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## Study of serum fibrinogen level in type 2 diabetes mellitus

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### Abstract

**Objective:** To estimate the level of fibrinogen in patients with type 2 diabetes mellitus.

**Methods:** We conducted a hospital based study of 100 random patients, divided into 4 groups, 25 in each group and compared serum fibrinogen between the group during the study period from November 2019 to April 2021.

The patients will be sub classified into four groups:

- Patients with type 2 diabetes mellitus without complications (Group – A).
- Patients with type 2 diabetes mellitus with microvascular complications (Group – B).
- Patients with type 2 diabetes mellitus with macrovascular complications (Group – C).
- Patients with type2 diabetes mellitus with both microvascular and macrovascular complications (Group – D).

**Results:** The difference between serum fibrinogen levels among 4 groups were statistically significant ( $p < 0.001$ )

**Conclusion:** Fibrinogen could be potential marker for prediction and prevention of microvascular and macrovascular complication.

**Keywords:** Type 2 diabetes mellitus, serum fibrinogen

### Introduction

Diabetes is one of the largest global health emergencies of this century, ranking among the 10 leading causes of mortality <sup>[1]</sup>. According to the World Health Organization (WHO), noncommunicable diseases (NCDs) accounted for 74% of deaths globally in 2019, of which, diabetes resulted in 1.6 million deaths, thus becoming the ninth leading cause of death globally <sup>[1]</sup>. According to the International Diabetes Federation (IDF), 8.8% of the adult population have diabetes, with men having slightly higher rates (9.6%) than women (9.0%) <sup>[1]</sup>. India is frequently referred to as the diabetic capital of the world as it has the highest number of cases in the world. In the Indian Council of Medical Research the largest nationally representative epidemiological survey conducted in India on diabetes and prediabetes, showed the prevalence of diabetes ranged from 3.5 to 8.7% in rural to 5.8 to 15.5% in urban areas <sup>[1]</sup>.

The real burden of the disease is however due to its macro and micro vascular complications. Coronary artery disease is the leading cause of death among adult diabetics and accounts for about three times as many deaths among diabetics as among non-diabetics. It is now being increasingly appreciated that the traditional risk factors (smoking, obesity, hypercholesterolemia, family history, physical inactivity, diabetes mellitus, hypertension) for cardiovascular disease may account for only one half to two thirds of the actual risk. It becomes important to try and identify other risk factors, especially those that can be easily modified.

Fibrinogen is one such factor. Elevation of plasma viscosity due to increase in fibrinogen concentration significantly contributes to the microvascular disorder in diabetics.<sup>3,4</sup> Similarly many studies have shown elevated fibrinogen to be an important risk factor for coronary artery disease <sup>[2, 3]</sup>. Studies showed that fibrinogen may be involved in development of atherosclerotic lesions <sup>[4]</sup>. To conclude among the various hematological factors, elevated fibrinogen as a risk factor in diabetes plays an important role in the development of complications <sup>[5]</sup>. Fibrinogen levels can be reduced considerably by life style interventions and probably drugs there is possibility that measurement of fibrinogen may help in disease

prediction or prevention.

**Inclusion criteria**

Type 2 diabetes mellitus is diagnosed if any of the following is present with normal or elevated C – peptide level,

- 1) Fasting blood sugar value in total venous sample >126mg/dl
- 2) Postprandial blood sugar value in total venous sample >200mg/dl
- 3) HbA1c value in total venous sample ≥ 6.5%

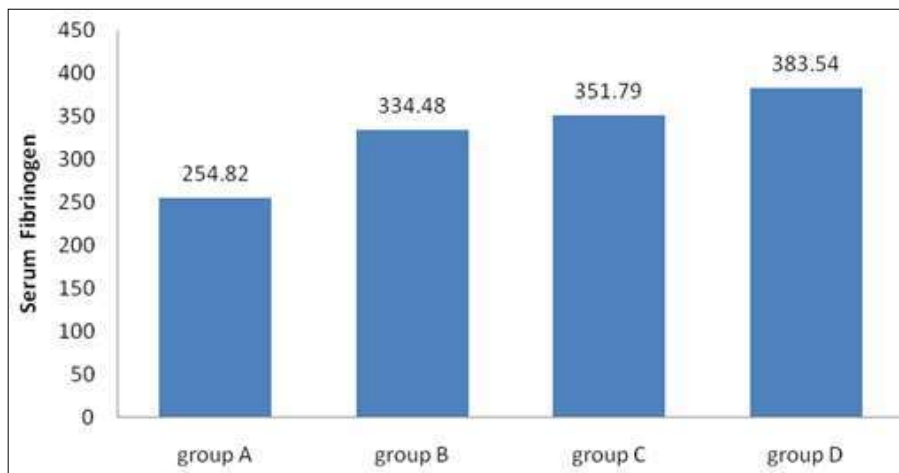
**Exclusion criteria**

- 1) Patients on anti coagulant therapy and also past history of anti coagulation therapy.
- 2) Body Mass Index >30  
BMI is calculated by following formula,  
Body mass index = weight in kilogram ÷ height in metre <sup>[2]</sup>
- 3) Patients with Systolic blood pressure >140 mmHg and/or Diastolic blood pressure >90mmHg in sphygmomanometer

**Results**

**Table 1:** Serum fibrinogen levels of the study participants (N=100)

Serum fibrinogen levels	Group A (N=25)	Group B (N=25)	Group C (N=25)	Group D (N=25)
Mean(mg/dl)	254.82	334.48	351.79	383.54
Std deviation	56.36	51.74	73.04	73.93
Upper limit	278.09	355.84	381.94	414.05
Lower limit	231.56	313.12	321.64	353.02



The above table and figure shows that mean serum fibrinogen levels were  
 254.82 mg/dl - group A  
 334.48 mg/dl - group B  
 351.79 mg/dl - group C  
 383.54 mg/dl - group D

**Graph 1:** Serum fibrinogen levels of the study participants (N=100)

**Table 2:** Comparison of serum fibrinogen levels among the study participants

Comparison of serum fibrinogen among the groups	P value
DM alone& DM with microvascular Complications	p< 0.001 (very significant)
DM alone & DM with macrovascular Complications	p< 0.001 (very significant)
DM alone & DM with macrovascular and microvascular complications	p< 0.001 (very significant)

In order to ascertain whether differences between the fibrinogen levels among 4 groups were statistically significant, p value was calculated using one way anova and Tukey-Kramer Multiple Comparisons Test. The above table shows that the p value is less than 0.01 in all the 3 comparisons indicating that differences in the mean fibrinogen levels are significant.

**Discussion**

This study was a hospital based study in 100 type 2 DM patients attending RMMCH medicine OPD. They were divided into 4 groups of 25 each. Group A patients had Diabetes Mellitus without any complications. Group B had patients of DM with microvascular complications (diabetic

retinopathy/neuropathy/nephropathy). Group C had patients of DM with macrovascular complications (CVA/CAD/PAD). Group D patients of DM with both micro and macrovascular complications. Serum fibrinogen is an inflammatory marker and has a role in pathogenesis of inflammation, atherosclerosis, thrombogenesis and development of vascular complications in type-2 diabetes mellitus patients. The various possible mechanisms for hyperfibrinogenemia in diabetics could be that a procoagulant state often exists in people of diabetes. In our study, the mean age of the study participants was 49.8 years. 17% in the age of 30-40 years, 36% in 40-50 years, 34% in 50-60 years and 13% were above 60 years. 62% of were males and 38% were females.

In our study among the micro vascular complications group B diabetes mellitus patients, the common complication was diabetic nephropathy (48%) followed by diabetic neuropathy (44%) and diabetic retinopathy (36%). Similar findings were found by Madan *et al.* in their study that nephropathy was most common complication than retinopathy and neuropathy [7]. Among the macro vascular complications group C diabetes mellitus patients, the common complication was coronary artery disease (60%), followed by cerebrovascular disease (44%) and peripheral artery disease (PAD) (24%).

In our study among the group D diabetes mellitus patients, the common microvascular complication was diabetic nephropathy (72%) followed by diabetic retinopathy (56%) and diabetic neuropathy (12%). Among the macro vascular complications in group D diabetes mellitus patients, the common complication was coronary artery disease (60%), followed by cerebrovascular disease (40%) and PAD (16%).

The present study found that the mean serum fibrinogen levels were 254.82 mg/dl in group A patients, 334.48 mg/dl in group B patients, 351.79 mg/dl in group C patients and 383.54 mg/dl in group D patients.

The results from this study showed fibrinogen levels to be significantly higher in diabetic patients who had both micro and macro vascular complications than those who had diabetes with micro vascular complications, diabetes with macro vascular complications and diabetes without complications. Our study showed that the p value was less than 0.01 in all the 3 comparisons indicating that differences in the mean fibrinogen levels are significant. Thus fibrinogen levels are potential markers of CAD/stroke as well as micro vascular complications like retinopathy, nephropathy etc. The results were similar to various other studies around the world. In a study by Bruno *et al.* involving 1574 diabetics in north Italy, fibrinogen was found to be significantly elevated in diabetes mellitus patients compared to non diabetics [9]. Similarly, Jensen *et al.* reported a progressive increase in Fibrinogen level in diabetics with complications [10]. In a study by Eriksson *et al.* in Stockholm area to assess the relationship between plasma fibrinogen and CAD in women, found the mean value for plasma fibrinogen to be significantly higher in CAD patients than in controls and it tended to be higher in diabetics than in non diabetics [11].

Asakawa *et al.* and Fujisawa *et al.* have shown that increased fibrinogen is associated with worsening renal function and also retinopathy [12, 13]. Recent studies have shown that certain polymorphisms in fibrinogen gene is associated with elevated levels of fibrinogen in type 2 DM. Similar findings have been shown in India by Neetha Kuzhuppilly *et al.* in a study at Kasturba Medical College, Manipal, Karnataka [15].

In our study we found that the mean fibrinogen level was slightly higher in males (337.73 mg/dl) than females (320.44 mg/dl), the p value was greater than 0.05 indicating that the differences in male and female mean fibrinogen levels is not significant. Similar findings were reported by Archana *et al.* in their study that the males had mean fibrinogen level of  $342 \pm 156$  mg/dl and females had mean fibrinogen of  $301 \pm 110$  mg/dl which were lower but was not statistically significant. [16] This result was in contrast to other studies by Klein *et al.* [14] Jain *et al.* [17] where the levels were slightly higher in females but the difference was also not significant.

## Conclusion

In our study, we conclude that the serum fibrinogen levels were found to be significantly higher in diabetic patients who had both micro and macro vascular complications than those who had diabetes with microvascular complications, diabetes with macro vascular complications and diabetes without complications and the comparison was found to be statistically significant.

Serum fibrinogen levels had a positive correlation with age and HBA1C levels. From our study, we can recommend that estimation of fibrinogen in a subset of patients who have poor glycemic control and with increasing age if fibrinogen levels are found high strict control measures should be initiated. Fibrinogen levels could be a potential marker for the prediction and prevention of macrovascular or microvascular complications. Fibrinogen levels before initiating treatment and during on-going treatment could be a potential indicator for overall efficacy of therapy and life style modifications and the risk reduction. Further studies can be done to study the serum fibrinogen level in diabetic patients with complications and effect of interventions done to reduce the fibrinogen levels.

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