



Evaluation of plasma fibrinogen levels in type 2 diabetes mellitus and its co relation with HbA1c levels

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ABSTRACT

Background: Diabetes mellitus comprises a group of common metabolic disorder where increased fibrinogen level can act as a thrombogenic factor. Diabetic patients have higher cardiovascular morbidity than non diabetic subjects. Several studies have shown that haemostatic factor especially hyperfibrinogenaemia is implicated as a source of atherosclerosis.

Material and method : A study was conducted to compare fibrinogen levels between 30 type 2 diabetes patients and 10 age and sex matched healthy controls. Their fibrinogen levels are compared and correlated with risk factors like glycosylated haemoglobin ,age ,sex ,smoking ,body mass index(kg/m2),and hypertension.

Results : It was seen that in diabetic patients ,the plasma fibrinogen levels were higher than non diabetic even though it was not statistically significant.(327.37 ±47.25 vs 327.1±72.45: p > 0.05) . The study re established co relation between HbA1c and fibrinogen levels of the diabetic patient is positive i.e.,poorer the glycaemic status, higher the fibrinogen levels. (r=0.21).

Conclusion : It can be concluded that fibrinogen levels are increased in diabetic subjects which is associated with glycemic index .This contributes to the excess cardiovascular morbidity and mortality.

KEYWORDS : Glycosylated haemoglobin, MI, fibrinogen.

Introduction

Diabetes mellitus comprises a group of common metabolic disorders that share the phenotype of hyperglycemia. The worldwide prevalence of diabetes mellitus has risen dramatically over the past two decades and the prevalence of type 2 diabetes mellitus is expected to rise more rapidly in future because of increasing obesity and reduced activity levels.. Studies have shown that formation of an occlusive thrombus, on a damaged atherosclerotic lesion is the most common precipitating factor of acute myocardial infarction. Evidence also suggests that fibrinogen has a role; both in the early stages of plaque formation and late complications of cardiovascular disease. The excess cardiovascular morbidity and mortality among diabetics have not been fully explained by major risk factors such as hypertension, cigarette smoking and hypercholesterolemia. Increased attention is being paid to, disordered hemostatic mechanism in pathogenesis of both large vessel and small vessel disease in diabetes. Fibrinogen, itself is determined by several modifiable and non-modifiable determinants like age, sex, smoking, body mass index (BMI), hypertension, alcoholism, glycemic control, lipid profile and urine albumin excretion rate. The present study was undertaken to know the levels of fibrinogen in type 2 diabetes mellitus and its relation with glycemic control. Several studies have shown that haemostatic factor especially hyperfibrinogenemia is implicated as a source of atherosclerosis and its complications. Studies have reported that fibrinogen levels were higher in diabetics than in controls. In view of above concepts and due to paucity of similar studies in Indian patients, this study had been undertaken to know the significance of fibrinogen as risk factor in type 2 diabetes mellitus and its relation with glycemic control.¹⁰

METHODS

The proposed comparative and cross-sectional observational study was conducted at Bangalore Medical College & Research Institute and Bowring & Lady Curzon hospital, Bengaluru. The subjects (type 2 DM patients) was drawn from among the patients who attended Bangalore Medical College Hospital & Research Centre, Bengaluru and healthy subjects (age and sex matched) from relative accompanied with the patients. The type 2 DM patients and healthy subjects (age and sex matched) were included in group 1 and group 2 respectively for the study. Institutional Ethics Committee permission was sought. Individual informed consent was taken before enrolment subjects (including type 2 diabetes patients and healthy subjects) for the study. Clinical presentation, history of type 2 diabetes and other socio-demographic baseline data were collected by using pre-structured questionnaire in both type 2

diabetic patients and in controls. The various parameters which were studied include age of the patient (in years), sex, smoking history, blood pressure (mm Hg), BMI (kg/m2), history of ischemic heart disease (IHD), plasma fibrinogen levels (mg/dl) by Claus method and glycosylated hemoglobin (%) by immunoturbidimetric test method .Plasma fibrinogen levels, glycated hemoglobin were measured in both the cases and controls. Fibrinogen level was measured by "Claus method" using automated Sysmex CA 600 series. HbA1C was measured by "particle enhanced immunoturbidimetric test" using Erba Mannheim Kit and reader II. Glycosylated Hemoglobin (GHb) is normal adult hemoglobin (HbA1) which is covalently bonded to a glucose molecule. GHb concentration is dependent on the average blood glucose concentration. Results were calculated automatically by the instrument.

Results

In the present study fibrinogen levels were estimated in 30 type 2 diabetes mellitus subjects and 10 age and sex matched controls. Fibrinogen levels were correlated with age, sex, smoking, hypertension (HTN), BMI and glycosylated hemoglobin (HbA1C). ean age in the present series was 58.83 years for cases and 61.7 years for controls. The youngest age was 39 years. The eldest age was 85 years. The maximum numbers of patients were in the age group 51–70 years (50%). Among the 30 patients studied 50% were males and 50% were females. In this study M:F ratio is 1:1. The mean plasma fibrinogen in cases was 327.37 ± 97.25 mg/dl. Lowest value was 121 mg/dl and highest value was 540 mg/dl. The mean plasma fibrinogen in controls was 327.1 ± 72.45 mg/dl. Lowest value was 259 mg/dl and highest value was 461 mg/dl. Cases had a higher fibrinogen when compared to controls and normal range (200–350 mg/dl) and it was not statistically significant (P>0.05), Table 1. In this, it was found in study population that, as age advances fibrinogen did not increase and was statistically insignificant. In cases, males had mean fibrinogen of 336.53 ± 96 mg/dl and females had mean fibrinogen of 318.2 ± 100.4 mg/dl which were higher but was not statistically significant. In control, males had mean fibrinogen of 317.17 ± 68.96 mg/dl and females had mean fibrinogen of 342 ± 85.6 mg/dl which were lower but was not statistically significant. There were 8 (26%) smokers among cases and 5 (50%) in controls. In cases and controls, smokers had higher fibrinogen levels than non smokers and were statistically insignificant (P>0.05). In cases, smokers had 330 ± 98.54 mg/dl and non smokers had 326.4 ± 99.1 mg/dl fibrinogen levels. In controls smokers had 342.4 ± 50.64 mg/dl and non smokers had 311.8 ± 93.06 mg/dl fibrinogen levels. In diabetic hypertensive patients

mean fibrinogen level was 329.41 ± 102.5 mg/dl and in diabetic normotensive 321.75 ± 87.07 mg/dl. Diabetic hypertensive patients had higher fibrinogen level than diabetic normotensive which was statistically insignificant. In cases obese individuals had higher fibrinogen level than non obese and which was statistically not significant. In diabetic obese individuals mean fibrinogen was 360 ± 141.06 mg/dl and in non obese individuals, mean fibrinogen was 323.74 ± 94.24 mg/dl., Table 2. The mean HbA1c value in cases was $10.39 \pm 3.04\%$. Lowest value was 4.4% and highest value was 18%. Cases had a higher HbA1c value when compared to normal range (4.2–6.2%). The correlation between HbA1c and fibrinogen levels of the diabetic patient is positive i.e., poorer the glycemic status, higher the fibrinogen levels ($r=0.21$),

Discussion

There are various studies showing increased levels of fibrinogen in diabetic patients above the normal range (150-350 mg/dl).In our study many diabetic patients had above normal or on higher side of normal range .Only one patient had low fibrinogen value of 121mg/dl with HbA1c 6.4. This could have led to lowered mean fibrinogen levels (327.37 ± 97.25) in the whole group of cases. But still the fibrinogen levels are on the higher side of normal range in most patients signifying a pro coagulant state in patients .

The mechanism by which fibrinogen increases cardiovascular risks are not fully understood .Fibrinogen plays important role in development of atherosclerosis starting from the stage of plaque formation till formation of occlusive thrombus over a ruptured atherosclerotic plaque,which is the most common precipitating cause of MI⁽¹⁾

Studies have shown association with age, hypertension , smoking, IHD,BMI^(1,2) which was not found statistically significant in our study. Probably it is due to the sample size.

Fibrinogen level plays an important role in the development of stroke and myocardial infarction although causality cannot be inferred from the data⁽³⁾.In a study done by Jain A et al ,fibrinogen was associated with glycemic control and urine albumin excretion rate in a statistically significant manner⁽²⁾. Plasma fibrinogen levels is influenced by many factors .It increases with age, body mass index ,smoking and diabetes and post menopause and is related to fasting, serum insulin ,LDL cholesterol ,lipoprotein (a) and leucocyte count. Conversely it decreases with HDL cholesterol , hormone replacement therapy.

Hence further studies with larger sample size and research to discovery of lowering of variables of fibrinogen is going on. Thus reducing chance of stroke and cardiovascular events in diabetes.

Table no 1 . Descriptive statistics in diabetics and controls

	Cases	Controls	
Number	30	10	
Age (Mean)	58.83 yrs	61.7 yrs	
Fibrinogen	327.37 ± 97.25	327.1 ± 72.45	
HbA1c	$10.393.04$	5.85 ± 0.69	P<0.001

In our study fibrinogen levels were higher in cases compared to controls but this was not statistically significant. This was similar to study done by Nuha muhsin.⁽¹¹⁾. But statistically significant difference was found by several other studies.^(1,2,4,9,10)

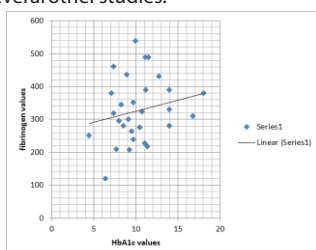


Fig 1 . Correlation of HbA1c values and fibrinogen in diabetics.

In our study there was a positive co relation ($r=0.21$) between fibrinogen levels and HbA1c levels in diabetics i.e.,poorer the glycemic status higher the fibrinogen levels.This is similar to Bembde AS¹,Jain A et al²,Purushothaman et al⁴,DR Kafle⁵ et al¹,Harsoor S⁷ et al,Ying Zhao⁹ et al.

In our study among cases there was no significant correlation between age and fibrinogen levels but among controls there was a significant co relation ($r=0.646$). There are similar findings by various studies^(4,9,10,11). But few studies have found significant correlation between fibrinogen levels and increasing age^(1,2,5,7). Thus there is no consensus about this variable.

In our study among cases and in control group there was no co relation between fibrinogen levels and sex of the patient. This was similar to study conducted by Bembde AS¹,Jain A et al²,DR Kafle⁵ et al,Ying Zhao⁹ et al.

In our study there is no significant difference in fibrinogen levels between hypertensives and normotensives in both cases and control group. This is similar to Harsoor S⁷ et al .Many authors have found association between hypertension and fibrinogen levels among diabetics. (Bembde AS¹,Jain A et al²,DR Kafle⁵ et al,Gupta P et al.¹⁰)

In our study there was no co relation of fibrinogen levels with BMI (kg/m2). Cases were grouped as obese or non obese depending on whether their BMI was more than 30 or not. This was similar to Ying Zhao⁹ et al. But significant co relation was found by Bembde AS¹,Jain A et al²,DR Kafle et al⁵ and Harsoor S et al⁷.

In our study no co relation was found between fibrinogen levels and smoking .There were 8(26%) smokers among cases and 5(50%) smokers among controls.This was similar to study done by Jain A et al⁽²⁾.But few studies have found significant co relation of rising fibrinogen levels with smoking among cases and controls (Bembde AS¹,DR Kafle et al⁵,Wilhelmsen Let al³).

Conclusion .

Diabetics have higher fibrinogen levels compared to controls which is positively co related with HbA1c levels ($r=0.21$). There is no significant correlation of fibrinogen levels with age, sex , smoking , hypertension ,BMI among diabetics. But there was significant correlation of fibrinogen levels with age among control group ($r=0.646$). Hence large scale studies are required to know as to how to lower this fibrinogen levels in diabetics .

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