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Original Research Article

A COMPARATIVE STUDY OF COAGULATION PROFILE OF TYPE 2 DIABETIC INDIVIDUALS WITH HEALTHY INDIVIDUALS

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Abstract

Background: The presence of chronically elevated blood glucose levels in individuals with diabetes mellitus leads to the development of coagulopathies. This is primarily attributed to the process of glycation, which involves the binding of glucose molecules to various proteins involved in the clotting mechanism, such as haemoglobin, prothrombin, and fibrinogen. The abbreviation APTT, which stands for activated partial thromboplastin time, and the abbreviation PT, which stands for prothrombin time, are indicators of a hypercoagulable state. This state is characterized by an elevated risk of thrombosis and negative cardiovascular consequences. A comparative study of coagulation profile of type 2 diabetic individuals with healthy individuals. **Materials and Methods:** This study was conducted on 80 individuals of which 40 were Type-2 DM(Study group)& 40 were healthy individuals (control group) of age group 40-75 yrs with duration of diabetes more than 3yrs in the Department of Physiology VDGMC Latur; Maharashtra. The diagnostic criteria for diabetes mellitus are established by the National Diabetes Data Group and the World Health Organization (WHO). **Result:** The average age of patients diagnosed with type 2 Diabetes Mellitus was 53.85 ± 5.89 years, while the average age of healthy patients was 37.81 ± 5.11 years. The values for PT, APTT, and INR in patients with type 2 diabetes and non-diabetic patients were found to be 14.72 ± 3.02, 26.87 ± 3.35, and 1.10 ± 0.25, and 15.46 ± 3.80, 1.09 ± 0.23, and 36.18 ± 10.32, respectively. The results indicate that the levels of PT and INR did not show a statistically significant difference between cases and healthy patients. **Conclusion:** The Activated Partial Thromboplastin Time (APTT) was shorter in Type-2 diabetes mellitus individuals than healthy individuals. This laboratory evidence of shortened APTT in diabetic individuals could therefore be the expression of hypercoagulable state.

INTRODUCTION

Diabetes mellitus (DM) represents a significant global health concern. Type 2 diabetes mellitus (DM), which is distinguished by the presence of insulin resistance, accounts for approximately 90% of diabetes cases on a global scale. Diabetes mellitus is characterized by hyperglycemia & biochemical alterations in carbohydrate; protein and lipid metabolism.[1] DM due to defect in insulin secretion is Type1DM(IDDM) & DM due to decreased sensitivity of tissues to insulin (insulin resistance) is Type 2 DM(NIDDM).[2] Diabetes mellitus is commonly associated with both microvascular & macrovascular complications with increased risk of coronary artery disease.[3-5]DM is heterogeneous disorder that affects cellular metabolism in variety of ways & coagulation indices are adversely affected. Individuals diagnosed with diabetes mellitus (DM) are at a significantly elevated risk of experiencing atherothrombotic events. It has been observed that approximately 80% of patients with DM succumb to a thrombotic demise, with 75% of these fatalities attributed to complications arising from cardiovascular disorders. Hence coagulation profile must be a part of Investigations requested by clinicians in diabetes mellitus.

Therefore aim of our study is to compare coagulation status of Type 2diabetic individuals with healthy individuals by doing coagulation tests:

1) PT, INR &
2) APTT

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Prothrombin time is a laboratory screening test used to detect disorders involving activity of the factors 1,II,III,IV, V, VII,& X of the extrinsic & common pathways. APTT is used to screen for abnormalities of intrinsic and common pathways involving activity of factors 1, II, V, VIII, IX- XI, & XII. Shortened clotting times, could therefore be the expression of a hypercoagulable state.[6]

MATERIALS AND METHODS

This study was conducted on 80 individuals of which 40 were Type-2 DM(Study group)& 40 were healthy individuals (control group) of age group 40-75 yrs with duration of diabetes more than 3yrs in the Department of Physiology VDGMC Latur; Maharashtra.

The diagnostic criteria for diabetes mellitus are established by the National Diabetes Data Group and the World Health Organization (WHO). These criteria include the presence of symptoms of diabetes in addition to specific blood sugar measurements. These measurements consist of a random blood sugar level exceeding 200mg%, a fasting blood sugar level exceeding 126mg%, or a postprandial blood sugar level exceeding 200mg%.The diagnostic criteria for diabetes mellitus are established by the National Diabetes Data Group and adopted by the World Health Organization (WHO). These criteria consist of the presence of diabetes symptoms in addition to a random blood sugar level exceeding 200mg%. If the fasting blood sugar level exceeds 126mg% or the postprandial blood sugar level exceeds 200mg%, it indicates a potential health concern. The subjects with Type-1 DM, heart disease, on anticoagulant therapy, renal disease, liver disease, dengue, malaria, history of thrombo-embolism and cancer patients were excluded.

Methodology

Under all aseptic conditions, 5ml blood samples were collected from Group-1 & Group -2 individuals from anticubital veins using 22G number needles. Collected samples from both the patients and controls transferred in clean container or tube having 3.2% trisodium citrate (1:9). Immediately mixed the blood with anticoagulant to avoid foam formation. Centrifuge the samples for 15 minat approximately 3000rpm & collect the plasma in separate tubes. Fresh plasma is preferred for testing as it performs bests when tested immediately. Samples may be tested within 2hrs at 25 degree centigrade & within 3hrs at 2-8 degree centigrade. Take haemostatic reagent into a test tube respectively for doing PT INR & APTT; add patient plasma into test tube. Incubate test tube containing plasma and reagent; PT INR and APTT were measured on coagulometer model –ECL 105 coagulometer model. Our laboratory ranges are PT (11-16sec); INR (0.9-1.3); APTT(22-37sec). Statistical analysis done by applying impaired test.

RESULTS

The average age of patients diagnosed with type 2 Diabetes Mellitus was 53.85 ± 5.89 years, while the average age of healthy patients was 37.81 ± 5.11 years. It is worth noting that a significant proportion of both groups fell within their sixth decade of life. No statistically significant difference was observed between the genders of patients with type 2 diabetes and those without diabetes. There was no statistically significant disparity observed in the platelet count and total calcium level between individuals diagnosed with type 2 diabetes and those without diabetes. [Table 1] presents the data collected in the study. The values for PT, APTT, and INR in patients with type 2 diabetes and non-diabetic patients were found to be 14.72 ± 3.02, 26.87 ± 3.35, and 1.10 ± 0.25, and 15.46 ± 3.80, 1.09 ± 0.23, and 36.18 ± 10.32, respectively. The results indicate that the levels of PT and INR did not show a statistically significant difference between cases and healthy patients. However, the APTT levels exhibited a high level of statistical significance in distinguishing between the two groups. The data presented in [Table 2].

Table 1: Basic profile of the participants

Parameters	Cases (40) Mean ± SD	Control Mean ± SD	P-Value
Age (years)	53.85 ± 5.89	37.81 ± 5.11	<0.0001
Gender			0.41
Male	18 (45)	16 (40)	
Female	22(55)	24 (60)	
Occupation			<0.0001
Unemployed	4 (10)	2 (5)	
Informal	28 (70)	16 (40)	
Formal	8 (20.0)	22 (55)	
SBP (mmHg)	145.85 ± 11.74	119.11 ± 10.74	<0.0001
DBP (mmHg)	81.01 ± 12.15	77.16 ± 6.89	0.36
FBG (mmol/L)	12.02 ± 2.66	4.66 ± 0.77	<0.0001
WHR (cm)	0.95 ± 0.11	0.84 ± 0.11	<0.0001
BMI (Kg/m^2)	22.22 ± 2.44	21.36 ± 2.96	0.22
PLT × $10^3/mm^3$	181.55 ± 15.69	169.61 ± 16.55	0.45

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Table 2: Mean of PT, INR and APTT in case and control groups

Parameters	Cases	Control	P-Value
PT	14.72 ± 3.02	15.46 ± 3.80	0.344 (NS
INR	1.10 ± 0.25	1.09 ± 0.23	0.321 (NS)
APTT	26.87 ± 3.35	36.18 ± 10.32	0.0001 (Highly Significant)

Table 3: Regression analysis of PT, INR and APTT

	OR (95% CI)	
Parameters	**Male**	**Female**
PT	1.00 (0.22–1.88)	1.88 (0.58–6.15)
INR	1.11 (0.25–1.79)	1.82 (0.49–6.02)
APTT	1.05 (0.19–2.15)	2.98 (0.82–10.29)

DISCUSSION

DM is a multifaceted condition that exerts an impact on cellular metabolism through various mechanisms, notably leading to significant alterations in coagulation parameters. The presence of elevated blood glucose levels in individuals with diabetes is associated with an increase in fibrinogen levels, a protein involved in blood clotting. This hyperfibrinogenemia condition also triggers the activation of the coagulation cascade, leading to an enhanced production of thrombin and the breakdown of fibrinogen into smaller fragments. These fragments, known as fibrinogen degradation products, have the potential to stimulate the synthesis of fibrinogen in the liver. The PT, APTT, and fibrinogen tests are commonly used as standard screening tests to assess the functioning of the coagulation system. These tests are widely recognized for their effectiveness in monitoring the efficacy of therapeutic anticoagulation.[7] Diabetes is correlated with an elevated likelihood of developing micro- and macro-vascular complications, thereby establishing it as a condition that promotes blood clot formation.[2] Elevated levels of fibrinogen have been identified as a significant and autonomous risk factor for cardiovascular diseases. The prothrombotic state has emerged as a newly acknowledged element of the metabolic syndrome. Individuals diagnosed with metabolic syndrome, such as type 2 diabetes mellitus (T2DM), demonstrate a distinct configuration of coagulation factors that either enhance the formation of blood clots or impede their dissolution.[8]

Our study demonstrates a decrease in activated partial thromboplastin time (APTT) among individuals with type 2 Diabetes mellitus, potentially indicating the presence of a hypercoagulable state. The activated partial thromboplastin time (APTT) serves as an indicator of a defect in the intrinsic common pathway, whereas the prothrombin time (PT) is indicative of the extrinsic pathway. The abbreviation APTT may be reduced due to the buildup of activated clotting factors in the bloodstream, which occurs as a result of increased coagulation activation within the body.[9,10]

The findings of our study are corroborated by previous research conducted on patients with Type-2 diabetes mellitus, specifically in relation to shortened activated partial thromboplastin time (APTT). Zhao et al,[11] P. Chan et al,[12] and Sunita S. Dhule et al,[6] have all reported similar results. These studies collectively demonstrated that shortened activated partial thromboplastin time (APTT) values are associated with a hypercoagulable state and an elevated risk of thromboembolism.

The results of our study align with prior research studies that have also observed decreased activated partial thromboplastin time (APTT) and prothrombin time (PT) in individuals with diabetes when compared to a control group without diabetes.[9] Lippi et al,[9] conducted an epidemiological study to examine the correlation between plasma glucose levels and activated partial thromboplastin time (APTT) in individuals diagnosed with type 2 diabetes mellitus. The study revealed a significant reduction in APTT among patients with diabetes. Nevertheless, a case-control study conducted by Madan et al,[13] yielded inconclusive results as it failed to identify any statistically significant disparity in activated partial thromboplastin time (APTT) between individuals with type 2 diabetes and those without the condition. The study conducted by Medan et al. (year) employed a comparatively smaller sample size in the control group (30 participants) compared to the experimental group (40 participants) in this particular study. This discrepancy, along with variations in population demographics, could potentially explain the observed variance. In comparison to the control group, the type 2 diabetic individuals exhibited shorter PT and INR values.

This study provides additional support for the previously reported shorter activated partial thromboplastin time (APTT) observed by Acang and Jalil.[14] However, it contradicts the results of Zhao et al,[11] who found no significant reduction in prothrombin time (PT) values among patients with type 2 diabetes in a case-control study conducted at Zhejiang University in China. Madan et al. (2013) similarly observed no significant variation in PT between individuals with type 2 diabetes. The observed disparities in coagulation test outcomes may be attributed to variations in sample size, racial demographics, and geographical distribution.

The insignificant PT INR results in our study support the hypothesis that there is less involvement of extrinsic pathway in hypercoagulability state in

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diabetic conditions due to the fact that injury occurring to the vascular system in diabetic patients does not involve release of tissue factor(TF) from outside of vascular system.

CONCLUSION

The Activated Partial Thromboplastin Time (APTT) was shorter in Type-2 diabetes mellitus individuals than healthy individuals. This laboratory evidence of shortened APTT in diabetic individuals could therefore be the expression of hypercoagulable state.

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