significant change in calculated BMI in Group A and Group-B

DISCUSSION

The present study was done on 32 diabetic patients, and 52 diabetic patients with Hypertension and 30 normals were taken as controls. Various parameters like FBS, PPBS, PT, APTT and BMI of these patients were compared with controls. Diabetic patients comprised Group-A and Diabetic patients with Hypertension comprised Group-B. In comparison with controls FBS, PPBS, BMI and APTT values were highly elevated $P < 0.001$ indicating that Group A patients had higher BMI, higher Blood glucose levels and prolonged APTT (but still within the normal range) PT did not show any significant variation. Abnormalities in both lipid metabolism and plasma coagulation system have been considered to contribute to the development of Atherosclerotic changes and Thrombotic events in Diabetic patients. The present study did not show any thrombotic tendency in comparison with the controls as

seen by a prolonged APTT value in diabetic patients. This finding is correlated to the findings of Fatherlrahman Mahdi Hassan in the year 2009⁽⁴⁾ of 50 diabetic patients and 10 controls where there was no difference between APTT values which is not correlated to the present study though the difference is not significant between controls and Diabetics. PT was shortened significantly. Patients with Type-II Diabetes Mellitus also show higher BMI when compared with normal individuals. Hypercoagulation in abdominal obesity is thought to be caused primarily by the synthesis of factors activating coagulation and inhibiting fibrinolysis in adipose tissue. These findings are correlated well with the findings of Acang N, Jalil FD in the year 1993⁽¹⁾, 60 diabetic patients and 60 controls. The mean \pm SD of PT is 10.1 ± 1.31 seconds in diabetic patients Vs 11.04 ± 0.93 seconds in controls. Whereas APTT is 29.2 ± 3.69 sec. Vs 32.16 ± 3.77 sec. They found PT and APTT were shorter in diabetic patients when compared to controls.

A similar findings were found in the study done by D.L.Sauls, A.C. Banini, et al., in the year 2006⁽³⁾ of 41 diabetic patients and 39 controls. They found PT (11.3 ± 0.5 Vs 11.9 ± 0.6 sec.) and APTT values (26.6 ± 3.7 Vs 29.3 ± 3.4 sec.) were shorter in diabetes when compared with controls. According to their study APTT values were shortened which was not seen in the present study. The study done by OO Alao, DO Damulak, et al. in the year 2010⁽⁶⁾ of 50 Type-II Diabetic patients were compared with 50 control's. PT and APTT values were found to be prolonged ($P < 0.005$). This is not correlated to the present study where PT was shortened in diabetics though APTT was prolonged. The study done by Ritu Madan, Baupta, Sumita Saluja, et al 2009⁽⁸⁾ of 60 type-II diabetic patients were compared with 30 non-diabetic patients. They found no difference in PT ($P=0.05$) and APTT ($P=0.05$) values in diabetics verses control's. This indicates that Diabetic patients need not always have a hypercoagulable state PT could be shortened too which is correlated to the present study. Many studies have shown both procoagulant and Anticoagulant status in Diabetics. Because Diabetes Mellitus is multifactorial disease the coagulation profile may be affected by several factors which have yet to be investigated. In the present study on comparison of Group-B with controls parameters like PT, APTT, BMI and PPBS showed a significant elevation in Group-B patients which was statistically significant ($P < 0.001$). The study done by Cristiana Catena, Laura Zingaro, et al., in the year 2000⁽²⁾, coagulation abnormalities were assessed in 382 patients with essential hypertension and compared with controls ,they found that PT and APTT values did not show significant values which is not correlated to the present study. In a study done by R.S.El-Hagracy, G.M. Kamal, et al., in the year 2010⁽¹⁰⁾, 60 Type II Diabetic patients were divided into Group I having 30 patients without history (or) clinically detected heart disease and Group – II having 30 patients with history of Myocardial infarction. These subjects were compared with 20 controls. The levels of tissue factor pathway Inhibitor and factor VIIa were compared b/n these patients and controls. The results showed that the values of TF, TFPI and Factor VIIa were higher in diabetic group

when compared to controls. These values were significantly higher in hypertensives and dyslipidemia but not in smokers. This indicates that Diabetic patients with hypertensive patients have procoagulant status when compared with controls. All these studies do not show much change in Hypertensive patients with regards to PT and APTT values. Some studies have shown a procoagulant state which is different from the results obtained in the present study where PT and APTT values are prolonged. This indicates that there is a tendency for bleeding in these patients. In the present study on comparison of PT and APTT values between Group-A and Group – B showed highly significant prolongation in PT and APTT values. P value < 0.001 . BMI did not show any significant variation between the two groups. Leonardo A. Sechi, Laura Zingaro, et al., in the year 2003⁽⁵⁾, has investigated 352 patients with Mild to moderate essential Hypertension and diabetic patients with hypertension on parameters like PT, APTT and BMI. They found that hypertensive patients had greater BMI than controls. There was no significant difference in PT and APTT which is not correlated to the present study.

CONCLUSION

The present study shows significant difference in PT and APTT values between Group-A and Group-B where there is a prolongation in these values in Group-B patients which should be kept in mind before undertaking any surgical procedure for patients with Diabetes mellitus and hypertension. These findings suggest that haemorrhagic tendencies and complications should not be entirely ruled out among diabetics, and should born in mind during the management of these patients. It would also be helpful to incorporate coagulation screening (PT, APTT) as routine tests for better management of Diabetic patients. Obesity enhances thrombotic tendency through up regulation of Tissue Factor, altered expression of proteins participating in the coagulation cascade as well as atherosclerosis. The positive correlation of procoagulant markers (PT & APTT) and BMI reinforces the importance of Glucose optimal control in T2DM patients.

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