

A Study on Correlation of Plasma Fibrinogen Levels with Glycemic Status in Type-2 Diabetes Mellitus Patients at A Tertiary Care Hospital in Rajasthan

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Conflict of interest: Nil

Abstract

Background: Diabetes is a common endocrinological disorder which can lead to serious cardiovascular events. Increased fibrinogen levels can exaggerate these thrombotic complications in diabetics than non-diabetic individuals. Along with other major risk factors like hypertension, cigarette smoking and hypercholesterolemia, glycemic status of an individual can cause atherosclerosis.

Aims & objectives: To correlate plasma fibrinogen levels with glycemic status in type 2 diabetes mellitus patients at a tertiary care hospital in Rajasthan

Material & Methods- This cross-sectional observational study recruited 85 patients with type 2 diabetes mellitus and 85 healthy subjects in age range of 18-75 yrs who visited the Department of Medicine of our tertiary care hospital from February 2022 to August 2022. Group D- Patients with type 2 diabetes mellitus (n= 85); Group H - Healthy subjects (n= 85). Demographic variables, Clinical signs & symptoms, clinical history were recorded. Parameters studied were age, sex, body mass index, smoking history, history of ischemic cardiac disease, blood pressure. Biochemical investigation carried out were plasma fibrinogen levels (mg/dl) by Clauss method and glycosylated hemoglobin (%) by immuno-turbidimetric test method, fasting & post parandial blood sugar levels (FBS, PPBS), glycated hemoglobin, and lipid profile (TC, TG, HDL and LDL) in both the groups.

Results: This cross-sectional study recruited total 170 patients; 85 patients in each Group. No significant difference with respect to age, gender & height of the patients in both groups. In Group D, 39 patients were hypertensive, 14 had history of ischemic heart disease & 25 were smokers. Statistically significant difference was noted between the both the groups with respect to variables i.e. Hypertension, IHD, Smoking, Weight & BMI ($p < .05$). In Group D, mean FBS, mean PPBS, mean plasma fibrinogen levels, mean LDL, mean HDL, mean TG, mean TC & HbA1C levels were statistically significant higher as compared to Group H (p value < 0.001). In Group D, statistically significant correlation of fibrinogen levels with age, smoking, hypertension, ischemic heart disease, high BMI, high HbA1c levels were noted. Poorer the glycemic status, higher the fibrinogen levels. In Group H, statistically significant correlation of fibrinogen levels with smoking & high BMI were noted.

Conclusion: The glycemic status of diabetic individual correlates significantly with fibrinogen levels, thus proper management should be undertaken to improve the glycemic status & prevent cardiovascular complications.

Keywords: fibrinogen, type 2 diabetes mellitus, ischemic heart disease count.

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Introduction

Across the globe, Diabetes is becoming a potential metabolic disorder affecting 10.5% of the population in 2022 with an increase to 12.2% by 2045. [1] It is a chronic disease characterized by hyperglycemia & altered carbohydrates, fats, and protein metabolism. The prevalence of diabetes and impaired fasting blood glucose levels in India was 9.3% and 24.5% respectively. Older individuals had an increased risk for diabetes & were sixteen times more aware.[2] In type 2 diabetes, peripheral insulin resistance leads to metabolic syndrome, nonalcoholic fatty liver disease & type 2 diabetes mellitus. Its prevalence is about 90% of the total global diabetic population. In India, increased prevalence of Type 2 DM is due to decreased activity & increased obesity. [3]

High mortality & morbidity in DM patients are caused by thrombotic complications & serious cardiovascular events. The leading risk factors lean towards a hypercoagulable state occurring in diabetics due to altered hemostatic mechanism and increased levels of fibrinogen in plasma. Apart from major risk factors like hypertension, cigarette smoking and hypercholesterolemia, rise in plasma fibrinogen levels.[4]

Fibrinogen plays an important role in coagulation cascade & determines viscosity of blood, platelet aggregation, and thrombus formation. Various factors modify the plasma levels of fibrinogen in type 2 diabetics like age, sex, smoking, body mass index (BMI), hypertension, glycemic status, alcoholism, lipid profile and urine albumin excretion rate.[5] It plays a significant role in initiation of atherosclerotic plaque formation & its associated complications.

Anjula J et al 2001 reported higher fibrinogen levels in diabetics than in controls. [6]

Bruno et al 1996 stated occlusive thrombus formation on a damaged atherosclerotic lesion to be the most common precipitating factor for acute ischemic events.[7] Gupta P et al.2016 concluded that fibrinogen levels are raised in type 2 DM with and without chronic heart disease. Hyperfibrinogenemia could be a contributing factor to the excess cardiovascular morbidity and mortality in diabetics. [8] Ghongade PV 2020 concluded plasma fibrinogen level to be significantly associated with glycemic control & duration of DM (in years). Therapeutic approaches to reduce plasma fibrinogen levels could prevent cardiovascular complications in diabetics.[9]

Hence, this cross-sectional study was aimed to correlate plasma fibrinogen levels with glycemic status in type 2 diabetes mellitus patients. Other parameters correlated were fasting plasma glucose(FBS),serum total cholesterol (TC),triglyceride (TG) & high density lipoprotein cholesterol (HDL),Low-density lipoprotein cholesterol (LDL)& HbA1C levels. The early detection, proper monitoring & timely management can help reduce morbidity and mortality associated with type 2 DM.

Material & Methods

This cross-sectional observational study recruited 85 patients with type 2 diabetes mellitus and 85 healthy subjects in age range of 18-75 yrs who visited the Department of Medicine of our tertiary care hospital from February 2022 to August 2022.

Group D- Patients with type 2 diabetes mellitus (n= 85)

Group H - Healthy subjects (n= 85)

Approval sought from institutional ethics committee and written informed consent was taken before start of study.

Demographic variables, Clinical signs & symptoms, clinical history were recorded for both the Groups. The various parameters studied were age, sex, Body mass index, smoking history, history of ischemic cardiac disease, blood pressure. Biochemical investigation carried out were plasma fibrinogen levels (mg/dl) by Clauss method and glycosylated hemoglobin (%) by immuno-turbidimetric test method, fasting & post parandial blood sugar levels (FBS, PPBS) and lipid profile (TC, TG, HDL and LDL) in both the groups. The reference values considered as fasting plasma glucose (75- 100 mg/dl), serum TC (130-250 mg/dl), TG (<160 mg/dl), and HDL (30-55 mg/dl), LDL (70-165 mg/dl) & HbA1C (<5.7%). Type 2 Diabetes mellitus was defined as FBS of ≥ 126 mg/dl or as receiving anti-hyperglycemic drug treatment.

Statistical Analysis: The collected data was analyzed using SPSS version 2.0 software. The student test was used to find the significant difference among the groups & Chi square test was used to find the correlation between the variables. P value ≤ 0.05 was considered statistically significant.

Results

This cross-sectional study recruited total 170 patients; 85 patients in each Group. There was no significant difference with respect to age, gender & height of the patients in both groups. In Group D, 39 patients were hypertensive & with history of IHD were 14 while it was nil for Group H. In Group D, 25 were smokers ,39 patients were hypertensives, 14 had history of IHD. Statistically significant difference was noted between the both the groups with respect to variables i.e. Hypertension, IHD, Smoking, Weight & BMI ($p < .05$). (Table 1)

In Group D, mean FBS, mean PPBS, mean plasma fibrinogen levels, mean LDL, mean HDL, mean TG, mean TC & HbA1C levels were statistically significant higher as compared to Group H (p value < 0.001). (Table 2)

In Group D, statistically significant correlation of fibrinogen levels with age, smoking, hypertension, IHD, high BMI, high HbA1c levels were noted. Poorer the glycemic status, higher the fibrinogen levels. In Group H, statistically significant correlation of fibrinogen levels with smoking & high BMI were noted. (Table 3)

Table 1: Demographic Variables

Demographic Variables	Group D	Group H	P value
No of subjects	85	85	>.05
Mean age (in yrs)	53.32 \pm 12.65	52.71 \pm 11	>.05
Hypertension (mm Hg)	39	Nil	<.05
IHD	14	Nil	<.05
Smoking	25	18	<.05
Weight (kg)	69.58 \pm 9.31	66.34 \pm 7.95	<.05
Height (meters)	1.65 \pm 0.06	1.66 \pm 0.06	>.05
BMI(kg/m ²)	26.21 \pm 2.75	24.53 \pm 1.54	<.05

Table 2: Biochemical Investigations Values of Group D & Group H

Biochemical Investigations	Group D (mean \pm SD)	Group H (mean \pm SD)	P value
FBS	192.24 \pm 83.11	95.24 \pm 15.63	0.001
PPBS	347.73 \pm 121.32	142.56 \pm 50.51	0.001
Fibrinogen	391.71 \pm 135.45	319.03 \pm 99.02	0.001
LDL	131.73 \pm 33.41	101.67 \pm 26.82	0.001
HDL	38.98 \pm 4.91	43.87 \pm 2.32	0.001
TG levels	146.83 \pm 54.11	98.53 \pm 33.31	0.001

Cholesterol	198.53±47.82	163.21±29.21	0.001
HbA1C	9.78±2.51	5.32±0.34	0.001

Table 3: Correlation between fibrinogen levels in Group D and Group H with other parameters

Study Parameters	Group D	Group H
Age	P<0.05	P>0.05
Sex	P>0.05	P>0.05
Smoker	P<0.05	P<0.05
Hypertension	P<0.05	-
IHD	P<0.05	-
BMI	P<0.05	P<0.05
HbA1c	P<0.05	-

Discussion

Hyper fibrinogenemia in DM cases may be a sequela of low-grade inflammation & high levels of circulating cytokines especially interleukin-6 which stimulate hepatocytes to produce fibrinogen. This stands to be an important link between inflammation and hypercoagulable state. Peripheral insulin resistance and hyperglycemia directly affect plasma fibrinogen levels, the concentrations of which are correlated with insulin and pro-insulin levels in healthy subjects. An increase in quantity of coagulation factors such as von-Willebrand factor, fibrinogen, plasminogen activator inhibitor 1, factor VII and thrombin antithrombin complexes result in a procoagulant state .[10]

Hyperfibrinogenemia are due to increased blood viscosity, inflammation and endothelial injury, platelet aggregation occur. Fibrinogen degradation products (FDPs) are formed which bind low-density lipoprotein & sequester more fibrinogen & FDPs stimulating smooth cell proliferation and migration, thus promoting atherosclerosis and thrombus formation. Also, hyperfibrinogenemia is associated with age, smoking, hypertension, glycemic control, and duration of type 2 DM. Higher fibrinogen level implicates increased risk for CAD. [11]

In the present study ,65% of the patients were in 50-70yrs age range. Similarly, Bembde et al observed 69% of diabetics in age group 51–70 years .12In Group D, mean FBS levels and mean PPBS levels were higher than Group H which was statistically significant (p value <0.001). In Group D, mean plasma fibrinogen levels were higher than Group H which was statistically significant (p value <0.001). It was observed that as age progresses increase in fibrinogen was statistically significant. Similarly, Gupta P et al 2016, observed higher mean plasma fibrinogen levels in diabetic group than controls. Also fibrinogen was significantly higher in diabetic patients with coronary artery disease(CAD) than those having only diabetes.8 Similar findings were noted by James et al [13] and Bembde AS et al [12], with statistically significant higher fibrinogen levels in CAD patients than without the disease.

In the present study, fibrinogen levels were significantly associated with HbA1c levels. Increase in fibrinogen levels were noted with increase in the HbA1c values. Similar findings were noted by Gupta P et al but no significant association observed between duration of diabetes and fibrinogen level .[8]

In the present study, in Group D, mean LDL, mean HDL, mean TG, mean cholesterol were higher than Group H which was statistically significant (p value <0.001). Gupta P et al study demonstrated significantly higher levels of cholesterol, LDL and triglycerides in the diabetic group.[8]

In the present study, in Group D, HbA1C levels were higher than Group H which was statistically significant (p value <0.001) which represents a poor long term glycaemic status. Long-term hyperglycemia causes endothelium damage by increased formation of advanced glycation end products by glycosylation of proteins and lipids. In Ghongade et al 9 study, mean HbA1c value was 8.02±1.88 % in diabetics while in Mohan V et al 2022, levels were 9.2% in type 2 DM. [14]

Conclusion

The study concludes significantly higher levels of fibrinogen in comparison to non-diabetic control individuals. The parameters correlated with the cardiovascular risk variables like age, smoking, hypertension, ischemic heart disease, high BMI, high HbA1c levels. This suggests that plasma fibrinogen levels play an important role to play in pathogenesis role in diabetes. The glycaemic status of diabetic individual correlates with fibrinogen levels, thus proper management should be undertaken to improve the glycaemic status & prevent cardiovascular complications.

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