ORIGINAL ARTICLE

Association of Serum Fibrinogen with Hemoglobin A1c among Type 2 Diabetics patients and non-diabetics

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ABSTRACT

Objective: To detect the plasma fibrinogen levels in type 2 diabetes mellitus patients by taking non-diabetes healthy individuals as control and correlation between plasma fibrinogen levels and glycemic status.

Methods: This case control study was conducted at department of Pathology NICVD Karachi, from November 2018 to November 2019. Diagnosed cases of type 2 DM of >18 years of age and irrespective of gender were included in the study and non-diabetic healthy individuals were taken as control. All the study subjects were assessed regarding glucose level, HbA1c level and Fibrinogen measurement. Data was collected via study proforma and analysis was done by using SPSS version 20.

Results: Mean of fibrinogen level was 331.48±63.5 among diabetes group and mean fibrinogen level was 246.19±18.2 in non-diabetes group (p=<0.01). Average of hemoglobin A1c among type 2 diabetes cases and in non-diabetes cases was found to be 9.40±1.1 and 6.12±0.5 respectively (p=<0.01). Mean fibrinogen level was significantly associated with elevated glycemic status (p=<0.01). Average systolic blood pressure and diastolic blood pressure were also high among those who had Glycemic status (Hba1c) >8% (p=<0.01).

Conclusion: There was significant positive association of fibrinogen with glycemic status in type 2 DM patients.

Keywords: Fibrinogen, hemoglobin A1c, type 2 diabetes mellitus

INTRODUCTION

Type 2 diabetes mellitus is the most frequent health problem for the people globally specifically in developing and under developed nations. Type 2 diabetes mellitus (T2DM) is the 6th foremost basis for mortality and morbidity at global level. [1,2] Worldwide, incidence of T2DM is around one in each eleven grownups and this problem is at peak specifically in Asia.[3] According to a public grounded review study conducted in Pakistan, occurrence of type 2 T2DM by screening test of glycated haemoglobin (HbA1c) evaluated about the occurrence of T2DM and pre-diabetes in Pakistan as 16.98% and10.91% respectively. [4] Individuals with T2DM are comparatively at raised chances for developing the macrovascular problems like peripheral vessel disorders, coronary artery disease and cerebral vessels' disease as well as also the micro-vascular dysfunctions like diabetic nephropathy, diabetic neuropathy, and diabetic retinopathy. [5] Such complications may prime to trouble quality of life as well as peaked chances for death.[6] Unfortunately, in Pakistan, there are more than nineteen million individuals assessed to be with T2DM. [7] Statistics recommended that reference line plasma fibrinogen may perhaps expect and assess early the chances for cardiovascular accidents among overall non diabetic people. [8,9] Although, fibrinogen had been also thought as enhancing the risk for developing the atherosclerosis as well as cardiovascular risk among the patients with T2DM and the fibrinogen levels are found positively correlated to HbA1c. [10,11,12] Fibrinogen, being the symbol for thrombosis as well as inflammation, and is allied with disturbance in cardiovascular physiology, i.e., can be able to detect vascular intima-media thickening and asymptomatic atherosclerosis.[13] This study has been designed to evaluate the association of fibrinogen levels with glycemic control among T2DM patients. The objectives are to detect the plasma fibrinogen levels in T2DM and non-diabetics and to compare and correlate the values of plasma fibrinogen levels with glycemic status in these patients.

METHODOLOGY

This cases control study conducted at Department of Pathology NICVD Karachi from November 2018 to November 2019. Diagnosed cases of type 2 DM of >18 years of age and irrespective of gender were included in this study. Patients having malignancy, infections, glomerulonephritis, coronary artery disease, stroke, connective tissue disorder and with history of trauma were excluded from this study. All the study subjects were assessed regarding glucose level, HbA1c level and Fibrinogen measurement. Glucose was measured by hexokinase (HK) method/ G-6-PDH on Architect ci-8200. HbA1c was measured by Boronate affinity High Performance Liquid Chromatography (HPLC) on Trinity Biotech (Hb 9210 Premier). Fibrinogen was measured on Coagulation analyzer (OCG-102).The test was performed by inserting the test strip into analyzer. The time elapsed between start of test and clot formation is directly proportional to amount of Fibrinogen present in sample. All the data was collected via study proforma. Data analysis was done by using SPSS version 20.

RESULTS

Total 152 individuals were studied, followed by 87 diabetes type II patients and 64 healthy individuals. Mean fibrinogen level was 331.48±63.5 among diabetes type II patients, which was significantly higher as compared to non-diabetes

healthy individuals as 246.19±18.2 (p=0.001). Mean hemoglobin A1c level was 9.40±1.1 in type II diabetes group and 6.12±0.5 was in non-diabetes group (p=0.001). Mean fasting blood sugar among type 2 diabetes cases 153.6±22.5. Table No.1

Serum fibrinogen mean level was 232.6±14 among those who had Glycemic status (Hba1c) <7% and 240.7±23 was in those had Glycemic status (Hba1c) 7-8%, while mean serum fibrinogen level was significantly higher 344.6±56 among those who had Glycemic status (Hba1c)>8% (p=0.001). However systolic blood pressure and diastolic blood pressure were also significantly higher among those who had Glycemic status (Hba1c)>8% p-values were quite significant as showed in table.2

Table No.1: Serum Fibrinogen in diabetic and non-diabetic groups (n=152)

Group Statistics					
	Groups	N	Mean	Std. Deviation	P value
Fibrinogen(mg/dl)	Type 2 Diabetic	87	331.48	63.566	<0.01**
	Non diabetic	64	246.19	18.246	
Hemoglobin a1c(%)	Type 2 Diabetic	87	9.405	1.1913	<0.01**
	Non diabetic	64	6.126	.5782	
Fasting blood sugar(mg/dl)	Type 2 Diabetic	87	153.61	22.548	<0.01**
	Non diabetic	64	111.16	1.394	

** shows statistically high significance i.e., <0.01

Table No. 2: Serum fibrinogen according to glycemic status (n=152)

| Glycemic status (Hba1c)		N	Mean	Std. Deviation	95% Confidence Interval for Mean		P value
					Lower Bound	Upper Bound	
Fibrinogen	<7.0%	64	232.6	14.6	228.9	236.2	<0.01**
	7.0-8.0%	11	240.7	23.3	225.0	256.4	
	>8.0	76	344.6	56.3	331.7	357.5	
	Total	151	289.5	69.3	278.4	300.7	
hemoglobina1c	<7.0%	64	6.1	.57	5.9	6.2	
	7.0-8.0%	11	7.9	.15	7.8	8.0	<0.01**
	>8.0	76	9.6	1.12	9.3	9.8	
	Total	151	8.0	1.8	7.7	8.3	
Systolic blood pressure	<7.0%	64	118.4	4.4	117.3	119.5	
	7.0-8.0%	11	115.4	6.8	110.8	120.0	<0.01**
	>8.0	76	127.5	8.2	125.6	129.4	
	Total	151	122.7	8.3	121.4	124.1	
Diastolic blood pressure	<7.0%	64	79.37	2.2	78.80	79.9	
	7.0-8.0%	11	84.09	4.9	80.79	87.3	<0.01**
	>8.0	76	84.80	4.9	83.66	85.9	
	Total	151	82.45	4.8	81.67	83.2	

** statistically significant
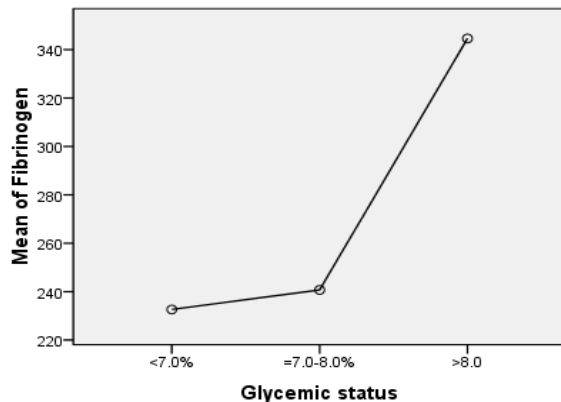
Figure No. 1: Serum fibrinogen according to glycemic status

DISCUSSION

Fibrinogen also known as Factor I, is the foremost clotting factor in blood and is glycoprotein in nature as well as it circulates as a dimer comprised of 03 pairs of polypeptide chain. It has been found related with developing cardiovascular complications unusually. [14] In present study, when fibrinogen levels compared between T2DM group and non-diabetic group, then significant difference revealed in two groups with (p- value<0.01) In this study, glycemic status of study population revealed in significant positive association with serum fibrinogen levels, Systolic blood pressure and diastolic blood pressure. Parallel to this study, Pase MA, et al. [15] found that among the diabetic foot ulcer patients, fibrinogen revealed to be in positive correlation with HbA1C as well as also found eloquently elevated amongst those presented with uncontrolled

T2DM. Insistently increases in fibrinogen had been associated with thickening in vascular intima, so elevated chances for developing cardiovascular morbidity, specifically among T2DM cases. [10] Yahang SH et al. [7] also revealed that cardiovascular morbidity increases with increases in fibrinogen levels among T2DM cases. Factor I, plays its role in developing ischemic heart disease by causing cross-linking and adherence of platelets, expansion to formation of thrombus, and increases in viscosity of blood and subsequently advance to plaque and narrowing in lumen of vessels. Desai KP et al. [17] also found elevated fibrinogen in T2DM patients but not significant association with Hba1c, that might be due to smaller sample size i.e, 30 T2DM patients. Although, in point of facts, augmented levels of glucose actually encourage oxidative stress as well as formation of extremely reactive products, i.e., methylglyoxal, that make structural modifications as well as the efficient impairments of fibrinogen. The glycation status in molecule of fibrinogen is twice to thrice times augmented in T2DM as compared to non-diabetic. These alterations in fibrinogen glycation among diabetic found connected to glycemic switch watched by HbA$_{1c}$ levels. [18]

CONCLUSION
There is positive association of fibrinogen, systolic and diastolic blood pressure with glycemic status in T2DM patients.

REFERENCES
1. Cho N, Shaw JE, Karuranga S, Huang Y, da Rocha Fernandes JD, Ohlrogge AW, Malanda B. IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045. Diabetes research and clinical practice. 2018 Apr 1;138:271-81.
2. Uddin F, Ali B, Junaid N. Prevalence of diabetic complications in newly diagnosed type 2 diabetes patients in Pakistan: findings from national registry. Journal of Ayub Medical College Abbottabad. 2019 Jan 15;30(4-Sup).
3. Zheng, Y., Ley, S. & Hu, F. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nat Rev Endocrinol 14, 88–98 (2018).
4. Aamir AH, Ul-Haq Z, Mahar SA, Qureshi FM, Ahmad I, Jawa A, Sheikh A, Raza A, Fazid S, Jadoon Z, Ishtiaq O. Diabetes Prevalence Survey of Pakistan (DPS-PAK): prevalence of type 2 diabetes mellitus and prediabetes using HbA1c: a population-based survey from Pakistan. BMJ open. 2019 Feb 1;9(2):e025300.
5. Abro M, Zafar AB, Fawwad A, Mustafa N, Tahir B, Riaz M, Basit A. Prevalence of diabetic micro vascular complications at a tertiary care unit of Karachi, Pakistan. International Journal of Diabetes in Developing Countries. 2019 Apr 1;39(2):325-30.
6. Valencia WM, Florez H. How to prevent the microvascular complications of type 2 diabetes beyond glucose control. BMJ. 2017;356:i6505.
7. Saeedi P, Petersohn I, Salpea P, Malanda B, Karuranga S, Unwin N, Colagiuri S, Guariguata L, Motala AA, Ogurtsova K, Shaw JE. Global and regional diabetes prevalence estimates for 2019 and projections for 2030 and 2045: Results from the International Diabetes Federation Diabetes Atlas. Diabetes research and clinical practice. 2019 Nov 1;157:107843.
8. Kaptoge S , Di Angelantonio E , Pennells L , et al . C-reactive protein, fibrinogen, and cardiovascular disease prediction. N Engl J Med 2012;367:1310–20.
9. De Luca G, Verdoia M, Cassetti E, Schaffer A, Cavallino C, Bolzani V, Marino P, Novara Atherosclerosis Study Group. High fibrinogen level is an independent predictor of presence and extent of coronary artery disease among Italian population. Journal of thrombosis and thrombolysis. 2011 May 1;31(4):458-63.
10. Razak MK, Sultan AA. The importance of measurement of plasma fibrinogen level among patients with type-2 diabetes mellitus. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2019 Mar 1;13(2):1151-8
11. R. Barazzoni, M. Zanetti, G. Davanzo, E. Kiwanuka, P. Carraro, A. Tiengo, P. Tessari, Increased Fibrinogen Production in Type 2 Diabetic Patients without Detectable Vascular Complications: Correlation with Plasma Glucagon Concentrations, The Journal of Clinical Endocrinology & Metabolism, 2000; 85(9): 3121-25.
12. Bembde AS. A study of plasma fibrinogen level in type-2 diabetes mellitus and its relation to glycemic control. Indian J Hematol Blood Transfus. 2012;28(2):105-108.
13. Yang SH, Du Y, Zhang Y, Li XL, Li S, Xu RX, Zhu CG, Guo YL, Wu NQ, Qing P, Gao Y. Serum fibrinogen and cardiovascular events in Chinese patients with type 2 diabetes and stable coronary artery disease: a prospective observational study. BMJ open. 2017 Jun 1;7(6):e015041.
14. Mahendra JV, Kumar SD, Anuradha TS, Talikoti P, Nagaraj RS, Vishali V. Plasma fibrinogen in type 2 diabetic patients with metabolic syndrome and its relation with ischemic heart disease (IHD) and retinopathy. Journal of clinical and diagnostic research: JCDR. 2015 Jan;9(1):BC18.
15. Pase MA, Gatot D, Lindarto D. Association of fibrinogen with HbA1C in diabetic foot ulcer.2018
16. Green D, Foiles N, Chan C, Schreiner PJ, Liu K. Elevated fibrinogen levels and subsequent subclinical atherosclerosis: the CARDIA Study. Atherosclerosis. 2009 Feb;202(2):623-31.
17. Desai KP, Roopakala MS, Silvia CW, Kumar KP. Evaluation of plasma fibrinogen levels in type 2 diabetes mellitus. International Journal of Diabetes in Developing Countries. 2012 Dec 1;32(4):209-13.
18. Luzak B, Boncler M, Kosmalski M, Mnich E, Stanczyk L, Przygodzki T, Watala C. Fibrinogen Glycation and Presence of Glucose Impair Fibrin Polymerization—An In Vitro Study of Isolated Fibrinogen and Plasma from Patients with Diabetes Mellitus. Biomolecules. 2020 Jun;10(6):877.