IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

A COMPARITIVE STUDY OF PROTHROMBIN TIME AND ACTIVATED PARTIAL THROMBOPLASTIN TIME IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

[1]ASHNA P J, [2]APARNA T R,

[1]PhD Scholar, Srenivas University mukkam, Mangloore , [2]BSC MLT Student, Presentation college, puthenvelikara, .

Abstract: INTRODUCTION:Diabetes mellitus is a disorder of multiple aetiologies characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism that result from defects in insulin secretion, insulin action or both. A hypercoagulable state is observed in diabetic patients due to abnormalities in several plasma proteins in blood coagulation. Measurement of PT and APTT are usually done in patients with a suspected coagulation disorder. AIM: To evaluate and compare the association between PT and APTT in patients with Diabetes mellitus. METHOD: In this study100 samples were included, 50 diabetic patients and 50 healthy non-diabetic individuals of age group 40 to 80 years were subjected to Prothrombin time and Activated partial thromboplastin time. The study was conducted at pathology laboratory in Presentation Center of Allied Sciences, Puthenvelikara. RESULT:The mean PT value in diabetic patients was 19.44 ±1.97 and in non-diabetic was 15.14 ±1.47 with a P value of 0.0001.The mean INR value in diabetic patients was 1.43 ±0.22 and in non-diabetic was 0.9 ±0.15 with a P value of 0.0001.The mean APTT value in diabetic patients was 47.72 ±4.45 and in non-diabetic was 37.96 ±2.61 with a P value of 0.0001. A stastically significant difference was seen among diabetic patients and non-diabetic healthy individuals.The PT value in males and females was 19.60 ±2.04 and 19.22 ±1.9 with a P value of 0.56.The mean APTT value in males and females was 48.28 ±4.47 and 47±4.44 with a P value of 0.31.There was no significant difference seen among the PT and APTT values in males and females. CONCLUSION:The present study observes a significant association between type 2 diabetes mellitus and coagulation parameters. Patients with type 2 DM have increased level of PT and APTT when compared to healthy individuals. Diabetic patients are more prone to develop coagulation disorders,so routine examination of PT, INR and APTT are done for the better management of diabetic patients .

Index Terms **–** Hyperglycemia, PT, APTT, Coagulation disorders.

I. INTRODUCTION

Diabetes mellitus is a major epidemic all over the world. The WHO defines DM as a disorder of multiple aetiologies characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism that result from defects in insulin secretion, insulin action or both.(1) In 2017, the International Diabetes Federation estimated that 451 million adults are diagnosed with Diabetes mellitus worldwide, and the number would increase to 693 million in 2045.(2) DM is broadly divided into 2 types, type1 DM (IDDM) is caused by autoimmune destruction of pancreatic beta cells resulting in an absolute deficiency in insulin and type 2 DM (NIDDM) occurs due to insulin resistance or lack of enough insulin. Diabetes is a major health problem with about 80% of diabetic patients having Type 2 DM (NIDDM) while about 20% have Type 1 DM(IDDM).(3)

The Patients with diabetes mellitus have a high risk of atherothrombotic CVD.[4] The microvascular and macrovascular systems are involved in the major complications that result from DM. Nephropathy, retinopathy and neuropathy are the most common microvascular complications while stroke, CAD and PAD are the most common macrovascular complications.[5] Thrombotic events are responsible for 80% of diabetic deaths, with 75%-80% of these deaths resulting from cardiovascular events.[6] Thrombin plays an important role in blood coagulation. Patients with diabetic mellitus have symptoms of hypercoagulability and hypofibrinolysis.[7] A hypercoagulable prothrombin state is observed in diabetic patients.[8] This state enhance cardiovascular risk by increasing the thrombus within a coronary or cerebral artery, contributing to the development of atherosclerotic lesions.The abnormalities observed involve all stages of coagulation, affecting both thrombus formation and its inhibition, fibrinolysis, platelet and endothelial functions. The 2 plasma levels of many clotting factors including fibrinogen, factor VII, factor VIII, factor XI, factor XII, kallikerin and vWF are increased in diabetes.[9] This hypercoagulability is due to an imbalance between the endothelial surface and the blood clotting factors. Measurement of PT and APTT are usually done in patients with a suspected coagulation disorder. This coagulation tests provide information about how much thrombin can be generated in plasma after the activation of the extrinsic and intrinsic coagulation pathways. PT is used to detect abnormalities of factor I, factor II, factor V, factor VII and factor X of extrinsic and common pathways.[10] PT is the most commonly used coagulation test in routine laboratories. In this test tissue thromboplastin and calcium ions are added to plasma which activate extrinsic clotting factors, resulting in the generation of thrombin and formation of fibrin clot. Activated partial thromboplastin time is used to screen abnormalities of factor I, factor II, factor V, factor VIII, factor IX, factor XI and factor XII of the intrinsic and common pathways.[11] In this test, the addition of a platelet substitute, factor XII activator, and calcium chloride results in the formation of stable clots. Prolonged PT and APTT is a clinical indicator to detect the deficiency of coagulation factors or the presence of coagulation inhibitors.[12] In the present study, patients were divided into two groups based on their age and GRBS level as diabetic and non-diabetic individuals. The purpose of the present study is to evaluate and compare the coagulation tests PT and APTT in diabetic patients and non-diabetic individuals.

II. MATERIALS AND METHODS

A total number of 100 subjects were recruited for the study. Apparently diabetic patients and healthy, males and females of age group 40 to 80 years were included in the study.

2.1 INCLUSION CRITERIA ¬ DM individuals diagnosed by GRBS between the age group of 40-80 years. ¬ Healthy non-diabetic individuals between the age group of 40-80 years .

2.2 EXCLUSION CRITERIA ¬ Patients on anticoagulant therapy ¬ Pregnant women ¬ Individuals who were recently undergone surgery ¬ Patients who did not give consent

2.3 BLOOD COLLECTION

A written consent were obtained from the individuals who participated in this study and also explains about the study protocol and venous blood collection method to each individual.

2.4 MATERIALS

- Disposable single use syringe
- Tourniquet
- cotton
- 70% alcohol
- 3.2% Tri-sodium citrate tube(2ml)

2.5 SAMPLING METHOD

- Prepare the appropriate syringe or needle.
- Put the tourniquet on the upper arm (not too tightly and do not leave it longer than 1 minute).
- Sterilize the site with 70% alcohol in an anti-clock wise direction
- Then insert the needle at an angle of 20-300 to the site .
- When the needle entered the vein, blood is withdrawn into the syringe.
- Release the tourniquet and remove the needle from body.
- Put cotton immediately on the puncture site and hold adequate pressure to avoid formation of a hematoma.
- Dispense 1.8ml blood into trisodium citrate tube and mix well.

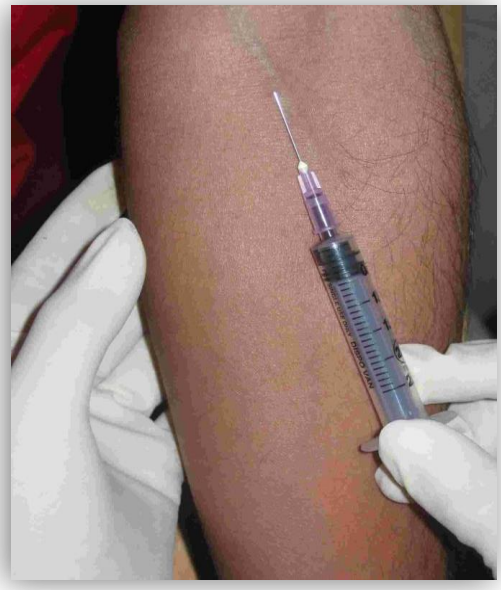


Fig 1 : venous blood collection

2.6 SAMPLE PREPARATION

- After blood collection immediately mix the blood with anticoagulant avoiding the foam formation.
- Centrifuge the sample for 15 minutes at approximately 2000g (3000 rpm).
- Collect the plasma in a separate tube.

2.7 PROTHROMBIN TIME (PT) TEST

2.7.1MATERIALS

- LIQUIPLASTIN Reagent
- Platelet poor plasma
- Glass test tubes
- Micropipettes(100µl and 200 µl)
- Waterbath at 37°C
- Stop Watch

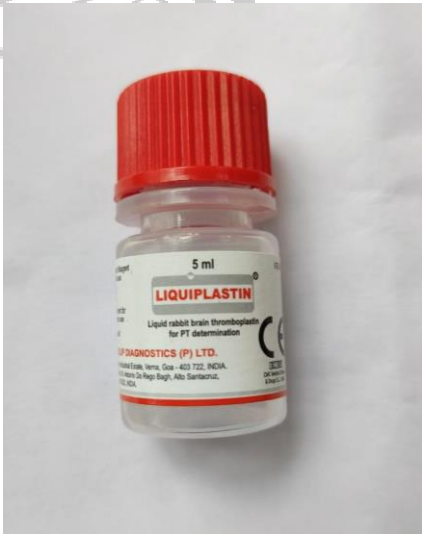


Fig 2: liquiplastin reagent for determination of prothrombin time

2.7.2METHOD

- Bring the reagent to room temperature(20-30°C)
- Shake the reagent gently and properly before use.
- Pipette 200 µl of well mixed reagent into a test tube.
- Pipette 100 µl of plasma into a test tube.

- Incubate the test tubes containing reagent and plasma in waterbath at 37°C for 3-5 minutes.
- Add 200 µl of well mixed reagent pre-warmed to 37°C to the tube containing plasma.
- Start the stop watch
- Gently tilt the tube back and forth and stop the stop watch as soon as the first fibrin strand is visible and which initiates gel formation.
- Measure the time taken for clot formation in seconds.
- Repeat the test 3times and record the average PT value.

2.7.3 INR Calculation

$$INR = (R)^{ISI}$$

R = Diabetic patient PT / Mean normal PT

ISI of reagent = 1.5

2.8 ACTIVATED PARTIAL THROMBOPLASTIN TIME (APTT)

2.8.1 MATERIALS

- LIQUICELIN-E APTT Reagent
- Platelet poor plasma
- Calcium Chloride
- Glass test tubes
- Micropipette(100µl)
- Waterbath at 37°C
- Stop Watch

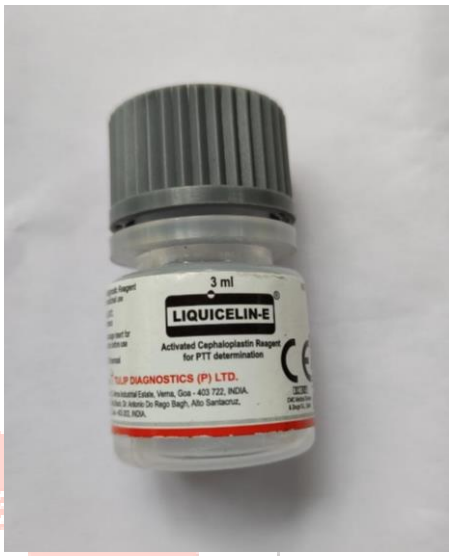


Fig 3 : LIQUICELIN-E APTT Reagent

2.8.2 METHOD

- Bring the reagent to room temperature(20-30°C)
- Shake the reagent gently and properly before use.
- Pipette 100 µl of well mixed reagent and Calcium Chloride in separate test tubes and incubate in waterbath at 37°C for 3-5 minutes.
- Pipette 100 µl of plasma into a test tube and incubate in waterbath at 37°C for 3-5 minutes.
- Add 100 µl plasma to the tube containing pre-warmed reagent and incubate for 3-5 minutes
- After 3 minutes, add 100 µl of well mixed Calcium Chloride pre-warmed to 37°C to the tube containing APTT reagent and plasma.
- Start the stop watch
- Gently tilt the tube back and forth and stop the stop watch as soon as the first fibrin strand is visible and which initiates gel formation.
- Measure the time taken for clot formation in seconds.
- Repeat the test 3times and record the average APTT value.

3. RESULTS AND DISCUSSION

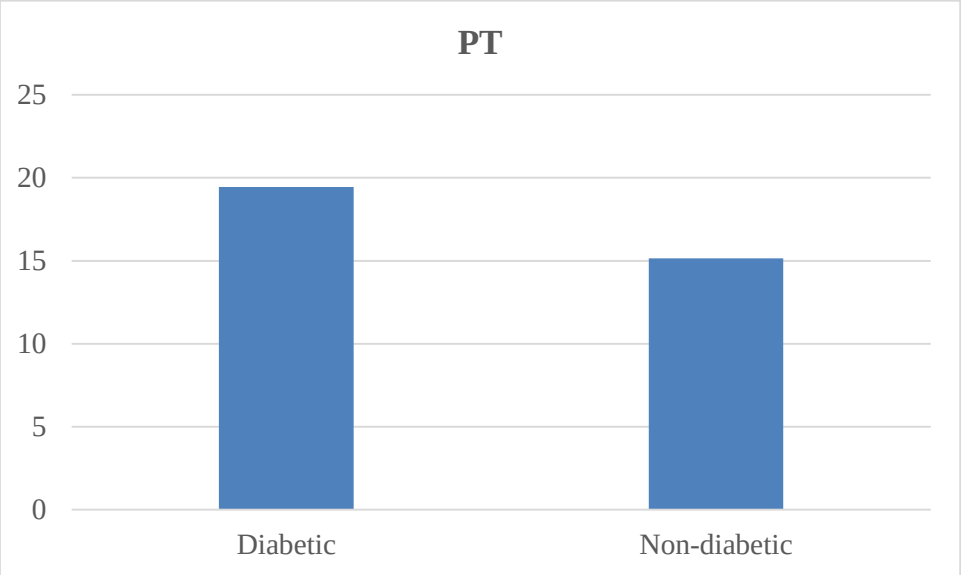
A total of 100 samples were included in this study, 50 Diabetic patients and 50 Non-diabetic individuals.

Table-1: PT of Diabetic patient and Non-diabetic

PT	N	Mean	SD	t-test	P value
Diabetic	50	19.44	1.97	12.37	0.0001
Non-diabetic	50	15.14	1.47		

Table-1 shows the mean PT value in diabetic patients was 19.44 ±1.97 and in Non-diabetic was 15.14 ±1.47. P value was 0.0001. A significant difference was seen among Diabetic and Non-diabetic individuals.

Graph-1: Mean value of PT



Graph-2: SD of PT

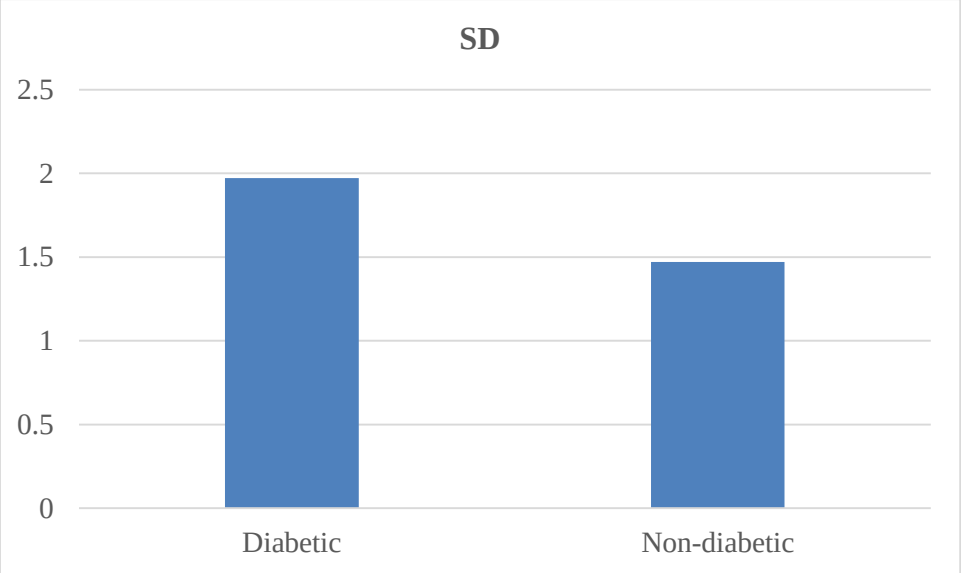


Table-2: INR of Diabetic patient and Non-diabetic

INR	N	Mean	SD	t-test	P value
Diabetic	50	1.43	0.9	14.07	0.0001
Non-diabetic	50	0.22	0.15		

Table-2 shows the mean INR value in diabetic patients was 1.43 ±0.9 and in Non-diabetic was 0.22 ±0.15. P value was 0.0001. A significant difference was seen among Diabetic and Non-diabetic individuals.

Graph 3 : Mean INR value for diabetic and non diabetic patients

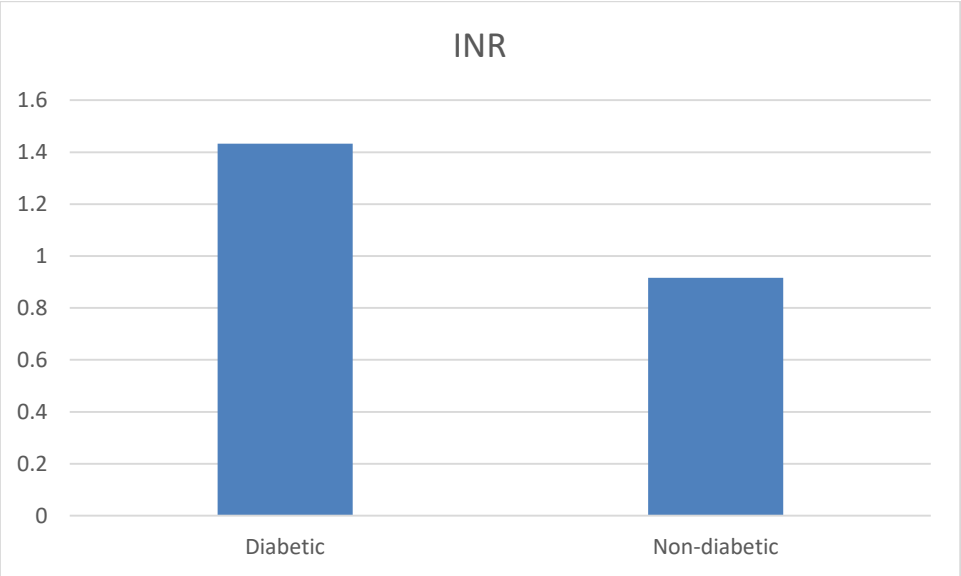
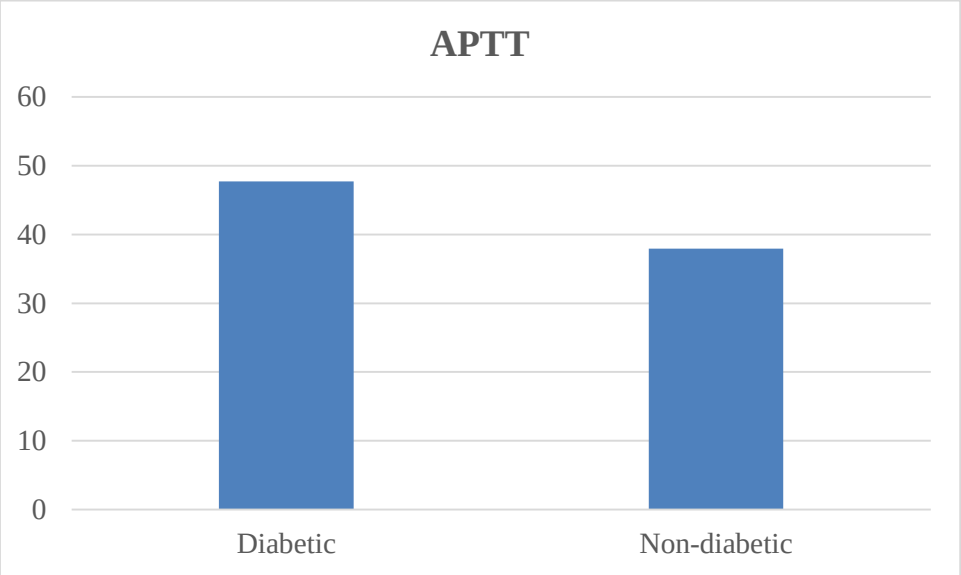


Table-3: APTT of Diabetic patient and Non-diabetic

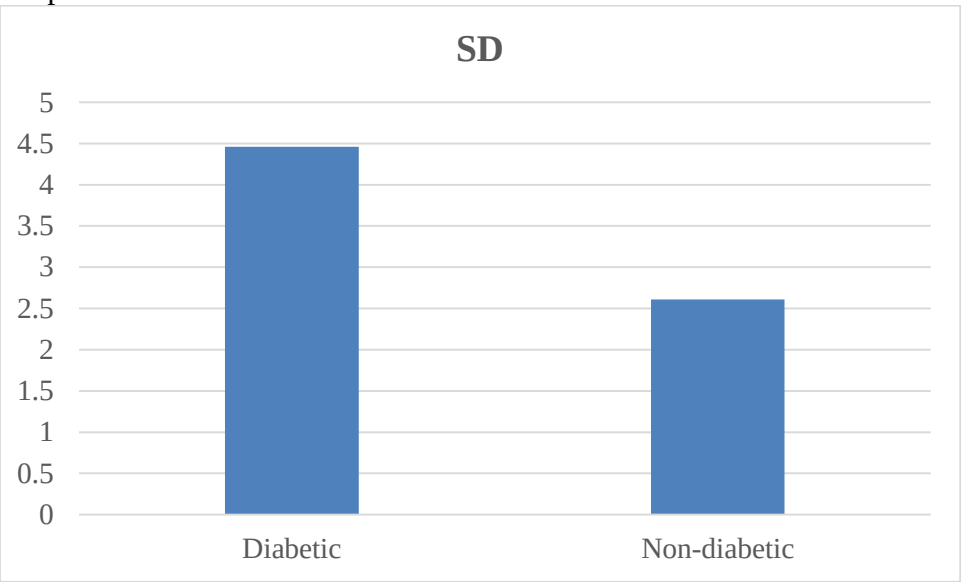
APTT	N	Mean	SD	t-test	P value
Diabetic	50	47.72	4.45	13.37	0.0001
Non-diabetic	50	37.96	2.61		

Table-3 shows the mean APTT value in diabetic patients was 47.72 ±4.45 and in Non-diabetic was 37. 96 ±2.61. P value was 0.0001. A significant difference was seen among Diabetic and Non-diabetic individuals.

Graph-4: Mean value of APTT



Graph-5: SD of APTT



. The present study was conducted at pathology laboratory of Presentation Center of Allied Science, Puthenvelikara. A total of 100 cases were analyzed, out of which 50 diabetic cases and 50 healthy individuals who served as controls were taken up for the study. This current study aimed to evaluate and compare the association between PT and APTT in patients with type 2 diabetes mellitus.

In this study, it was observed that the mean PT value in diabetic patients and non-diabetic individual was 19.44 ±1.97 and 15.14 ±1.47, the P value was 0.0001 (< 0.05). A significant difference was seen among the PT value of Diabetic and Non-diabetic individuals.The mean INR value in diabetic patients was 1.43 ±0.9 and in non-diabetic was 0.22 ±0.15. P value was 0.0001. A significant difference was seen among the INR value of Diabetic and Non-diabetic individuals.The mean APTT value in diabetic patients and Non-diabetic individual was 47.72 ±4.45 and 37. 96 ±2.61, the P value was 0.0001. A significant difference was seen among the APTT value of Diabetic and Non-diabetic individuals.

This observation agree with findings of Thukral et al " Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) in Type 2 Diabetes Mellitus, a Case Control Study. International Journal of Contemporary Medical Research, Volume 5, Issue 8, August 2018. He observed that there were significantly higher PT and APTT values in diabetic patients, when compared to healthy individuals[13]. Also agree with findings of Y. Abdulrahaman and M.K. Dallatu et al "Evaluation of Prothrombin Time and Activated Partial Thromboplastin in Patients with Diabetes Mellitus, Nigerian Journal of Basic and Applied Science (March, 2012), 20(1): 60-63. They concluded that the values of PT and APTT was significantly increased in untreated diabetic patients when compared to control group.[14]

This observation disagree with the findings of Fayeza Karim et al "Coagulation Impairment in Type 2 Diabetes Mellitus 26J Bangladesh Soc Physiol. 2015, June; 10(1): 26-29. He concluded that the PT and APTT were significantly lower in diabetes mellitus than those of control group[15].

4 CONCLUSION

In our study "A COMPARITIVE STUDY OF PROTHROMBIN TIME AND ACTIVATED PARTIAL THROMBOPLASTIN TIME IN PATIENTS WITH TYPE 2 DIABETES MELLITUS " We concluded that, there is a significant association between Type 2 Diabetes mellitus and coagulation parameters. Patients suffering from type 2 diabetes mellitus were found to have increased level of PT and APTT when compared to healthy individuals. Diabetic patients are more prone to develop coagulation impairment, so routine examination of PT, INR and APTT are done for the better management of diabetic patients .

REFERENCES

[1] WHO. Diagnosis and Classification of diabetes mellitus and its complications. World Health Organization Department of Non Communicable Disease Surveillance.
[2] IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045.
[3] Ostenson CG. The pathophysiology of type 2 diabetes mellitus: An overview. 2001; 171:241
[4] Sapkota B, Shrestha SK, Poudel S. Association of activated partial thromboplastin time and fibrinogen level in patients with type II diabetes mellitus. BMC Research Notes. 2013;6:1-5
[5] Nazimek-Siewniak B, Moczulski D, Grzeszczac W. Risk of macrovascular and microvascular complications in Type 2 Diabetes: results of longitudinal study design. J Diabetes Complications. 2002;16(4):271–6.
[6] Fuller JH, Stevens LK, Wang SL. Risk Factors for Cardiovascular mortality and morbidity: the WHO Multinational Study of Vascular Disease in Diabetes. Diabetologia. 2001;4(Suppl 2):S54–64.
[7] Carr ME. Diabetes mellitus: a hypercoagulable state. J Diabetes Complications. 2001; 15(1): 44-54
[8] Sumitra Dash, RJ Dash. Levels of natural anticoagulants , antithrombin iii and protein C in diabetes vascular disease. Bahrain Medical Bulletin. 1995;17(4).
[9] M E Carr. J Diabetes complications .DM:a hypercoagulable state
[10] Iazbik, C., Couto, G., Gray, T.L. and Kociba, G. (2001). Effect of storage conditions on hemostatic parameters of canine plasma obtained for transfusion. American Journal of Veterinary Research, 62:734–735
[11] Anna Leticia Soares, Marinez de Oliviera Sousa, Ana Paula Salles Moura Fernandez, Maria das Gracas Carvalho. Haemostatic changes in patients with type 2 diabetes mellitus. Rev. Bras. Hematol. Hemoter. 2010;32(6).
[12] Ramdas Nayak, Essentials in Hematology and Clinical pathology, Jaypee Brothers Medical Publishers, 01 Feb 2017.
[13] Thukral S, Hussain S, Bhat S, Kaur N, Reddy A. Prothrombin time (PT) and activated partial thromboplastin time (APTT) in type 2 diabetes mellitus, a case control study. International Journal of Contemporary Medical Research. 2018;5(8):H5-9.
[14] Abdulrahaman Y, Dallatu MK. Evaluation of prothrombin time and activated partial thromboplastin in patients with diabetes mellitus. Nigerian journal of basic and applied sciences. 2012;20(1):60-3.
[15] https://www.researchgate.net/publication/283184882_Coagulation_Impairment_in_Type_2_Diabetes_Mellitus