



Comparative Study Of Serum Fibrinogen Level And Hba1c Level In Type 2 Diabetes Mellitus

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Abstract

Introduction : Diabetes mellitus comprises a group of common metabolic disorders where increased fibrinogen levels can act as a thrombogenic factor. Diabetic patients have higher cardiovascular morbidity than non-diabetic subjects. Several studies have shown that haemostatic factor especially hyperfibrinogenemia is implicated as a source of atherosclerosis and its complications.

Objective: To explore the association between serum fibrinogen level and HbA1C level in patients with type 2 diabetes mellitus.

Methods: We have selected hundred random T2DM patients came to our hospital and compared fibrinogen level with HbA1C levels during the study period between November 2019 - April 2021 at Rajah Muthiah Medical College & Hospital, Annamalai University, Chidambaram, India . pre-structured and pre-tested proforma was used to collect the data. Informed consent was taken from all cases and control subjects. Base line data including age and sex, detailed medical history including conventional risk factors, clinical examinations and relevant investigations were included as part of the methodology. For blood investigations, 5ml of blood was collected under aseptic precautions from selected subjects on overnight fasting of 12 hours. Fasting and 2 hours postprandial blood sample were collected for the analysis in the below mentioned vacuum evacuated tubes. Fluoride EDTA vacuum evacuated tubes for estimation of blood glucose and glycated hemoglobin. Clot activator vacuum evacuated tubes for estimation of serum ferritin. Serum obtained following centrifugation was used for estimation of serum ferritin. Fresh random mid stream urine sample was collected in a sterile container for estimation of micro albumin .

Results: The mean fibrinogen level is slightly higher in males than females ,the p value is greater than 0.05 indicating that the differences in male and female mean fibrinogen levels is not significant. mean fibrinogen levels in patients with HbA1c > 7% was compared with HbA1c < 7%, The difference is statistically significant implying that fibrinogen levels increases with poor glycaemic control. Mean fibrinogen level in complicated Type 2 Diabetes mellitus was high 450.43 ± 108.51 mg/ dl as compared to uncomplicated cases 372.30 ± 123.78 mg/dl ($p=0.0001$). Mean HbA1c in total Diabetes mellitus cases was 8.02 ± 1.88 mg/dl with a range of 5.50-14.50 mg/dl. A positive correlation was found between HbA1c and mean fibrinogen level ($r=0.782$, $p= 0.001$) in type 2 Diabetes mellitus. Duration of diabetes in years showed a significant correlation with mean fibrinogen levels ($r=0.295$, $p=0.002$).

Conclusion: Fibrinogen can be used as an indicator for prediction and prevention of microvascular and macrovascular complication of Diabetes Mellitus.2-Fibrinogen level increases with poor glycemic control (indicated by increased HbA1C).

Keywords: Type 2 diabetes mellitus, serum fibrinogen, HbA1C

Introduction

Chronic hyperglycemia in type 2 DM leads to oxidative stress created by an imbalance of pro-oxidants, involves glucose auto-oxidation, protein glycation, polyol pathway and over production of superoxide radicals which causes oxidative stress. This oxidative stress leads to complications in type 2 DM. The long term hyperglycemic status favours glycation reactions leading to formation of advanced glycated end products (AGE). This causes tissue damage by cross linking of collagen. Therefore complications in type 2 DM are dependent on glycemic control. Iron is present in almost all cells of the body. About 75% of total iron is hemoglobin (Hb), 5% is in myoglobin and 15% in ferritin. Ferritin is ubiquitous intra cellular protein that stores iron and releases it in controlled fashion. It acts as a buffer against iron deficiency and iron overload. The relationship between iron metabolism and type 2 DM is bi-directional. Iron influences glucose metabolism, even in the absence of significant iron overload. Iron is a potent pro-oxidant that increases cell oxidative stress causing inhibition of insulin internalization and actions, resulting in hyperinsulinemia and insulin resistance. Free iron exerts a positive feedback on ferritin synthesis and oxidative stress increases the release of iron from ferritin. The abnormalities in ferritin metabolism following glycation in hyperglycemic state might be a primary cause of hyperferritinaemia in type 2 DM. Glycated ferritin has longer half-life. Glycation of transferrin decreases its ability to bind ferrous ion and by increasing the pool of free iron and stimulates ferritin synthesis. Thus, type 2 DM is associated with abnormalities of ferritin metabolism resulting in parallel increase of serum ferritin levels. In this study estimation of serum ferritin will be carried out in patients with type 2 diabetes mellitus and a correlation of these values with the glycated hemoglobin will be studied. Hence we are exploring

the possibility of using serum ferritin for screening persons at high risk of diabetic complications.

Methods: We have selected hundred random T2DM patients came to our hospital and compared fibrinogen level with HbA1C levels during the study period between November 2019 - April 2021 at Rajah Muthiah Medical College & Hospital, Annamalai University, Chidambaram, India . pre-structured and pre-tested proforma was used to collect the data. Informed consent was taken from all cases and control subjects. Base line data including age and sex, detailed medical history including conventional risk factors, clinical examinations and relevant investigations were included as part of the methodology. For blood investigations, 5ml of blood was collected under aseptic precautions from selected subjects on overnight fasting of 12 hours. Fasting and 2 hours postprandial blood sample were collected for the analysis in the below mentioned vacuum evacuated tubes. Fluoride EDTA vacuum evacuated tubes for estimation of blood glucose and glycated hemoglobin. Clot activator vacuum evacuated tubes for estimation of serum ferritin. Serum obtained following centrifugation was used for estimation of serum ferritin. Fresh random mid stream urine sample was collected in a sterile container for estimation of micro albumin

Inclusion Criteria:

Type2 diabetes mellitus is diagnosed if any of the following is present with normal or raised C – peptide level,

1. Fasting blood sugar >126mg/dl
2. Postprandial blood sugar >200mg/dl
3. HbA1c value \geq 6.5%

Exclusion Criteria:

1. Patients on anti-coagulant treatment.

2. Body Mass Index >30, calculated by Body mass index = weight in kilogram ÷ height in metre ²
3. Patients with Systolic blood pressure >140 mmHg and/or Diastolic blood pressure >90mmHg in sphygmomanometer.

Results

Table :1 Distribution of the total study participants according to age (N=100)

Age	Male (N)	Female (N)	%
30-40 years	7	10	17
40-50 years	24	12	36
50-60 years	23	11	34
Above 60 years	8	5	13

The above table shows that the average age of the study participants is 49.8 years. 17% were in the age group of 30-40 years, 36% in 40-50 years, 34% in 50-60 years and 13% were above 60 years. 62% of the study participants were males and 38% were females.

Table :2 Serum fibrinogen value among the male and female study participants : (N=100)

Gender	N	Mean Serum fibrinogen levels (mg/dl)	P value
Male	62	337.73	0.293
Female	38	320.44	

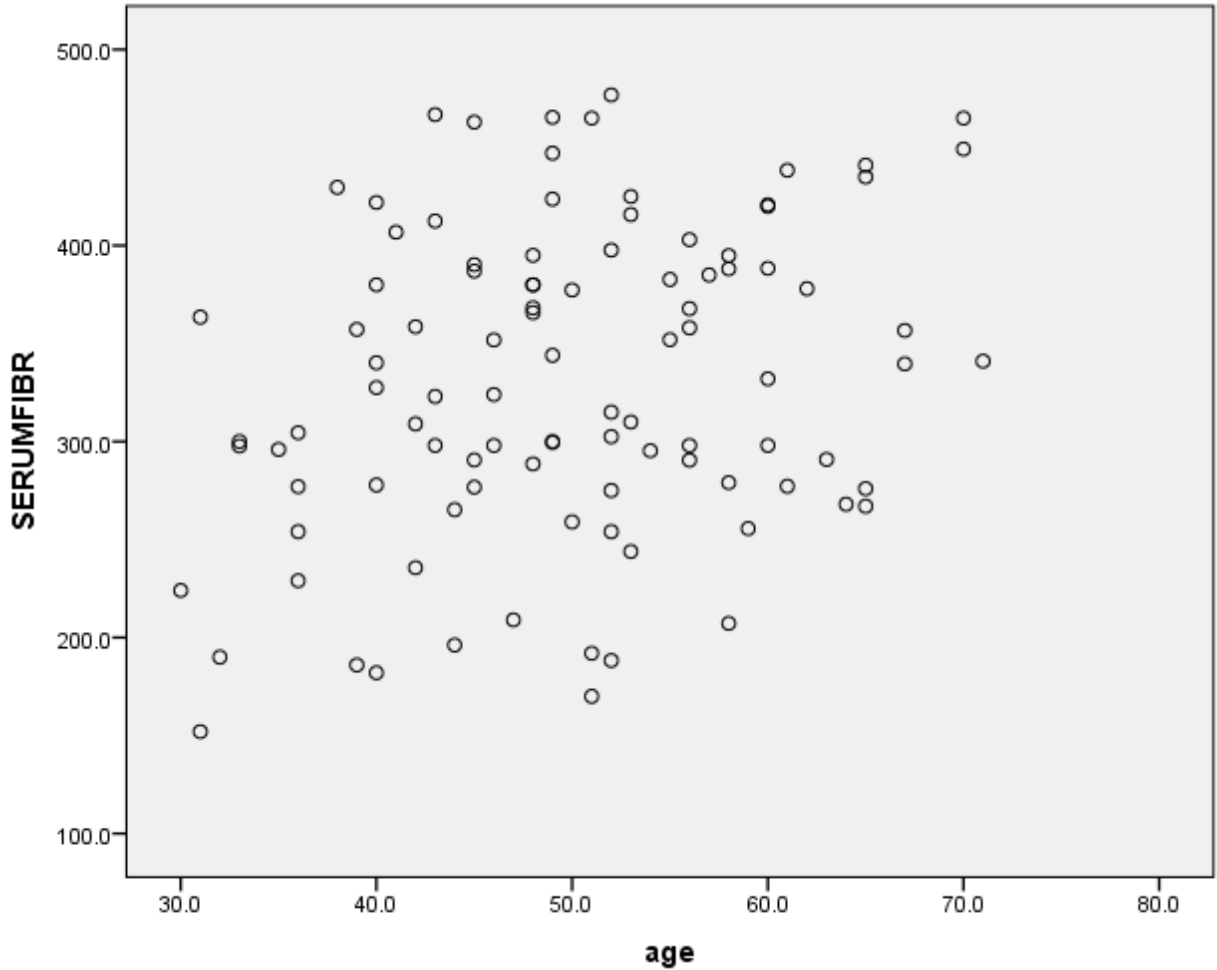
The above table shows that the mean fibrinogen level is slightly higher in males than females ,the p value is greater than 0.05 indicating that the differences in male and female mean fibrinogen levels is not significant.

Table :3 Comparison of serum fibrinogen levels and HBA1C levels among the study participants:

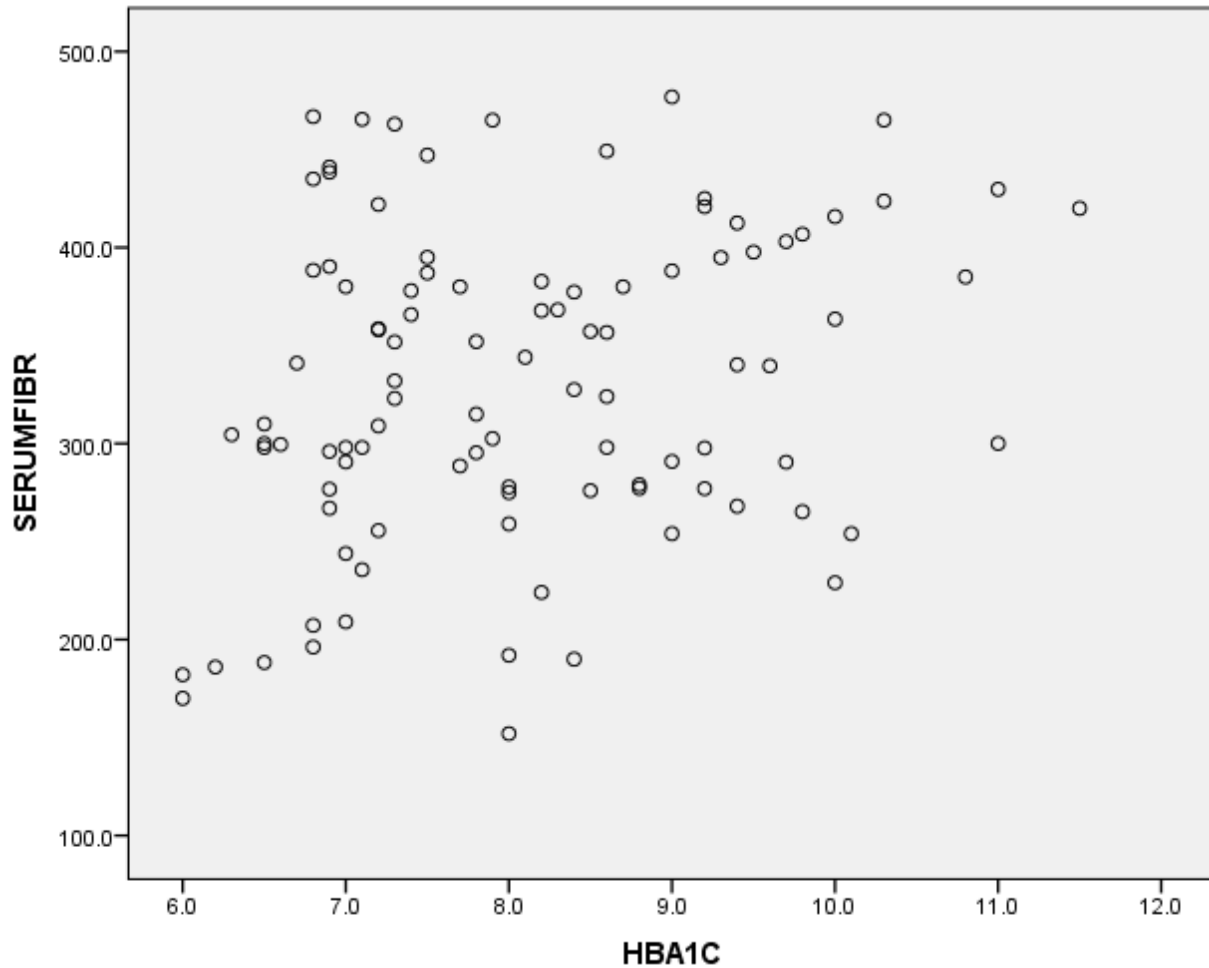
Group	N	Mean Serum fibrinogen levels (mg/dl)	P value
HBA1C level < 7	26	300.14	0.02
HBA1C level > 7	74	342.05	

The above table and figure shows that the mean fibrinogen levels in patients with HbA1c > 7% was compared with HbA1c < 7%, The difference is statistically significant implying that fibrinogen levels increases with poor glycaemic control.

Figure 1: Correlation of age and fibrinogen levels of the study participants : (N=100).



The above figure shows that serum Fibrinogen levels show a positive correlation with age implying that fibrinogen levels increase with age and this was significant statistically. ($r=0.275$ p value = 0.01).

Figure 2: Correlation of HBA1C and fibrinogen levels of the study participants: (N=100):

The above figure shows that serum Fibrinogen levels show a positive correlation with a HBA1C levels implying that fibrinogen levels increase with increasing HBA1C levels and this was found to be statistically significant. ($r=0.257$ p value = 0.01).

Discussion

This study was a hospital based study in 100 T2DM patients attending RMMCH General Medicine OPD. Serum fibrinogen is an inflammatory marker and plays a role in pathogenesis of inflammation, atherosclerosis, thrombogenesis and development of vascular complications in Type-2 diabetes mellitus patients. In diabetics the reason for hyperfibrinogenemia could be due to procoagulant state existing in diabetics. In our study, the average 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 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. Recent studies have stated 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 (337.73mg/dl) than females (320.44 mg/dl), the p value was greater than 0.05 indicating that there is no significant difference serum fibrinogen level between sexes. Similar findings were reported by Archana et al in their study that the males had mean fibrinogen level of 342 ± 156 mg/dl and females had mean fibrinogen of 301 ± 110 mg/dl which were lower but was not statistically significant.¹⁶ This

result was in contrast to other studies by Klein et al¹⁴ Jain et al¹⁷ where the levels were slightly higher in females but the difference was also not significant. In our study, in order to find out whether the glycaemic control affected fibrinogen levels, the mean fibrinogen levels in patients with HbA1c > 7% was compared with HbA1c < 7% and the results showed that the mean fibrinogen levels in patients with HbA1c > 7% was 342.05 mg/dl higher than in HbA1c < 7% 300.14(mg/dl), The difference is statistically significant (p =0.02) implying that fibrinogen levels increases with poor glycaemic control. We also found that that serum Fibrinogen levels show a positive correlation with a HBA1C levels implying that serum level of fibrinogen increasing HBA1C levels and this was found to be statistically significant.(r=0.257 p value = 0.01. This has been shown in studies by Bruno et al, Klein et al, Kafle et al and Bembde et al . The relation between diabetic control and fibrinogen levels could be due to (a) decreased plasmin mediated degradation of glycosilated fibrinogen (b) deficiency of insulin in diabetic's results in differential protein synthesis i.e., 29% reduction in albumin synthesis and 50% elevation in fibrinogen synthesis. In our study , we have found that that serum Fibrinogen levels show a positive correlation with age implying that fibrinogen levels hike up with age and this was found to be statistically significant.(r =0.275 p value = 0.01). This goes hand in hand with a study done by Jain et al that fibrinogen levels were associated with age (r = 0.873) and other variables like body mass index (r = 0.898), triglyceride level (r = 0.9396), cholesterol level (r = 0.99), glycosylated hemoglobin (r = 0.99) and urine albumin excretion rate (r = 0.930) in diabetics, in a significant manner.

Conclusion

In our study, Serum fibrinogen levels has a positive correlation with age and HBA1C levels. As per our study, we recommend, estimation of fibrinogen in a subset of patients who have poor glycaemic control, and also with increasing age. And if fibrinogen levels are found high strict control measures should be initiated. Fibrinogen level can be a vital marker for the indication 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 to know whether interventions done to reduce the fibrinogen levels has any role in patient's wellbeing.

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