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Plasma Fibrinogen Levels and Peripheral Neuropathy in Type 2 Diabetes Mellitus: A Correlative Study

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ABSTRACT

Background: Peripheral neuropathy (PN) is a prominent complication in persons with type 2 diabetes mellitus (T2DM) and has a major influence on morbidity. Emerging evidence suggests that elevated plasma fibrinogen (FIB) levels, which are indicative of inflammation and coagulation, may be linked to various diabetic complications. Nevertheless, there hasn't been much research done on the connection between PN and plasma fibrinogen levels in T2DM.

Objective: This study aimed to investigate the correlation between plasma fibrinogen levels and the presence of PN in patients with T2DM.

Patients and methods: A cross-sectional study that included 120 patients diagnosed with T2DM. They were divided into 2 equal groups: Group I contained 60 patients with diabetic peripheral neuropathy (DPN) and group II that involved 60 patients without DPN.

Results: The study revealed a significant increase in serum fibrinogen levels in patients with diabetic neuropathy. Those with diabetic neuropathy had a mean fibrinogen level of 11.585 ± 4.256, compared to 1.798 ± 0.566 in patients without neuropathy (p-value < 0.001). Furthermore, the study indicated that plasma fibrinogen levels were significantly higher in patients with severe diabetic neuropathy, with a mean of 14.813 ± 3.713, followed by those with moderate neuropathy (mean 10.315 ± 2.562), and the lowest levels were observed in patients with mild neuropathy (mean 8.331 ± 3.558), with a p-value of 0.001.

Conclusion: Increased plasma fibrinogen levels are substantially related with DPN in patients with T2DM. These results indicate that plasma fibrinogen could potentially act as a biomarker for identifying T2DM patients who are at increased risk of developing PN.

Keywords: Plasma fibrinogen, DPN, T2DM.

INTRODUCTION

DPN is one of the most significant and prevalent complications of T2DM. It notably affects both morbidity and mortality, severely diminishing patients' quality of life and creating substantial challenges in long-term diabetes management. DPN impacts sensory, motor, and autonomic nerves and affects over 60% of T2DM patients [(1, 2)].

Those with insulin resistance and T2DM often show increased levels of plasminogen activator inhibitors, especially PAI-1 alongside fibrinogen. These factors contribute to enhanced blood clotting and reduced fibrinolysis, which can lead to arterial thrombosis [(3)]. Elevated plasma levels of CRP and fibrinogen are markers of higher risks for vascular complications and cardiovascular death in diabetic individuals [(4)].

Fibrinogen is a glycoprotein generated by the liver that plays an important function in blood coagulation. It is necessary for maintaining healthy blood flow by regulating coagulation, platelet aggregation, and endothelial activities. Elevated fibrinogen levels have been associated with nerve degeneration, though the exact mechanisms remain unclear [(5)]. High fibrinogen levels can disrupt circulation and promote clot formation, potentially causing ischemia in small blood vessels and affecting the nutrition of nerve tissues. Furthermore, hyperfibrinogenemia can impair endothelial function, increase vascular permeability, and exacerbate inflammation, all contributing to nerve damage [(6)].

Studies suggest a link between DPN and plasma fibrinogen levels, although the precise function of fibrinogen in DPN has not been extensively reported. This research investigated the relationship between fibrinogen and DPN and explored their potential as biomarkers for diagnosing DPN.

PATIENTS AND METHODS

This cross-sectional observational study was carried out at the Outpatient Clinic, Ain Shams University Hospital between March and July 2023.
We enrolled 120 patients with a confirmed diagnosis of T2DM who were divided into two cohorts:

- Group I: 60 T2DM patients with PN.
- Group II: 60 T2DM patients without PN.

Inclusion criteria: Patients aged 40 to 75 years who were diagnosed with T2DM. For group I: Patients with clinical evidence of PN confirmed using the Michigan Neuropathy Screening Instrument (MNSI). For group II: Patients without any clinical evidence of PN.

Exclusion criteria: Patients with T1DM. Patients with other causes of neuropathy (e.g., alcoholism, vitamin deficiencies & chronic renal failure). Patients with acute

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or chronic infections, inflammatory diseases, and malignancies. Patients on anticoagulant therapy.

All participants were subjected to:

- **Demographic and clinical data collection including** age, sex, duration of diabetes, BMI, and medication history (Collected through patient interviews and medical record reviews).
- **Peripheral neuropathy assessment**: PN was assessed using the Michigan neuropathy screening instrument (MNSI) [7]. It included two separate assessments: A patient-reported symptom questionnaire and a clinical examination. The clinical examination involved testing for sensation using a 10-g monofilament and vibration perception using a tuning fork.
- **The first part of** the MNSI screening tool comprises of 15 self-administered "yes" or "no" questions about foot feeling such as pain, numbness, and temperature sensitivity (figure 1). A higher score suggests more neuropathic symptoms.
- **The second part of the MNSI** is a brief physical examination involving:
- The physical examination component that involves the assessment of the feet for signs of neuropathy (figure 2). This includes:

1. Inspection:

- Checking for the presence of foot deformities, calluses, or infections.
- Scoring: Each abnormal finding (deformities, calluses, infections) typically scores 1 point, contributing to a maximum of 10 points.

2. Assessment of Ankle Reflexes:

- Evaluating the presence or absence of ankle reflexes.
- Scoring: Absent reflexes score 0 points, reduced reflexes score 0.5 points, and normal reflexes score 1 point for each ankle.

3. Vibration Perception:

- Using a 128 Hz tuning fork at the great toe and the medial malleolus to assess vibration perception.
- Scoring: The ability to sense vibration is scored as either normal or reduced/absent.

4. Monofilament Test:

- Using a 10-gram monofilament to test pressure sensation at various sites on the feet.
- Scoring: Inability to feel the monofilament at four out of ten sites is indicative of neuropathy and is scored accordingly.

- **Total Scoring**

The total MNSI score is a combination of the questionnaire and physical examination scores. Here is a typical scoring method:

- Questionnaire: Each "yes" response scores 1 point. The total possible score ranges from 0 to 15.
- Physical Examination: Each abnormal finding in the physical exam is scored, with total points varying based on the specific scoring system used.

- **Interpretation:**

- *0-2 points*: No neuropathy
- *3-5 points*: Mild neuropathy
- *6-8 points*: Moderate neuropathy
- *> 8 points*: Severe neuropathy.

Laboratory testing: Fasting blood glucose (FBS), 2 hours postprandial (2hpp), glycated hemoglobin (HbA1c %), and lipid profile. eGFR calculated using Cockcroft-Gault Equation:

$$eGFR\ (mL/min) = \frac{(140-\text{Age})\times\text{weight (kg)}\times(0.85\text{ if female})}{72\times\text{serum creatinine mg/dl}}$$

- Plasma fibrinogen levels were measured using an ELISA kit.

Appendix A: MICHIGAN NEUROPATHY SCREENING INSTRUMENT

Patient version

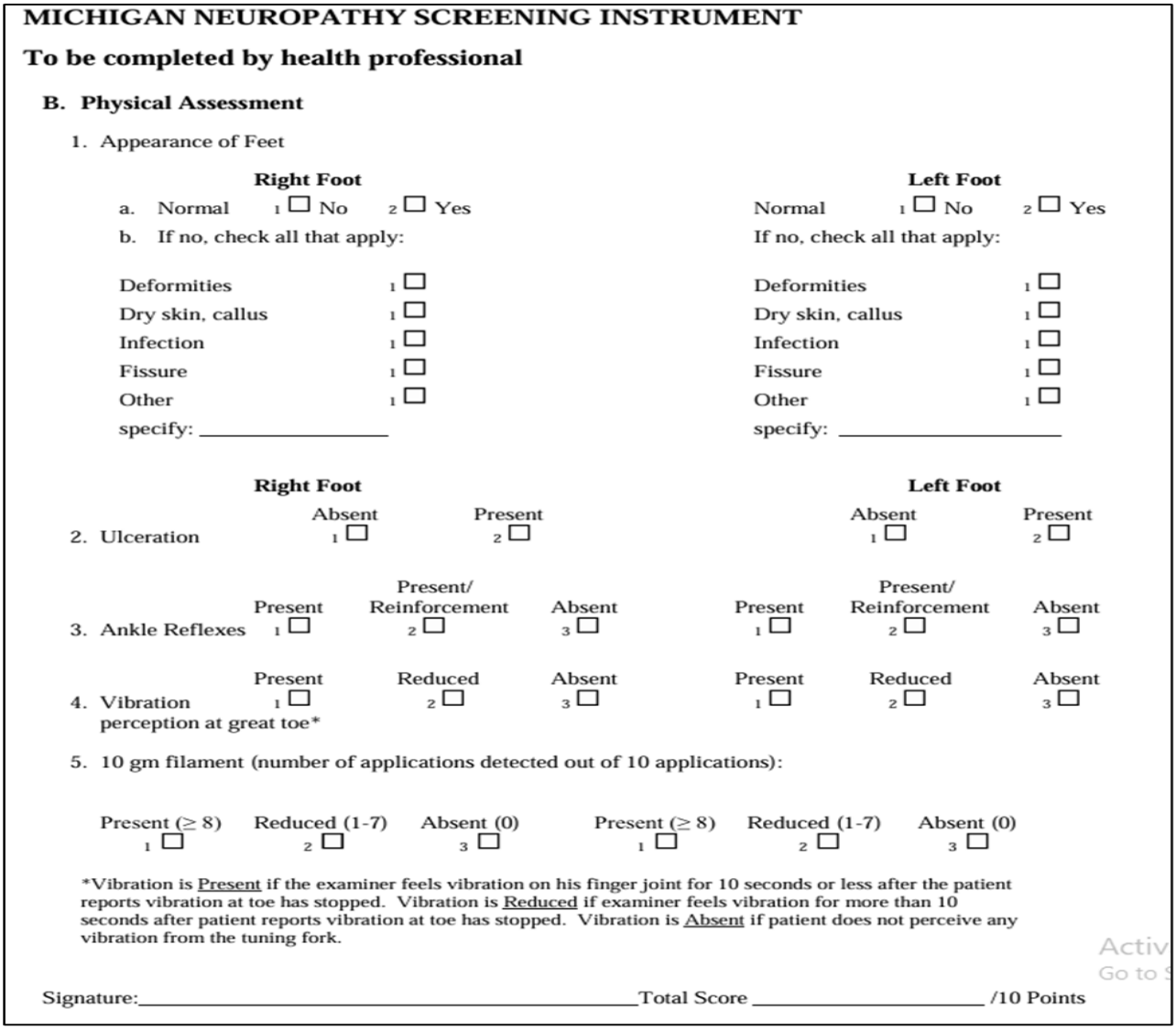
A. History (To be completed by the person with diabetes)

Please take a few minutes to answer the following questions about the feeling in your legs and feet. Check yes or no based on how you usually feel. Thank you.

1.	Are your legs and/or feet numb?	☐ No	☐ Yes
2.	Do you ever have any burning pain in your legs and/or feet?	☐ No	☐ Yes
3.	Are your feet too sensitive to touch?	☐ No	☐ Yes
4.	Do you get muscle cramps in your legs and/or feet?	☐ No	☐ Yes
5.	Do you ever have any prickling feelings in your legs or feet?	☐ No	☐ Yes
6.	Does it hurt when the bed covers touch your skin?	☐ No	☐ Yes
7.	When you get into the tub or shower, are you able to tell the hot water from the cold water?	☐ No	☐ Yes
8.	Have you ever had an open sore on your foot?	☐ No	☐ Yes
9.	Has your doctor ever told you that you have diabetic neuropathy?	☐ No	☐ Yes
10.	Do you feel weak all over most of the time?	☐ No	☐ Yes
11.	Are your symptoms worse at night?	☐ No	☐ Yes
12.	Do your legs hurt when you walk?	☐ No	☐ Yes
13.	Are you able to sense your feet when you walk?	☐ No	☐ Yes
14.	Is the skin on your feet so dry that it cracks open?	☐ No	☐ Yes
15.	Have you ever had an amputation?	☐ No	☐ Yes

Total: _____

Figure (1): MNSI (questionnaire part)



MICHIGAN NEUROPATHY SCREENING INSTRUMENT

To be completed by health professional

B. Physical Assessment

1. Appearance of Feet

	Right Foot	Left Foot
a. Normal	1 ☐ No 2 ☐ Yes	Normal 1 ☐ No 2 ☐ Yes
b. If no, check all that apply:		If no, check all that apply:
Deformities	1 ☐	Deformities 1 ☐
Dry skin, callus	1 ☐	Dry skin, callus 1 ☐
Infection	1 ☐	Infection 1 ☐
Fissure	1 ☐	Fissure 1 ☐
Other	1 ☐	Other 1 ☐
specify: _____		specify: _____

	Right Foot			Left Foot		
2. Ulceration	Absent 1 ☐	Present 2 ☐		Absent 1 ☐	Present 2 ☐	
3. Ankle Reflexes	Present 1 ☐	Present/ Reinforcement 2 ☐	Absent 3 ☐	Present 1 ☐	Present/ Reinforcement 2 ☐	Absent 3 ☐
4. Vibration perception at great toe*	Present 1 ☐	Reduced 2 ☐	Absent 3 ☐	Present 1 ☐	Reduced 2 ☐	Absent 3 ☐

5. 10 gm filament (number of applications detected out of 10 applications):

Right Foot			Left Foot		
Present (≥ 8) 1 ☐	Reduced (1-7) 2 ☐	Absent (0) 3 ☐	Present (≥ 8) 1 ☐	Reduced (1-7) 2 ☐	Absent (0) 3 ☐

*Vibration is Present if the examiner feels vibration on his finger joint for 10 seconds or less after the patient reports vibration at toe has stopped. Vibration is Reduced if examiner feels vibration for more than 10 seconds after patient reports vibration at toe has stopped. Vibration is Absent if patient does not perceive any vibration from the tuning fork.

Signature:_____Total Score _____ /10 Points

Figure (2): MNSI (physical examination part).

Ethical approval: All patients who were part of our study gave their informed consents, and we received ethical approval from The Research Ethics Committee of Faculty of Medicine, Ain Shams University. The Helsinki Declaration was adhered to at every stage of the investigation.

Statistical analysis

SPSS Version 20.0 was used to analyze the data. The clinical and demographic parameters of the study population were compiled using descriptive statistics. The frequencies and relative percentages used to depict the qualitative data. One can use the X^2-test to determine the difference between two or more qualitative variable groups. The statistical information was presented as Mean ± SD. To compare the two groups' plasma fibrinogen levels, the independent t-test or the Mann-Whitney U test were employed. The link between the levels of plasma fibrinogen and the severity of PN was evaluated using Pearson or Spearman' correlation coefficient calculation. In order to account for any confounding variables, multiple regression analysis was used. When it was equal to or less than 0.05, the p-value was deemed significant.

RESULTS

Group I included 60 type 2 diabetic patients with diabetic neuropathy (20 males, 40 females), their mean age was 51.76 ± 7.688 years. Group II included 60 type 2 diabetic patients without diabetic neuropathy (24 males, 36 females), their mean age was 55.733 ± 8.898 years (Table 1, 2). There were no significant differences in gender distribution, smoking status, or hypertension prevalence between T2DM patients with PN and those without PN (Table 1).

Table (1): Comparison between the two studied groups regarding gender, smoking, and hypertension status

		Group				T-Test	
		T2DM patients with DPN		T2DM without DPN		t	P-value
Chi-Square		N	%	N	%	X2	P-value
Gender	Male	20	33.33	24	40.00	0.287	0.592
	Female	40	66.67	36	60.00		
Smoking	No	52	86.67	56	93.33	0.741	0.389
	Yes	8	13.33	4	6.67		
Hypertension	No	32	53.33	38	63.33	0.617	0.432
	Yes	28	46.67	22	36.67		

There was no significant difference in age, BMI, and eGFR, between patients with and without PN ($p > 0.05$). Patients with PN had diabetes for a significantly longer duration (mean 7.3 years) compared to those without PN (mean 4.3 years, $p = 0.019$). The albumin to creatinine ratio (ACR) was significantly higher in patients with PN (mean 61.341 mg/g) compared to those without (mean 15.710 mg/g, $p < 0.001$) indicating a higher degree of kidney damage in patients with DPN. Serum Fibrinogen was significantly higher in patients with PN (mean 11.585 mg/dl) compared to those without (mean 1.798 mg/dl, $p < 0.001$). Patients with PN demonstrated significantly poorer lipid and glycemic control compared to those without neuropathy. This was indicated by higher total cholesterol, triglycerides, LDL-c, fasting blood sugar, 2-hour postprandial glucose, and HbA1c levels, as well as lower HDL-c levels (Table 2).

Table (2): Comparison between T2DM patients with and without peripheral neuropathy regarding clinical and biochemical variables

Variable	T2DM patients with DPN (N=60)	T2DM patients without DPN. (N=60)	t	P value
Age (year)	57.167 ± 7.688 42- 70	55.733 ± 8.898 41 – 71	0.668	0.507
Duration of DM (year)	7.3080 ±5.839 0.08-20	4.300±3.515 0.5-12	2.418	0.019*
BMI (kg/m^2)	29.870 ± 4.530 24.08 - 43.2	32.512 ± 6.367 19.9 - 52.8	-1.852	0.069
eGFR (ml/min)	81.157 ± 19.99	76.320 ± 18.89	0.556	0.580
ACR (mg/g)	61.341 ± 14.88	15.710 ± 3.81	4.773	<0.001*
S. Fibrinogen (mg/dl)	11.585 ± 2.6	1.798 ± 0.43	12.486	<0.001*
Total cholesterol (mg/dl)	224.900 ± 38.587	198.333 ± 45.116	2.451	0.017*
Triglyceride (mg/dl)	179.733 ± 43.71	147.967 ± 35.11	2.300	0.025*
HDL-c (mg/dl)	44.397 ± 9.100	53.983 ± 13.12	-2.647	0.010*
LDL-c (mg/dl)	144.370 ± 5.383	117.609 ± 28.10	2.408	0.019*
FBS (mg/dl)	189.800 ± 45.97	144.167 ± 35.52	2.561	0.013*
2h pp (mg/dl)	234.567 ± 57.92	193.633 ± 46.54	2.182	0.033*
HBA1c (%)	10.000 ± 2.413	7.577 ± 1.154	4.962	<0.001*

T2DM Patients group with DPN had neuropathy severity that was distributed as follows: 26.67% had mild neuropathy, 33.33% had moderate neuropathy, and 40% had severe neuropathy. The majority of patients (73.33%) fall into the moderate or severe categories, indicating that a significant portion of the cases experienced more advanced stages of neuropathy (Table 3).

Table (3): The classification of the cases with DPN regarding the degree of severity of the neuropathy

Severity of the neuropathy		
	N	%
Mild	16	26.67
Moderate	20	33.33
Severe	24	40.00
Total	60	100.00

The mean serum fibrinogen levels were significantly higher in patients with more severe PN (P-value = 0.001) (Table 4 & Figure 3).

Mild DPN: Mean = 8.331 mg/dl. Moderate DPN: Mean = 10.315 mg/dl. Severe DPN: Mean = 14.813 mg/dl.

Table (4): Relationship between S. Fibrinogen and severity of DPN

Severity	S. Fibrinogen (mg/dl)				ANOVA	
	N	Mean	±	SD	F	P-value
Mild	16	8.331	±	3.558	10.183	0.001*
Moderate	20	10.315	±	2.562		
Severe	24	14.813	±	3.713		

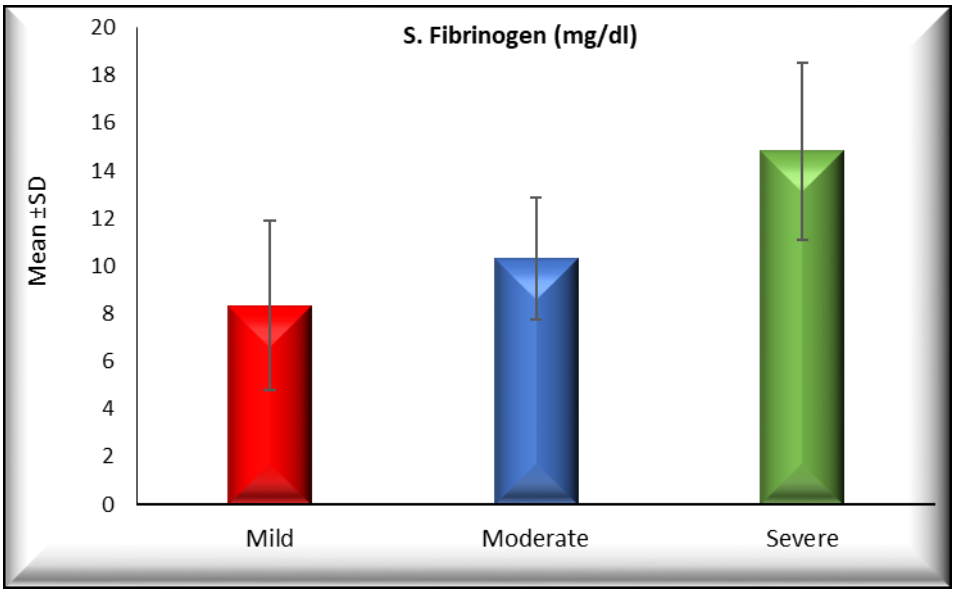


Figure (4): Relationship between s. fibrinogen and severity of DPN.

S. Fibrinogen levels showed significant positive correlations with age ($p = 0.009$), duration of diabetes ($p < 0.001$), fasting glucose ($p = 0.007$), 2-hour postprandial glucose ($p = 0.010$), HbA1c ($p < 0.001$), total cholesterol ($p = 0.003$), triglycerides ($p = 0.022$), LDL-c ($p = 0.013$), and albumin/creatinine ratio ($p = 0.002$). On the other hand, there was a significant negative correlation between S. fibrinogen and HDL-c (p-value 0.016). BMI, eGFR, and creatinine did not show significant correlations with S. fibrinogen (Table 5 & figures 4a & 4b).

Table (5): Correlation between S. fibrinogen and different clinical and biochemical variables

Correlations		
	S. Fibrinogen (mg/dl)	
	R	P-value
Age (Years)	0.468	0.009*
BMI (kg/m^2)	0.151	0.426
Duration of DM (Years)	0.636	<0.001*
eGFR (ml/min)	0.276	0.140
FBS (mg/dl)	0.483	0.007*
2h pp (mg/dl)	0.465	0.010*
HBA1c (%)	0.679	<0.001*
Total cholesterol (mg/dl)	0.520	0.003*
Triglyceride (mg/dl)	0.418	0.022*
HDL (mg/dl)	- 0.435	0.016*
LDL (mg/dl)	0.449	0.013*
Albumin/creatinine ratio	0.538	0.002*

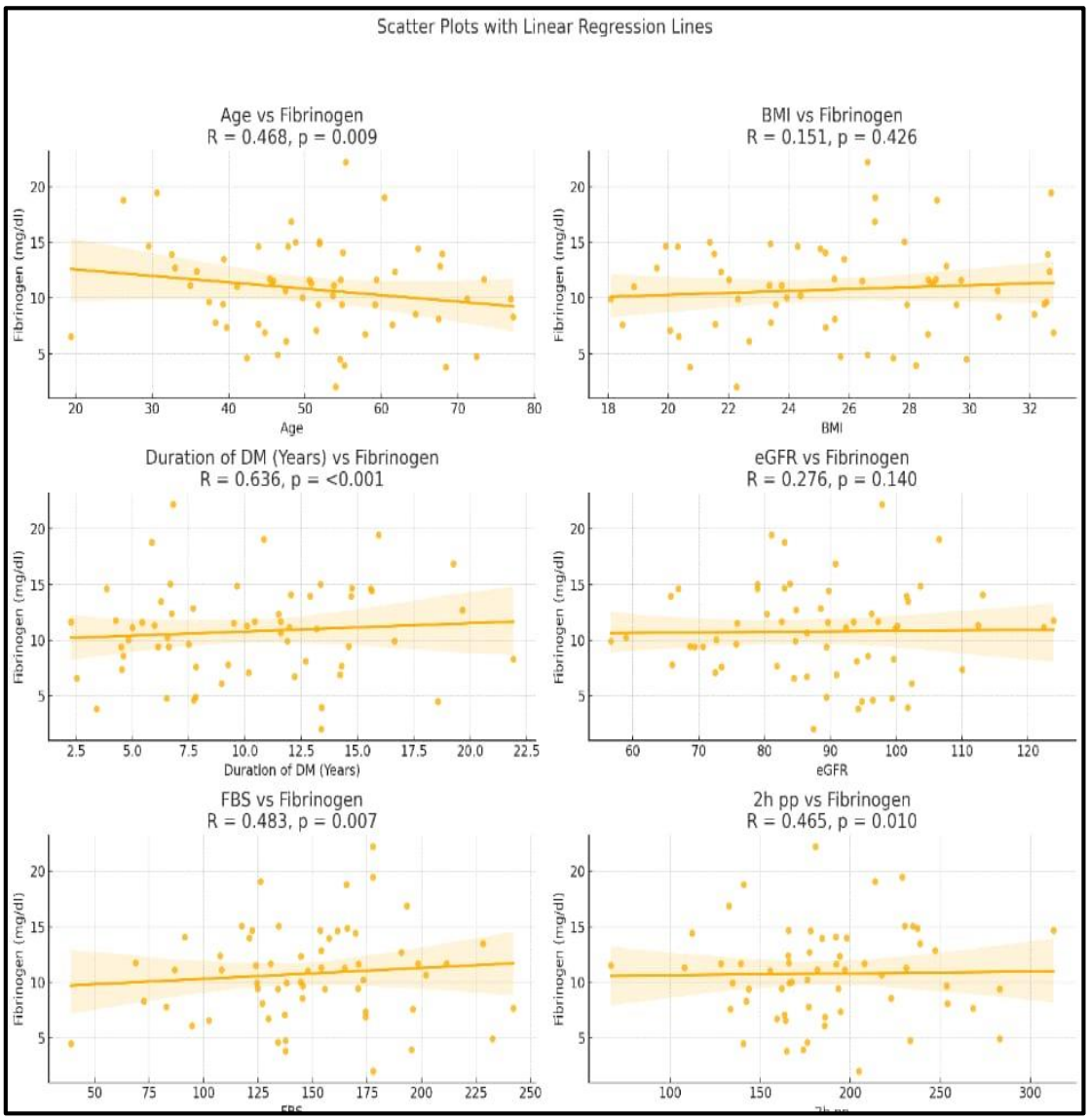


Figure (4a): Relationship between S. fibrinogen and different clinical and biochemical variables

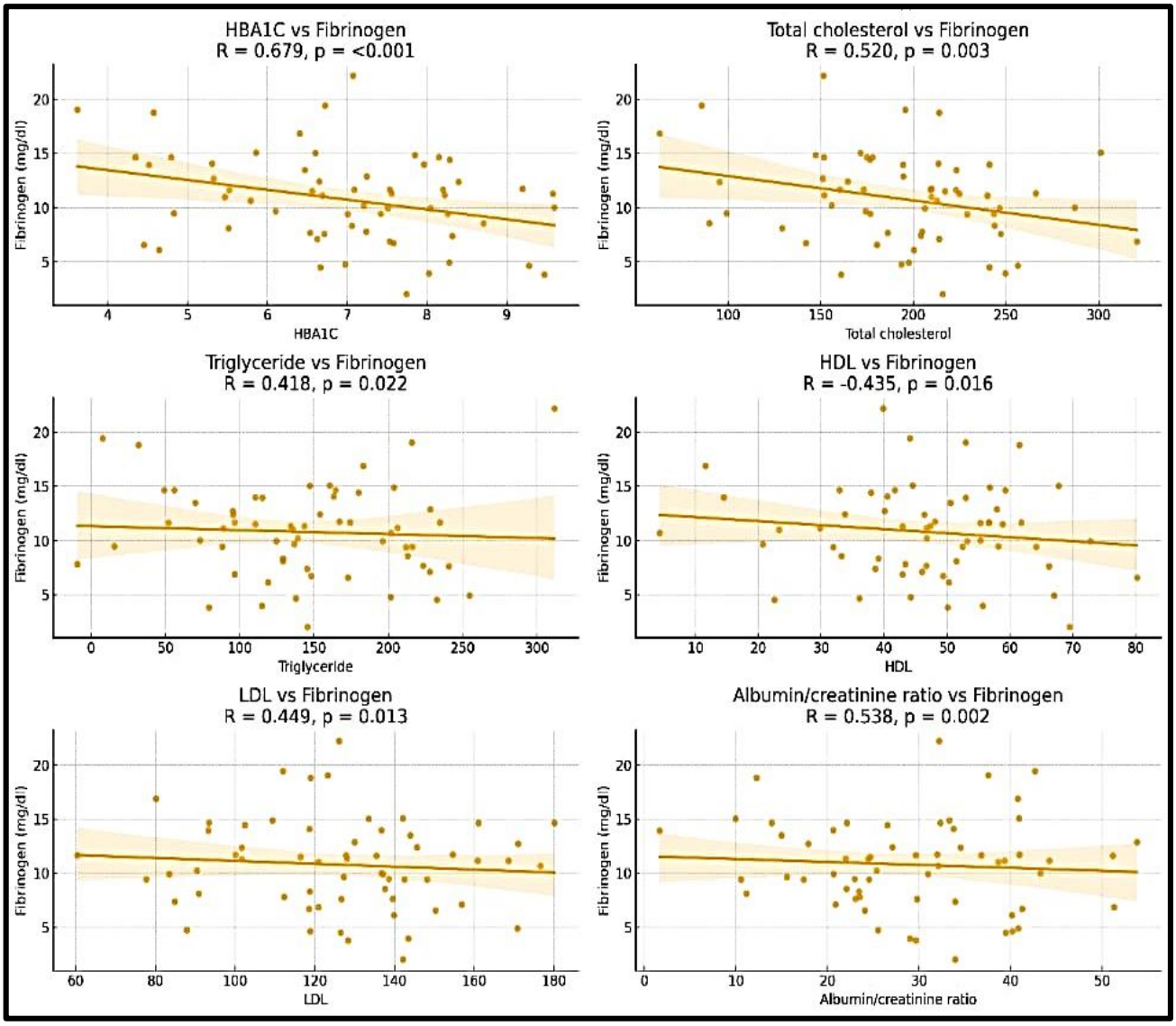


Figure (4b): Relationship between S. fibrinogen and different clinical and biochemical variables

On performing multiple linear regression analysis to understand the relationship between the severity of PN and multiple independent variables or predictors, duration of DM and serum fibrinogen levels were significantly correlated with the severity of PN. Specifically, a longer duration of DM and higher fibrinogen levels were associated with increased severity of PN, highlighting their potential role as important factors in the progression of neuropathy. Additionally, the 2-hour postprandial glucose level showed a borderline significant correlation with PN severity, suggesting a potential, albeit not definitive, relationship that warrants further investigation. Other variables, including age, fasting glucose, HBA1c, total cholesterol, triglycerides, HDL, LDL, and albumin/creatinine ratio did not demonstrate significant correlations with PN severity (Table 6).

Table (6): Multiple linear regression analysis to understand the relationship between the severity of peripheral neuropathy and multiple independent variables**.**

Covariables	B	Std. Error	Beta	T	P-value
Age (Years)	-0.055	0.069	-0.100	-0.806	0.431
Duration of DM (Years)	0.329	0.106	0.451	3.090	0.007*
Fasting	-0.001	0.007	-0.022	-0.150	0.882
2h pp (mg/dl)	0.016	0.008	0.289	2.078	0.053*
HBA1c (%)	0.249	0.249	0.141	1.000	0.331
Total cholesterol (mg/dl)	-0.021	0.019	-0.191	-1.099	0.287
Triglyceride (mg/dl)	-0.007	0.008	-0.102	-0.880	0.391
HDL-c (mg/dl)	0.027	0.051	0.057	0.522	0.608
LDL-c (mg/dl)	0.031	0.015	0.211	2.044	0.057
Albumin/create ratio	0.008	0.008	0.090	0.928	0.366
S. fibrinogen (mg/dl)	1.173	0.530	0.226	2.214	0.041*

Dependent Variable: Severity of PN

The ROC curve analysis indicated that serum fibrinogen (with a cutoff value of >2.8 mg/dl) was an excellent diagnostic marker for diabetic neuropathy, achieving perfect sensitivity, specificity, PPV, NPV, and accuracy. This implies that using serum fibrinogen levels above 2.8 mg/dl can perfectly discriminate between diabetic patients with and without neuropathy (Table 7 & figure 5).

Table (7): ROC curve analysis for the diagnostic value of s. fibrinogen in discrimination between Diabetic patients with and without PN.

ROC curve between Cases and Controls						
	Cutoff	**Sens.**	**Spec.**	**PPV**	**NPV**	**Accuracy**
S. fibrinogen (mg/dl)	>2.8	100.0	100.0	100.0	100.0	100%

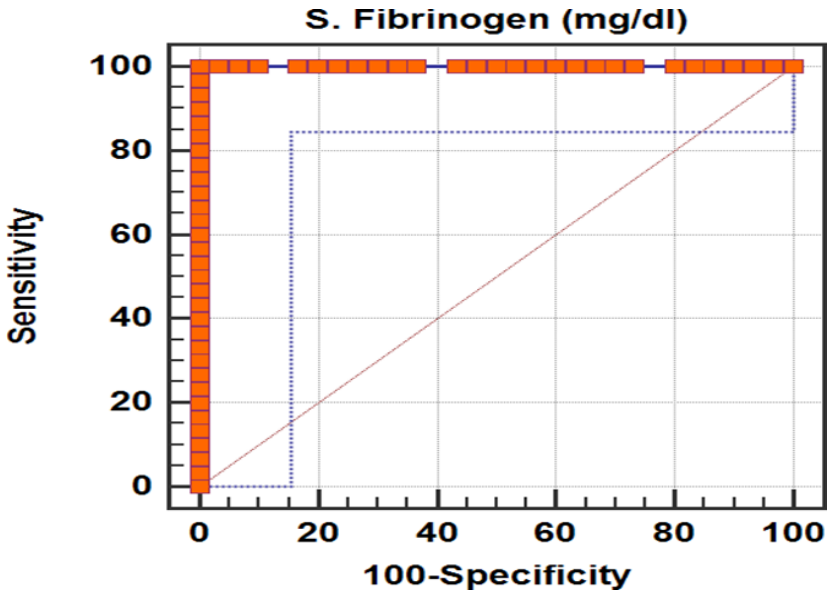


Figure (5): ROC curve analysis for s. fibrinogen as a predictor of diabetic neuropathy.

DISCUSSION

Fibrinogen is a large hexameric protein composed of Aα, Bβ, and γ chains linked by disulfide bonds, with an approximate molecular weight of 340,000 Daltons. Elevated levels of fibrinogen increase blood viscosity and enhance clot formation, which can aggravate microcirculatory insults such as ischemia and hypoxia. As an inflammatory marker, FIB contributes to endothelial damage, altered blood flow, and thrombosis, all of which are involved in diabetic complications [10].

In our study, patients with DPN exhibited significantly higher fibrinogen levels compared to those without neuropathy. The mean FIB levels were 11.585 mg/dl in patients with neuropathy versus 1.798 mg/dl in those without ($p < 0.001$). Additionally, our study reported a significant correlation between the severity of DPN and serum fibrinogen levels. Specifically, patients with more severe DPN who exhibited higher serum fibrinogen levels. These results align with a previous study involving 561 T2DM patients, which also found significantly higher fibrinogen levels in those with neuropathy ($p < 0.001$) [11]. Similarly, Another study involving 121 T2DM patients with DPN observed higher plasma fibrinogen levels in asymptomatic T2DM patients compared to healthy controls, with symptomatic individuals having much greater amounts than asymptomatic ones ($p < 0.01$) [12]. Therefore, we could conclude that as the severity of peripheral neuropathy increases, serum fibrinogen levels also tend to increase significantly. This relationship suggests that serum fibrinogen could potentially serve as a biomarker for the severity of PN.

Long-term hyperglycemia in diabetic patients can elevate fibrinogen levels due to disruptions in glucose metabolism, leading to overproduction of sorbitol and subsequent oxidative stress [13]. Such oxidative stress damages nerve cells and triggers chronic inflammatory responses. Fibrinogen functions as an inflammatory mediator by binding to β3 integrin receptors and triggering the activation of the epidermal growth factor receptor on nerve cells, This process disrupts nerve axon growth and is linked to diabetic neuropathy [11]. Therefore, elevated fibrinogen levels in patients with neuropathy underscore its potential as a key biomarker for identifying diabetic complications.

In this study, patients with DPN were diabetics for much longer, averaging 7.308 ± 5.839 years, compared to those without neuropathy, who had an average duration of 4.300 ± 3.515 years ($p = 0.019$). This observation aligns with a cohort study that demonstrated a significant correlation between the duration of diabetes and DPN ($p < 0.001$) [14]. Additionally, a comprehensive review of 16 studies, encompassing a total of 12,116 cases and including both cross-sectional and case-control designs, found a strong

association between a longer duration of diabetes and an elevated risk of DPN [15].

In our investigation, the albumin/creatinine ratio was significantly higher in patients with DPN, with a mean of 61.341 ± 50.684, compared to those without neuropathy, who had a mean of 15.710 ± 13.176 (p = 0.004*). This result is supported by a retrospective study involving 185 type 2 diabetes patients. After a two-year follow-up, they observed a significant relationship between the albumin/creatinine ratio and the occurrence of DPN. Their ROC curve analysis indicated that a ≥ 30% increase in the albumin/creatinine ratio could elevate the risk for new-onset DPN [16]. Further support comes from a study involving 124 T2DM. Among the 56 patients with peripheral neuropathy, 50 exhibited microalbuminuria, while only 10 out of 68 patients without neuropathy had microalbuminuria. The mean albumin/creatinine ratio was significantly higher in those with neuropathy (47.71 ± 27.08 mg/dl) compared to those without neuropathy (16.05 ± 5.99 mg/dl) (p < 0.0001). This finding emphasizes the association between microalbuminuria and neuropathy [17].

Additionally, our study revealed that patients with DPN had poorer glycemic and lipid control, with higher levels of T. cholesterol, TG, LDL-c, fasting blood sugar, 2-hour postprandial glucose, and HbA1c, as well as lower HDL-c levels. These findings underscore the critical need for stringent glycemic and lipid management to mitigate diabetic complications such as neuropathy. Poor control of these parameters is known to exacerbate diabetic complications, including neuropathy [18].

Consistent with this, a recent research found a positive correlation between LDL levels and diabetic peripheral neuropathy [19]. However, a different study involving a larger sample of T2DM patients over an extended period did not find an association, potentially due to variations in study design, participant characteristics, or ethnicity [18].

In addition, our study revealed significantly higher triglyceride levels in patients with diabetic neuropathy (mean of 179.733 ± 58.474) compared to those without (147.967 ± 48.008) (p = 0.025). This aligns with other research indicating that hypertriglyceridemia is a significant independent risk factor for DPN [20]. Conversely, another study did not find a significant association between triglyceride levels and neuropathy [18].

In our study, the distribution of neuropathy severity indicated that a substantial majority, specifically 73.33% of the patients were classified into moderate or severe categories. The advanced stage of neuropathy observed among these patients emphasized the critical need for proactive and early intervention strategies to manage and potentially mitigate the progression of neuropathy.

Our study identified a significant positive correlation between plasma fibrinogen levels and various factors, such as patient age, duration of diabetes, fasting blood glucose, 2-hour postprandial glucose, HbA1c, T. cholesterol, TG, LDL-c, and the albumin/creatinine ratio. Conversely, an inverse relationship was observed with HDL-c levels. These findings align with those reported in several prior studies [11, 15, 21].

Multiple linear regression analysis identified the duration of diabetes and serum fibrinogen levels as key predictors of neuropathy severity. The 2-hour postprandial glucose level displayed a borderline significant correlation, indicating a potential link that may warrant further investigation. Other factors, such as age, fasting glucose, HbA1c, T. cholesterol, TG, HDL-c, LDL-c, and the albumin/creatinine ratio did not exhibit significant correlations with neuropathy severity in this analysis. These results support the idea that chronic glycemic exposure and inflammatory markers have a greater impact on neuropathy severity compared to individual metabolic parameters [22, 23].

Study limitations: A narrow geographic focus, a brief research period, and a small sample size. The results' significance and generalizability may be affected by these variables. Future studies should include bigger sample numbers and longer study durations to overcome these constraints and more convincingly validate and corroborate the findings.

CONCLUSION

The duration of diabetes and serum fibrinogen levels were key predictors of DPN severity. These results underscore the importance of managing both glycemic control and inflammatory markers to reduce the risk and slow the progression of neuropathy. The significant association between fibrinogen levels and neuropathy severity indicates its potential as both a diagnostic and prognostic marker in clinical settings. Future research should aim to further clarify the roles of these and other factors in neuropathy progression and focus on developing targeted interventions to enhance patient outcomes.

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