DOI: 10.7860/NJLM/2026/79870.3015

Original Article

Pathology Section

Plasma Fibrinogen Levels and their Association with Glycaemic Control and Microvascular Complications in Type 2 Diabetes Mellitus: A Cross-sectional Study

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ABSTRACT

Introduction: Type 2 Diabetes Mellitus (T2DM) is a global health burden associated with chronic hyperglycaemia and vascular complications. Dysregulation of haemostatic pathways particularly hyperfibrinogenaemia is increasingly recognised as a contributor to both atherosclerosis and microvascular damage in diabetes. Despite this, plasma fibrinogen is not routinely measured in diabetic patients. Evaluating its relationship with glycaemic control and end-organ complications could identify a low-cost, accessible marker for early risk stratification.

Aim: To evaluate plasma fibrinogen levels in patients with T2DM, assess their association with glycaemic control, and determine their relationship with microvascular complications (retinopathy, neuropathy, and nephropathy).

Materials and Methods: This cross-sectional observational study was in the Department of Pathology, Inlaks and Budhrani Hospital, a tertiary care hospital serving patients across socioeconomic strata in Pune, Maharashtra, India, from June 2022 to May 2023. A total of 84 patients with T2DM were enrolled. Parameters assessed included plasma fibrinogen (Clauss assay), Glycated Haemoglobin (HbA1c) (turbidimetric inhibition immunoassay), fasting and postprandial blood glucose, fasting lipid profile, renal function tests (blood urea, serum creatinine), complete blood count, and clinical assessment for microvascular complications (retinopathy, neuropathy, nephropathy). Statistical analysis was performed using GraphPad Prism v8.0.2 (GraphPad Software, San Diego, CA, USA) and included Spearman's rho (ρ) and the Mann-Whitney U test.

Results: The median plasma fibrinogen level was 298.9 mg/dL {Interquartile Range (IQR): 230.7-400.5 mg/dL}, and the median HbA1c was 7.80% (IQR: 6.50-10.60%). A strong positive correlation was observed between fibrinogen and HbA1c (Spearman's rho=0.807; p<0.0001). Microvascular complications were present in 26.19% of patients (n=22). Fibrinogen levels were significantly higher in patients with microvascular complications {median (IQR): 410.8 (330.0-462.7) mg/dL} than in those without complications {268.2 (224.0-366.5) mg/dL; Mann-Whitney U=1065; p<0.0001; rank-biserial r=0.562}. No significant association was found between fibrinogen and age (p=0.075), gender (p=0.474) or Body Mass Index (BMI) (p=0.953).

Conclusion: Plasma fibrinogen is strongly and significantly associated with both poor glycaemic control and microvascular complications in T2DM. The statistically significant elevation in fibrinogen among patients with complications, combined with its strong correlation with HbA1c, supports an association between poor glycaemic control, hypercoagulability, and microvascular complications in T2DM. These findings suggest that plasma fibrinogen may have potential as an adjunctive biomarker for vascular risk assessment in T2DM. Prospective multicentre studies are needed to determine whether fibrinogen has predictive value for complication onset and progression.

Keywords: Clauss assay, Hypercoagulability, Microangiopathy, Nephropathy, Neuropathy, Poor glycaemic control, Retinopathy

INTRODUCTION

Diabetes mellitus is a major global health concern, ranking among the top ten causes of death and contributing significantly to the burden of non communicable diseases. In India, the burden is particularly striking; prevalence rose from 7.1% in 2009 to 8.9% in 2019, with nearly 57% of cases remaining undiagnosed, representing approximately 43.9 million individuals living with untreated disease [1]. Beyond its sheer prevalence, the true cost of diabetes lies in its complications. Microvascular damage affecting the retina, kidney, and peripheral nerves, reduces quality of life, drives dialysis dependency, causes preventable blindness, and substantially increases mortality and healthcare expenditure [1,2]. Early identification of patients at highest risk for these complications remains one of the most clinically urgent challenges in diabetology.

Chronic hyperglycaemia reflected by elevated Glycated Haemoglobin (HbA1c), drives microvascular injury through multiple converging pathways including oxidative stress, endothelial dysfunction, activation of the polyol and hexosamine pathways, and accumulation of advanced glycation end products [3,4]. Alongside these metabolic mechanisms, dysregulation of the coagulation system has emerged as a critical and underappreciated contributor to microvascular damage in diabetes. T2DM is associated with elevated fibrinogen, increased thromboxane A2, reduced platelet synthesis of nitric oxide, and increased Plasminogen Activator Inhibitor-1 (PAI-1) release, collectively creating a prothrombotic, hypofibrinolytic milieu that promotes capillary occlusion and endothelial injury at the microvascular level [5-7]. During states of chronic low-grade inflammation, as seen in persistent hyperglycaemia interleukin-6 acts as the key mediator of increased hepatic fibrinogen synthesis, driving fibrinogen levels well above the normal reference range of 200-400 mg/dL [6,7]. Elevated fibrinogen in this context reflects not simply a generic inflammatory response but a constellation of diabetes-driven pathological processes, making it a particularly relevant biomarker for risk stratification in T2DM.

Crucially, poor glycaemic control leads to glycation of fibrinogen itself. Glycated fibrinogen produces structurally abnormal fibrin clots: denser, with thinner fibres, reduced porosity, and markedly resistant

to fibrinolysis, providing a direct mechanistic link between HbA1c and the hypercoagulable state observed in poorly controlled diabetes [6,7]. Elevated fibrinogen further increases plasma viscosity, promotes platelet aggregation, and generates fibrinogen degradation products that impair endothelial function and promote capillary basement membrane thickening- processes that directly accelerate microvascular injury in the retina, kidney, and peripheral nerves [4,7,8].

What makes fibrinogen particularly attractive as a clinical biomarker is its practicality. Unlike many emerging coagulation markers - von Willebrand factor, PAI-1, thrombin-antithrombin complexes, or factor VII- fibrinogen is measurable by the Clauss assay, the internationally recommended and widely used method of choice for fibrinogen function assessment [9,10]. This practical advantage is especially relevant in resource-limited settings such as community and district-level hospitals across India, where complex coagulation panels are not feasible. If fibrinogen reliably reflects glycaemic burden and complication status, it may complement existing approaches to risk stratification in patients with T2DM [2,9].

Despite this potential, the evidence base remains limited, particularly in the Indian population, where the phenotype of T2DM differs from Western cohorts in terms of earlier age of onset, leaner body habitus, and distinct patterns of complication progression [1]. Existing studies have examined fibrinogen largely in isolation or focused predominantly on macrovascular outcomes [11]; few have simultaneously evaluated its relationship with both glycaemic control and microvascular complications in a South Asian cohort [8,12,13]. This combined analysis- fibrinogen, HbA1c, and microvascular end-organ damage assessed together in an Indian tertiary care population- represents the specific gap the present study was designed to address.

The primary aim of the present study was to evaluate plasma fibrinogen levels in patients with T2DM and assess their association with glycaemic control. The objectives were to assess fibrinogen levels in relation to the presence of microvascular complications including retinopathy, neuropathy, and nephropathy, to examine the relationship between fibrinogen and demographic variables such as age, gender, and BMI and to determine whether routine plasma fibrinogen measurement could add clinical value to diabetic risk stratification in a tertiary care setting in India.

MATERIALS AND METHODS

A cross-sectional observational study was conducted in the Department of Pathology, Inlaks and Budhrani Hospital, a tertiary care hospital serving patients across socioeconomic strata in Pune, Maharashtra, India. The study was conducted over a period of 12 months, from June 2022 to May 2023. Ethical approval was obtained from the Institutional Ethics Committee of Inlaks and Budhrani Hospital (IEC Registration No. IEC/2022/273). The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrollment, following a detailed explanation of the study purpose, procedures, and their right to withdraw at any time without consequence.

Patients diagnosed with T2DM, with or without microvascular complications, attending the Medicine Outpatient Department (OPD) and Inpatient Department (IPD) were enrolled.

Diagnostic criteria for T2DM were defined according to the American Diabetes Association (ADA) 2022 guidelines: fasting plasma glucose ≥126 mg/dL, or 2-hour plasma glucose ≥200 mg/dL during an oral glucose tolerance test, or HbA1c ≥6.5%, or random plasma glucose ≥200 mg/dL in a patient with classic symptoms of hyperglycaemia [14].

Microvascular complications were defined as follows:

- Diabetic retinopathy was diagnosed by a consultant ophthalmologist on the basis of fundoscopic examination, using the International Clinical Diabetic Retinopathy severity scale [15].
- Diabetic neuropathy was defined as the presence of symptoms (numbness, tingling, burning pain in the extremities) with supportive clinical signs (reduced vibration sense, absent ankle reflexes), consistent with the criteria of the Toronto Diabetic Neuropathy Expert Group [4].
- Diabetic nephropathy was defined as persistent albuminuria (urinary albumin-to-creatinine ratio >30 mg/g on at least two occasions) in the absence of other primary renal disease, consistent with Kidney Disease: Improving Global Outcomes (KDIGO) criteria [16].

Glycaemic control was classified based on HbA1c. Patients with HbA1c <7.0% were considered to have controlled diabetes, and those with HbA1c ≥7.0% were classified as having suboptimal or poor glycaemic control, in accordance with ADA targets [2].

Inclusion criteria:

- Diagnosed cases of T2DM as per ADA 2022 criteria;
- Patients managed on Oral Hypoglycaemic Agents (OHAs) at the time of enrollment;
- Age 18 years and above;
- Willingness to provide written informed consent.

Exclusion criteria:

- Type 1 diabetes mellitus;
- Patients on insulin therapy were excluded because exogenous insulin independently influences fibrinogen levels and coagulation parameters, which would confound the primary outcome measure [7];
- Patients on anticoagulant therapy were excluded because anticoagulants directly alter coagulation parameters and may affect the interpretation of fibrinogen and other coagulation assay results;
- Patients on aspirin therapy were excluded because aspirin inhibits platelet function and may influence coagulation-related parameters, potentially confounding the study results;
- Patients with known hepatic disease were excluded because fibrinogen is synthesised in the liver, and hepatic dysfunction could independently alter fibrinogen levels;
- Patients with active infection, malignancy, or other acute inflammatory conditions were excluded because fibrinogen is an acute-phase reactant, and these conditions could independently increase fibrinogen levels and confound the study results.

Sample size calculation: Sample size was determined by using the effect sizes from the previously published study (Bembde AS [11]) and with the help of following formula:

$n = (Z\ \alpha/2 \times \sigma / me)^2$

Where:

- σ= 139 mg/dL (published Standard Deviation (SD) of plasma fibrinogen levels)
- $Z\ \alpha/2$= 1.96 (standard normal deviate at 95% confidence interval)
- me= 30 mg/dL (margin of error)
- $n = (1.96 \times 139/30)^2 = (9.083)^2 = 82.47 \approx 83$

A minimum sample size of 83 patients was therefore required. A total of 84 patients were enrolled to account for potential data loss or incomplete records, giving a final study sample of 84 participants.

Consecutive sampling was employed to minimise selection bias. All patients with T2DM attending the medicine OPD and IPD during the study period who met the eligibility criteria were approached for enrollment in the order of their attendance, until the required sample size was achieved. This method was chosen over convenience sampling to ensure systematic and reproducible patient selection, reducing the risk of operator-driven bias in enrollment.

Study Procedure

For each participant, demographic and clinical details were recorded, including age, gender, BMI, duration of diabetes, and presence of microvascular complications. The following laboratory and clinical investigations were performed:

1. Fasting and postprandial blood glucose;
2. Fasting lipid profile;
3. HbA1c by turbidimetric inhibition immunoassay;
4. Plasma fibrinogen by Clauss assay;
5. Blood urea and serum creatinine;
6. Complete blood count including total leucocyte count, differential count, haemoglobin, Erythrocyte Sedimentation Rate (ESR), haematocrit, and platelet count;
7. Electrocardiogram (ECG) -to exclude patients with acute cardiac events that could independently elevate fibrinogen as an acute-phase reactant;
8. Chest X-ray- to exclude active pulmonary infection or malignancy, conditions that independently elevate fibrinogen and would confound results.

STATISTICAL ANALYSIS

Normality of continuous variables was assessed using the Shapiro-Wilk test. Fibrinogen was normally distributed (W=0.982, p=0.298); HbA1c was non normally distributed (W=0.895, p<0.001). The correlation analysis involved a non normally distributed variable (HbA1c), Spearman's rank correlation coefficient (ρ) was used. Comparisons between patients with and without microvascular complications were performed using the Mann-Whitney U test because one comparison group was relatively small (n=22). Continuous variables are presented as mean±SD for descriptive purposes, with median and IQR additionally reported for plasma fibrinogen and HbA1c to facilitate interpretation of the non parametric analyses. Categorical variables are presented as frequencies and percentages. Patients with microvascular complications were classified as the "complicated" group and those without microvascular complications as the "uncomplicated" group. A p-value<0.05 was considered statistically significant. Data analysis was performed using GraphPad Prism v8.0.2 (GraphPad Software, San Diego, CA, USA).

RESULTS

A total of 84 patients were enrolled, slightly exceeding the calculated minimum sample size of 83. The mean age of participants was 48.63±9.02 years. The cohort comprised 43 males (51.19%) and 41 females (48.81%). The mean Body Mass Index (BMI) was 24.87±1.87 kg/m². Baseline haematological and biochemical parameters are summarised in [Table/Fig-1]. Complete blood count parameters, ECG, and chest X-ray findings were reviewed prior to enrollment to exclude active cardiac, pulmonary, infectious, or known inflammatory conditions.

Duration of diabetes: Among the study population, 55.95% of participants (n=47) had a diabetes duration of more than five years, while 44.05% (n=37) had a duration of five years or less.

Patients with diabetes duration greater than five years demonstrated higher plasma fibrinogen levels {median (IQR): 340.3 (245.2-429.6) mg/dL; mean±SD: 336.1±119.9 mg/dL} compared to those with disease duration of five years or less {median (IQR): 265.9 (207.7-349.2) mg/dL; mean±SD: 275.9±103.0 mg/dL}.

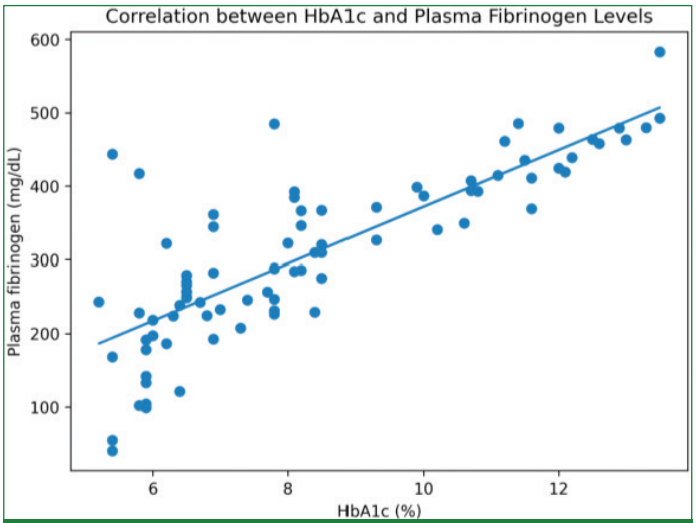
Duration of diabetes was analysed as an ordinal binary variable (>5 years vs ≤5 years). A statistically significant correlation was observed between duration of diabetes and plasma fibrinogen levels (Spearman's rho=0.262; p=0.016).

Parameters	Mean±SD	Reference range
Fasting blood glucose (mg/dL)	160±30	70-110 mg/dL
Postprandial blood glucose (mg/dL)	245±55	<140 mg/dL
BMI (kg/m²)	24.87±1.87	18.5-24.9 kg/m²
Lipid Profile		
Total cholesterol (mg/dL)	205±42	<200 mg/dL
Triglycerides (mg/dL)	185±60	<150 mg/dL
HDL cholesterol (mg/dL)	38±7	Male: >40 mg/dL; Female: >50 mg/dL
LDL cholesterol (mg/dL)	122±30	<100 mg/dL
VLDL cholesterol (mg/dL)	36±12	5-40 mg/dL
HbA1c (%)	8.39±2.4	4.0-5.6 %
Plasma fibrinogen (mg/dL)	309.6±116.1	200-400 mg/dL
Blood urea (mg/dL)	31±10	15-40 mg/dL
Serum creatinine (mg/dL)	1.0±0.3	0.6-1.2 mg/dL
Haemoglobin (g/dL)	12.7±1.8	Male: 13-17 g/dL; Female: 12-15 g/dL
Total leukocyte count (/mm³)	9,700±2,400	4,000-11,000 /mm³
Differential leukocyte count (%)	Neutrophils: 62±9; Lymphocytes: 30±9; Monocytes: 5±3, Eosinophils: 3±2	Neutrophils: 40-75%; Lymphocytes: 20-45%; Monocytes: 2-10%; Eosinophils: 1-6%
ESR (mm/hr)	24±10	Male: 0-15 mm/hr; Female: 0-20 mm/hr
Haematocrit (%)	38±5	Male: 40-54%; Female: 36-48%
Platelet count (×10³/mm³)	269±61	150-450 ×10³/mm³

[Table/Fig-1]: Biochemical and haematological parameters in all Type 2 Diabetes Mellitus (T2DM) patients.
HDL: High-density lipoprotein; LDL: Low-density lipoprotein; VLDL: Very-low-density lipoprotein

Glycaemic control and plasma fibrinogen levels: The median HbA1c level across the entire cohort was 7.80% (IQR: 6.50-10.60%) {mean±SD: 8.39±2.45%}. HbA1c values ranged from 5.2% to 13.5%, with 41.67% of patients (n=35) having HbA1c <7.0% and 11.90% (n=10) having HbA1c >12.0%. The median plasma fibrinogen level was 298.9 mg/dL (IQR: 230.7-400.5 mg/dL) {mean±SD: 309.6±116.1 mg/dL} across the full cohort.

A significant positive correlation was observed between fibrinogen and HbA1c levels (Spearman's rho=0.807; p<0.0001) [Table/Fig-2].

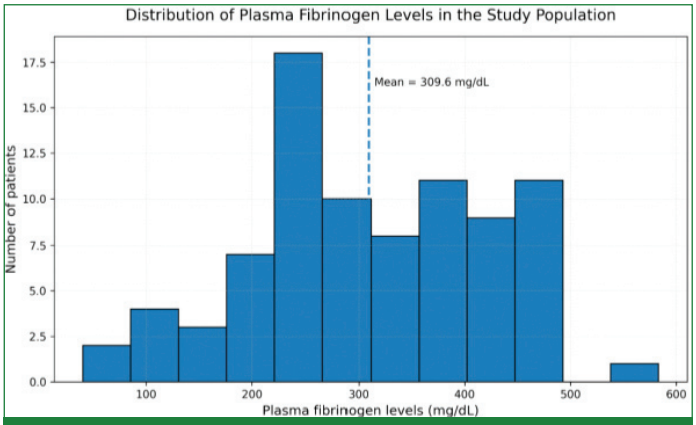


[Table/Fig-2]: Scatterplot showing positive correlation between HbA1c (%) and plasma fibrinogen (mg/dL) with trend line.

The distribution of plasma fibrinogen levels among the study population is shown in [Table/Fig-3].

Microvascular complications: Microvascular complications were identified in 22/84 (26.19%) patients. Retinopathy was present in 13/84 (15.48%) patients, nephropathy in 11/84 (13.10%), and

neuropathy in 12/84 (14.29%) [Table/Fig-4]. Among patients with microvascular complications (n=22), 4/22 (18.18%) had retinopathy only, 3/22 (13.64%) had nephropathy only, and 4/22 (18.18%) had neuropathy only. Among those with overlapping complications, 3/22 (13.64%) had concurrent retinopathy and nephropathy only, 3/22 (13.64%) had concurrent retinopathy and neuropathy only, and 2/22 (9.09%) had concurrent nephropathy and neuropathy only. All three microvascular complications were present concurrently in 3/22 (13.64%) of the complicated group. All patients with one or more microvascular complications were classified as the "complicated" group for statistical analysis.

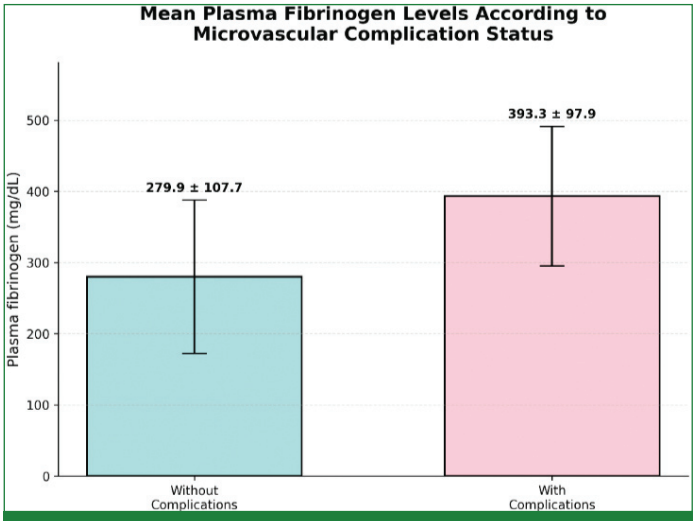


[Table/Fig-3]: Histogram showing frequency distribution of plasma fibrinogen values (mg/dL) across the study population.

Complication	n (%)
Retinopathy	13 (15.48)
Nephropathy	11 (13.10)
Neuropathy	12 (14.29)
≥1 microvascular complication	22 (26.19)

[Table/Fig-4]: Distribution of microvascular complications among study participants (N=84).

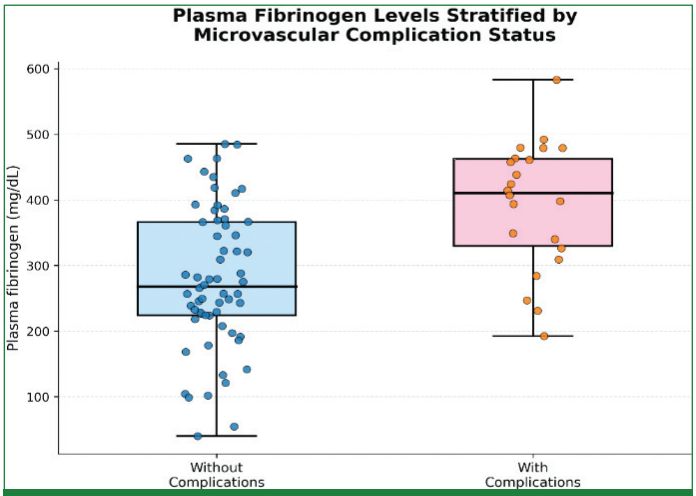
Fibrinogen levels by complication status: Patients with microvascular complications had significantly higher plasma fibrinogen levels {median (IQR): 410.8 (330.0-462.7) mg/dL; mean±SD: 393.3±97.9 mg/dL} compared to those without complications {268.2 (224.0-366.5) mg/dL; mean±SD: 279.9±107.7 mg/dL; Mann-Whitney U=1065.0; p<0.0001, rank-biserial r=0.562} [Table/Fig-5].



[Table/Fig-5]: Bar chart comparing mean plasma fibrinogen levels (mg/dL) in patients with and without microvascular complications. Error bars represent Standard Deviation (SD).

The distribution of plasma fibrinogen levels according to microvascular complication status is shown in [Table/Fig-6].

Gender and BMI analysis: Median plasma fibrinogen levels were 322.5 mg/dL (IQR: 235.7-417.9 mg/dL, mean: 317.3±115.6 mg/dL) in male participants and 284.5 mg/dL (IQR: 226.5-392.9 mg/dL, 301.5±117.5 mg/dL) in female participants. The difference was not statistically significant (Mann-Whitney U=962, p=0.474). Similarly, no significant correlation was observed between plasma fibrinogen levels and BMI (Spearman's rho= -0.007, p=0.953).



[Table/Fig-6]: Box plot of plasma fibrinogen levels stratified by microvascular complication status, demonstrating higher median fibrinogen and greater variability in the complicated group. Individual data points and outliers are overlaid.

Age correlation: Fibrinogen levels did not demonstrate a statistically significant correlation with age in this cohort (Spearman's rho= 0.195; p=0.075).

DISCUSSION

The present study evaluated plasma fibrinogen levels in 84 patients with T2DM and examined their association with glycaemic control (HbA1c) and the presence of microvascular complications. The mean fibrinogen level across the cohort was 309.6±116.1 mg/dL (median 298.9 mg/dL) against a mean HbA1c of 8.39±2.45% (median 7.80%), indicating suboptimal glycaemic control in the majority of participants.

Age distribution: The mean age of participants was 48.6±9.0 years, lower than that reported by Ghongade PV et al., (53.58±11.1 years in uncomplicated and 57.85±11.33 years in complicated T2DM) and Agarwal C et al., (55.63±7.49 years) [13,17]. This younger age profile is consistent with epidemiological observations that T2DM in India commonly presents during the fourth and fifth decades of life [1].

Glycaemic control: The mean HbA1c in the present cohort was 8.39±2.45% (median 7.80%), indicating suboptimal glycaemic control and was comparable to findings by Bembde AS (8.5±1.69%) and the IMPACT India programme, which reported an average HbA1c of 8.56% among Indian patients with type 2 diabetes [11,18]. The relatively wide SD reflects inclusion of patients across a broad spectrum of glycaemic control. Patients with microvascular complications had higher mean HbA1c levels than those without complications (10.80±2.05% vs 7.53±1.98%). A strong positive correlation was observed between HbA1c and plasma fibrinogen levels (Spearman's rho=0.807; p<0.0001), consistent with previous studies linking poor glycaemic control to hypercoagulability [6,7,11].

Duration of diabetes and fibrinogen: A statistically significant positive correlation was observed between duration of diabetes and plasma fibrinogen levels (Spearman's rho=0.262; p=0.016), with patients having disease duration greater than five years demonstrating higher mean fibrinogen levels (336.1±119.9 mg/dL, median 340.3 mg/dL) than those with shorter duration (275.9±103.0 mg/dL, median 265.9 mg/dL). Longer disease duration is associated with cumulative hyperglycaemic exposure, endothelial dysfunction, and chronic low-grade inflammation, all of which may contribute to

increased fibrinogen synthesis [5,7,11]. However, given the cross-sectional design, causality cannot be inferred.

Plasma fibrinogen levels and variability: The mean plasma fibrinogen level in the present study was 309.6±116.1 mg/dL (median 298.9 mg/dL), in keeping with previous studies reporting elevated fibrinogen levels in T2DM populations. Khan TM et al., reported fibrinogen levels of approximately 428±10 mg/dL in diabetic cohorts, while Kafle DR et al., similarly observed elevated fibrinogen levels in diabetic patients, particularly those with coexisting coronary artery disease [8,12]. The relatively wide SD in the present cohort reflects heterogeneity in glycaemic control, disease duration, and microvascular complication status. Within-group SDs were narrower (97.9 mg/dL in the complicated group and 107.7 mg/dL in the uncomplicated group), supporting that the overall variability primarily reflects between-group heterogeneity rather than measurement inconsistency.

Fibrinogen and microvascular complications: Patients with microvascular complications demonstrated significantly higher plasma fibrinogen levels (median 410.8 mg/dL; mean 393.3±97.9 mg/dL) compared to those without complications (median 268.2 mg/dL; mean 279.9±107.7 mg/dL; Mann-Whitney U=1065; $p<0.0001$; rank-biserial r=0.562, indicating a large effect). This marked elevation in the complicated group is consistent with findings reported by Bembde AS, Kafle DR and Shrestha P, and Nimmala SG et al., [11,12,19]. Poor glycaemic control promotes endothelial dysfunction, low-grade inflammation, and accumulation of advanced glycation end products, contributing to both microvascular damage and increased fibrinogen synthesis. However, fibrinogen is a non specific acute-phase reactant influenced by infection, obesity, dyslipidaemia, smoking, and hypertension, all of which may contribute to elevated levels in T2DM patients [4,7]. Patel HV et al., similarly reported significantly higher fibrinogen levels in patients with dyslipidaemia and poor glycaemic control [5]. Therefore, the observed elevation in fibrinogen may partly reflect broader systemic inflammation rather than microvascular disease alone, limiting its specificity as a biomarker.

Pathophysiological mechanisms: The pathophysiological mechanisms linking diabetes to hyperfibrinogenaemia are multifactorial. Insulin resistance and chronic hyperglycaemia stimulate hepatic fibrinogen production through proinflammatory cytokines such as interleukin-6 [7]. Diabetes is also associated with dysregulation of other coagulation factors, including von Willebrand factor, PAI-1, factor VII, and thrombin-antithrombin complexes, contributing to a prothrombotic state [6,7]. Glycosylated fibrinogen formed during poor glycaemic control produces denser fibrin clots that are resistant to fibrinolysis, contributing to the hypercoagulable state observed in T2DM. These structural abnormalities may explain the particularly strong correlation between fibrinogen and HbA1c observed in this study ($\rho=0.807$, $p<0.0001$).

Age gender and BMI: Fibrinogen levels showed no statistically significant correlation with age (Spearman's rho=0.195; p=0.075), gender (p=0.474), or BMI (Spearman's rho=-0.007; p=0.953) in the present study.

The absence of a significant age-fibrinogen correlation contrasts with findings by Bembde AS, Ghongade PV et al., and Drenos F et al., who reported positive correlations, possibly related to slower hepatic clearance and smoking [11,13,20]. The relatively narrow age range of the present cohort (48.6±9.0 years) may have limited the ability to detect this association. However, unmeasured confounders such as hypertension, smoking history, dyslipidaemia, and medication use may also have influenced fibrinogen levels.

The absence of a significant gender difference is consistent with Bembde AS, although Li T et al., reported sex-specific associations between fibrinogen and coronary atherosclerotic plaque subtypes, suggesting that hormonal influences may be more relevant in macrovascular disease [11,21].

The absence of a fibrinogen-BMI correlation differs from findings by Patel HV et al., Bembde AS and Ghongade PV et al., who reported higher fibrinogen levels in overweight and obese patients [5,11,13]. The relatively narrow BMI range in the present cohort (24.9±1.9 kg/m^2) may have limited the ability to detect this association and should not be generalised to populations with wider BMI distribution.

Clinical utility of plasma fibrinogen in diabetic risk stratification: The significant association between plasma fibrinogen, poor glycaemic control, and microvascular complications observed in the present study, together with the large effect size observed between patients with and without complications (rank-biserial r=0.562), suggests that fibrinogen may have potential as an adjunctive biomarker for vascular risk assessment in T2DM. Given that the Clauss assay is inexpensive, standardised, and widely available, fibrinogen measurement may be particularly relevant in resource-limited settings. However, the present findings are associative in nature and do not establish predictive utility. Prospective longitudinal studies are required to determine whether fibrinogen provides incremental value in identifying patients at risk of developing diabetic complications.

Limitation(s)

The present study is limited by its cross-sectional design and single-centre setting which restrict causal inference and predictive assessment of microvascular complications. Potential confounding factors such as smoking, hypertension, dyslipidaemia, obesity, and medication use were not adjusted for and may have influenced fibrinogen levels. In addition, fibrinogen is a non specific acute-phase reactant, which limits its specificity for microvascular disease. The severity of microvascular complications was not stratified, and exclusion of insulin-treated patients may limit generalisability to advanced T2DM populations.

CONCLUSION(S)

Plasma fibrinogen is elevated in patients with T2DM, particularly in those with microvascular complications, and is positively associated with poor glycaemic control. These findings support the biological link between dysglycaemia, inflammation, coagulation abnormalities, and diabetic microvascular injury. However, fibrinogen is a non specific acute-phase reactant, and its elevation may be influenced by other inflammatory and cardiovascular conditions. Therefore, the observed associations should be interpreted cautiously, particularly given the cross-sectional study design. Larger prospective multicentre studies with appropriate confounder adjustment are required to establish the independent predictive value and clinical utility of plasma fibrinogen in risk stratification of T2DM.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jan 28, 2026
- Manual Googling: Jul 02, 2026
- iThenticate Software: Jul 07, 2026 (4%)

ETYMOLOGY: Author Origin

EMENDATIONS: 7

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? Yes
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Jan 27, 2026**
Date of Peer Review: **Apr 06, 2026**
Date of Acceptance: **Jul 08, 2026**
Date of Publishing: **Oct 01, 2026**