Fibrinogen Level in Non-Insulin Dependent Diabetes Mellitus (NIDDM)

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Abstract: Background: Diabetes mellitus is the most common metabolic disorder characterized by metabolic abnormalities and long term complications. The presence of high levels of plasma fibrinogen is predictive of vascular complications and cardiovascular death in patients with diabetes mellitus. The increased prevalence of Coronary Artery Disease (CAD) in diabetic patients makes it important to evaluate changes in plasma fibrinogen. Aim and Objectives: The present study was undertaken to estimate plasma fibrinogen level in patients with diabetes type II and its correlation with glycemic control. Methods and materials: The study was conducted in Al Wahda hospital, and from different clinic in Derna city. The study included 53 patients with diabetic mellitus type II and 19 non diabetics (as control) without coronary artery disease (CAD). Plasma fibrinogen level was estimated in all cases and controls, and it’s correlated with glycemic control in diabetic. Results: Mean plasma fibrinogen level in patients with diabetic mellitus type II was high (447±22.2mg/dl) as compared to controls (198±0.82 mg/dl), which was found to be statistically highly significant (p=0.001). Our study showed fibrinogen to be significantly associated with the glycocylated hemoglobin (HbA1c) Fibrinogen level increased as the value of HbA1c became higher (459±22.8 mg/ dl ) when HBA1C ≥ 7%. Conclusion: Patients with type 2 diabetes mellitus had a higher plasma fibrinogen level. Fibrinogen level was significantly correlated with glycemic control. Keywords: Fibrinogen, Diabetes mellitus, HbA1c, Derna, Libya.

Introduction
The prevalence of diabetes has increased over the past decade and has been predicted to increase in the future. According to WHO, about 180 million people have diabetes. According to the current trend, more than 360 million people will have the disease by 2030 [1]. The prevalence of both type 1 and type 2 diabetes mellitus is increasing worldwide, but the prevalence of type 2 diabetes mellitus is expected to rise exponentially in future because of increasing obesity and reduced activity levels [2]. Diabetes increases the morbidity and mortality due to its propensity to develop micro and macroangiopathy [3].

Fibrinogen is a coagulation protein which is an important determinant of blood viscosity and platelet aggregation [4]. There are a number of mechanisms that explains the increased concentration of plasma fibrinogen in diabetic patients. Since the glycosylated fibrinogen is less susceptible to plasmin degradation its level remains increased in diabetic patients with poor glycaemic control [5]. This increased plasma fibrinogen level leads to a state of hypercoagulability which contribute to the development and progression of atherosclerosis and it will increases the stroke risk associated with large aortic plaque [6].

Fibrinogen may be indirectly associated with vascular disease as a marker of unstable lesions [7]. There is possibility that measurement (or modification) of fibrinogen may help in disease prediction or prevention. Studies have shown that formation of an occlusive thrombus on a damaged
Atherosclerotic lesion is the most common precipitating cause of acute myocardial infarction. Evidence also suggests that, in addition to having a role in the late complications of cardiovascular disease, fibrinogen may be involved in the development of atherosclerotic lesions beginning with the early stages of plaque formation [2]. Persons with type 2 diabetes mellitus are at increased risk for cardiovascular-related illness and death, but this excess risk is not completely explained by an increased prevalence of the major conventional cardiovascular risk factors (for example, smoking, hypertension, hypercholesterolemia and obesity). Researchers have suspected that fibrinogen is involved in the excess rate of cardiovascular disease in patients with non-insulin dependent diabetes mellitus [3, 4].

**Aim of the study** was to measure fibrinogen level among diabetic patient and compared with control and to compare plasma fibrinogen level in controlled diabetics and uncontrolled according to HBA1C.

**Materials and methods**

**Patients study**
The study was conducted in Al Wahda hospital, and from clinic of diabetic. The study included 53 diabetic patients and 18 non-diabetics (as control) without Coronary Artery Disease (CAD).

All the diabetic and non-diabetic subjects underwent complete clinical evaluation with specific reference to any micro-and macro-vascular complications.

Fifty three patients with mean of age 55.09±12.23 years, range 21-80 years, 22 (41.5 %) was male and 31 (58.5 %) was female, and twenty was healthy (non-diabetic) as control with mean of age 39.05±13.18 range from 21 to 62 years old.

**Samples collection**
Venous blood collected using sterile disposable plastic syringe after cleaning the venepuncture area with 70% ethanol, the blood was add to the anticoagulant at ratio of 2.5ml to 0.5ml of citrate (3.2% (0.109M) buffered sodium citrate and gently mixed. The sample was centrifuge at 1300 rpm for 15min to obtain platelet poor plasma (ppp). The ppp placed into plastic tube for fibrinogen assay.

Two ml was collected in EDTA vials for HbA1c. The FBS was analyzed in samples collected in sodium fluoride. Early morning samples were drawn for estimating fasting blood glucose levels. Samples were maintained at room temperature and analyzed within one hour of collection.

Blood glucose levels were tested using automated biochemistry analyzer and that of HbA1c by the high-performance liquid chromatography method.

**Statistical analysis**
All the continuous variables were presented as Mean ± SD. The comparison between two variables was done with the help of students T test. A P value of less than 0.05 is considered to be statistically significant.

**Results**
This study covered 72 study participants, divided into two study groups. Fifty three participants who diagnosed with NIDDM cases group (74%) and 19 healthy participants (26%) acted as control group. Concerning the age, Mean age was 50.86±14.3, about two thirds of the study participants were more than 35 years in age (78%) whiles only (22%) of them were less than 40 years in age. Similarly, more than half of the study participants (59%) were females.

The clinical characteristics was shown in table 1.
Table 1. Clinical characteristics of patients and control

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients with DM</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of cases</td>
<td>53</td>
<td>19</td>
</tr>
<tr>
<td>Mean of age ± SD</td>
<td>55.09±12.23</td>
<td>39.05±13.18</td>
</tr>
<tr>
<td>Male</td>
<td>22</td>
<td>8</td>
</tr>
<tr>
<td>Female</td>
<td>31</td>
<td>11</td>
</tr>
<tr>
<td>Duration of DM (years)</td>
<td>10.55±7.14</td>
<td>-</td>
</tr>
</tbody>
</table>

Hypertension

<table>
<thead>
<tr>
<th></th>
<th>Patients</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>27</td>
<td>-</td>
</tr>
<tr>
<td>No</td>
<td>26</td>
<td>-</td>
</tr>
<tr>
<td>FBS mg/dl</td>
<td>176±52.61</td>
<td>-</td>
</tr>
<tr>
<td>HBA1c %</td>
<td>8.92±1.8</td>
<td>-</td>
</tr>
</tbody>
</table>

The mean fibrinogen level was 447±22.2 mg/dl in diabetic whereas in healthy (control group) was 198±82 mg/dl there was a high significant different between patients and healthy group (P= 0.002) as in table 2.

Table 2. Plasma fibrinogen levels in diabetics and non-diabetics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control</th>
<th>Patients</th>
<th>t-test</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrinogen (mg/dl)</td>
<td>198±82</td>
<td>447±22.2</td>
<td>8.70</td>
<td>.002</td>
</tr>
</tbody>
</table>

Mean level of fibrinogen was also significantly high in relation to level of glycosylated haemoglobin as shown in table 3.

Table 3. Relationship of serum fibrinogen with glycosylated haemoglobin

<table>
<thead>
<tr>
<th>Parameter</th>
<th>HBA1c &lt;7(n=) Mean ± SD</th>
<th>HBA1c ≥7(n=) Mean ± SD</th>
<th>t-test</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrinogen (mg/dl)</td>
<td>413±207</td>
<td>459±228</td>
<td>11.4</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Discussion

Plasma fibrinogen is an important component of the coagulation cascade as well as a major determinant of blood viscosity and blood flow. Increasing evidence from epidemiological studies suggest that elevated plasma fibrinogen levels are associated with an increased risk of cardiovascular disorders including ischemic heart disease, stroke and others like thromboembolism [8, 9]. It has been reported that high fibrinogen concentration enhances the risk of cardiovascular disease in diabetic patients [10-12].

There are a number of mechanisms to explain increased fibrinogen levels in DM. Diabetes is associated with low grade inflammation and as a result Interleukin 6 are elevated in these patients. This cytokine stimulates hepatocytes to produce fibrinogen representing an important link between inflammation and hypercoagulation [8].

Insulin resistance in type 2 DM also is associated with increased hepatic fibrinogen production in response to insulin [8]. Increased fibrinogen synthesis has also been demonstrated post prandially in type 2 DM but not in healthy controls further suggesting hepatic dysregulation of fibrinogen synthesis in this condition [9]. In diabetic patients there is increased rate of fibrinogen clearance with shorter fibrinogen circulating half-life. This means that the rate of synthesis is even more than that indicated by plasma level.

Fibrinogen synthesis is regulated by a feedback mechanism by thrombin activation [11]. In diabetics thrombin formation is induced by free radicals. Hyperglycemia and insulin resistance and the consequent oxidative stress may give rise to increased thrombin formation [12].
In this study fibrinogen level was significantly higher in diabetic type 2 than in control 447±222 mg/dl whereas in healthy (control group) was 198±82 mg/dl (P = 0.002), these results were in agreement with other study by Archana et al. they found a higher plasma fibrinogen levels in type 2 diabetes mellitus patients (656 mg/dl) as compared to controls (324±139 mg/dl) which were statistically significant p. value <0.01 [13]. Similar results were found by Kalfe et al. where they reported high mean fibrinogen level (341±70) in diabetic patients compared to healthy non diabetic control (216±43) [14].

Our study showed fibrinogen to be significantly associated with the glycocyalted hemoglobin (HbA1c). Fibrinogen level increased as the value of HbA1c became higher, this result was in agreement with Sanjay Dhawale who found serum fibrinogen level was higher in uncontrolled diabetic HBA1C higher than 7% [15].

**Conclusion**

Serum fibrinogen level was found to be higher in type 2 diabetic patients as compared to non-diabetic and Serum fibrinogen level was higher in patients having uncontrolled diabetes. Patients with diabetic mellitus has significant increase in fibrinogen level, which may indicator hypercoaguable factor that may lead to thrombotic tendency.

**Acknowledgment**

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**Conflict of Interest**

We hereby declare that there is no conflict of interest.

**References**

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