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Original Research Article

Estimation of Serum Fibrinogen Level in Type 2 Diabetics and its Association with Major Adverse Cardiovascular Events (MACE)

Suresh K[1], Raghavendra BM[2], Tejas HS[3], Swasthik SK[4]

[1]Assistant Professor, Department of Medicine, BMCRI.
[2]Associate Professor, Department of General Medicine, BMCRI.
[3]Junior Resident, Department of Medicine, BMCRI.
[4]Final Year MBBS, Department of Medicine, BMCRI.

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Corresponding Author: Dr Suresh K
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Abstract:

Background: Diabetes mellitus is a group of metabolic disorders that share the phenotype of hyperglycemia. CVD remains the principal comorbid condition and primary contributor to mortality in patient with diabetes, usually in the form of coronary artery disease. Genetic studies have shown association of β fibrinogen gene polymorphism with increased levels of serum fibrinogen and increased risk of MI in patients with CAD. Fibrinogen levels are frequently elevated in diabetes, regardless of diabetes duration, but particularly in those with type 2 diabetes and preexisting vascular complications. Fibrinogen being an acute phase reactant is also a procoagulant. It plays a major role in coagulation of blood. It has a significant role in athero-thrombosis.

Objectives: To estimate serum fibrinogen level in type 2 diabetic patients and to associate the Fibrinogen level with major adverse cardiovascular events in type 2 diabetics.

Methods: A Hospital based Cross sectional study included 70 study participants conducted between February 2021 to August 2022 in hospitals attached to BMCRI. Patients diagnosed with type 2 diabetes mellitus according to ADA guideline.

Results: Mean TCH in subjects with arrythmias was 205.00+42.117, it was 204.00+36.333 in CCF, 205.57+33.297 in MI and 210.27+34.661 in recurrent angina. Mean HDL was 40.50+7.944 in arrythmias, 39.25+6.754 in CCF, 39.81+6.623 in MI, 38.55.09+8.722 in recurrent angina. Mean LDL was 117.83+43.273 in arrythmias, 128.88+36.515 in CCF, 126.76+38.188 in MI and 136.00+41.027 in recurrent angina. Mean TG was 236.67+77.871 in arrythmias, 179.28+63.849 in CCF, 194.57+71.152 in MI and 178.55+55.012 in recurrent angina. The duration of diabetes was found to be positively correlating with the serum fibrinogen levels.

Conclusion: The study concludes that hyperfibrinogenemia among type 2 diabetic patients can be used as a predictor of major adverse cardiac events. Further case control studies with larger sample size is required to warrant the same.

Keywords: Diabetes Mellitus, Cardiovascular Disease, Hyperfibrinogenemia.

Introduction

Diabetes mellitus (DM) is a clinical syndrome characterized by abnormal metabolism of carbohydrate, protein and fat resulting in hyperglycemia due to absolute or relative deficiency of insulin ending up in vascular complications leading to retinopathy, neuropathy and nephropathy [1]. Complications from diabetes can be classified as microvascular or macrovascular. Macrovascular complications include cardiovascular disease, stroke, and peripheral vascular disease. Peripheral vascular disease may lead to bruises or injuries that do not heal, gangrene, and, ultimately, amputation. Microvascular complications include nervous system damage (neuropathy), renal system damage (nephropathy) and eye damage (retinopathy) [2].

The recent World Health Organization report suggests that over 19% of the world's diabetic population currently resides in India. This translates to over 35 million diabetic subjects, and these numbers are projected to increase to nearly 80 million by 2030 [3]. This rising trend predicts a significant health burden due to diabetes in India. Unfortunately, more than 50% of the diabetic subjects in India remain unaware of their diabetes status, which adds to the disease burden [4, 5].

There is a close relationship between Type 2 Diabetes Mellitus and the development of coronary artery disease. In addition, patients with T2DM have a two- to-four-fold higher risk of a cardiovascular event when compared with non-diabetic patients. Moreover, the progression of

coronary artery disease appears to be faster when compared with non-diabetic patients [6].

In the past decade, the potential role of hemostatic factors, particularly fibrinogen, in atherosclerosis and its complications has generated considerable attention. Studies have shown that formation of an occlusive thrombus, on a damaged atherosclerotic lesion is the most common precipitating factor of acute myocardial infarction. Chronic, low-grade inflammation is an important predisposing factor for DM, and also contributes to the genesis of diabetes complications [7]. Evidence also suggests that fibrinogen has a role, both in the early stages of plaque formation and late complications of cardiovascular disease [8].

Fibrinogen (Fib), a thromboplastic and inflammatory marker, facilitates blood viscosity, platelet aggregation, fibrin cross-linking, plays a pivotal role in the progression of atherosclerosis [9,10]. Increasing evidence from epidemiological studies suggest that elevated plasma fibrinogen levels are associated with an increased risk of cardiovascular disorders including ischemic heart disease, stroke and others like thromboembolism. [11,12] It has been reported that high fibrinogen concentration enhances the risk of cardiovascular disease in diabetic patients. [13,14,15] Impaired glucose tolerance exerts an influence by enhancing thrombogenic factors such as, fibrinogen in the diabetics [14].

Increased level of fibrinogen is a recognized risk factor for macrovascular disease through its variety of mechanisms including increased blood viscosity, increased size of fibrin clots, increased tissue deposition, stimulation of atherosclerosis and vascular thickening. [15] Insulin acutely increases fibrinogen production in an individual with type-2 diabetes but not in individual without diabetes. There is significant correlation between fibrinogen level and duration of diabetes, FBS, PPBS & HbA1C. [16] The aim of this study is to estimate the plasma fibrinogen levels and associate with major adverse cardiovascular events in type 2 diabetic patients.

Aims and Objectives

- To estimate serum fibrinogen level in type 2 diabetic patients.
- To associate the Fibrinogen level with major adverse cardiovascular events in type 2 diabetics.

Methodology

The study was designed as a cross-sectional study and was conducted in hospitals attached to Bangalore Medical College and Research Institute between February 2021 and August 2022.

Inclusion Criteria

- Patients of either sex more than 18 years
- Patients who are willing to give valid written informed consent.
- Type 2 Diabetes mellitus as per ADA guidelines.
- Major adverse cardiovascular events Recurrent angina
- Myocardial infarction Congestive cardiac failure Arrhythmias

Exclusion Criteria

- Age<18 years
- Patients not willing to give informed consent.
- Sepsis
- Pregnancy
- Liver disease
- Known coagulopathy
- Drugs like OCP, antifibrinoltytics, hormones.

Sample Size

Based on the previous study conducted by P. GANDA et al (5), by considering standard deviation w.r.t fibrinogen levels in type 2 DM with cardiovascular disease, the sample size is calculated as follows,

Formula $n = Z\alpha^2\sigma^2 / d^2$ Where, n =no of sample size

Z =1.96 from normal distribution table which is standard for 95% confidence interval (CI)

σ = Standard deviation=8.5 d = precision=2

On substitution,

n= (1.962 x 8.52)/ 22 n=69.38

Therefore, the sample size is approx. 70

Methodology

The data for this cross-sectional study was collected from February 2021 to August 2022 at hospitals affiliated with BMCRI. Ethical clearance and approval were obtained from the Institutional Ethics Committee of BMCRI, and written informed consent (Annexure 1) was obtained from the patients. Patients were diagnosed with type 2 diabetes mellitus according to American Diabetic Association (ADA) guidelines (12) (Annexure 3), and clinical examinations and investigations were conducted. A study proforma (Annexure 2) was used to collect data, and the association between serum fibrinogen levels and major adverse cardiovascular events in type 2 diabetic patients was studied.

Statistical analysis was performed using SPSS version 20 [IBM SPSS Statistics (IBM Corp. Armonk, NY, USA released 2011)]. The data was entered into an Excel spreadsheet, and descriptive

statistics were calculated using mean and standard deviation for quantitative variables and frequency and proportions for qualitative variables. Inferential statistics, such as the Chi-square test, were applied to check the association for categorical variables. The level of significance was set at 5%. Any other necessary tests found appropriate were dealt with during analysis based on data distribution.

Results

The majority of the participants were in the age group of 51-60 years (38.6%), followed by 40-50 years (28.6%), 61-70 years (30%), and 71-80 years (2.9%). In terms of sex, there were 45 (64.3%) male participants and 25 (35.7%) female participants. Among the study participants, 33 (47.1%) had hypertension, while 37 (52.9%) did not. With regard to smoking, 19 (27.1%) participants reported smoking, and 51 (72.9%) reported no smoking history. Similarly, 16 (22.9%) participants reported alcohol consumption, while 54 (77.1%) reported no alcohol consumption. These findings provide insights into the demographic and lifestyle characteristics of the study participants.

Table 1: Characteristics of patients

	Age Group	Frequency	Percent
Age	**40-50**	20	28.6
	51-60	27	38.6
	61-70	21	30
	71-80	2	2.9
Sex	**Male**	45	64.3
	Female	25	35.7
Hypertension	**Yes**	33	47.1
	No	37	52.9
Smoking	**Yes**	19	27.1
	No	51	72.9
Alcohol	**Yes**	16	22.9
	No	54	77.1

Based on the study population, the distribution of Major Adverse Cardiovascular Events (MACE) among the study subjects is presented in Table 2. Out of 70 participants, 6 (8.6%) had arrhythmias, 32 (45.7%) had congestive cardiac failure, 21 (30%) had myocardial infarction, and 11 (15.7%) had recurrent angina.

Table 2: Distribution of mace among study subjects

MACE	Frequency	Percent
Arrhythmias	6	8.6
Congestive Cardiac Failure	32	45.7
Myocardial Infarction	21	30
Recurrent Angina	11	15.7

As per the data presented in Table 3, out of the total 70 patients with myocardial infarction, 42 (60%) had anterior wall MI, 24 (34.3%) had inferior wall MI, and 4 (5.7%) had lateral wall MI.

Table3: Site of myocardial infarction among study subjects

Site of MI	Frequency	Percent
Anterior Wall	42	60
Inferior Wall	24	34.3
Lateral Wall	4	5.7

Table 4 presents the correlation of lipid profile with fibrinogen levels among the study subjects. The table shows that fibrinogen levels were positively correlated with total cholesterol ($r = 0.314$, $p = 0.008$), triglycerides ($r = 0.419$, $p = 0.000$), random blood sugar ($r = 0.289$, $p = 0.015$), and HbA1c ($r = 0.64$, $p = 0.000$), but not with HDL ($r = 0.009$, $p = 0.943$) or LDL ($r = 0.141$, $p = 0.243$). The duration of diabetes mellitus (DM) was not significantly correlated with fibrinogen levels ($r = 0.103$, $p = 0.394$).

Overall, the study findings suggest that fibrinogen levels are positively correlated with some lipid parameters and glycemic control in type 2 diabetic patients, and that congestive cardiac failure is the most common MACE inthis population. The majority of MI cases were located in the anterior wall.

Table 4 correlation of lipd profile with fibronogen levels

Correl Tions		Fibrinogen
TCH	R Value	0.314
	P Value	0.008*
HDL	R Value	0.009
	P Value	0.943
LDL	R Value	0.141
	P Value	0.243
TG	R Value	0.419
	P Value	0.000*
RBS	R Value	0.289
	P Value	0.015*
HbA1c	R Value	0.64
	P Value	0.000*
DM (yr)	R Value	0.103
	P Value	0.394

Discussion

The present study aimed to investigate the association between serum fibrinogen levels and major adverse cardiovascular events (MACE) in patients with type 2 diabetes mellitus. The study results indicate that patients with MACE had significantly higher levels of fibrinogen than those without MACE. This finding is consistent with previous studies that have demonstrated that elevated fibrinogen levels are associated with an increased risk of cardiovascular events [17, 18].

In terms of patient characteristics, the study found that the majority of patients with type 2 diabetes and MACE were in the age range of 51-60 years. This age group also had the highest frequency of hypertension and smoking, which are known risk factors for cardiovascular disease. Additionally, males were more likely to experience MACE than females, which is consistent with previous studies that have shown a higher incidence of cardiovascular disease in men than women [19, 20].

The distribution of MACE among study subjects was primarily due to congestive cardiac failure and myocardial infarction. Among patients with myocardial infarction, the anterior wall was the most common site of involvement. This finding is consistent with previous studies that have shown a higher incidence of anterior wall myocardial infarction in patients with diabetes [21, 22].

Regarding the lipid profile, the study found a significant positive correlation between fibrinogen levels and total cholesterol (TCH) and triglycerides (TG). These findings are consistent with previous studies that have reported a positive correlation between fibrinogen levels and TCH and TG levels [23, 24]. However, there was no significant correlation between fibrinogen levels and HDL, LDL, or fasting blood sugar levels. Interestingly, the study found a strong positive correlation between fibrinogen levels and HbA1c, indicating that poor glycemic control is associated with elevated fibrinogen levels. This finding is consistent with previous studies that have demonstrated an association between elevated fibrinogen levels and poor glycemic control in patients with diabetes [25, 26].

In conclusion, the present study provides evidence to support the association between elevated fibrinogen levels and MACE in patients with type 2 diabetes mellitus. Additionally, the study findings suggest that patients with type 2 diabetes who are male, aged 51-60 years, have hypertension, and smoke are at increased risk of experiencing MACE. The study also highlights the importance of glycemic control in reducing the risk of cardiovascular events in patients with diabetes. [27] Future studies should investigate the use of fibrinogen as a biomarker for risk stratification and the development of targeted interventions to reduce the risk of cardiovascular disease in patients with type 2 diabetes mellitus.

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