

Study of the Plasma Fibrinogen Levels in Type 2 Diabetes Mellitus Patients in a Tertiary Care CentreD. K. Sivakumar¹, C. Ravindranath², S. Malathi³, S. Geetha⁴¹Associate Professor, Department of Medicine, Tamil Nadu Government Dental College & Hospital, Chennai, Tamil Nadu, India.²Assistant Professor, Department of Medicine, Tamil Nadu Government Dental College & Hospital, Chennai, Tamil Nadu, India.³Associate Professor, Department of Medicine, Kilpauk Medical College, Chennai, Tamil Nadu, India.⁴Associate Professor, Department of Medicine, Kilpauk Medical College, Chennai, Tamil Nadu, India.

Received: 01-10-2023 / Revised: 07-10-2023 / Accepted: 22-10-2023

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Conflict of interest: Nil

Abstract:

Background: For diabetic people, coronary artery disease is the main cause of death. In addition to the known traditional risk factors associated with complications of diabetes, there is a quest to find out newer markers to predict complications, especially vascular. Fibrinogen is one among such factors. Both medicine and changes in lifestyle can significantly lower fibrinogen levels. This raises the possibility that measuring plasma fibrinogen could aid in the diagnosis and prevention of illness. The aim of the present study was to monitor alterations in the plasma fibrinogen levels of patients with recently diagnosed type 2 diabetes mellitus in a tertiary care setting.

Methods: This was an observational case control study conducted among 100 patients aged 25 to 60 years with recently diagnosed type 2 diabetes mellitus who were hospitalised to the medical/diabetic ward and were visiting the outpatient department at Tamil Nadu Government Dental College, Chennai for 6 months (April 2023- September 2023) and were divided into 50 cases and 50 controls. In accordance with ADA guidelines, patients with newly detected type 2 diabetes mellitus were considered as cases. A comprehensive clinical examination and history were taken of each participant. Serum tubes were used to collect fresh peripheral venous blood samples, about 2 ml in volume, which were then submitted for electromagnetic viscosity measurement of blood glucose (postprandial, random, and fasting blood sugar) and serum fibrinogen levels.

Results: There was no statistically significant difference between the groups with respect to age and sex distribution. The case group had mean plasma fibrinogen levels that were greater than those of the controls. There was no statistically significant difference in plasma fibrinogen levels among the sexes. There was a positive link between all of the diabetes mellitus measures (RBS, FBS, PPBS, and HbA1c levels) and the plasma fibrinogen levels in individuals recently diagnosed with type 2 diabetes mellitus, but not in the control group.

Conclusion: According to this study, plasma fibrinogen and type 2 diabetes mellitus are positively correlated. Additionally, the relationship between plasma fibrinogen levels and other diabetes-related metrics, such as fasting blood sugar, postprandial blood sugar, and glycosylated haemoglobin, was found to be favourable. Thus, fibrinogen has the potential to be a marker for the early detection and treatment of microvascular and/or macrovascular problems in diabetic individuals.

Keywords: Plasma Fibrinogen Levels, Type 2 Diabetes Mellitus.

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Introduction

When compared to non-diabetics, people with diabetes mellitus die from coronary artery disease around three times more frequently than those without the condition. [1]

It's possible that just half of the risk for cardiovascular disease is associated with the traditional risk factors, which include smoking, high cholesterol, obesity, inactivity, and family

history. Therefore, it is now crucial to assess and pinpoint additional risk variables, particularly those that are simple to change. These include endogenous tissue plasminogen activator (tPA), homocysteine, plasminogen activator inhibitor type 1, C- reactive protein, and estrogen insufficiency.

Fibrinogen is one of these elements. It is the building block of fibrin and a crucial factor in

blood viscosity and platelet aggregation. The risk of microvascular problems in diabetic individuals might be considerably increased by elevated plasma viscosity brought on by elevated fibrinogen levels. [2] Similar to this, a number of studies have shown that a substantial risk factor for coronary events is increased fibrinogen levels. [3-5] Additionally, data indicates that increased fibrinogen levels, starting in the early phases of the creation of the plaque, may be involved in the development of atherosclerotic lesions. [6]

Increased fibrinogen levels in diabetics are a significant contributor in the development of problems. [7] Interleukin-6 production is elevated as a result of low-grade inflammation, which is frequently linked to diabetes mellitus. The liver's hepatocytes are stimulated by this interleukin-6 to create more fibrinogen, which is a crucial link between inflammation and the hypercoagulable state. [8]

Both medicine and changes in lifestyle can significantly lower fibrinogen levels. This raises the possibility that measuring plasma fibrinogen could aid in the diagnosis and prevention of illness. [9]

The current study's objectives were to monitor changes in plasma fibrinogen levels in individuals with newly diagnosed type 2 diabetes mellitus in a tertiary care facility and examine the relationships between plasma fibrinogen and a variety of variables, including age, sex, FBS, PPBS, and HbA1c.

Material and Methods

This was an observational case control study conducted among 100 patients aged 25 to 60 years, with recently diagnosed type 2 diabetes mellitus who were hospitalised to the medical/diabetic ward and were visiting the outpatient department at Tamil Nadu Government Dental College, Chennai for 6 months (April 2023- September 2023), and were divided into 50 cases and 50 controls.

Inclusion Criteria

- Age range: 25 to 60.
- Sexuality: Both genders.
- Individuals with newly diagnosed type 2 diabetes mellitus in accordance with ADA recommendations.

- Study participants who consented.

Exclusion Criteria

- Those unwilling to participate in the study.
- A well-known Type 2 Diabetes patient undergoing treatment.
- Known instance of diabetes type 1.
- ICU patients, expectant mothers, and post-operative patients.
- A bleeding diathesis case.
- Previous thrombotic incidents (cortical vein thrombosis, pulmonary embolism, and DVT);
- Cases of chronic kidney illness, cerebrovascular accident, and coronary artery disease that are known to exist;
- History of infection, autoimmune illness, and cancer.
- A comprehensive clinical examination and history were taken of each participant.
- A new peripheral venous blood sample, about 2 ml in volume, was drawn in serum tubes and submitted for the measurement of serum fibrinogen and blood glucose (fasting, postprandial, and random blood sugar) based on the electromagnetic viscosity measuring method.

Results

Majority of the subjects (50%) belonged to 41- 50 years age group and there was no statistically significant difference in the age distribution between the groups (p=0.675). Males were more in both the groups and there was no statistically significant difference between the groups (p-0.542).

Mean plasma fibrinogen levels were 314.3226±45.66938 among males and 306.63 ± 34.87 among females in the case group and the difference was not statistically significant.

Mean plasma fibrinogen levels (mg/dl) were 248.46± 38.83 among males and 240.50 ± 34.75 among females in the control group and the difference was not statistically significant.

The mean plasma fibrinogen levels were thus higher in the case group compared to the controls.

The incidence of comorbidities was higher in cases than in controls and the difference was statistically significant (p=0.009) as shown in Table.1

Table 1: Cross tabulation of co-morbidities among cases and controls

			Group		Total
			Cases	Control	
Comorbidities	COPD	Count	1	0	1
		% within Group	2.0%	0.0%	1.0%
	Hypothyroid	Count	2	0	2
		% within Group	4.0%	0.0%	2.0%
NIL	Count	38	50	88	

		% within Group	76.0%	100%	88.0%
	SHT	Count	7	0	7
		% within Group	14.0%	0.0%	7.0%
	SHT, COPD	Count	2	0	2
		% within Group	4.0%	0.0%	2.0%
Total		Count	50	50	100
		% within Group	100%	100%	100%
Pearson Chi Square =13.636**, p=0.009					

RBS, FBS and PPBS levels were higher in the cases compared to the control group and the difference was statistically significant (p=0.000). The plasma fibrinogen levels were higher (311.4 ± 41.68786 mg/dl) in the cases compared to controls (244.96 ± 36.94229 mg/dl). The difference was statistically significant (p=0.000).

Table 2: Plasma fibrinogen correlation with other biochemical assays (cases and controls)

Correlations							
		Age	RBS (mg/dl)	FBS (mg/dl)	PPBS (mg/dl)	HbA1c	INR
Plasma Fibrinogen MG/DL	Pearson Correlation	0.061	0.654**	0.679**	0.708**	0.776**	-0.032
	Sig.(2-tailed)	0.550	0.000	0.000	0.000	0.000	0.753
	N	100	100	100	100	100	100
** . Significant correlation is found at the 0.01 (2-tailed) level.							

When the entire cohort was considered, a significant correlation was observed between plasma fibrinogen levels and RBS, FBS, PPBS and HbA1c levels. The results are as depicted in table 2. We did not observe a correlation with either age or INR.

Table 3: Correlation of Plasma Fibrinogen with other biochemical measurements (cases only)

Correlations							
		Age	RBS (mg/dl)	FBS (mg/dl)	PPBS (mg/dl)	HbA1c	INR
Plasma Fibrinogen MG/DL	Pearson Correlation	0.237	0.485**	0.424**	0.453**	0.723**	-0.107
	Sig.(2-tailed)	0.098	0.000	.002	0.001	0.000	0.459
	N	50	50	50	50	50	50
** . There is a significant association at the 2-tailed 0.01 level.							

With respect to the case group alone, a significant correlation was observed between plasma fibrinogen levels and RBS, FBS, PPBS and HbA1c levels. The results are as depicted in table 3. We did not observe a correlation with either age or INR.

Table 4: Correlation of Plasma Fibrinogen with other biochemical measurements (controls only)

Correlations								
		Plasma Fibrinogen mg/dl	Age	RBS (mg/dl)	FBS (mg/dl)	PPBS (mg/dl)	HbA1c	INR
Plasma Fibrinogen mg/dl	Pearson Correlation	1	-0.011	-0.167	0.183	0.279*	0.250	-0.047
	Sig.(2-tailed)		0.940	0.245	0.204	0.050	0.080	0.748
	N	50	50	50	50	50	50	50
* The correlation is significant at the two-tailed 0.05 level;								
**The correlation is significant at the two-tailed 0.01 level.								

When the control group alone was taken into account, a significant correlation was observed between plasma fibrinogen levels and PPBS only. The results are as depicted in table 4.

Discussion

Of a total of 100 participants, 4% belonged to 25-30 years of age; 16% belonged to 31-40 years of age, while a majority 50% belonged to 41-50 years of age and 30% belonged to 50-60 years of age. Among both the cases and controls, a majority 50% (n=25) belonged to 41-50 years of age, 62% of the instances (n=31) involved men, whereas

38% (n=19) involved women. Among the controls, 44% (n=22) were female and 56% (n=28) were male.

In relation to the cases, 38% (n=38) did not have any co-morbidities, 2% (n=1) had hypothyroidism, 4% (n=2) had chronic obstructive lung disease, 14% (n=7) had systemic hypertension, and 4% (n=2) had both chronic hypertension and pulmonary sickness. There were no co-morbidities in the controls.

The mean plasma fibrinogen levels were higher among cases than in controls. Between cases, males

had a mean plasma fibrinogen concentration of 314.32 mg/dl and females a mean concentration of 306.63 mg/dl.

Whereas among controls it was 248.46 mg/dl for males and for females 240.50 mg/dl. Thus, higher levels of plasma fibrinogen were observed in both the sexes in cases compared to controls. The levels were 65.86 mg/dl higher in males and 66.13 mg/dl higher among females.

The mean random blood sugar value in cases was 248 mg/dl, which was substantially higher than the value in controls, which was 121 mg/dl.

The mean fasting blood sugar concentrations among the cases were substantially higher, at 127 mg/dl as opposed to 89 mg/dl for the controls.

When compared to controls, who had mean postprandial blood sugar of 137 mg/dl, cases had mean postprandial blood sugar that was considerably higher at 278 mg/dl.

A comparison of the patient's and control's mean HbA1c revealed that the case values were higher. (8.6% vs. 6.2%).

When compared to the control's mean plasma fibrinogen levels of 244.9 mg/dl, the case's mean plasma fibrinogen levels were higher at 311.4 mg/dl.

All the above differences were found to be statistically significant.

There was a positive link between all the diabetes mellitus measures (RBS, FBS, PPBS, and HbA1c levels) and compared to the control group, the plasma fibrinogen levels were higher in individuals with recently diagnosed type 2 diabetes mellitus.

The findings of the current study are consistent with those of the numerous preceding investigations. Fibrinogen levels in diabetes mellitus patients were shown to be considerably higher than in non-diabetics in a study conducted by Bruno et al. comprising 1574 diabetics in north Italy. [10] In a similar vein, Jensen et al. showed that diabetics with problems had fibrinogen levels that gradually rose. [11]

The mean plasma fibrinogen value was found to be significantly higher in patients with coronary artery disease than in controls in a study done in the Stockholm area by Eriksson et al. to evaluate the relationship between women's coronary heart disease and plasma fibrinogen. Furthermore, it tended to be higher in diabetics than in non-diabetics. [12] On admission, diabetic patients had higher fibrinogen and WBC counts than non-diabetic patients. Moreover, among diabetic patients, fibrinogen levels were greater in those who passed away during the follow-up. A research by Sanchez et al. evaluated the predictive

relationships between mortality and inflammatory markers in diabetic individuals with non-ST elevation acute coronary syndrome. [13]

James et al. comparable studies [14] It was shown that diabetics with CAD had greater fibrinogen levels than non-diabetics with CAD and non-diabetics, as reported by Kafle et al., [15] Taj Muhammad Khan et al. [16] and other studies. Maresca et al. have shown that high fibrinogen is a significant cardiovascular risk factor in diabetes mellitus. This implies that elevated fibrinogen levels might account for a portion of the heightened cardiovascular risk in individuals with type 2 diabetes that persists even after accounting for other risk factors. [17]

According to a study by Klein et al., fibrinogen levels rose in patients with peripheral vascular disease and retinopathy but did not correlate with the severity of retinopathy. The study included 909 type 1 diabetic patients enrolled in the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC). [18] According to studies by Asakawa et al. and Fujisawa et al., elevated fibrinogen is linked to worsening retinopathy and renal function. [19-20] Recent research has demonstrated an association between specific fibrinogen gene variants and higher fibrinogen levels in type 2 diabetes mellitus.

Neetha Kuzhuppilly et al. study at Kasturba Medical College in Manipal, Karnataka, produced similar results. A substantial association (Pearson correlation of 0.723) between plasma fibrinogen levels and HbA1c levels was found in our investigation. Studies by Bruno et al., Klein et al., and Kafle et al. have also demonstrated this.

Limitations of the Study

- The results may not accurately reflect a larger population because they were mostly derived from a limited number of patients.
- The length of type 2 diabetes mellitus was not considered in this study since the participants were newly diagnosed with the condition.
- Patients with type 1 diabetes mellitus were not included in the sample.
- Although microvascular and macrovascular problems are those that are linked to morbidity and mortality, they were not assessed in this investigation.
- Due to a high patient loss to follow-up, the impact of the treatment modality could not be compared to plasma fibrinogen levels.

Conclusion

According to this study, plasma fibrinogen and type 2 diabetes mellitus are positively correlated. Additionally, the relationship between plasma

fibrinogen levels and other diabetes-related metrics, such as fasting blood sugar, postprandial blood sugar, and glycosylated haemoglobin, was found to be favourable. Further research into the development of therapeutic modalities aimed at lowering fibrinogen levels and preventing complications has been made possible by the discovery of fibrinogen as a possible indicator for the early detection and management of microvascular and/or macrovascular problems in individuals with diabetes.

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