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EVALUATION OF D-DIMER LEVEL AMONG TYPE 2 DIABETES MELLITUS WITH NEPHROTIC SYNDROM IN SUDAN

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ABSTRACT
Diabetes mellitus is a leading cause of vascular morbidity and mortality, early disability, end stage renal diseases, blindness, and non-traumatic limb amputation. Hypercoagulability is one of many complications associated with diabetes mellitus which occurs due to hyperglycemia. Diabetic nephropathy is a serious complication that occurs in 20–40% of all diabetic patients. Plasma level of D-Dimer reflects the amount of lysed fibrin and hence is an accepted marker of hypercoagulability. The aim of this study was to evaluate the plasma D-dimer level in type 2 diabetes mellitus patients with nephrotic syndrome in Sudan. The study included 100 diabetic patients (50 patients with nephropathy and 50 patients without nephropathy). Their D-Dimer level and haemoglobin (Hb) A1c were measured and compared with 100 normal subjects as control. D-Dimer and HbA1c were measured using I-CHROMA™ system. 72% of the diabetic patients were uncontrolled with (HbA1c > 8.0 %). Our study revealed higher D-Dimer level among diabetic patients than the control (p value = 0.045). D-Dimer level was significantly higher among diabetic patients with nephrotic syndrome than diabetic patients without nephrotic syndrome (p value = 0.033). There was insignificant correlation between D-Dimer level, and HbA1c level (p value = 0.072). our study concluded that diabetic patients with nephrotic syndrome are associated with higher D-Dimer level, suggesting that hypercoagulability may be an important causative factor of nephrotic syndrome in patients with type 2 diabetes.

KEYWORDS: Diabetes Mellitus, D-Dimer, HbA1c, Hypercoagulability, Nephropathy.

INTRODUCTION
Diabetes mellitus is a syndrome characterized by chronic hyperglycemia, disturbed carbohydrate, fat, protein and acid base metabolism. It is a group of metabolic diseases resulting from defects in insulin secretion, insulin action or both.[1] Diabetes is a leading cause of mortality and early disability. It is a leading cause of end stage renal disease, blindness, and non-traumatic limb amputation]. Also, it increases the risk of cardiac, cerebral and peripheral vascular disease.[1] Microvascular complications are a major outcome in patients with type 2 DM. They have a significant burden on the patient's quality of life. They are also a leading cause of morbidity and mortality.[2] Hypercoagulability is one of many complications associated with diabetes mellitus which occurs due to hyperglycemia.[3] In type 2 diabetes mellitus, the endothelial layer can be affected, where the endothelial layer contributes to maintaining the blood flow by preventing platelets aggregation and its anticoagulant properties, and by stimulating fibrinolytic system.[4] Hyperglycemia directly contributes to endothelial injury through irreversible glycation of collagen and other subendothelial structure proteins of the vessel, forming advanced glycation end products (AGEs), which accumulate in the endothelium over time influenced by increase in blood sugar levels and are directly related to atherosclerosis.[5] The concept of hypercoagulability state or thrombophilia is thrombosis resulted from three interrelated factors: inflammation of blood vessels (vascular endothelial injury), and intrinsic alterations in the nature of the blood itself.[6] Diabetic nephropathy, which is defined as elevated urine albumin excretion or reduced glomerular filtration rate or both, is a serious complication that occurs in 20–40% of all diabetic patients.[7] D-dimer is a direct marker of fibrinolytic activity. It is a clinical screening marker of preceding coagulation activity.[8] It is known that D-dimer is associated with an increased risk of arterial thrombotic events, irrespective of baseline vascular disease, and diabetes. There is a need for simple markers that can help to identify patients at risk of hypercoagulability related complications. D-dimer is such a simple test. High – risk patients could thus be monitored and treated more intensely. The aim of this

study was to evaluate the plasma D-dimer level in type 2 diabetes mellitus patients with nephrotic syndrome in Sudan.

MATERIALS AND METHODS

This study was designed as a case control study. Following informed consent, 100 type 2 diabetic patients (50 patients with nephropathy and 50 patients without nephropathy) and 100 age and sex matched normal subjects as control were enrolled in this study. Diabetic individuals with known inherited or acquired coagulopathy, or any patients under anticoagulant therapy or a condition of hypercoagulability (pregnancy) were excluded. Five ml of venous blood sample was collected from each subject: 2.5ml was collected in 3.8 % tri-sodium citrate (9:1 vol/vol) for D-dimer analysis. Samples were kept in ice until centrifugation at 4000 RPM for 15 minutes at 4°C, plasma samples were immediately frozen and stored at -80°C for subsequent analysis; and 2.5 ml in EDTA anticoagulant for HbA1c measurement. D-Dimer and HbA1c were measured using I-CHROMA^{TM} system (Boditech – Korea). The test uses a sandwich immunodetection method. D-Dimer/or HbA1c is bound with an antibody in buffer and the antigen-antibody complexes are captured by antibodies that have been immobilized on the test strip as sample mixture migrates through nitrocellulose matrix. Signal intensity of fluorescence on detection antibody reflects the amount of the antigen captured and is processed by I-CHROMA^{TM} Reader to show D-Dimer/or HbA1c concentration in the specimen.

RESULT

In this study 100 type 2 diabetic patients (50 patients with nephropathy and 50 patients without nephropathy) and 100 age and sex matched normal subjects as control were enrolled. Male female ratio of the study group was 1.5, their age was 20 - 80 Years. 72 % of DM patients presented with poor glycemic control with Hb A1c greater than 8 %.

Mean D-Dimer level was significantly higher in case group than control group (table 1). There was no significant difference in mean D-Dimer level between male and female (table 2). There was insignificant correlation between D-Dimer level and HbA1c concentration (*p* value = 0.072) (figure.1).

Table 1: Comparison of the D-Dimer level between diabetic patients (Case) and control.

Parameter	Case (mean±SD)	Control (mean±SD)	*P*.Value
D-Dimer (ng/ml)	329.77 ±212.17	284.38 ± 75.11	0.045

Table 2: Comparison of the D-Dimer level between male and female.

Parameter	Male (mean±SD)	Female (mean±SD)	*P*.Value
D-Dimer (ng/ml)	317.9±208.2	347.6± 219.4	0.496

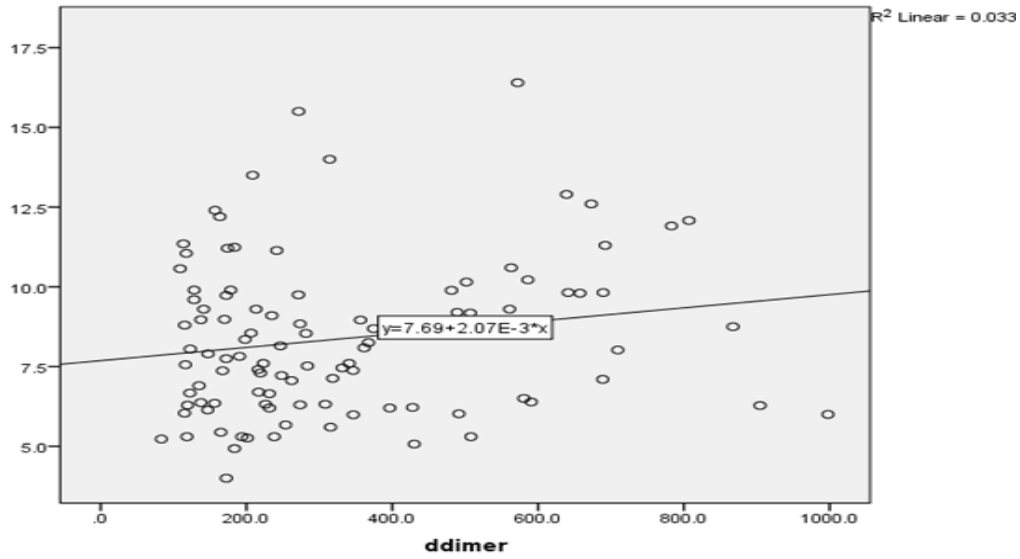

Figure 1: Correlation between D-dimer level and HbA1c concentration.

DISCUSSION

As hypercoagulability state is present in diabetic patients, the expression of a marker such as D-Dimer may be underestimated.[9] The current study was conducted in Khartoum state, Sudan among type 2diabetic patients. The study included 100 diabetic patients (50 patients with nephropathy and 50 patients without nephropathy). Their D-Dimer level and haemoglobin (Hb) A1c were measured and compared with 100 normal subjects as control. Most of the patients had poor glycemic control (72 %); this frequency was higher compared to previous reports among different populations.[10] Our result highlighted the urgent needs to develop an awareness plan as to reduce the incidence of

diabetes complications in future. This study found that the mean D-Dimer level was significantly higher in case group than control (P= 0.045). our result is in agreement with previous report.[11] Our findings also similar with the findings of Anna et-al who found that changes in D-dimer levels indicate diabetes disease progression to macrovascular complications. D-dimer levels that became increasingly higher than control as the disease progressed from pre-diabetes to cardiovascular complications.[12] Our study also revealed a significantly higher D-Dimer level among diabetic patients with nephropathy complication than diabetic patients without nephropathy with P= 0.033. Similar findings were previously reported[13] Further studies with more laboratory investigations and clinical data are needed for deep interpretation and accurate conclusion of the association of an elevated D-Dimer level with nephropathy complication in T2DM patients, which may reveal an important finding with a benefit for the management of such patients.

CONCLUSIONS

This study concluded that diabetic patients with nephrotic syndrome are associated with higher D-Dimer level, suggesting that hypercoagulability may be an important causative factor of nephrotic syndrome in patients with type 2 diabetes.

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