Diabetes & Metabolic Syndrome: Clinical Research & Reviews 13 (2019) 1151–1158

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Original Article

The importance of measurement of plasma fibrinogen level among patients with type- 2 diabetes mellitus

Manal Khudder Abdul Razak [a,*], Ali Adnan Sultan [b]

[a] University of Baghdad, Baghdad College of Medicine, Department of Medicine, Baghdad, Iraq
[b] Department of Medicine, Baghdad Teaching Hospital, Medical City, Baghdad, Iraq

ARTICLE INFO

Article history:
Received 11 January 2019
Accepted 23 January 2019

Keywords:
Fibrinogen
Type 2 diabetes mellitus
HbA1c

ABSTRACT

Background & aim: Fibrinogen has been implicated as a cause of atherosclerosis and its complications in patients with type 2 DM. We aimed to measure the plasma fibrinogen level in type 2 diabetics and to correlate it with the duration, type of treatment, HbA1c, smoking, lipid profile, diabetic retinopathy, hypertension and ischemic heart disease in comparison to control.
Methods: A case control single center study included 50 patients with type 2 DM between the ages of 35–85 y who were randomly selected from the medical units of Baghdad Teaching Hospital compared to 30 non-diabetics as a control. After taking verbal consents; plasma fibrinogen levels were estimated and correlated with aimed variables. Odds ratios with 95% CI were calculated and regression analysis was performed for correlations. $P \leq 0.05$ was considered statistically significant.
Results: There were statistically significant differences regarding total cholesterol, TG, and LDL between cases and control. Mean HbA1c of diabetics was $8.31 \pm 1.75\%$ ($P < 0.001$). Cases showed plasma fibrinogen of (4.01 ± 1.89 g/dL) compared to (2.79 ± 0.55 g/dL) of control ($P < 0.001$). ROC curve revealed that the AUC was (0.679 ± 0.06, 95%CI = 0.561–0.797, $P < 0.008$). The sensitivity and specificity of the test at cut off value of 3.05 g/dL were 0.62 and 0.567 respectively. There was a significant correlation between fibrinogen level and each of HbA1c ($r = 0.497$, $P < 0.001$) and TG ($r = 0.359$, $P = 0.01$).
Conclusions: HbA1c has a significant positive effect on plasma fibrinogen and it is important to measure plasma fibrinogen level in patients with type 2 DM.

1. Introduction

1.1. Diabetes mellitus

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of DM are caused by a complex interaction of genetics and environmental factors [1]. Although the prevalence of both type 1 and type 2 DM is increasing worldwide, the prevalence of type 2 DM is rising much more rapidly, presumably because of increasing obesity, reduced activity levels as countries become more industrialized, and the aging of the population [2]. Chronic hyperglycemia contributes for initiation and progression of micro and macrovascular complication in diabetics [3].

DM is associated with elevated fibrinogen, increased thromboxane A2, reduced platelet nitric oxide synthesis, as well as increased plasminogen activator inhibitor-1 (PAI-1) release from platelets leading to inhibition of thrombolysis [4].

1.2. Fibrinogen

It is synthesized in the liver and following activation of the coagulation pathway is converted to a fibrin monomer (by thrombin) which subsequently attaches to neighboring molecules through lateral aggregation, forming the backbone of the blood clot [5]. The normal range of fibrinogen in the blood is 200–400 mg/dl. Fibrinogen, itself is determined by several modifiable and non-modifiable determinants like age, sex, smoking, body mass index (BMI), hypertension, alcoholism, glycemic control, lipid profile and urine albumin excretion rate [6].

* Corresponding author. Baghdad College of Medicine, University of Baghdad, Bab al- Muadham Campus, Baghdad, Iraq.
E-mail address: manal.aladhadh@meciq.edu.iq (M.K. Abdul Razak).

https://doi.org/10.1016/j.dsx.2019.01.049
1871-4021/

1.3. Fibrinogen and DM

Elevated levels of fibrinogen are observed in diabetes and likely reflects increased hepatic production through the actions of inflammatory cytokines and insulin. In vivo hyperglycemia in poorly controlled diabetes patients is known to cause glycation of fibrinogen which causes an alteration in the structure and function of the molecule and contributes to the ex-vivo formation of a rigid and dense clot with thinner fibrin fibers and fewer pores. These clots are increasingly resistant to fibrinolysis compared to non-diabetes clots and are associated with increased cardiovascular risk [7]. High levels of fibrinogen in the blood, which are associated with advancing age, obesity, physical inactivity, diabetes, and smoking, appear to raise the risk of cardiovascular disease [8].

Scientists aren't certain whether hyperfibrinogenemia is a cause or simply a marker of cardiovascular disease. It's possible that hyperfibrinogenemia is simply a result of the chronic inflammation that characterizes atherosclerosis, or the buildup of fatty plaques on blood vessel walls that leads to cardiovascular disease. On the other hand, hyperfibrinogenemia may actively increase blood thickness, affect interactions between blood platelets, or trigger other mechanisms that directly promote the formation of atherosclerotic plaques on blood vessel walls [6].

2. Aim of study

The aim of the study was to measure plasma fibrinogen level in patients with type 2 DM and to correlate it with the duration of DN, type of treatment, HbA1c, smoking, lipid profile, diabetic retinopathy, hypertension and ischemic heart disease in comparison to non-diabetic control group.

3. Patients and methods

3.1. Study design

This was a case control single center study, conducted in Baghdad Teaching Hospital/Medical City Complex from Feb 2018 to July 2018.

3.2. Study protocol

This study included 2 groups; a group of 50 patients with type 2 DM as cases between the ages of 30–85 years of either gender who were selected randomly from the outpatient's clinic and medical units of Baghdad Teaching Hospital and a group of 30 non-diabetic participants as control. The study protocol was approved by the ethical committee of the Iraqi Council of Medical specialization.

3.3. Exclusion criteria were

1. Acute severe infectious or inflammatory disease.
2. Acute coronary syndrome.
3. Chronic liver dysfunction.
4. Severe renal insufficiency.
5. Pregnancy.
6. Various cancers.

3.4. Definitions

Hypertension is considered if the recorded systolic blood pressure $\geq$140 mmHg and or diastolic blood pressure $\geq$90 mmHg, or if the patient was on current antihypertensive therapy [25].

Diabetes Mellitus is defined as the use of insulin or glucose-lowering medication on admission, or a diet for diabetes documented in medical history. The diagnosis of "undiagnosed diabetes mellitus" was made if patients with fasting glucose >7.0 mmol/L or random glucose >11.1 mmol/L together with an admission HbA1c >6.5% according to the latest American Diabetes Association (ADA) recommendations [26].

3.5. Procedure

Venous blood samples, 1.8 ml were collected in a vacutainer tubes containing 0.105 mol/L buffered sodium citrate. Citrated blood samples were centrifuged for 10 min. The fibrinogen level was measured in the fibrinogen program on the automated instrument-coagulometer (CA-50-Sysmex). The automated device will automatically quantify the plasma fibrinogen level with limit of error of 3.2%. The reference value of serum fibrinogen that was used by our lab was 1.8–3.5 g/L.

3.6. Measurments

All participants (patients and control subjects) were tested by drawing a blood sample for the following:

- Glycosylated hemoglobin (HbA1c) level was measured regardless of whether they had been fasting, by a spectrophotometer.
- Fasting lipid profile included total cholesterol (TC), low density lipoprotein cholesterol (LDL- C), high density lipoprotein cholesterol (HDL- C) and triglycerides (TG).
- Plasma fibrinogen level.

Patients with (HbA1C) $\leq$ 7% were considered as having adequate glycemic control while those with (HbA1C) > 7% were considered as having poor glycemic control according to the latest ADA guidelines [27].

3.7. Statistical analysis

Statistical package for Social Sciences (SPSS version 20) was used for data analysis, and Microsoft Excel to generate graphs. Continuous variables were expressed as a mean $\pm$ standard deviation (SD), while categorical variables were expressed as frequency and percentages. For bivariate analysis, the student's test (*t*-test) was used to compare means of continuous variables, and Pearson's Chi square to compare the categorical variables. Bivariate logistic regression test was used to evaluate the significant association between fibrinogen levels and covariates. Odds ratios (OR) with 95% confidence interval (CI) were calculated from this test. Regression analysis was performed using plasma fibrinogen as dependent variable and HbA1c as independent variable. The statistical tests were two-sided, and a $P \leq 0.05$ was considered statistically significant.

4. Results

In the present study; plasma fibrinogen levels were estimated in 50 patients with type 2 DM and 30 control. Fibrinogen levels were correlated with age, gender, smoking, duration of DM, HTN, IHD, and (HbA1c).

4.1. Demographic and clinical characteristics of patients (50) and control (30)

The mean age of diabetic patients was 59.04 $\pm$ 12.2 years with age range of 38–86 years which was higher than that of control group (mean age was 53.67 $\pm$ 8.9 years with age range of 40–73

years) with a statistically significant difference ($P = 0.039$). Gender and smoking habit did not differ significantly between the two groups ($P = 0.729$ and $P = 0.226$ respectively). Although both hypertension and smoking were more frequent among diabetic patients [28 (56%) and 20 (40%) respectively] than controls [14 (46.67%) and 8 (26.67%) respectively], the difference did not reach a statistically significant level ($P = 0.418$, $P = 0.19$ respectively). More than one quarter of diabetic patients 14 (28%) had retinopathy, and the majority of them 39 (78%) are taking oral hypoglycemic agents as a treatment for diabetes. Mean duration of DM was 15.42 ± 7.61 years with range of 3–33 years as illustrated in Table 1.

4.2. Laboratory characteristics of patients and control

The laboratory characteristics of the study sample showed that the mean values of HbA1c% in patients and controls were 8.31 ± 1.75% and 5.82 ± 0.51% respectively with a statistically highly significant difference ($P < 0.001$). Likewise, the majority of lipid profile items were higher in patients than controls with highly significant differences ($P < 0.001$). The only exception was HDL-C which was very similar in patients and controls ($P = 0.706$) as illustrated in Table 2.

4.3. Plasma levels of fibrinogen

Patients with T2DM showed higher plasma level of fibrinogen (4.01 ± 1.89 g/dL) than controls (2.79 ± 0.55 g/dL) with a statistically highly significant difference ($P < 0.001$) as illustrated in Fig. 1.

4.3.1. Diagnostic value of fibrinogen

As there was a highly significant difference in plasma level of fibrinogen between cases and controls; it is reasonable to evaluate the diagnostic value of fibrinogen for differentiation between diabetic and healthy individuals. Fig. 2 shows ROC curve between patients and controls. The test revealed that the area under the curve (AUC) was [0.679 ± 0.06 (standard error), 95% CI = 0.561–0.797, $P < 0.008$]. The sensitivity and specificity of the test at cut off value of 3.05 g/dL were 0.62 and 0.567 respectively, indicating a moderate discrimination value.

4.4. Association of fibrinogen with different factors in diabetic patients

4.4.1. Gender

Although, female patients showed higher plasma level of fibrinogen (4.19 ± 2.3 mg/dL) than male patients (3.82 ± 1.29 mg/dL), the difference was not statistically significant ($P = 0.496$) as shown in Fig. 3.

4.4.2. Smoking

Interestingly, non-smokers showed higher plasma levels of fibrinogen than smokers (4.46 ± 1.88 mg/dL vs. 3.35 ± 1.75 mg/dL) with a statistically significant difference ($P = 0.043$) as illustrated in Fig. 4.

4.4.3. Retinopathy

Diabetic patients who developed retinopathy had slightly higher plasma level of fibrinogen than those with no such complication (4.68 ± 1.94 mg/dL vs. 3.76 ± 1.83 mg/dL); however, the difference was not statistically significant ($P = 0.123$) as illustrated in Fig. 5.

4.4.4. Mode of treatment of DM

As illustrated in Fig. 6; patients using oral hypoglycemic medication had higher level of plasma fibrinogen (4.28 ± 1.81 mg/dL) than those using insulin (3.09 ± 1.99 mg/dL). The statistical analysis revealed a marginal significant difference between the two groups ($P = 0.066$).

4.4.5. Ischemic heart disease

As illustrated in Fig. 7; plasma levels of fibrinogen in diabetic patients with and without IHD were 4.33 ± 11.95 mg/dL and 3.76 ± 1.83 mg/dL respectively. Student t-test revealed no statistically significant difference between the two groups ($P = 0.275$).

4.4.6. Hypertension

Almost diabetic patients with and without hypertension had similar level of plasma fibrinogen (about 4 mg/dl) with no statistically significant difference ($P = 0.985$) as shown in Fig. 8.

Table 1
Demographic and clinical data of diabetic patients and control.

Characteristic	Diabetic patients (50)	Control (30)	P-value
Age, years (mean ± SD*)	59.04 ± 12.2	53.67 ± 8.9	0.039
Gender, No. (%)			
Male	23 (46%)	15 (50%)	0.729
Female	27 (54%)	15 (50%)	
Hypertension, No. (%)			
Hypertensive	28 (56%)	14 (46.67%)	0.418
Normotensive	22 (44%)	16 (53.33%)	
Current Smoking, No. (%)			
Yes	20 (40%)	8 (26.67%)	0.226
No	30 (60%)	22 (73.33%)	
Ischemic heart diseases, No. (%)			
Present	23 (46%)	6 (20%)	0.19
Absent	27 (54%)	24 (80%)	
Retinopathy, No. (%)			
Present	14 (28%)	……..	……
Absent	36 (72%)		
Medication, No. (%)			
Oral hypoglycemic agents	39 (78%)	……	…….
Insulin	11 (22%)		
Duration of diabetes, years (mean ± SD)	15.42 ± 7.61	……	……

*: Standard deviation.

Table 2
Laboratory data of diabetic patients and control.

Characteristic	Diabetic patients (50)	Healthy control (30)	P-value
HbA1c% (mean ± SD*)	8.31 ± 1.75	5.82 ± 0.51	<0.001**
TG§, mg/dL (mean ± SD)	188.72 ± 49.27	150.53 ± 24.82	<0.001
TC∞, mg/dL (mean ± SD)	266.34 ± 60.1	194.47 ± 36.76	<0.001
LDL- C■, mg/dL (mean ± SD)	170.78 ± 52.47	116.7 ± 25.62	<0.001
HDL- C●, mg/dL (mean ± SD)	69.54 ± 14.69	68.4 ± 9.56	0.706

*: Standard deviation, **: Highly significant, §: Triglyceride, ∞: Total cholesterol, ■: Low density lipoprotein, ●: High density lipoprotein.

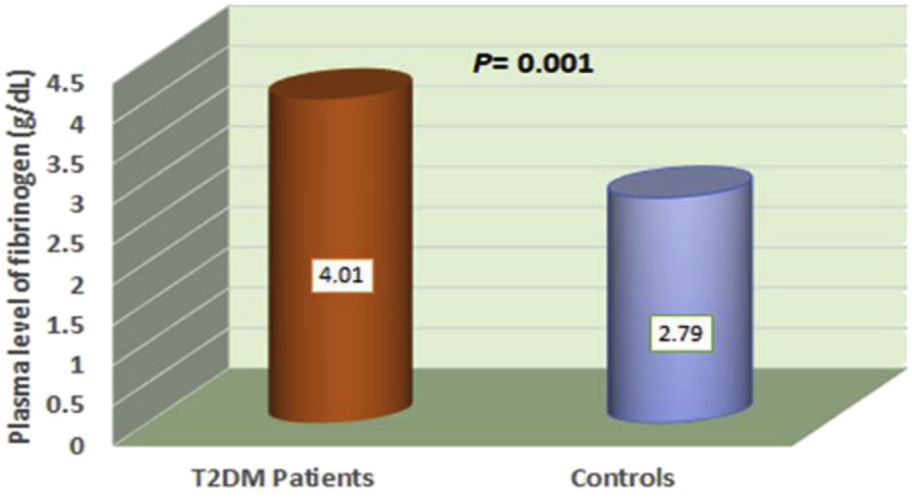

Fig. 1. Mean plasma fibrinogen concentration in diabetic patients and controls.

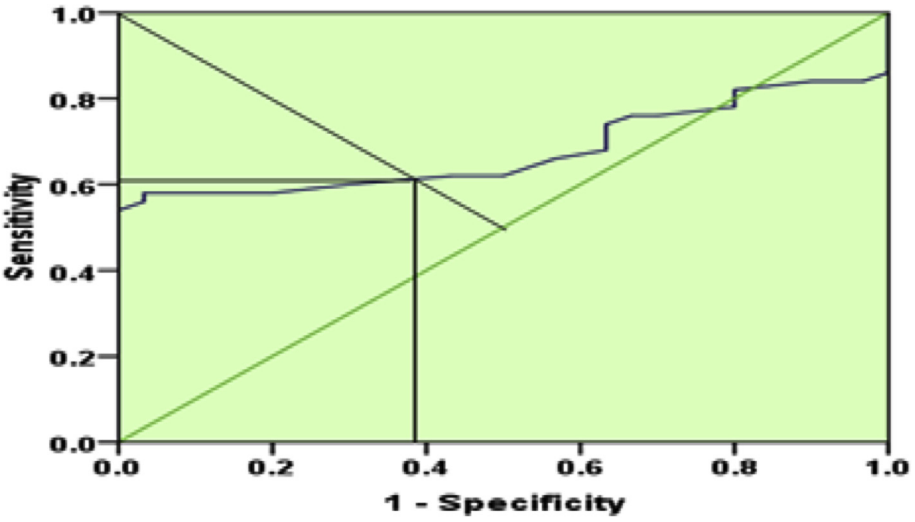

Fig. 2. Receiver-operating characteristic (ROC) curve for fibrinogen in the context of discrimination of diabetic patients from healthy control.

4.5. Correlation between plasma fibrinogen and different continuous variables

Table 3 shows the results of Pearson's correlation between fibrinogen and the other continuous variables. There was a moderate positive significant correlation between fibrinogen and each of HbA1c ($r = 0.497$, $P < 0.0001$) and TG ($r = 0.359$, $P = 0.01$).

4.6. Predictors of hyperfibrinogenemia

According to the results of the previous analysis, HbA1c%, no smoking and TG were significantly correlated with plasma levels of fibrinogen. Accordingly, these variables were incorporated in logistic regression model as independent variables, while plasma fibrinogen as dependent variable to find out the quantitative impact of these variable on plasma levels of fibrinogen. For this analysis, ≤3.5 g/dl was considered as a normal level of fibrinogen, and <7% was considered as normal level for HbA1c, while <150 mg/dl was considered as a normal level of TG. The result of this model is illustrated in Table 4. HbA1c% was significantly associated with fibrinogen level (OR = 10.13, 95%CI = 1.89–54.12, $P = 0.007$). In contrast TG was not significantly associated with fibrinogen level ($P = 0.924$), while, smoking was inversely associated with fibrinogen level (OR = 0.29, 95%C = 0.09–0.94, $P = 0.039$).

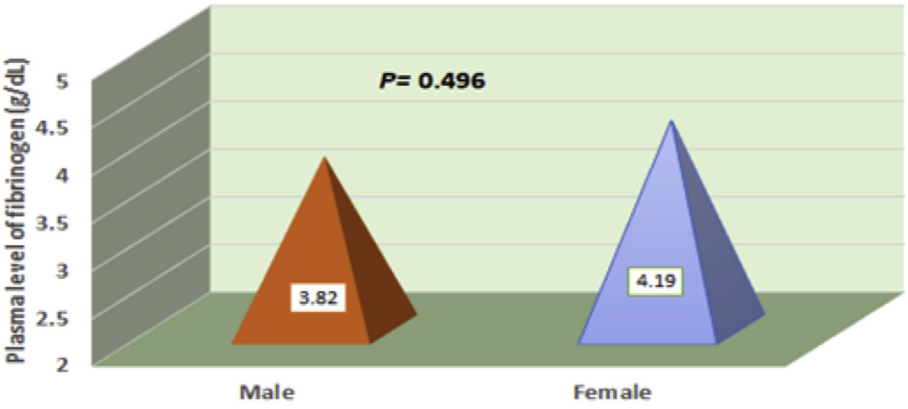

Fig. 3. Mean plasma fibrinogen level in male and female patients.

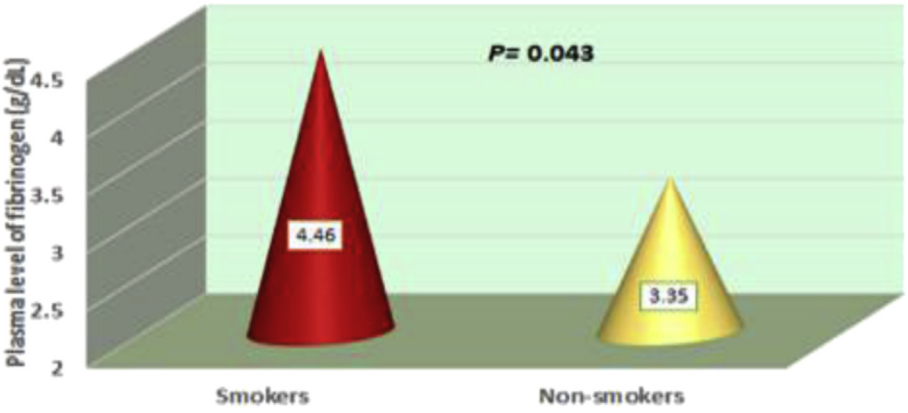

Fig. 4. Mean plasma fibrinogen level in smoker and non-smoker patients.

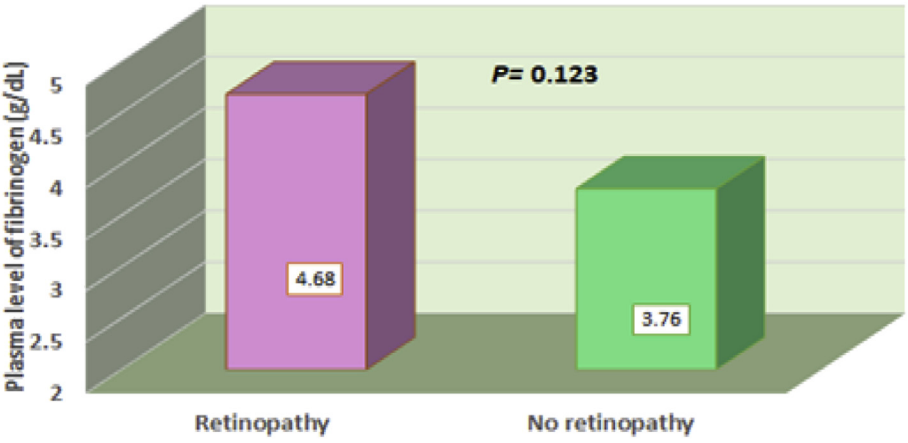

Fig. 5. Mean plasma fibrinogen level in diabetic patients with and without retinopathy.

4.7. Linear regression analysis

For further illustration of the association between plasma level of fibrinogen and HbA1c, linear regression analysis was performed, in which plasma fibrinogen was the dependent variable and HbA1c was the independent variable. Fig. 9 shows the results of this analysis. HbA1c% has a significant positive effect on plasma fibrinogen ($R^2 = 0.21$) which implies that 21% of change in plasma fibrinogen is attributed to the change in HbA1c%.

5. Discussion

The present study was conducted to evaluate the importance of measuring plasma fibrinogen in patients with type 2 DM, and to study its correlation with parameters like age, gender, current smoking, duration of diabetes, type of treatment, lipid profile, glycosylated hemoglobin, hypertension and ischemic heart disease. In our study, 50 patients with type 2 DM were studied compared to 30 non-diabetic participants as a control.

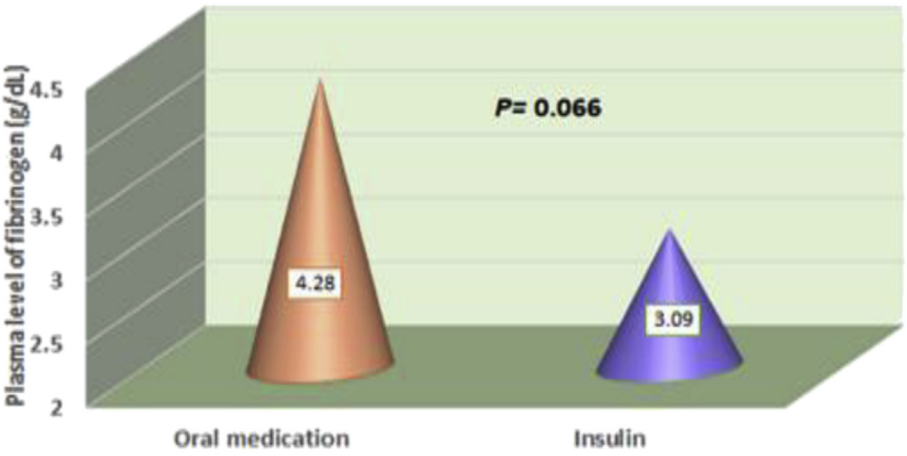

Fig. 6. Mean plasma fibrinogen level in diabetic patients using oral hypoglycemic medications and insulin.

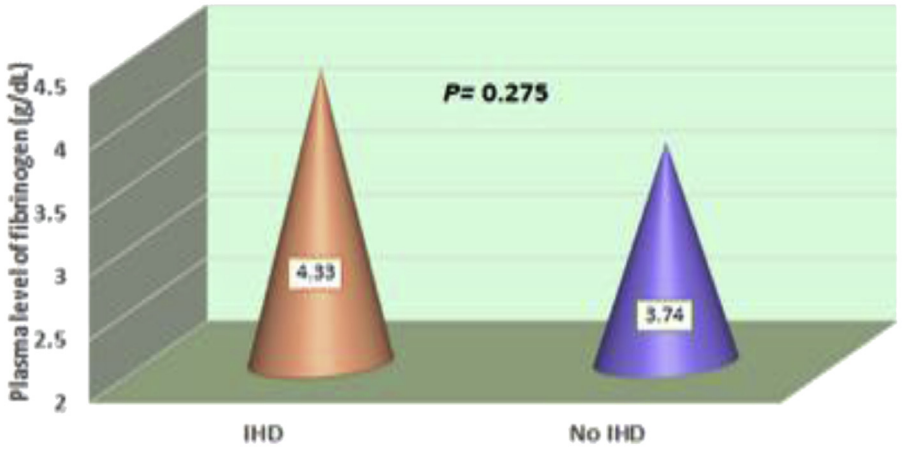

Fig. 7. Mean plasma fibrinogen level in diabetic patients with and without ischemic heart disease.

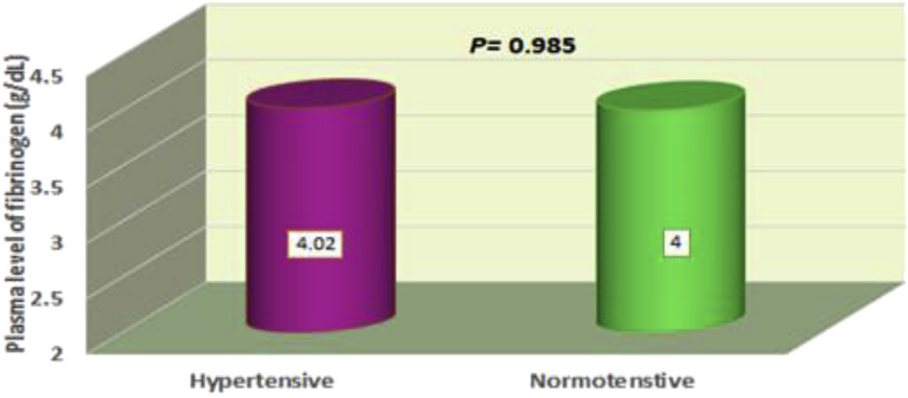

Fig. 8. Mean plasma fibrinogen level in diabetics with and without hypertension.

Table 3
Pearson's correlation between fibrinogen and different variables in diabetic patients.

Fibrinogen	HbA1c	TC ∞	TG§	LDL■	HDL●	Age	Duration
Correlation	0.497	0.269	0.359	0.16	0.007	0.133	−0.071
P-value	0.0001	0.059	0.01	0.267	0.267	0.358	0.622

§: Triglyceride, ∞: Total cholesterol, ■: Low density lipoprotein, ●: High density lipoprotein.

In present study, plasma fibrinogen level was significantly higher in all diabetic patients compared to non-diabetic control with statistically highly significant difference ($P < 0.001$). Similar result was found in a study by (Kalfe D. R.& Shrestha P., 2010) [9] in which they reported a high mean fibrinogen level (341 ± 70) in diabetic patients compared to non-diabetic control (216 ± 43).

Diabetes is associated with low grade inflammation and as a

Table 4
Predictors for hyperfibrinogenemia.

Variables	Normal plasma fibrinogen (21)	Hyper-fibrinogenemia (29)	*P*-value	OR* (95% CI)
HBA1c%				
<7	9 (42.86%)	2 (6.9%)		1.0 (Reference)
≥7	12 (57.71%)	27 (93.1%)	0.007	10.13 (1.89–54.12)
TG (mg/dL)				
<150	2 (9.52%)	3(10.34%)		1.0 (Reference)
≥150	19 (90.48%)	26 (89.66%)	0.924	1.09 (0.17–0.22)
Smoking				
Smokers	12 (57.14%)	8 (27.59%)		1.0 (Reference)
Non-smokers	9 (42.86%)	21(72.41%)	0.039	0.29 (0.09–0.94)

*: Odds ratio.

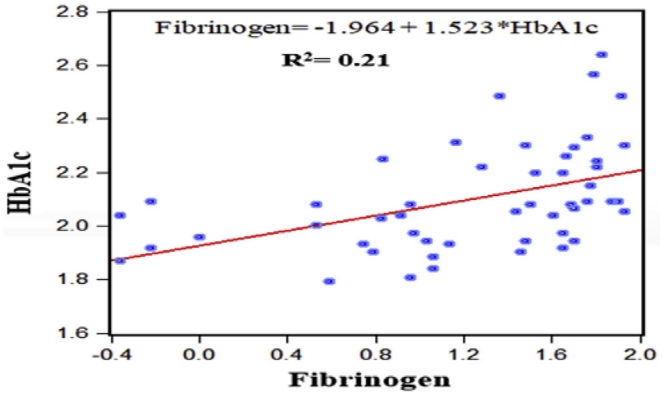

Fig. 9. Scatter diagram for linear regression analysis of plasma fibrinogen and HbA1c.

result Interleukin 6 is elevated in these patients. This cytokine stimulates hepatocytes to produce fibrinogen representing an important link between inflammation and hypercoagulation. Also, Insulin resistance in type 2 DM is associated with increased hepatic fibrinogen production in response to insulin (Ajjan R.& Grant P.J., 2006) [10].

In diabetic patients there is increased rate of fibrinogen clearance with shorter fibrinogen circulating half-life. This means that the rate of synthesis is even more than that indicated by plasma level. In addition, an association between oxidative stress and plasma fibrinogen has been observed in type 2 diabetics (Farah R., 2008) [11]. In diabetics; thrombin formation is induced by free radicals. Hyperglycemia and insulin resistance and the consequent oxidative stress may give rise to increased thrombin formation [12].

In present study; although, female patients showed higher plasma level of fibrinogen than male patients, the difference was not statistically significant ($P = 0.496$). Similar result was found in (Jain A. et al., 2001) study [13].

In present study; HbA1c was significantly associated with fibrinogen level in diabetic patients. Similar results were found in other studies like (Bembde A. S, 2012) study [14] and (Hong L.F. et al., 2014) study [15], where there was a significant correlation between plasma fibrinogen and HbA1c ($r = 0.167$, $p < 0.001$).

The correlation between glycemic control and fibrinogen levels could be due to the facts that glycosylate hemoglobin is less susceptible to plasmin degradation and relative insulin deficiency in diabetic patients results in differential protein synthesis i.e., 29% decrease in albumin synthesis and 50% increase in fibrinogen synthesis (Pierpaola D. F., 1991) [16].

The present study revealed no statistically significant difference between plasma levels of fibrinogen in diabetic patients and IHD ($P = 0.275$).

Lowe G., 2014; studied the association of fibrinogen with the risk of major macrovascular events, microvascular complications, and mortality in patients with type 2 diabetes who participated in the Action in Diabetes and Vascular Disease: Preterax and Diamicron Modified Release Controlled Evaluation (ADVANCE) Study. Plasma CRP, fibrinogen and IL-6 levels were determined in a case-cohort study (n = 3865) with type 2 diabetes and baseline CVD or risk factors in the ADVANCE Study. All 3 were associated with an increased risk of macrovascular events and death in analyses adjusted for age, sex, and treatment groups. After further adjustment, only IL-6 was an independent predictor of macrovascular events (hazard ratio per SD increase 1.37 [95% CI 1.24–1.51]) and death (1.35 [1.23–1.49]). After adjustment, none of the markers predicted microvascular complications. They conclude that CRP or fibrinogen levels, did not add significantly to the prediction of macrovascular events and mortality in individuals with type 2 diabetes who have baseline CVD or risk factors [17].

On the contrary, Gargano Heart Study showed that fibrinogen was a predictor of incident major cardiovascular events after adjusting for sex, age, smoking habit and BMI status in patients with diabetes [18].

Lawlor, 2005; found that fibrinogen predict CHD but may not be causally related to it [19].

Part of explanation of such different association between fibrinogen level and IHD is related to selection criteria of diabetics with CVE regarding stability and ethnicity (Albert M. A., 2007) [20].

Papageorgiou, 2010, identified that the plasma fibrinogen was a strong predictor of silent myocardial ischemia in diabetic patients, which makes it possible to identify the individuals with high cardiovascular risk [21].

The correlation between smoking and plasma fibrinogen level is a matter of debate. Interestingly in present study; we found that the plasma fibrinogen level in smoker diabetics is lower than non-smokers; this is in agreement to a study done by (Jain A. et al., 2001) [13] in which no correlation was found between fibrinogen levels and smoking. But few studies have found significant correlation of rising fibrinogen levels with smoking among cases and controls like (Bembde A. S., 2012) [14] and Wilhelmsen L., 2017) [22].

Multiple risk factors that affect the fibrinogen level and which patient has more than the others of these may play the role in this discrepancy in this result.

In present study; diabetic patients who developed retinopathy had slightly higher plasma level of fibrinogen than those with no such a complication (4.68 ± 1.94 mg/dL Vs. 3.76 ± 1.83 mg/dL). This is similar to the study done by (Neetha & Vijaya, 2010) [23]. Their study demonstrates that plasma fibrinogen levels are significantly elevated in patients with diabetic retinopathy. This finding is in agreement with the report of (Asakawa H., 2000) [24] who found that plasma fibrinogen is independently associated with existence of diabetic retinopathy, but not significantly different when comparing different grades of retinopathy.

In present study; the patients on insulin therapy had lower

serum fibrinogen levels as compared to those on oral hypoglycemic agents and the statistical analysis revealed a marginal significant difference between the two groups ($P = 0.066$). As we know insulin causes intensive glycemic control leading to potential beneficial effects but a possible adverse effect in increasing fibrinogen level. Similar study was done by (Emanuele et al., 1998) [25] in which they found that intensive insulin therapy beneficially reduced serum TG, TC and HDL- C but it causes transient elevation in plasma fibrinogen level, a possible thrombogenic effect.

A study by (Tessari P. et al., 2006) [26] concluded the insulin effect to increase fibrinogen synthesis in type 2 diabetic patients (by 50%) but not in nondiabetic.

We thought that our small sample size is the cause behind this different result noticing that in our study there was only 11 (22%) patient from the total number of 50 diabetics were taking insulin.

In present study; there was no significant difference in fibrinogen levels between hypertensives and normotensives in both cases and control group ($P = 0.985$). Many authors have found association between hypertension and fibrinogen levels among diabetics like (Harsoor, S., & Kinagi, A., 2014) [26], and (Bembde A. S., 2012) [14].

6. Conclusions

This study showed a positive moderate significant correlation between fibrinogen and HbA1c and linear regression analysis showed that HbA1c has a significant positive effect on plasma fibrinogen. This study concluded that it is important to measure plasma fibrinogen level in patients with type 2 DM as part of management plan.

Acknowledgement

We acknowledge the work of the paramedical staff in the medical units and clinical laboratory of Baghdad Teaching Hospital for their technical help. Also we acknowledge the effort of Dr. Qasem in preparing the statistical analysis.

References

[1] Alvin CP. Diabetes mellites: diagnosis, classification, and pathophysiology. In: Braunwald E, Faucei AS, Kasper DL, Hauser SL, Longo DL, Larry JJ, editors. Harrison's principles of internal medicine. nineteenth ed. New York: McGraw Hill Medical Publishing division; 2016. p. 2399.
[2] Alvin CP. Diabetes mellitus. In: Braunwald E, Faucei AS, Kasper DL, Hauser SL, Longo DL, Larry JJ, editors. Harrison's principles of internal medicine. fifteenth ed. New York: McGraw Hill Medical Publishing division; 2001. p. 2109–37.
[3] Maritime A, Sanders R, Watkins J. Diabetes, oxidative stress, and antioxidants A review. J Biochem Mol Toxicol 2003;17:24–38.
[4] Kreutz RP, Nystrom P, Kreutz Y. Inhibition of platelet aggregation by prostaglandin E1 (PGE1) in diabetic patients during therapy with clopidogrel and aspirin. Platelets 2013;24(2):145–50.
[5] Ajjan R, Grant PJ. Coagulation and atherothrombotic disease. Atherosclerosis 2006;186:240–59.
[6] Anjula J, Gupta HL, Narayan S. Hyperfibrinogenemia in patients of diabetes mellitus in relation to glycemic control and urinary albumin excretion rate. JAPI 2001;49:227–30.
[7] Pieters M, Van Zyl DG, Rheeder P, Jerling JC, Loots du T, van der Westhuizen FH, et al. Glycation of fibrinogen in uncontrolled diabetic patients and the effects of glycaemic control on fibrinogen glycation. Thromb Res 2007;120:439–46.
[8] 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. J Cin Diagn Res 2015;9(1):BC18–21.
[9] Kafle DR, Shrestha P. Study of fibrinogen in patient with diabetes mellitus. NMCJ 2010;12(1):34–7.
[10] Ajjan R, Grant PJ. Coagulation and atherothrombotic disease. Atherosclerosis 2006;186:240–59.
[11] Farah R, Shurtz-Swirski R, Lapin O. Intensification of oxidative stress and inflammation in type 2 diabetes despite antihyperglycemic treatment. Cardiovasc Diabetol 2008;7:20.
[12] Ceriello A, Giacomello R, Stel G, Motz E, Taboga C, Tonutti L, et al. Hyperglycemia- induced thrombin formation in diabetes: a possible role of oxidative stress. Diabetes 1995;44(8):924–8.
[13] Jain A, Gupta H, Narayan S. Hyperfibrinogenemia in patients of diabetes mellitus in relation to glycemic control and urinary albumin excretion rate. J Assoc Phys India 2001;49:227–30.
[14] 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):105–8.
[15] Hong LF, Li XL, Luo SH, Guo YL, Zhu CG, Qing P, et al. Association of Fibrinogen with Severity of Stable Coronary Artery Disease in Patients with Type 2 Diabetic Mellitus. Dis Markers. Volume 2014, Article ID 485687. https://www.hindawi.com/journals/dm/2014/485687.
[16] Pierpaola DF, Margaret GG, Haymond MW. Differential effects of insulin deficiency on albumin and fibrinogen synthesis in humans. J Clin Invest 1991;88:833–40.
[17] Lowe G, Woodward M, Hillis G, Rumley A, Li Q. Circulating inflammatory markers and the risk of vascular complications and mortality in people with type 2 diabetes and cardiovascular disease or risk factors: the ADVANCE study. Diabetes 2014;63(3):1115–23.
[18] Pacilli A, De Cosmo S, Trischitta V, Bacci S. Role of relationship between HbA1c, brinogen and HDL-cholesterol on cardiovascular disease in patients with type 2 diabetes mellitus. Atherosclerosis 2013;228:247–8.
[19] Lawlor DA, Smith GD, Rumley A, Lowe GDO, Ebrahim S. Association of fibrinogen and C-reactive protein with prevalent and incident coronary heart disease are attenuated by adjustment for confounding factors. British Women's Heart and Health study. Thromb Haemostasis 2005;93:955–63.
[20] Albert MA. Inflammatory biomarkers, race/ethnicity and cardiovascular disease. Nutr Rev 2007;65:234–8.
[21] Papageorgiou N, Tousoulis D, Siasos G, Stefanadis C. Is fibrinogen a marker of inflammation in coronary artery disease? Hellenic J Cardiol 2010;51(1):1–9.
[22] Wilhelmsen L, Svärdsudd K, Korsan-Bengtsen K, Larsson B, Welin L, Tibblin G. Fibrinogen as a risk factor for stroke and myocardial infarction. N Engl J Med 2017;311(8):501–5.
[23] Neetha Kuzhuppilly IR, Vijaya Pai H. Plasma fibrinogen levels and its relation to diabetic retinopathy. Kerala J. Ophthalmol 2010;22(4).
[24] Asakawa H, Tokunaga K, Kawakami F. Elevation of fibrinogen and thrombin-antithrombin III complex levels of type 2 diabetes mellitus patients with retinopathy and nephropathy. J Diabet Complicat 2000;14:121–6.
[25] Emanuele N, Azad N, Abraira C, Henderson W, Colwell J, Levin S, et al. Effect of intensive glycemic control on fibrinogen, lipids and lipoprotein. Arch Intern Med 1998;158:2485–90.
[26] Tessari P, Kiwanuka E, Millioni R, Vettore M, Puricelli L, Zanetti M, et al. Albumin and fibrinogen synthesis and insulin effect in type 2 diabetic patients with normoalbuminuria. Diabetes Care 2006;29:323–8.
[27] Harsoor S, Kinagi A. Correlation of Plasma Fibrinogen with Blood Pressure, BMI, Lipid Pro le and Glycemic Status in Type II D M". J Evol Med Dent Sci 2014;3(68):14615–27.