DETERMINATION OF PROTEIN C LEVEL IN TYPE 2 DIABETIC PATIENTS IN SUDAN

Eman Albager Mohamed Osman*[1] and Mahdi H. A. Abdalla[2]

[1]Department of Hematology, Faculty of Medical Laboratory Sciences, Al-Neelain University, Khartoum, Sudan.
[2]Associate Professor of Hematology, Department of Hematology, Faculty of Medical Laboratory Sciences, Omdurman Ahlia University, Khartoum, Sudan.

*Corresponding Author: Eman Albager Mohamed Osman

Department of Hematology, Faculty of Medical Laboratory Sciences, Al-Neelain University, Khartoum, Sudan.

ABSTRACT

Protein C is a precursor to a serine protease present in plasma that plays an important physiological role in the regulation of blood coagulation. Protein C deficiency causes thrombophilia or hypercoagulability and increased risk of venous thrombosis. The aim of this study was to measure protein C level among type 2 diabetes mellitus patients in Sudan. A total of 90 samples were collected (45 patients with type 2 DM and 45 healthy controls), 50 were males and 40 were females, their age ranged between 18 to 52years. the protein C level was measured by Enzyme Linked Immunosorbent Assay ELIZA method, to correlate the protein C level with patient, s, age, gender and HBA1c. Data were analyzed by using statistical package for the social science (SPSS). The present study showed that mean PC level among case group (50± 12.4) was significantly lower than control group (83±12 (P-value 0.000).

KEYWORDS: Protein C, Type 2 diabetic mellitus, Sudan.

INTRODUCTION

Diabetes mellitus (DM) is characterized by hyperglycemia accompanied with the biochemical alterations in carbohydrate, protein and lipid metabolism.[1] Due to the increasing number of diabetics, this disease has acquired a character of "epidemic" in recent decades. In 2000, the number of diabetics worldwide was approximately 151 million, estimates are that in 2010 this will reach 221 million and by 2025, 324 million.[2] It is believed that changes in human behavior, environment and lifestyle are favoring an increase in the number of obese and diabetic individuals.[3] According to WHO, diagnostic criteria of diabetes mellitus are fasting blood glucose e"7.0 mmol/l, and 2 hours after glucose <1.11mmol/l and HbA1c <6.5%.[4]

There are Two types of diabetes mellitus are the most prevalent: type-1 diabetes is characterized by autoimmune destruction of pancreatic beta cells resulting in an absolute deficiency in insulin. and type 2 diabetes (T2DM or adult-onset), which corresponds to approximately 90% of cases of diabetes worldwide, is characterized by insulin resistance and/or reduced production of insulin.[5] Patients suffering from diabetes mellitus a high probability of developing acute cardiovascular disease, in particular myocardial infarct and cerebrovascular stork.[6] Cardiovascular disease (CVD) is the leading cause of disability and premature

mortality in patients with diabetes.[7] About 80% patients with diabetes may die due to thromboembolic CVD.[8] Much attention has been devoted to the pathogenic factors, altered haemostatic balance, including abnormalities in platelet function, increase in blood coagulability and altered fibrinolytic system.[9] Since most of these abnormalities indicate a hypercoagulable and hypofibrinolytic state leading to enhance intravascular fibrin deposition they have been linked to the high risk for cardiovascular morbidity and mortality among these patients.[10] Coagulation abnormalities with decreased level of antithrombin III, protein C and protein S has been reported in DM with elevated clotting factors.[11]

Protein C is a precursor to a serine protease present in plasma that plays an important physiological role in the regulation of blood coagulation.[12] Protein C is a vitamin K dependent factor, which, in its active form, inactivates coagulation factor Va and VIIIa. Protein S, another vitamin K dependent factor serves as a cofactor of activated protein C.[13] APC was demonstrated to show profibrinolytic activity by inactivating plasminogen activator inhibitor. Since severe thrombosis was observed in patients with protein C deficiency. Protein C might play a critical role in antithrombotic process. Protein C might be consumed by developing the hypercoagulable state. Two types of PC deficiency states

are recognized, in type I deficiency the plasma concentration of PC is reduced both in functional and immunological assay, reflecting a genetic defect causing a reduced biosynthesis of PC. Type II deficiency is characterized by normal protein C antigen levels, but with decreased functional activity. This type of defect reflect the synthesis of abnormal molecules with reduced function, the mutation in the PC gene have been characterized in a recently published data base.[14] Because of the critical role that protein C play as an anticoagulant those deficiencies in PC or APC resistance lead to significant risk of forming blood clots.

MATERIALS AND METHODS
This was a case-control study, conducted in Khartoum, Sudan during the period of April 2017 to August 2017. 90 samples were included (45 samples of type 2 Diabetic patient's individuals and 45 samples of healthy individuals as control).

Five ml of venous blood was collected: 2.5 ml in 3.8% Trisodiume citrate (1:9 volume of sodium citrate solution), and 2.5 in EDTA container. Haemoglobin A1c (HBA1c) was measured using NYco Card READER II.

Protein C was measured using Enzyme Linked Immunosorbent Assay ELISA commercial assay kit from Aesku, Diagnostics, Germany (normal range: 70-140%), Data were analyzed by using statistical package for the social science (SPSS) Version 23.

RESULTS
This study was conducted in Khartoum Sudan Among 90 individuals. There were divided into two groups 45 were patients with type 2 diabetes mellitus who considered as cases and 45 apparently healthy individuals who considered as control. Our study revealed statistically significant difference between cases and controls concerning protein C concentration. Mean PC level among case group (50± 12.4) was significantly lower than control group (83±12 (P-value 0.000). as shown in table 4.1. While there was no correlation between Protein C concentration and HbA1c Concentration among study group (R value=0.145, P value=0.349) as shown in figure 4.1.

Table (4.1): Protein C Level among study population (CASE& control).

Parameter	Case NO (45)	Control NO (45)	P. Value
Protein C Mean (SD)	50 ± (12.4)	83± (12)	**0.000**
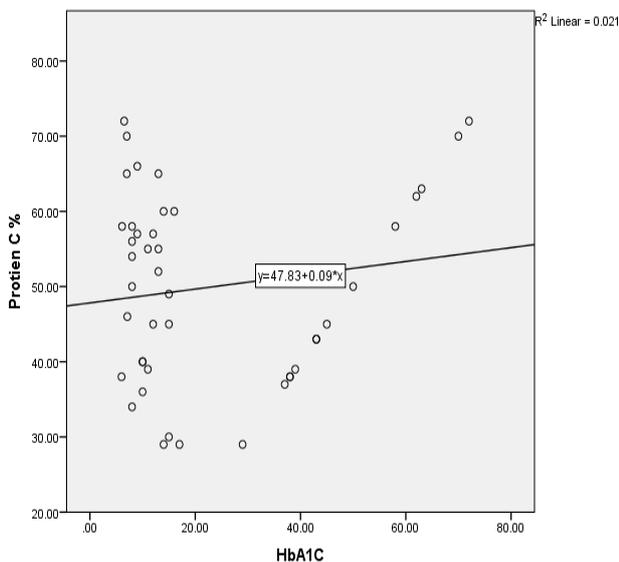
R Value= 0.145, P value= 0.349
Figure 4.1 scatter dot plot of HbA1C Correlation with Protein C among Diabetic Patients.

DISCUSSION
Diabetes mellitus patients have a high probability of developing acute cardiovascular disease, in particular myocardial infarction and cerebrovascular stroke.

It has been suggested that diabetes can be associated with hypercoagulability in abroad sense, which is related to the development of vascular complication.

Ninety patients were enrolled in this study (45 were diabetic patients and the others were healthy controls). Our study revealed statistically significant difference between cases and controls concerning protein C level (Mean=50 ± 12.4 and 83± 12, P value=0.000 respectively). While there was no correlation between Protein C and HbA1c concentration among study group (R value=0.145, P value=0.349). Also non-significant association between protein C level and age and gender was detected (p value= 0.739 and gender p value=0.325).

In our study the mean of protein C level was significantly lower than that of the healthy control group (P < 0.00) Our observation was matched with berna ASLAN[15] and Nantarat komanasin[16], Ceriello.[17] Saito et al.[18] found that the PC-Ag levels of the diabetic patients were higher than that of the control group.

These finding suggested that increased thrombin production in diabetes mellitus causes enhanced activation of protein C in the circulation and in turn enhanced clearance from the blood.[17]

This study revealed low protein C in type 2 diabetic patients, the decrease in protein C level is due to improper synthesis of protein C in the liver. Also decrease in protein C level maybe due to the increase in clearance in diabetic patients. This abnormal decrease in protein C level promote the hypercoagubale state in diabetic patients which leads to venous thrombosis.

CONCLUSION
The study findings concluded that plasma protein C level decreases in patients with diabetic mellitus and these changes are not influenced HbA1c.

ACKNOWLEDGMENT

REFERENCES
1. Jabeen F, Rizvi HA, Aziz F, Wasti AZ. Hyperglycemic induced variations in Hematological Indices in Type 2 Diabetics. Int J Adv Res., 2013; 1(8): 322-34.
2. Cheng D. Prevalence, predisposition and prevention of type II diabetes. Nutr Metab (Lond), 2005; 2: 29.
3. Zimmet P, Alberti KG, Shaw J. Global and societal implications of the diabetes epidemic. Nature, 2001; 414(6865): 782-7.
4. Seino Y, Nanjo K, Tajima N, Kadowaki T, Kashiwagi A, Araki E. Report of the committee on the classification and diagnostic criteria of Diabetes Mellitus. J Diabetes invest, 2010; 1(5): 212-28.
5. Zimmet P, Alberti KG, Shaw J. Global and societal implications of the diabetes epidemic. Nature, 2001; 414(6865): 782-7.
6. Colwell JAVascular thrombosis in type II diabetes mellitus. Diabetes, 1993; 42: 8_11.
7. Alao O, Damulak D, Joseph D, Puepet F. Haemostatic Profile of Patients with Type 2 Diabetes Mellitus in Northern Nigeria. Int J Endocrinol, 2010; 6(1): 122-32.
8. Colwell JA, Nesto RW. The Platelet in Diabetes. Diabetes Care, 2003; 26(7): 2181–8.
9. H.C. Kwaan, Changes in blood coagulation, platelet function and plasminogen-plasmin system in diabetes, Diabetes, 1992; 4(2): 32–35.
10. T.Vukovich, S.Proidl, P.Knoble, H. Teufelsbauer, C. Schnack and G. Schernthaner, The effect of insulin treatment on the balance between tissue plasminogen activator and plasminogen activator inhibitor-1 in type 2 diabetic patients, Thromb Haemst, 1992; 68: 253–256.
11. Madan R, Gupta B, Saluja S, Kansr UC, Tripathi BK, Guliani BP. Coagulation Profile in Diabetes and its Association with Diabetic Microvascular Complications. JAPI, 2010; 58: 481-9.
12. Stenflo J. J. Biol. Chem., 1976; 251: 355-363.
13. WALKER F.J. The regulation of activated protein C by a new protein: A possible function of bovine protein S. J.Biol. Chem., 1980; 255: 5521-5524.
14. Reitsma PH, Bernardi F, Doig RG et al. Protein C deficiency: a database of mutations, 1995 update. Thromb Haemost, 1995; 73: 876- 889.
15. Berna ASLAN, Nezaket EREN, Þebnem CÜÚERLÜ, Fatma M.LD.R, Nihal Y.CELResearch and Training Hospital, Biochemistry Laboratory, Üstanbul – TurkeyReceived, 2004 April 15.
16. Nantarat komanasin, chatler pongchaiyakul, thongchai patipanwat, youwalak theerajetkual, and paisal mongkolwongroj Department of clinical microscopy, faculty of associated medical science, khon kaen university, 2003; 32: 3-2437.
17. Ceriello A, Quatraro A, Dello Russo P et al. Protein C deficiency in insulin dependent diabetes: A hyperglycemia-related phenomenon. Thromb. Haemost, 1990; 64: 104-107.
18. Saito M, Kumabashiri I, Jokaji H, et al. The levels of protein C and protein S in plasma in patients with type II diabetes mellitus. Thromb Res., 1988; 52: 479-486.