IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 22, Issue 6 Ser.6 (June. 2023), PP 25-29
www.iosrjournals.org

A Study Of Plasma Fibrinogen Level In Type 2 Diabetes Mellitus And Its Relation To Glycemic Control

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Abstract
Introduction*: Diabetes mellitus refers to a group of common metabolic disorders that share the phenotype of hyper-glycemia. T2DM is a long term metabolic disorder that is characterized by high blood sugar, insulin resistance, and relative lack of insulin.Impaired glucose tolerance exerts an influence by enhancing thrombogenic factors such as, fibrinogen in the diabetics.Poor glycemic control has been reported to be associated with hyperfibrinogenemia and its complications. Plasma fibrinogen is an important component of the coagulation cascade as well as a major determinant of blood viscosity and blood flow.*
Method*: This cross-sectional study was conducted at SRN hospital MLN medical college; a tertiary care centre, Prayagraj (U.P).To estimate plasma fibrinogen level and its association with microalbuminuria and glycemic control in patients with type 2 diabetes mellitus. A total of 150 diabetic patients out of which 111 were males and 39 were females with age above 18 years were selected. Subjects underwent OGTT and glucose profile (FPG, PPBS, HbA1c) values were observed. Serum fibrinogen other parameters like KFT,S.lipid profile,LFT, urine micralbumin were also measured. 2DEcho was performed and fundus was assessed. Fibrinogen levels were compared with glycemic control of the study participants.*
Conclusion*: It has observed that fibrinogen levels was significantly correlated with glycemic control of the study population.*
Keywords*: Fibrinogen level,Type 2 Diabetes,Microalbuminuria,Glycemic Control.*

Date of Submission: 01-06-2023 Date of Acceptance: 10-06-2023

I. INTRODUCTION

Diabetes mellitus (DM) refers to a group of common metabolic disorders that is characterized by chronic hyperglycemia. Depending on etiology of the DM factors contributing to hyperglycemia include reduced insulin secretion, decreased glucose utilization and increased glucose production. Several distinct types of DM are caused by a complex interaction of genetics and environmental factors. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems.
Etiologic Classification of Diabetes Mellitus[1].

I. Type 1 diabetes (beta cell destruction, usually leading to absolute insulin deficiency)

- Immune-mediated
- Idiopathic

II. Type 2 diabetes (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly insulin secretory defect with insulin resistance)

III. Other specific types of diabetes

- Genetic defects of beta cell function
- Genetic defects in insulin action
- Diseases of the exocrine pancreas—pancreatitis, pancreatectomy, neoplasia.
- Endocrinopathies- acromegaly, Cushing's syndrome, glucagonoma etc.
- Drug- or chemical-induced
- Infections—congenital rubella, cytomegalovirus, coxsackievirus.
- Uncommon forms of immune-mediated diabetes— "stiff-person" syndrome etc.
- Other genetic syndromes sometimes associated with diabetes like Turners

IV. Gestational diabetes mellitus (GDM)

Criteria for the Diagnosis of DM

1.Symptoms of diabetes plus random blood glucose concentration ≥11.1 mmol/l (200 mg/dl) a or
2.Fasting plasma glucose ≥7.0 mmol/l(126 mg/dl)b or
3.HbA1c > 6.5%c or
4.Two-hour plasma glucose ≥11.1 mmol/l (200 mg/dl) during an oral glucose tolerance test d

Fibrinogen is one of the most important coagulation factors in the final common pathway of coagulation. It is a dimeric glycoprotein synthesized in the liver and has a molecular weight of 340,000.The plasma half-life of fibrinogen is 3 to 5 days[24].Elevation of plasma viscosity due to increase in fibrinogen concentration significantly contributes to the microvascular disorder in diabetics[25,26]. Similarly many studies have shown elevated fibrinogen to be an important risk factor for coronary artery disease[27-29]. Evidence also suggests that fibrinogen may be involved in the development of atherosclerotic lesions beginning with the early stages of plaque formation[30].Normal serum fibrinogen level in Indian population is 200-400 mg/dl.Regarding the relationship between fibrinogen and glycemic control in T2DM, only a few research have been conducted.

AIIMS AND OBJECTIVE

1.To estimate plasma fibrinogen level and its association with glycemic control in patients with type 2 diabetes mellitus.
2.To study relationship between fibrinogen level and HbA1c Levels in patients of type 2 diabetes mellitus.

II. Materials and Methods

This Cross-sectional study was conducted in SRN Hospital and MLN medical college, Prayagraj, Uttar Pradesh, India, from July 2021 to September 2022.150 Patients (male and female) attending Medicine OPD and IPD in Swaroop Rani Hospital, Prayagraj, Uttar Pradesh, India.

Inclusion Criteria:

- Age group >18-years, fulfilling diagnostic criteria of T2DM (as per ADA guidelines).
- Diagnostic criteria for T2DM:
- Fasting blood sugar >126mg/dl.
- Post prandial blood sugar >200 mg/dl.
- HBA1C >6.5%.
- Known case of T2DM on antidiabetic drugs

Exclusion Criteria:

- Patients less than 18 years of age
- Patients with a history of chronic alcohol intake and chronic smoking.
- Patients on anticoagulation therapy or having any bleeding diathesis
- Patients with a history of chronic liver disease.

After this, patients will go through needed investigations to fulfill aims and objective of the study.The findings from this study would clarify the significance of fibrinogen level as an indicator of glycemic control in patients of type 2 Diabetes mellitus.

III. Observation and Results

Age distribution of patients

Age intervals	No of patients	Percent
35-50 years	31	20.7
51-65 years	104	69.3
>65 years	15	10.0
Total	150	100.0

Majority 104 (69.3%) were in the age range of 51-65 years and 31 (20.7%) were in the age range of 35-50 years and 15 (10%) were more than 65 years. Mean age was 56.61±8.02 and median was 56; patients all together were in the age range of 38 to 95 years.

Gender distribution of study population.

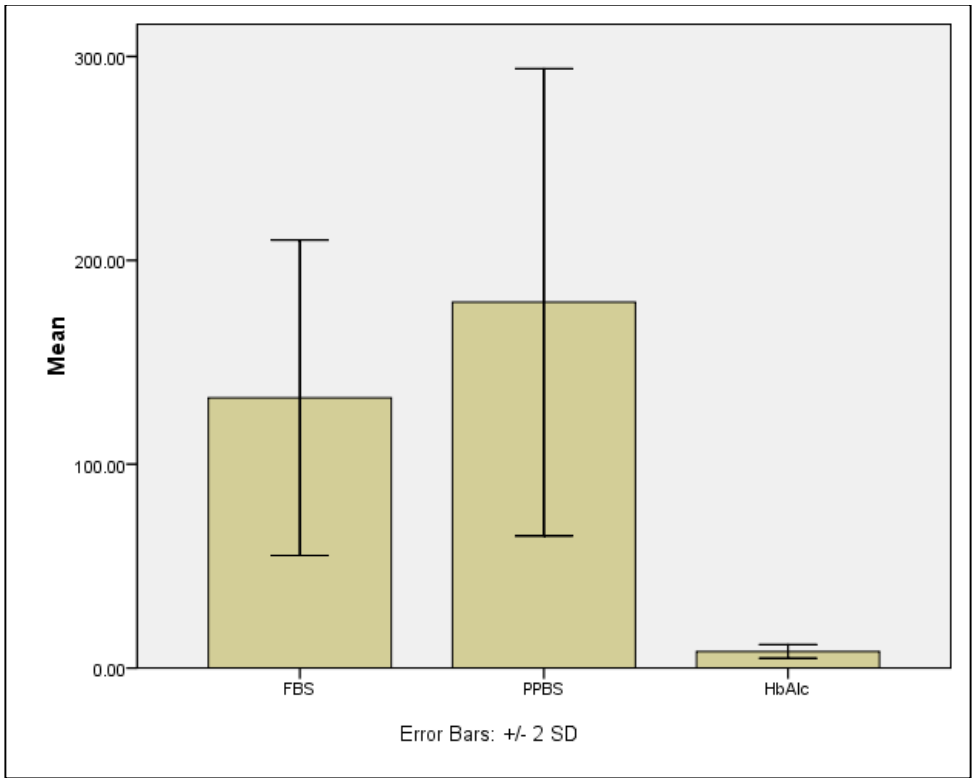
SEX	No of patients	Percent
Female	39	26.0
Male	111	74.0
Total	150	100.0

In the study, there were 39 (26%) males and 111 (74%) females.

Description of Diabetes parameters.

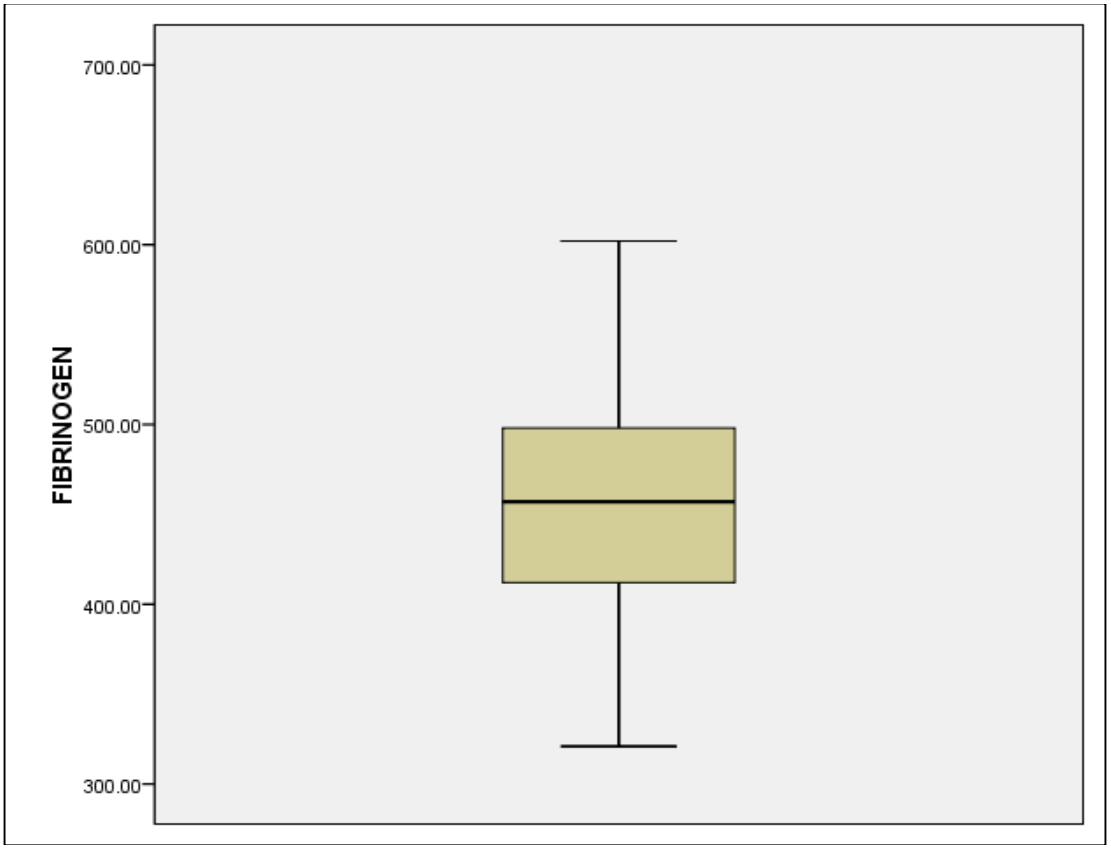
	Mean	SD	Median	Min	Max	Valid N
FBS (mg/dl)	132.58	38.70	121.00	88.00	276.00	150
PPBS (mg/dl)	179.45	57.30	176.00	96.00	433.00	150
HbA1c(%)	8.15	1.67	7.60	5.70	14.00	150

Mean FBS was 132.58±38.7 (mg/dl) and median was 121 (mg/dl); range was 88 to 276 (mg/dl).
Mean PPBS was 179.45±57.3 (mg/dl) and median was 176 (mg/dl); range was 96 to 433 (mg/dl).
Mean HbA1c was 8.15±1.67 (%) and median was 7.6 (%); range was 5.7 to 14(%).



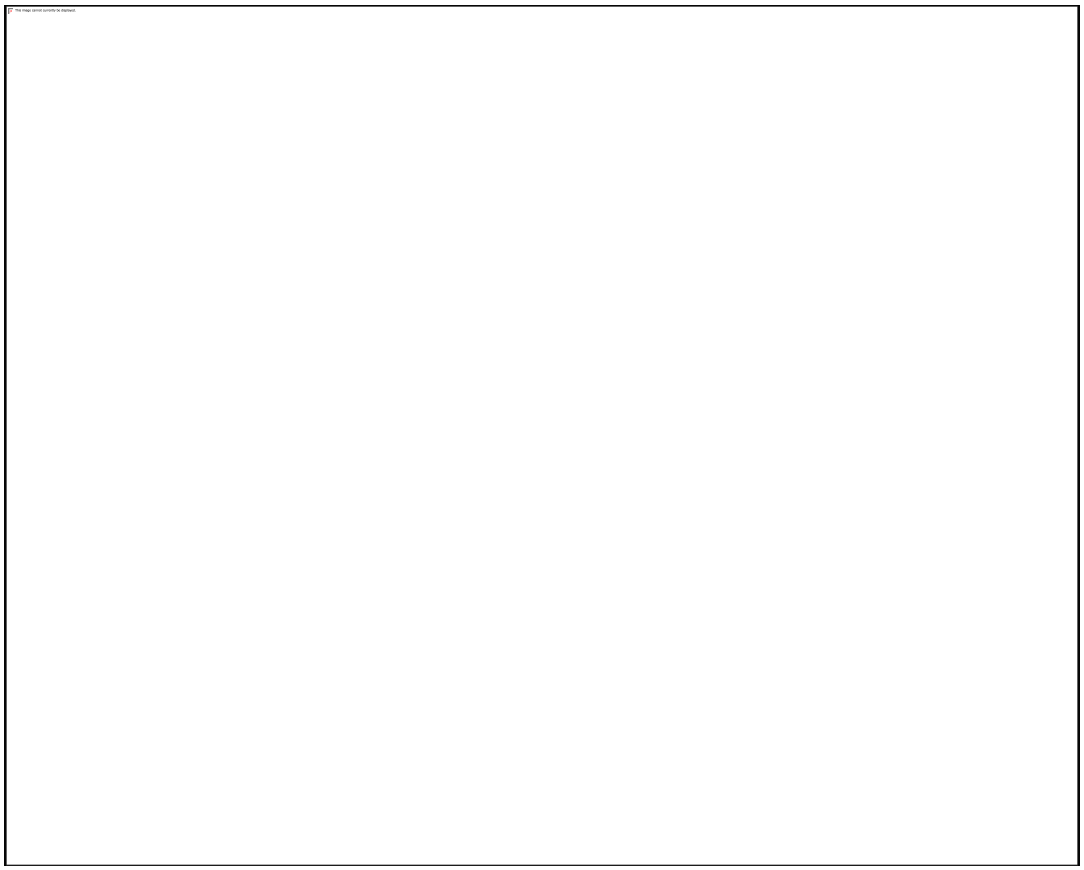
Description of Plasma Fibrinogen.

	Mean	SD	Median	Min	Max	Valid N
PLASMA FIBRINOGEN (mg/dl)	462.81	59.21	457.00	321.00	602.00	150



Mean Plasma Fibrinogen was 462.81±59.21 (mg/dl) and median was 457 (mg/dl); range was 321 to 602 (mg/dl).

Correlation of HbAIc with Plasma Fibrinogen in the study population.



HbA1c shows a significant strong positive correlation with fibrinogen with r= 0.855 and p value = <0.001**.**
FBS was correlated with Plasma Fibrinogen, a significant positive correlation was found.
PPBS was correlated with Plasma Fibrinogen, a significant positive correlation was found.
Discussion
One hundred fifty diabetes patients aged between 38 to 95 years with a mean age of 56.61±8.02 were selected for the study. The age distribution of the study population was as below,

- Between 51- 65 years -69.3%
- 35 and 50 years- 31.7%
- >65 years- 10%

This age distribution was similar to that reported in another study, such as by Bembde, (2019). Our study's mean were as following Hemoglobin(10.36±1.47 g/dl), TLC(9613.87±3834.55 cells/mm3), S urea(63.01±42.5 mg/dl), S creatinine(2.25±2.34 mg/dl), urine micral(203.28±174.06 mg/dl), S bilirubin(1.12±0.89 mg/dl), S albumin (3.73±0.43 g/dl), ALP(359.1±186.19 U/L), SGOT(55.88±63.65 U/L), SGPT(52.48±56.34 U/L), FBS(132.58±38.7 mg/dl), PPBS(179.45±57.3 mg/dl), total cholesterol (234.57±73.79 mg/dl), HDL (62.75±10.41 mg/dl), PT/INR (1.12±0.33) and 2DECHO (EF %) (49.07±8.7 %).Our study's mean HbA1c was 8.15±1.67.

The mean fibrinogen was found to be 462.81±59.21mg/dl, with a range of 321 to 602mg/dl.The correlation between HbA1c and fibrinogen levels of the diabetic patient was found to be significantly positive, i.e., the poorer the glycemic status, the higher the fibrinogen levels (r = 0.855).This statistically significant correlation could be due to a number of factors such as

- glycosylated fibrinogen being less susceptible to plasmin degradation
- relative insulin deficiency in diabetics resulting in differential protein synthesis causing 29% decrease in albumin synthesis and 50% increase in fibrinogen synthesis[59].

In this study, blood sugars, both FBS and PPBS, were also found to be significantly positively correlated with Fibrinogen levels.

IV. Conclusion

The mean Plasma Fibrinogen in our study was found to be 462.81±59.21 (mg/dl) which was higher than the range of 200-400 mg/dl found in normal individuals . HbA1c levels in the study cohort were positively correlated with plasma fibrinogen levels of study population with p value of <0.001 . It was statistically significant and implied poorer glycemic status was associated with higher Plasma fibrinogen levels (r = 0.855).

Blood sugar levels both FBS and PPBS were significantly positively correlated with Plasma Fibrinogen which further strengthened the above finding of poorer sugar control being associated with higher fibrinogen level.

V. LIMITATION OF STUDY:

Study had following limitations.The result were obtained from cross sectional survey of small number of patients which may not be representative of entire population.

The study sample did not include type 1 Diabetes mellitus patients and the duration of diabetes mellitus was not considered.

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