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ORIGINAL ARTICLE

Assessment of Variations in PT, APTT and Platelet Count and Their Correlation with Glycated Hemoglobin in Type 2 Diabetes mellitus

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ABSTRACT

Background: Diabetic patients are at higher risk of cardiovascular disease than non-diabetics. Elevated glucose level in Type 2 Diabetes mellitus (T2DM) can induce variations in blood composition and blood vesicles, which lead towards coagulation abnormalities and cardiovascular disease. Prothrombin Time (PT) Activated Partial Thromboplastin Time (APTT) and platelet count are commonly used tests to assess the coagulation abnormalities of blood.

Objectives: To evaluate the variations in PT, APTT and platelet count in T2DM and their correlation with glycated hemoglobin.

Methodology: This cross sectional study was performed at Asia Diagnostic Center, Islamabad. Pre-diagnosed 52 adults with Type 2 Diabetes mellitus, from 35 to 65 years of age, and 52 sex and age matched healthy subjects were considered as control in this study. Glycosylated Hemoglobin (HbA1c), APTT, PT and platelet counts were measured in both groups.

Results: PT and APTT were significantly lower in T2DM patients (p value < 0.0001) and platelet count was slightly higher in T2DM (p value = 0.13) than the control group. PT (r^2= -0.23) and APTT (r^2= -0.16) were negatively correlated with HbA1c, while platelet count was positively correlated with HbA1c (r^2=0.23) in T2DM group.

Conclusion: From our study, it was concluded that low PT and APTT with relatively high platelet count in T2DM than control group may induce coagulopathies that can lead toward thrombosis in T2DM patients.

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INTRODUCTION

Diabetes mellitus is the most common disease, which is associated with hyperglycemia. It is mainly divided in to two types. First is Type 1 diabetes that is called as Insulin Dependent Diabetes mellitus (IDDM) and second is Type 2 diabetes that is Non-Insulin Dependent Diabetes mellitus (NIDDM)[1]. In these two types, different genetical and

environmental factors are involved that can cause the destruction of β-cells of pancreas or they suppress its function[2]. Diabetic patients are prone to develop a number of serious life threatening health complications, resulting in increased mortality rate[3]. Persistent high level of blood glucose in T2DM causes generalized endovascular injury, which affects the heart, eyes, kidneys, muscles and nerves[4]. Worldwide prevalence of diabetes is 8.5%, amongst which 7.3% men and 9.6% women are the affectees[5]. International Diabetic Federation (IDF) states that Pakistan is at number seven among the countries with highest prevalence of diabetes. About 6.9 million were diabetic in 2007 and it is assumed that there will be 11.5 million diabetic people by the end of 2025[6]. Diabetes mellitus is frequently associated with hypercoagulability resulting in 2 to 4 time higher risk of thrombosis[7]. The main mechanisms of increased risk of thrombosis in diabetes are diverse, and involve multiple pathways[8].

Diabetic patients having endovascular dysfunction result in premature atherosclerosis, which enhance the chances of a thrombus. These diabetic patients have a high tendency of thrombosis because of increased activation of thrombocytes, excessive activation of prethrombotic coagulation factors, and decreased fibrinolysis[9]. Pre-thrombosis status can be determined by elevated plasma levels of fibrinogen, elevated Plasminogen Activator Inhibitor (PAI)-1 and abnormal platelet function[10]. Different studies reported different types of variations in coagulation profiles among diabetic patients[9].

This study was aimed to determine the variation in PT, APTT and platelet count in T2DM patients along with the analysis of correlation of these coagulation profile parameters with glycemic control (HbA1c) in T2DM.

MATERIALS AND METHODS

This cross sectional study was performed at Asia Diagnostic Center, Islamabad from 1st January, 2019 to 31st December, 2019. Already diagnosed Type 2 diabetic patients (both male and females) from 35 to 65 years were diagnosed according to the 1998 World Health Organization (WHO) guidelines[11] were taken as cases. Males and females having same age group were taken as control. Patients who had a previous history of susceptibility to hypercoagulation, such as patients with a history of venous thromboembolism, hereditary coagulopathy, malignancy, gestation, recent surgery, hyperthyroidism, Type 1 diabetes, liver and kidney disease were excluded from this study[12]. Coagulopathies were excluded by medical history, physical examination for Petechiae, and bruises and lab investigations for thrombocytosis.

Eventually, the study included 52 pre-diagnosed Type 2 diabetic patients and 52 non-diabetic healthy individuals as controls. T2DM was confirmed by medical history of adult onset of hyperglycemia, fasting glucose level >126mg/dl and negative urinary ketones[11]. Venous blood samples were collected in sodium citrate tubes for Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) tests. Ethylene Diamine Tetra Acetic Acid (EDTA) tubes were used for HbA1c and platelet count. PT and APTT tests were measured by a coagulation analyzer Sysmax 50. Platelet count were measured by an automated blood analyzer Sysmex XP and HbA1c was measured on a Point-of-Care testing device I-Chroma. I-Chroma was an instrument of choice to measure HbA1c because it is being used for determination of HbA1c in different studies[13], due to user friendly operation. This also covers the unavailability of High Performance Liquid Chromatography (HPLC); a reference method for HbA1c measurement.

RESULTS

Microsoft excel was used for analysis and presentation of data in tabular form. Frequency and %age distribution of males and females in this study is given in Table **1**.

Table 1. Frequency and Percentage Distribution of Males and Females.

Patients	T2DM %	Control group
Male	32 (61%)	28 (54%)
Females	20 (38%)	24 (46%)
Total	52	52

Table 2. Comparison of PT, APTT and Platelet Count Mean by Two Sample t-test.

Tests	Control group	T2DM	p-value
PT	12.3 ± 1.3	9.4 ± 1.2	<0.0001
APTT	32.5 ± 2.1	27.6 ± 3.1	<0.0001
Platelet Count	266.6 ± 42.8	280.8 ± 52.7	0.1366

Table 3. Pearson Correlation Coefficient of PT, APTT and Platelet Count with HbA1c (9.2 ± 1.2) in T2DM.

Test Parameter	Pearson Correlation of co-efficient with HbA1c
PT	-0.23
APTT	-0.16
Platelet Count	0.223

The mean levels of PT, APTT, and platelet count between T2DM and the control group were compared with a two-sample t-test, as shown in Table **2**. P-value < 0.05 was considered significant. Mean PT (9.4 ± 1.2) was significantly lower in diabetic group when it was compared in control group (12.3 ± 1.3) ($p < 0.0001$). The mean APTT (27.6 ± 3.1) in the T2DM group was also lower than that in the control group (32.5 ± 2.1). The average platelet count of T2DM patients (280.8 ± 52.7) was slightly higher than that of the control group (266.6 ± 42.8), but the p value of 0.1366 was not significantly different.

Correlation analysis of PT, APTT and platelet count with blood glucose control (HbA1c) was performed with Pearson correlation. Table **3** shows the Pearson correlation coefficients of coagulation parameters with HbA1c. We observed a weak negative correlation of PT, APTT and a weak positive correlation of platelet count with HbA1c in T2DM.

DISCUSSION

Our results indicates the tendency of coagulation profile towards hypercoagulability in T2DM. We observed decrease in PT, APTT and increased platelet in T2DM group as compared with control group. T2DM patients are considered to be more susceptible than non-diabetic patients to macrovascular complications and thrombotic events[14]. Type 1 or Type 2 diabetic patients with increased activation of the coagulation system has been previously reported. This coagulation activation is an important factor in the occurrence of vascular complications of diabetes[15]. Many researches have shown that coagulation activation markers such as antithrombin-thrombin complex and prothrombin activating fragments are elevated in diabetes. The plasma levels of coagulation factors, such as fibrinogen level, Factor VII, VIII, XI, XII (Kallikrein) and von villi brond Factor (vWF) are increased in diabetes[16].

T2DM is correlated with decreased APTT and elevated fibrinogen levels[12]. Similar results were reported for PT and APTT in a study conducted by Ephraim *et al* in 2017[9]. Here, we also performed correlation of PT, APPT and platelet count with HbA1c in T2DM and the results were also supporting the tendency of hypercoagulability with poor glycemic control. The UK Prospective Diabetes Study (UKPDS) has shown that the risk of complications in patients with T2DM is closely related to previous hyperglycemia. Decrease in HbA1c may reduce the risk of complications, HbA1c within the normal range (<6.0%) is good indicator of lowest risk of atherosclerosis[17]. In a study conducted by Kaur *et al.* in 2018, they also observed that diabetic patients develop complications according to the glycemic control and risk of microvascular complication and thrombus formation is decreased with good glycemic control[14]. Some studies indicate that strength of clot formation is correlated with blood sugar level in diabetes[18]. In diabetic patients with non-insulin dependence, there is structural damage and functional impairment of the endothelium, which has proven to be essential for stimulating different coagulation factors. It is believed that high levels of von villi brand factor (vWF) in DM indicate excessive activation of coagulation factors in diabetes,

which may result in shorter PT and APTT in diabetic patients than the healthy control, as shown in Table **2** of our study[19]. Diabetic patients are at high risk of developing hypercoagulability and good glycemic control can reduce the risk of thrombosis[20].

CONCLUSION

This study concluded that mean PT and APTT are shorter and mean platelet count is higher in T2DM patients than controls, and that is the indication of hypercoagulability and higher tendency of thrombus formation in T2DM patients. Decrease in PT, APTT and increase in platelet count are also associated with glycemic control status of the T2DM patients. Therefore, it can be said that T2DM induce hypercoagulability and tendency of thrombus formation which is associated with glycemic status of the patient.

ETHICAL APROVAL

Ethical approval for the study was obtained from Ethical Board of Medical Laboratory Technology, University of Haripur, Pakistan.

CONFLICTS OF INTEREST

The authors declare that there is no conflict of interest regarding the publication of this article.

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LIST OF ABBREVIATIONS

APTT	Activated Partial Prothrombin Time
DM	Diabetes mellitus
EDTA	Ethylene Diamine Tetra Acetic acid
HbA1c	Glycosylated Hemoglobin
IDDM	Insulin Dependent Diabetes mellitus
IDF	International Diabetic Federation
NIDDM	Non-Insulin Dependent Diabetes mellitus
PAI-1	Plasminogen Activator Inhibitor-1
PT	Prothrombin Time
T2DM	Type 2 Diabetes mellitus
UKPDS	UK Prospective Diabetes Study
vWF	Von Willebrand Factor

REFERENCES

1. Bishop ML, Fody EP, Schoeff LE. Clinical chemistry: Techniques, principles, correlations/ [edited by] Michael L. Bishop, Edward P. Fody, Larry E. Schoeff.; 2010.
2. Zaccardi F, Webb DR, Yates T, Davies MJ. Pathophysiology of Type 1 and Type 2 diabetes mellitus: a 90-year perspective. Postgra Med J. 2016; 92(1084):63-9.
3. Cho N, Shaw J, Karuranga S, Huang Y, da Rocha Fernandes J, Ohlrogge A, *et al*. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes research and clinical practice. 2018; 138:271-81.
4. Chawla A, Chawla R, Jaggi S. Microvasular and macrovascular complications in diabetes mellitus: distinct or continuum? Indian J Endocrinol Metab. 2016; 20(4):546.
5. Bouguerra R, Alberti H, Salem LB, Rayana CB, Atti J, Gaigi S, *et al*. The global diabetes pandemic: the Tunisian experience. Eur J Clin Nutr. 2007; 61(2):160-5.
6. Meo SA, Zia I, Bukhari IA, Arain SA. Type 2 diabetes mellitus in Pakistan: Current prevalence and future forecast. J Pak Med Assoc. 2016; 66(12):1637-42.
7. Park HS, Gu J-Y, Yoo HJ, Han SE, Park CH, Kim YI, *et al*. Thrombin generation assay detects moderate-intensity statin-induced reduction of hypercoagulability in diabetes. Clin App Thrombosis / Hemostasis. 2018; 24(7):1095-101.
8. Tabit CE, Chung WB, Hamburg NM, Vita JA. Endothelial dysfunction in diabetes mellitus: Molecular mechanisms and clinical implications. Rev Endo Metab Dis. 2010; 11(1):61-74.
9. Ephraim RK, Awuku YA, Adu P, Ampomah LT, Adoba P, Panford S, *et al*. High risk of coagulopathy among Type-2 Diabetes mellitus clients at a municipal hospital in Ghana. Ghana Med J. 2017; 51(3):101-7.

10. Imperatore G, Riccardi G, Iovine C, Rivellese AA, Vaccaro O. Plasma fibrinogen: A new factor of the metabolic syndrome: A population-based study. Diab Care. 1998; 21(4):649-54.
11. Alberti KGMM, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus. Provisional report of a WHO consultation. Diab Med. 1998; 15(7):539-53.
12. Zhao Y, Zhang J, Zhang J, Wu J. Diabetes mellitus is associated with shortened activated partial thromboplastin time and increased fibrinogen values. PLoS One. 2011; 6(1):17-28.
13. Omer MA, Ali AE. Relationship between HbA1c levels and inflammatory biomarkers (C-reactive protein, IL6 and TNF-alpha) among Type 2 Diabetes mellitus-Khartoum-Sudan. Int J Med Biomed Sci. 2019; 3(3):10-32553
14. Kaur R, Kaur M, Singh J. Endothelial dysfunction and platelet hyperactivity in type 2 Diabetes mellitus: Molecular insights and therapeutic strategies. Cardio Diabetol. 2018; 17(1):1-7.
15. Erem C, Hacıhasanoğlu A, Çelik Ş, Ovalı E, Ersöz HÖ, Ukinç K, *et al*. Coagulation and fibrinolysis parameters in Type 2 diabetic patients with and without diabetic vascular complications. Med Princip Pract. 2005; 14(1):22-30.
16. Madan R, Gupt B, Saluja S, Kansra U, Tripathi B, Guliani B. Coagulation profile in diabetes and its association with diabetic microvascular complications. J Assoc Physicians India. 2010; 58:481-4.
17. Kodiatte TA, Manikyam UK, Rao SB, Jagadish TM, Reddy M, Lingaiah HKM, *et al*. Mean platelet volume in type 2 Diabetes mellitus. J Lab Physicians. 2012; 4(1):005-9.
18. Bryk AH, Siudut J, Broniatowska E, Bagoly Z, Baráth B, Katona É, *et al*. Sex-specific alteration to α2-antiplasmin incorporation in patients with type 2 diabetes. Thromb Res. 2020; 185:55-62.
19. Junbin H, Wenning W, Guizhi D, Li Y, Zhongpin L. Variations and clinical significance of coagulation and fibrinolysis parameters in patients with Diabetes mellitus. J Tongji Univ Nat Sci. 1998; 18(4):233-5.
20. Agarwal C, Bansal K, Pujani M, Singh K, Chauhan V, Rana D, *et al*. Association of coagulation profile with microvascular complications and glycemic control in Type 2 Diabetes mellitus-a study at a tertiary care center in Delhi. Hematol Transf Cell Therapy. 2019; 41(1):31-6.