The Association between Microalbuminuria and Plasma Fibrinogen Levels in Type 2 Diabetic Sudanese Patients

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Abstract

Aims: Increased plasma fibrinogen considered as one of the underlying complications caused by type 2 diabetic, proteins overproduction is associated with albuminuria in non-dibetic individuals. It is not known whether the presence of albuminuria in patients with type 2 diabetes mellitus is associated with greater albumin and fibrinogen production rates, so the present study was designed to investigate the association of the fibrinogen levels in type 2 diabetic patients with and without microalbuminuria compared with normal subjects.

Materials & Methods: Plasma fibrinogen level was assessed in 140 individuals; 110 diagnosed as type 2 diabetic patients, furthermore they were classified into two groups according to the urinary excretion rates of albumin, 55 patients with microalbuminuria, 55 patients without microalbuminuria, and 30 non diabetic subjects as control.

Results: Diabetic patients group had a higher mean value of plasma fibrinogen (M±SD = 3.751±0.934) compared with control group (M±SD= 3.296±0.590) (*P*= 0.013), and in diabetic patients subgroups; patients with microalbuminuria had a higher mean value of fibrinogen (M±SD= 4.039±0.976) compared to diabetic patients without microalbuminuria (M±SD= 3.463±0.798) (*P*= 0.001). In addition to that, the study noticed that, the plasma fibrinogen level was positively correlates with the duration of diabetes; (*P*= 0.002).

Conclusion: The study concluded that the plasma fibrinogen level was significantly elevated in Type 2 diabetic patients with microalbuminuria, and also the fibrinogen level correlates with duration of diabetes.

Key Words: Microalbuminuria, Fibrinogen, Diabetes, CVD, Sudan

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Introduction

Type 2 diabetes mellitus was thought to be a relatively benign condition, at least in the elderly, with relatively little effect on life expectancy (1). But it has now become obvious that type2 diabetes must be taken every bit as seriously as type 1 diabetes, because of its complications (in particular renal complication) (2). In addition to that, type 2 diabetes have an increasing impact on rates of morbidity and mortality in Sudan according to its diverse complications (3).

Fibrinogen is a strong and independent cardiovascular risk factor, its plasma concentration predicts cardiovascular events in general population (4). Fibrinogen level may also be increased in type 2 diabetes suggesting its contribution to the excess cardiovascular morbidity andmortality in this disease (5).

Microalbuminuria, defined as an increased urinary albumin excretion rate in the absence of clinically compromised renal function, and it has been recognized as an important biomarker to predict micro and macrovascular diabetic complication (6).

Fibrinogen and albumin are two liver synthesised proteins, with different functions. Patients with increased protein loss such like nephrotic syndrome and renal failure, production of albumin and fibrinogen increased (7), suggesting coordinate changes in hepatic protein production in response to albuminuria. Chronic complications of uncontrolled diabetes begins with loss of a small amount of albumin (Microalbuminuria) (8), this may lead to increase production of fibrinogen.

Besides that, there are different changes in hemostatic markers; and many studies have shown that diabetes is a hypercoagulable state, as results of enhanced vascular endothelial cell expression of tissue factor and Von Willebrand factor, increased platelet adhesiveness, elevated level of procoagulant factor, and decreased fibrinolytic activity (6). Fibrinogen, one of an important procoagulant and thrombogenic factors, elevation of plasma viscosity due to corresponding increase in fibrinogen concentration significantly contributes to the increase in blood viscosity has been shown to be an important component of microcirculatory disorders in diabetic patients (7).

The present study was designed to investigate the association between the plasma fibrinogen levels and microalbumiuria in Sudanese with type 2 diabetic mellitus.

Materials and Methods

This study is descriptive cross sectional case control study, conducted from April to August 2012, a total of 140 individual their aged ranged from 30-75 years; 110 (50% male, 50% female) diagnosed with type 2 diabetic mellitus, all of them are negative for C-reactive protein test (CRP), and 30 non diabetic apparently healthy individuals were included as control.

Venous blood sample (5.0 ml) was drawn from each diabetic patient and tested for the CRP using latex agglutination test in order to ensure that increasing of fibrinogen level not as a result of inflammatory response. According to the rates of urinary albumin excretion, which was assayed by NycoCard U-albumin (immunometric assay), patients were classified into two group; 55 patients with microalbuminuria, that their urinary albumin ranging between 20 and 200 mg/L), 55 patients without microalbuminuria their urinary albumin was <20 mg/L.

The study was approved by Alneelain University Ethics Committee and all subjects gave informed consent (Based on Helsinki Declaration), the informed consent was signed by them. Patient's information's were collected by a structured questionnaire.

Fibrinogen was assayed by the Clauss method using commercial reagent (FIBRI-PREST) and performed on the automated blood coagulation analyzer (Sysmex CA-500 series) for the diabetic patients and control group.

Results

The mean values of the fibrinogen in each group was determined, in diabetic group it was significantly higher (M±SD = 3.75±0.943 g/l), compared to control group (M±SD= 3.29±0.59 g/l P= 0.013) as shown in table (1), while in the diabetic patients subgroups; with microalbuminuria fibrinogen concentration was significantly higher (M±SD= 4.03±0.976 g/l), compared to patients without microalbuminuria (M±SD= 3.46±0.789 g/l, P= 0.001 as shown in table (2).

Furthermore, in diabetic group, there is significant correlation between fibrinogen levels and disease duration, (p = 0.002), shown in figure (1).

Table (1): The statistical difference between diabetic and control groups

Variables	Study group	Min.	Max.	Mean	Std. Deviation	P value
Fibrinogen (g/l)	Test group	1.89	6.43	3.75	0.93	0.013
	Control group	2	4	3.29	0.59	

Table (2): Statistical difference between diabetic subgroups

Variables	Study group	Min.	Max.	Mean	S.D	P value
Fibrinogen (g/l)	Patients with microalbuminuria	2.50	6.43	4.03	0.97	0.001
	Without microalbuminuria	1.89	5.85	3.46	0.79	

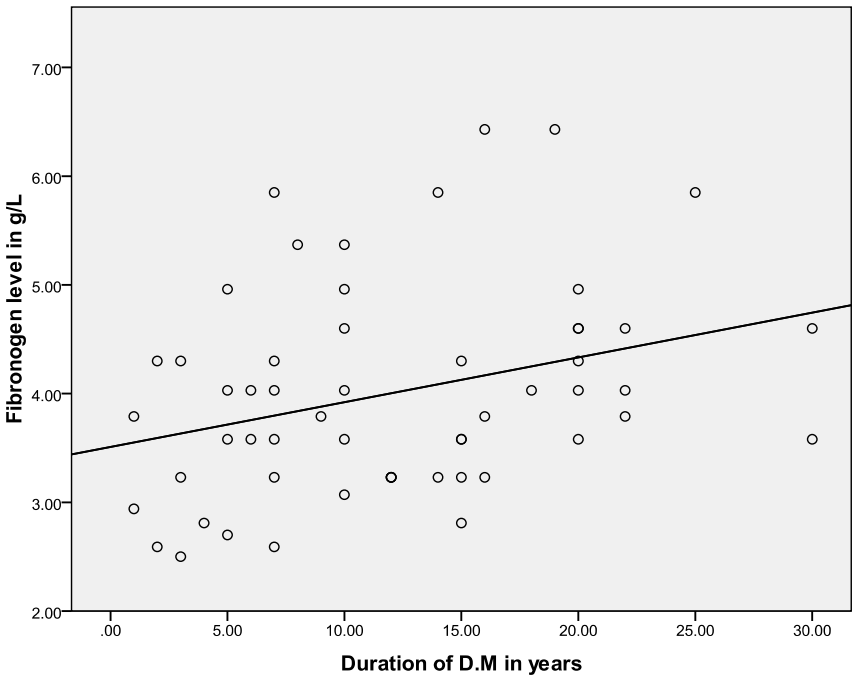

Figure (1): Correlation between the duration of the disease (Years) and Fibrinogen levels (g/l) in diabetic group.

Discussion

Microalbuminuria is early marker of nephropathy in diabetic patients (6). Because it might reflect widespread increased vascularpermeability causing organ damage, it was considered as risk factor for cardiovascular disease in diabetic type 2 patients (9). Increased fibrinogen in circulation also is a powerful and independent cardiovascular risk factor. It was hyposized that urinary albumin loss may leads to increased fibrinogen production, as liver response (10).

In Sudan, type 2 diabetes have an increasing impact on rates of morbidity and mortality, for that this study was done to assess the relationship between the plasma fibrinogen levels and urinary microalbumin in type 2 diabetic Sudanese patients. Study found significant difference in the mean value of fibrinogen as compared between diabetic group and non diabetic control group (P= 0.013). The hyperfibrinogenemia of type 2 diabetes in the study is also in agreement with a previous report of increased fibrinogen production in this disease (11-13).

In subgroups of diabetic patients; there is significant difference in the mean value of fibrinogen as compared between patients with microalbuminuria and patients without microalbuminuria ; (P=0.001), this finding was also reported previously (13). The study found the plasma fibrinogen levels significantly higher in pateints with long disease duration as compared with that pateints with short disease duration (p = 0.002).

The limitation of this study can be summarized into two things; firstly we did not study presence of other cardiovascular risk factors such as body mass index, hypertension, lipids profile, smoking, and other diabetes monitoring parameters such as HbA1c, which were associated with fibrinogen level as reported previously (14;15). Secondly, we did not consider age as study variable, however it had been reported that as age advances fibrinogen also increases and was statistically significant (14).

Conclusion

Finally, this study concluded that the diabetic patients with microalbuminuria tended to have hyperfibrinogenemia compared with diabetic patients without microalbuminuria. This finding provides a biological link between the excretion of microalbumin in urine and hyperfibrinogenemia, which is considered an important component of microvasculatory disorders in diabetic patients by increasing blood viscosity.

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