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RESEARCH ARTICLE

FIBRINOGEN LEVEL AMONG TYPE 2 DIABETIC SUDANESE PATIENTS WITH CORONARY ARTERIAL DISEASE

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ABSTRACT

Cardiovascular complications account for nearly 50% of deaths in type 2 diabetes mellitus. Several studies reported that haemostatic factor especially hyperfibrinogenemia is implicated as a source of atherosclerosis and its complications. This study aimed to determine fibrinogen level among type 2 diabetic Sudanese patients with coronary arterial diseases (CAD). Following informed consent, 150 subjects were enrolled: 50 known type 2 diabetic patients with stable coronary arterial disease; 50 known type 2 diabetic patients without history of heart disease and 50 healthy individual as controls. Fibrinogen level was measured by Clauss modified method. HbA1c was measured by "boronate binding assay (using NycoCard Kit). Fibrinogen level was found to be significantly higher in diabetic patients with CAD compared with diabetic patients without CAD (p-value 0.001), with no difference between males and females. Fibrinogen levels were significantly associated with HbA1c levels (p value 0.000) and the duration of diabetes (p value 0.048). Our study concluded that fibrinogen level is higher among type 2 diabetic patients with CAD than diabetic patients without CAD. The elevation of fibrinogen level was significantly associated with uncontrolled diabetes.

INTRODUCTION

Diabetes mellitus (DM) is a heterogeneous group of metabolic disorders characterized by chronic hyperglycemia with disturbances of carbohydrates, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both. DM is a major independent risk factor for cardiovascular diseases arising mainly from microvascular and macrovascular diseases including atherosclerosis and thrombosis. (Schneile *et al.,* 2006). Cardiovascular complications account for nearly 50% of deaths in type 2 diabetes mellitus and 25% in type 1 patients. Therefore, it is important to recognize various cardiovascular risk factors and modify them if possible by primary and secondary intervention (Anjula *et al.,* 2001). Several studies reported that haemostatic factor especially hyperfibrinogenemia is implicated as a source of atherosclerosis and its complications (Ernst *et al.,* 1993). Glycated hemoglobin (HbA1c) reflects the average blood glucose concentrations over the preceding 2 to 3 months. (Selvin *et al.,* 2007). It was used to evaluate glycaemic control, rather than glucose concentration. Poor glycemic control has been reported to be associated with increased vascular complications in diabetic patients (Kuusisti *et al*., 1994). Fibrinogen is the major coagulation protein in the blood from which fibrin clot is formed. It is an important determinant of plasma viscosity, platelet aggregation and thrombus formation, also it is an acute-phase reactant that increases in inflammatory states (Stec *et al.,* 2000 ; Kalfe *et al.,* 2010; Maple-brown *et al.,* 2010). Fibrinogen level can be reduced by life style that affects levels of established risk factors (such as regular exercise, smoking cessation, and moderate alcohol consumption) (Danish *et al.,* 2005). Many studies reported that plasma fibrinogen levels were higher in diabetic patients than in controls. This study aimed to determine fibrinogen level among type 2 diabetic Sudanese patients with coronary arterial diseases (CAD).

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MATERIALS AND METHODS

Following informed consent, one hundred and fifty subjects were enrolled: 50 known type 2 diabetic patients with stable CAD (diagnosis based on the history of prolonged chest pain, and angiographic study); 50 known type 2 diabetic patients without history of heart disease and 50 healthy individual as controls. Exclusion criteria were unstable angina pectoris, myocardial infarction within the last two months and acute or chronic heart failure. Patients with other known causes of hyperfibrinogenaemia such as pregnancy, smoking, and hypertension were also excluded from this study. Five ml of venous blood was collected from each subject: 2.5 ml in 3.8% trisodium citrate (9:1 vol/vol), kept on ice until centrifugation at 2500g for 30 minutes at 4°C, plasma samples were

immediately frozen and stored at - 80°C for subsequent coagulation analysis; and 2.5 ml in EDTA for Hb A1c estimation. Laboratory analysis was performed at the Department of Haematology, Faculty of Medical Laboratory Sciences, Alneelain University, Sudan. Fibrinogen level was measured by Clauss modified method using a test kit produced by (TECHNOCLONE GMBH, AUSTRIA). The method uses a functional assay based upon the time for fibrin clot formation, in brief, Diluted plasma is clotted with a high concentration of thrombin, and the concentration of fibrinogen is determined by comparing the plasma clotting time to a calibration curve of a reference plasma with a series of dilutions (1:5 –1:40). HbA1c was measured by "boronate binding assay" using NycoCard Kit and reader II. 5 µl of EDTA anticoagulated blood was added to reagent 1 (Buffer containing dye bound boronic acid and detergent), mixed well, and incubated for 3 minutes. Then, 25 µl of the mixture was added to the test device, and allowed to soak completely into the membrane, 25 µl of the washing solution was applied to the test device, allowed to soak completely into the membrane, and the result read within 5minutes by NycoCard reader II. Statistical analysis was performed using statistical package for social science (SPSS) software. Evaluation of patient's data was performed using the t-test and Pearson correlation test. Results with p value < 0.05 were considered statistically significant.

RESULTS

The male: female ratio was 1.3 and the median age was 62 year, with minimum age of 40 and maximum of 75 years. Mean duration of diabetes among the study group was 15 ± 11 years. All patients were tested for the fibrinogen level and HbA1c. Means fibrinogen levels were as follows: 456±99 mg/dl for diabetic patients with CAD; 387±101 mg/dl for diabetic patients without CAD; and 272±54 mg/dl for healthy controls. Mean fibrinogen level was significantly higher among diabetic patients when compared to controls (p value 0.000), it is higher among diabetic patients with CAD than those without CAD (p value 0.001).

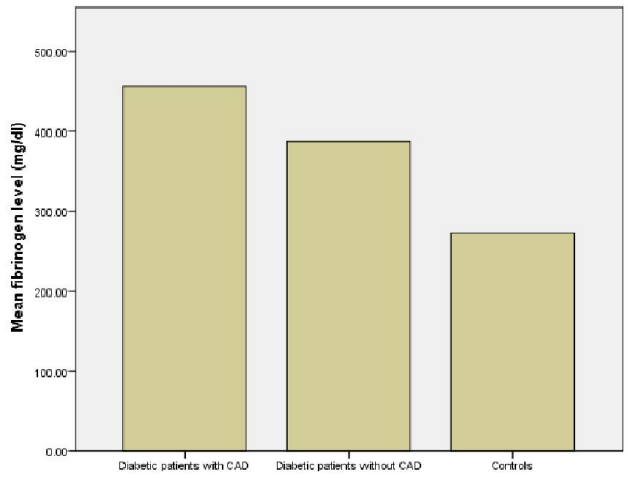

Fig. 1. Fibrinogen levels among different groups

Mean fibrinogen level among males was 410±106 mg/dl while for females it was 438±103 mg/dl, no significant difference was observed in the fibrinogen level between males and females. Mean HbA1c for diabetic patients was 9.2±2.3. Fibrinogen levels were significantly associated with HbA1c levels (p value 0.000), it was also significantly associated with the duration of the diabetes (p value 0.048). No significant association between fibrinogen levels and the duration of CAD (p value 0.592) or with age (p value 0.529) was observed.

DISCUSSION

Haemostatic factors, especially fibrinogen, have been implicated as a cause of atherosclerosis and its complications. Several previous studies have suggested an association between plasma fibrinogen and CAD, other investigations suggested that glycohemoglobin might affect plasma fibrinogen levels. This study included 50 diabetic patients with CAD and 50 diabetic patients without CAD their fibrinogen levels were measured and compared with 50 healthy individuals. We observed a significant increase in the mean of the fibrinogen level among Diabetic patients, when compared with the control group. Similar findings in previous studies have been reported (Lippi *et al.,* 2009; Festa *et al.,* 2002; Bembde, 2012). Fibrinogen levels were significantly increased among diabetic patients with CAD than patients without CAD, several studies have revealed the positive association of elevated plasma fibrinogen and of stable CAD (Gustavsson & Agardh, 2004; Lind *et al.,* 2001; Kafle & Shrestha, 2010). Hong *et at* suggested that elevated fibrinogen might confer to not only the presence of CAD but also the severity of coronary lesions in diabetic patients with stable CAD (Hong *et al.,* 2014). The elevation of fibrinogen level was significantly associated with uncontrolled diabetes which was indicated by an elevated HbA1c levels, previous studies have reported that glycohemoglobin was vital determinants of fibrinogen concentrations in type 2 diabetic patients (McBane *et al.,* 2010; Rogowski O *et al.,* 2008; Guardado-Mendoza R *et al.,* 2009).

Conclusion

Our study concluded that fibrinogen level is higher among type 2 diabetic patients with CAD than diabetic patients without CAD. The elevation of the fibrinogen level was significantly associated with uncontrolled diabetes.

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Authors contributions

Enass A. M. Khalid and Mahdi H.A. Abdalla conceived the idea of the study, collected and analyzed samples and data and wrote the manuscript.

REFERENCS

Anjula J, Gupta HL, Narayan S. 2001. Hyperfibrinogenemia in patients of diabetes mellitus in relation to glycemic control and urinary albumin excretion rate. *JAPI*.,49:227–230.

Bembde ASA. 2012. Study of Plasma Fibrinogen Level in Type-2 Diabetes Mellitus and its Relation to Glycemic Control. *Indian J Hematol Blood Transfus*., 28:105–108.

Danish J, Simon G, Thompson D *et al.* (Fibrinogen Studies Collaboration). 2005. Plasma fibrinogen level and the risk of major cardiovascular diseases and Nonvascular Mortality. *J Amer Med Assoc*., 294:1799-1809.

Ernst E, Ludwig KR. 1993. Fibrinogen as a cardiovascular risk factor: a meta-analysis and review of literature. *Ann Intern Med*., 118:956–963.

Festa A, D'Agostino R, Tracy RP, Haffner SM. 2002. Elevated levels of acute-phase proteins and plasminogen activator inhibitor-1 predict the development of type 2 diabetes: the insulin resistance atherosclerosis study. Diabetes, 51:1131–1137.

Guardado-Mendoza R, Jimenez-Ceja L, Pacheco- Carrasco MF, *et al.* 2009. Fibrinogen is associated with silent myocardial ischaemia in type 2 diabetes mellitus. ActaCardiologica, 64:523–530.

Gustavsson CG and Agardh CD. 2004. Markers of inflammation in patients with coronary artery disease are also associated with glycosylated haemoglobin A1c within the normal range. *European Heart Journal*., 25:2120–2124.

Hong LF, Li XL, Luo SH, Guo YL, Zhu CG, Qing P, Wu NO, and Li JJ. 2014. Association of Fibrinogen with Severity of Stable Coronary Artery Disease in Patients with Type 2 Diabetic Mellitus. Disease Markers, Article ID 485687, 8 pages.

Kafle DR and Shrestha P. 2010. Study of fibrinogen in patients with DM. Nepal Med Coll J, 12:34-7.

Kuusisto J, Mykkanen L, Pyorala K, Laakso M. 1994. NIDDM and its metabolic control predict coronary heart disease in elderlysubjects. Diabetes, 43:960-7.

Lind P, Hedblad B, Stavenow L *et al.* 2001. Influence of plasma fibrinogen levels on the incidence of myocardial infarction and death is modified by other inflammation-sensitive proteins: a long-term cohort study. Atheroscler Thromb Vasc Biol., 21:452–8.

Lippi G, Franchini M, Targher G, Montagnana M, Salvagno GL, Guidi GC, Favaloro EJ. 2009. Epidemiological association between fasting plasma glucose and shortened APTT. *Clin Biochem*., 42:118–120.

Maple-Brown LJ, Cunningham J, Nandi N, Hodge A, O'Dea K. 2010. Fibrinogen and associated risk factors in a high-risk population: urban Indigenous Australians, the DRUID Study. Cardiovasc Diabetol., 9:69.

McBane RD, Hardison RM, and Sobel BE. 2010. Comparison of plasminogen activator inhibitor-1, tissue type plasminogen activator antigen, fibrinogen, and D-dimer levels in various age decades in patients with tyype 2 diabetes mellitus and stable coronary artery disease (from the BARI 2D trial). *American Journal of Cardiology*, 105:17–24, 2010.

Rogowski O, Shapira I, Peretz H, and Berliner S. 2008 Glycohaemoglobin as a determinant of increased fibrinogen concentrations and low-grade inflammation in apparently healthy nondiabetic individuals. *Clinical Endocrinology*, 68:182–189, 2008.

Schneil O and Stendl E. 2006. Impaired glucose tolerance, diabetes and cardiovascular diseases. EndocrPract., 26:398-408.

Selvin E, Crainiceanu CM, Brancati FL, Coresh J. 2007. Short-term variability in measures of glycemia and implications for the classification of diabetes. *Arch Intern Med*., 167: 1545–1551.

Stec JJ, Silbershatz H, Tofler GH, Matheney TH, Sutherland PLipinska I, *et al*. 2000. Association of fibrinogen with cardiovascular risk factors and cardiovascular disease in the Framingham Offspring Population. Circulation, 102:1634-8.

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