



Prevalence of Coagulopathy and its Association with Glycemic Control Complications in Patients with Type 2 Diabetes Mellitus: A Literature Review

Dony Prasetya Nugraha^{1*}, Alvin T Harahap²

Pertamina Tarakan Hospital, Indonesia¹

Pertamina Central Hospital, Indonesia²

Emails: donypn360@gmail.com^{1*}

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Abstract

Type 2 diabetes mellitus (T2DM) is associated with hemostatic abnormalities that may contribute to vascular complications; however, the reported prevalence of coagulopathy and its relationship with glycemic control remain inconsistent across studies. This systematic literature review aimed to synthesize evidence regarding the prevalence of coagulopathy and its associations with glycemic control and diabetes-related complications. The review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines and included searches of Europe PMC and supplementary sources for studies published between 2021 and 2026. A total of 32 articles were included and critically appraised using Joanna Briggs Institute (JBI) appraisal tools. The findings were analyzed through narrative synthesis and bibliometric mapping using VOSviewer. One study reported a coagulopathy prevalence of 26.6%; however, variations in diagnostic definitions and laboratory thresholds precluded a pooled prevalence estimate. Poor glycemic control was associated with elevated fibrinogen, D-dimer, plasminogen activator inhibitor-1 (PAI-1), and selected platelet indices, whereas prothrombin time (PT) and activated partial thromboplastin time (aPTT) demonstrated inconsistent patterns. Fibrinogen-related markers were associated with diabetic retinopathy, diabetic kidney disease, and peripheral neuropathy, while D-dimer and coagulation factor XI were associated with cardiovascular outcomes. These findings suggested potential interactions among coagulation activation, impaired fibrinolysis, and diabetes-related vascular injury. Nevertheless, the predominance of cross-sectional studies limited causal inference. Hemostatic biomarkers may complement individualized risk assessment for diabetes-related complications; however, the available evidence does not support routine coagulation testing in all patients with T2DM. Further prospective, multicenter studies employing standardized diagnostic criteria and laboratory measurements are needed to establish the predictive validity and clinical utility of these biomarkers across diverse patient populations.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) has become a major contributor to chronic disease burden, disability, and premature mortality worldwide. The International Diabetes Federation (2025) estimated that 589 million adults aged 20–79 years were living with diabetes in 2024, representing 11.1% of the global adult population, or approximately one in nine adults. This number is projected to increase to 853 million by 2050. A similarly substantial burden has been observed in Indonesia, where the number of people living with diabetes increased from 5.7

million in 2000 to 20.4 million in 2024 and is projected to reach 28.6 million by 2050. Type 2 diabetes accounts for more than 90% of all diabetes cases, indicating that this increasing prevalence represents an expanding population at risk of vascular complications, including cardiovascular disease, stroke, diabetic kidney disease, retinopathy, neuropathy, and lower-extremity amputation. The World Health Organization (2024) reported that diabetes directly caused approximately 1.6 million deaths in 2021, while diabetes-related kidney disease accounted for an additional 530,000 deaths. Elevated blood glucose also contributed to approximately 11% of cardiovascular deaths worldwide. The magnitude of this burden underscores the importance of diabetes management strategies that extend beyond glycemic control to include the identification of pathophysiological abnormalities associated with vascular complications, particularly hemostatic disturbances that may remain undetected during routine clinical assessments.

Coagulopathy in patients with T2DM does not necessarily manifest as bleeding or prolonged coagulation times. In this context, hemostatic abnormalities may also include hypercoagulability, increased platelet reactivity, enhanced thrombin generation, elevated fibrinogen levels, and impaired fibrinolysis, collectively contributing to a prothrombotic state. Li et al., (2021) explained that hyperglycemia and insulin resistance promote platelet activation, alter coagulation factor concentrations and activities, and contribute to the formation of denser fibrin clots that are more resistant to fibrinolysis. Fibrinogen glycation, increased von Willebrand factor activity, elevated coagulation factors VII, VIII, XI, and XII, and impaired endogenous anticoagulant mechanisms may further shift the hemostatic balance toward thrombosis. Bryk-Wiązania and Undas (2021) additionally emphasized that increased plasminogen activator inhibitor-1 (PAI-1) and thrombin-activatable fibrinolysis inhibitor (TAFI) activity can suppress fibrin degradation, potentially prolonging thrombus persistence. These disturbances may be assessed using conventional coagulation parameters, including prothrombin time (PT), activated partial thromboplastin time (aPTT), the international normalized ratio (INR), and platelet count, alongside specialized biomarkers such as fibrinogen, D-dimer, PAI-1, and TAFI. Global hemostatic assays, including thromboelastography and thrombin generation assays, may provide additional information regarding coagulation dynamics. However, conventional PT and aPTT measurements do not reliably capture all aspects of diabetes-associated hypercoagulability. Variations in the selection of laboratory parameters, diagnostic criteria, and reference thresholds have therefore contributed to inconsistencies in the operational definition and reported prevalence of coagulopathy among patients with T2DM.

These differences in diagnostic definitions have been reflected in substantial variations in reported coagulopathy prevalence across clinical settings. Getu et al., (2022) investigated 357 patients with T2DM in Ethiopia and reported a coagulopathy prevalence of 26.6% (95% confidence interval [CI]: 22.1%–31.5%). Shortened PT was identified in 12.3% of patients, shortened aPTT in 8.7%, prolonged PT in 5.6%, prolonged aPTT in 3.9%, and thrombocytopenia in 5.3%. Similarly, Ebrahim et al., (2021) observed shorter PT values, lower INR values, and increased platelet distribution width and mean platelet volume among patients with T2DM

compared with healthy controls, although the magnitude of these abnormalities varied across laboratory parameters. In contrast, Labu et al., (2026) reported a coagulopathy prevalence of 98.96% among 96 patients with T2DM in Cameroon. Prolonged PT was observed in 98.96% of patients, shortened aPTT in 33.3%, thrombocytopenia in 28.1%, and hyperfibrinogenemia in 39.6%. The substantial difference between prevalence estimates of 26.6% and 98.96% should not be interpreted solely as evidence of biological variation between populations. Differences in laboratory reference intervals, diagnostic criteria, the number and types of parameters assessed, patient characteristics, medication exposure, complication status, and analytical procedures may contribute to these discrepancies. Consequently, the available prevalence estimates require systematic evaluation before meaningful comparisons or broader generalizations can be made.

The relationship between hemostatic abnormalities and glycemic control has also demonstrated inconsistent findings across studies. Habtu et al., (2024) compared 45 patients with good glycemic control and 45 patients with poor glycemic control in Ethiopia and identified statistically significant differences in PT and aPTT, whereas platelet counts did not differ significantly between groups. Selleh et al., (2023) reported more specific alterations in fibrinolytic regulation, demonstrating significantly elevated PAI-1 concentrations among patients with poor glycemic control. In contrast, TAFI, PT, aPTT, INR, and platelet counts showed no statistically significant differences between the glycemic control groups. At a reported PAI-1 cutoff of ≥ 161.70 pg/ μ L, elevated PAI-1 was associated with 13.71-fold higher odds of poor glycemic control, with an area under the receiver operating characteristic curve (AUC) of 0.85. Conversely, Labu et al., (2026) identified no statistically significant correlations between glycated hemoglobin (HbA1c) levels and the evaluated hemostatic parameters. Their analysis also revealed no significant differences in PT, aPTT, INR, platelet count, or fibrinogen concentrations between patients with HbA1c levels $\leq 7\%$ and those with levels $>7\%$. These contrasting findings suggest that the association between glycemic control and hemostatic dysfunction may depend on the specific biomarkers examined. Poor glycemic control may be associated with impaired fibrinolysis, particularly through increased PAI-1 activity, without necessarily producing consistent abnormalities in conventional coagulation tests or platelet counts.

The clinical relevance of diabetes-associated hemostatic abnormalities becomes particularly apparent when examining microvascular complications. Lim et al., (2021) investigated 147 patients with diabetes, including 120 patients with T2DM, using thromboelastography, calibrated automated thrombography, and overall hemostatic potential assays. Compared with 153 healthy controls, patients with diabetes exhibited higher maximum amplitude values on thromboelastography and increased overall hemostatic potential, indicating a more pronounced hypercoagulable profile, particularly among patients with T2DM and microvascular complications. Zhao et al., (2021) identified progressively elevated D-dimer concentrations across diabetic retinopathy severity categories, increasing from 0.39 mg/L among patients without retinopathy to 1.06 mg/L among those with nonproliferative diabetic retinopathy and 1.39 mg/L among those with proliferative diabetic retinopathy. Fibrinogen concentrations

similarly increased from 3.07 g/L to 4.38 g/L and 4.46 g/L across the corresponding groups. Zhuang et al., (2022) reported that the prevalence of diabetic peripheral neuropathy increased from 15.2% in the lowest D-dimer quartile to 42.7% in the highest quartile. Patients in the highest quartile had significantly greater adjusted odds of peripheral neuropathy than those in the lowest quartile (adjusted odds ratio [aOR] = 5.17). Furthermore, Merid et al., (2024) reported an overall prevalence of microvascular complications of 26.5% among patients with T2DM, including neuropathy in 13.2%, nephropathy in 12.4%, and retinopathy in 6.4%. Poor glycemic control was identified as one of the factors significantly associated with these complications. Collectively, these findings suggest that abnormalities in coagulation activation and fibrinolytic regulation may accompany the development or progression of diabetes-related microvascular complications.

Associations between hemostatic biomarkers and macrovascular complications further demonstrate that individual coagulation markers may differ in their prognostic relevance. Cheng et al., (2022) reported that patients with T2DM in the highest D-dimer quartile had 3.62-fold higher adjusted odds of a composite outcome comprising all-cause mortality, new cardiovascular events, or cardiovascular mortality compared with those in the lowest quartile. This association remained after adjustment for HbA1c, diabetes duration, hypertension, body mass index, lipid profile, smoking status, and treatment-related factors. These findings suggest that D-dimer, a biomarker reflecting cross-linked fibrin formation and degradation, may provide additional information for cardiovascular risk stratification. However, Brook et al., (2025) found no statistically significant difference in tissue factor pathway inhibitor (TFPI) concentrations between patients with diabetes who experienced atherothrombotic events and those who did not (40.1 vs. 34.4 ng/mL; $p = 0.35$). Similarly, Labu et al., (2026) reported no significant differences in D-dimer, fibrinogen, PT, aPTT, INR, or platelet counts between patients with T2DM with and without complications. These discrepancies indicate that no single hemostatic biomarker can adequately represent the full spectrum of coagulation abnormalities associated with diabetes. Although D-dimer has demonstrated associations with cardiovascular outcomes and peripheral neuropathy in certain populations, other markers, including TFPI, PT, and aPTT, have yielded statistically insignificant findings in different clinical settings.

The existing evidence remains fragmented across geographical regions, laboratory methods, operational definitions of coagulopathy, glycemic control classifications, and complication types. Getu et al., (2022) assessed coagulopathy using abnormalities in PT, aPTT, and platelet counts, whereas Selleh et al., (2023) investigated fibrinolytic biomarkers, including PAI-1 and TAFI. Zhao et al., (2021) focused on D-dimer and fibrinogen, while Lim et al., (2021) employed global hemostatic assays to characterize coagulation abnormalities. These methodological differences limit the direct comparability of prevalence estimates and highlight the need to classify findings according to diagnostic definitions and laboratory assessment methods. Furthermore, most available studies employed cross-sectional designs and recruited participants from single-center clinical settings, limiting the ability to establish temporal relationships among glycemic control, hemostatic abnormalities, and diabetes-related

complications. Potential confounding factors, including antiplatelet and anticoagulant therapy, obesity, hypertension, dyslipidemia, renal dysfunction, liver disease, acute infections, age, diabetes duration, and glucose-lowering medications, were not consistently controlled across studies. Differences in outcome classification further complicated evidence synthesis, as some investigations combined microvascular and macrovascular complications into broad categories, whereas others evaluated retinopathy, neuropathy, nephropathy, and cardiovascular outcomes separately. To date, no comprehensive synthesis has been identified that simultaneously evaluates coagulopathy prevalence, patterns of abnormal hemostatic parameters, associations with HbA1c or glycemic control categories, and relationships between coagulation biomarkers and microvascular and macrovascular complications among patients with T2DM.

A systematic literature review was therefore warranted to clarify whether variations in reported coagulopathy prevalence were primarily associated with patient characteristics, diagnostic definitions, or laboratory assessment methods. A structured synthesis could distinguish abnormalities detected through conventional coagulation testing from broader manifestations of hypercoagulability and impaired fibrinolysis, compare hemostatic profiles across glycemic control categories, and identify biomarkers most consistently associated with diabetic retinopathy, peripheral neuropathy, nephropathy, cardiovascular disease, and thrombotic events. Such an approach could also help explain inconsistencies in statistical associations across populations while critically evaluating the strength and clinical applicability of the available evidence. Accordingly, this systematic literature review aimed to synthesize evidence regarding the prevalence and patterns of coagulopathy among patients with T2DM, examine their associations with glycemic control, and evaluate the relationships between hemostatic abnormalities and diabetes-related microvascular and macrovascular complications.

METHOD

Study Design

This study employed a systematic literature review to identify, critically appraise, and synthesize primary studies examining the prevalence of coagulopathy and its associations with glycemic control and diabetes-related complications among patients with type 2 diabetes mellitus. The review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines for study identification, screening, eligibility assessment, and inclusion (Page et al., 2021). The search strategy was also reported in accordance with PRISMA-S recommendations to ensure transparency and reproducibility (Rethlefsen et al., 2021).

The findings from 32 eligible articles were synthesized descriptively and narratively without conducting a meta-analysis because of heterogeneity in study populations, coagulopathy definitions, laboratory parameters, glycemic control measures, and clinical outcomes. Methodological quality was critically appraised, and the extracted data were compared to identify consistent findings, discrepancies, and potential associations. Bibliometric analysis using VOSviewer complemented the narrative synthesis by examining keyword co-occurrence,

thematic clusters, temporal research trends, and term density. The review process included literature searching, study selection, data extraction, methodological quality assessment, narrative synthesis, and bibliometric mapping.

PICO Framework and Eligibility Criteria

The research question was formulated as follows: “What is the prevalence of coagulopathy, and how is it associated with glycemic control and complications in patients with type 2 diabetes mellitus?” The PICO framework was used to clarify the population, exposure, comparator groups, and outcomes analyzed. The intervention component was adapted to exposure because the study focused on exposure in the form of coagulation abnormalities, fibrinolytic disturbances, and platelet activity rather than on the administration of a therapeutic intervention.

Table 1. PICO Framework of the Study

Component	Description
Population	Adult patients diagnosed with type 2 diabetes mellitus
Intervention/Exposure	Coagulopathy or changes in hemostatic indicators, such as PT, INR, aPTT, fibrinogen, D-dimer, coagulation factors, fibrinolysis inhibitors, thrombin generation, thromboelastography, and platelet indicators
Comparison	Patients with good and poor glycemic control; patients with and without complications; patients with T2DM and healthy control groups
Outcome	Prevalence of coagulopathy, association of hemostatic indicators with HbA1c or other glycemic indicators, and association of coagulopathy with microvascular and macrovascular complications

Articles were included if they were published from 2021 up to the date of the final search; were primary human studies; involved adult patients with T2DM; assessed at least one indicator of coagulation, fibrinolysis, or platelet activity; and reported the prevalence of coagulopathy, its association with glycemic control, or its association with diabetes complications. Studies with mixed populations were eligible if results for the T2DM subgroup were available separately. Articles were also required to be available in full text through the publisher's website, PubMed Central, or a legitimate scientific repository. Publication languages were limited to English and Indonesian.

Table 2. Article Inclusion and Exclusion Criteria

Aspect	Inclusion criteria	Exclusion criteria
Publication	Published in 2021–2026, in English or Indonesian, and available in full text	Published before 2021, in other languages, or full text unavailable
Study type	Primary human studies presenting clinical patient data	Review articles, meta-analyses, editorials, case reports, conference abstracts, animal studies, or in vitro studies
Population	Adult patients with T2DM; mixed-population data may be used if T2DM results are available separately	Type 1 diabetes, gestational diabetes, diabetic ketoacidosis, or T2DM results cannot be separated
Variables	Assessment of coagulation, fibrinolysis, or platelet activity indicators together with indicators of glycemic control	No assessment of relevant hemostatic or glycemic-control indicators
Outcomes	Reports prevalence of coagulopathy or its association with glycemic control or T2DM complications	Irrelevant outcomes, coagulopathy primarily caused by another acute disease, or use of the same cohort data

Articles were excluded if they were literature reviews, systematic reviews, meta-analyses, editorials, commentaries, case reports, conference abstracts without full manuscripts, animal studies, or laboratory studies without patient data. Studies on type 1 diabetes, gestational diabetes, and diabetic ketoacidosis were excluded if they did not provide T2DM-specific results. Articles in which COVID-19, malignancy, trauma, surgery, or another acute disease was the primary cause of coagulation abnormalities were also excluded. Publications using the same cohort were checked based on author names, study site, data-collection period, and participant characteristics. When overlapping data were identified, the article with the most complete information was retained.

Search Strategy and Article Selection

The literature search covered the period from 2021 to 2026 using Europe PMC as the primary database. Additional searches were conducted through PubMed Central, the related articles feature, reference lists of relevant articles, and official publisher websites. The search strategy was constructed from three groups of terms: type 2 diabetes mellitus, coagulation or fibrinolytic disorders, and clinical outcomes. The main Boolean string used was:

(T2DM OR "type 2 diabetes") AND (coagulopathy OR coagulation) AND (HbA1c OR "glycemic control") AND complications

The search identified 488 records from databases and three additional articles through citation checking. A total of 491 titles and abstracts were screened, after which 361 records were excluded because they did not meet the population, exposure, design, or outcome criteria. Full texts were sought for 130 articles, but 48 articles could not be retrieved in full. Eighty-two articles underwent full-text assessment. At this stage, 50 articles were excluded because the population was not eligible, T2DM results could not be separated, hemostatic indicators were not reported, outcomes were irrelevant, primary data were insufficient, or overlapping cohorts were used. The final selection yielded 32 included articles.

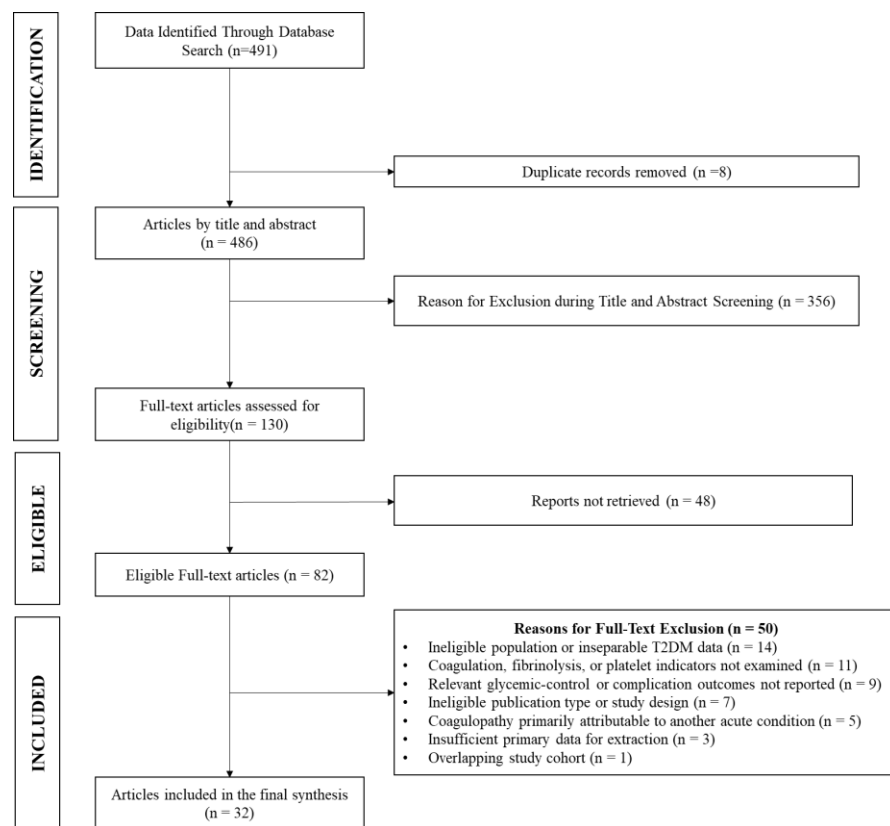


Figure 1. Flow Diagram of Article Selection Based on PRISMA 2020

Data Extraction and Analysis

Data were extracted using a structured form. Recorded data included author, publication year, country, study design, study setting, number of participants, age characteristics, T2DM duration, criteria for glycemic control, definition of coagulopathy, hemostatic parameters, type of complication, analytical method, main findings, and conclusions. Glycemic parameters included HbA1c, fasting blood glucose, random blood glucose, and estimated glucose disposal rate. Complications were grouped into retinopathy, nephropathy, peripheral neuropathy, autonomic neuropathy, diabetic foot, peripheral arterial disease, cardiovascular disease, and cardiovascular mortality.

Methodological quality was assessed using the Joanna Briggs Institute Critical Appraisal Tools according to study design, including checklists for analytical cross-sectional, case-control, cohort, and clinical-trial studies. Each item was rated as “yes,” “no,” “unclear,” or “not applicable.” Appraisal covered clarity of inclusion criteria, accuracy of exposure and outcome measurements, identification of confounding factors, control of confounding, and appropriateness of statistical analysis. Appraisal results were used to guide cautious interpretation and were not used as the sole basis for excluding articles.

Narrative synthesis was conducted across three analytical groups: prevalence and profile of coagulopathy, association between coagulopathy and glycemic control, and association between coagulopathy and T2DM complications. Each finding was entered into a comparison matrix to

assess the direction of association, statistical significance, the most frequently used indicators, consistent findings, and findings showing no association. Nonsignificant findings were retained so that the synthesis did not emphasize only positive results.

Bibliometric mapping was performed using VOSviewer version 1.6.21. Metadata consisting of titles, abstracts, keywords, authors, publication years, and DOIs from the 32 articles were prepared in a format readable by VOSviewer. The analysis used keyword co-occurrence with the full counting method and a minimum threshold of two occurrences. A thesaurus file was used to merge terms with the same meaning, such as “type 2 diabetes,” “type 2 diabetes mellitus,” and “T2DM,” and to remove generic terms that did not support interpretation.

VOSviewer results were presented as network visualization to show clusters and the strength of relationships among terms, overlay visualization to demonstrate shifts in themes according to the average publication year, and density visualization to depict the most frequently occurring terms. Node size indicates term frequency, lines indicate co-occurrence relationships, distance between nodes represents the closeness of relationships, and color indicates cluster or publication period. VOSviewer mapping was used as a complement to the narrative synthesis, while conclusions remained grounded in the content and methodological quality of the included articles.

RESULTS AND DISCUSSION

Characteristics and Methodological Quality of the Articles

This review analyzed 32 articles published between 2021 and 2024, with the most in 2022 (12; 37.5%) and 2023 (9; 28.1%). China contributed 22 articles (68.8%), Ethiopia 4 (12.5%), Poland 3 (9.4%), and Australia, Ghana, and Türkiye one each. Cross-sectional designs dominated (21; 65.6%), followed by case-control (6; 18.8%) and cohort studies (5; 15.6%). The largest clinical foci were coagulation and glycemic control without a specific complication and diabetic neuropathy (8 articles each), followed by cardiovascular outcomes (6), retinopathy (5), diabetic kidney disease (3), diabetic foot (1), and combined microvascular complications (1).

Based on the Joanna Briggs Institute tools, 23 articles (71.9%) were rated high quality and 9 (28.1%) moderate. Common limitations were the inability of cross-sectional designs to establish temporal sequence, limited control of confounding, single-hospital recruitment, and small samples. Two publications used the same 133 patients and were treated as two reports from one cohort. Fibrinogen was the most frequently used indicator (as concentration, FAR, FPR, or a thromboelastography parameter), alongside D-dimer, PT, aPTT, INR, platelet indices, TAFI, factor XI, FVIIa-AT complexes, thrombin generation, and fibrin clot properties. This variation broadens the picture of hemostatic disturbance but results in nonuniform definitions of coagulopathy.

Prevalence and Profile of Coagulopathy in T2DM

Prevalence could be derived only from articles that set abnormal cutoffs and reported the number of patients exceeding them; other articles presented mean differences, quartiles, correlations, or complication risks (Table 3).

Table 3. Prevalence and Profile of Hemostatic Abnormalities in Patients with T2DM

Indicator	Finding	Source
Overall coagulopathy (PT- and aPTT-based)	26.6% (95% CI 22.1–31.5)	Getu et al., (2022)
Shortened PT; shortened aPTT	12.3%; 8.7%	Getu et al., (2022)
Prolonged PT; prolonged aPTT	5.6%; 3.9% (95.0% and 92.8% corrected by mixing tests, suggesting factor deficiency)	Getu et al., (2022)
Factor XI above 120%	18.8%; associated with cardiovascular outcomes	Paszek et al., (2023)
Global assays (TEG-MA, OHP)	Higher than controls, indicating increased clot strength and fibrin-forming potential	Lim et al., (2021)
<i>FVIIa-AT complexes</i>	No difference from controls ($p = 0.30$)	Gastoł et al., (2024)

Getu et al., (2022) was the only article directly reporting overall coagulopathy prevalence (26.6%). This figure cannot be regarded as a cross-country prevalence because it came from a single hospital and used PT and aPTT as the basis for classification, and the factor XI figure (Paszek et al., 2023) is not equivalent to that definition. Lim et al., (2021) and Gastoł et al., (2024) also showed that a procoagulant state is not always reflected in a single test.

Association between Coagulopathy and Glycemic Control

Table 4. Association between Hemostatic Indicators and Glycemic Control

Hemostatic indicator	Association with glycemic indicator	Source
PT and aPTT	Longer with poor HbA1c control; platelet count did not differ	Habtu et al., (2024)
PT, aPTT, and INR	Negative correlation with fasting glucose	Ebrahim et al., (2021)
PAI-1 and TAFI	PAI-1 higher with poor HbA1c control; TAFI did not differ	Selleh et al., (2023)
aPTT and fibrinogen	eGDR correlated positively with aPTT and negatively with fibrinogen, mainly in men	Li et al., (2022)
<i>FVIIa-AT complexes</i>	Highest quartile had 27.4% higher HbA1c and 36.4% higher fasting glucose; HbA1c remained associated after adjustment	Gastoł et al., (2024)
<i>D-dimer</i>	Positive correlation with HbA1c; predicted cardiovascular events after adjustment	Cheng et al., (2022)
PDW	Positive correlation with HbA1c ($r = 0.334$; $p < 0.001$)	Kucuk et al., (2022)
Blood viscosity and fibrinogen	Weak direct correlation of viscosity with HbA1c; fibrinogen correlated more strongly	Sun et al., (2022)
Factor XI; TEG, thrombin generation, OHP	No significant or consistent association with HbA1c	Paszek et al., (2023); Lim et al., (2021)

Table 4 shows a more consistent association between poor glycemic control and increased PAI-1, D-dimer, PDW, fibrinogen, and FVIIa-AT complexes, whereas PT and aPTT moved in differing directions: Habtu et al., (2024) found prolongation with poor control, while Ebrahim et al., (2021), Li et al., (2022), and Selleh et al., (2023) supported shortened coagulation times

or increased inhibition of fibrinolysis. Factor XI and global assays showed no direct association with HbA1c, so HbA1c alone does not explain the variation in hemostasis in T2DM.

Association between Coagulopathy and T2DM Complications

Table 5. Association between Hemostatic Indicators and T2DM Complications
(condensed)

Complication	Hemostatic indicator	Main finding	Source
Cardiovascular events and mortality	<i>D-dimer</i> ; Dmax; thrombin	D-peak Highest D-dimer quartile OR 3.62; high D-Dmax and peak thrombin HR 5.43 and 5.65	Cheng et al., (2022); Bryk et al., (2021)
Infarction, stroke, or cardiovascular death	Factor XI > 120%	HR 10.94 for the composite outcome and 7.11 for cardiovascular death	Paszek et al., (2023)
Post-PCI MACCE; in-stent restenosis	FAR; PDW and fibrinogen	High FAR with diabetes gave the highest five-year risk; PDW and fibrinogen independently predicted restenosis	Wang et al., (2022); Chai et al., (2022)
Arterial stiffness	FAR	Associated with baPWV, particularly in men	Chen et al., (2023b)
Diabetic peripheral neuropathy (DPN)	Fibrinogen; <i>D-dimer</i> ; k value; FAR	Fibrinogen OR 1.172 (risk rose sharply near 3.75 g/L); D-dimer prevalence 42.7% in the highest quartile (OR 5.17); k value AUC 0.873; FAR predicted DPN better than fibrinogen or HbA1c	Xie et al., (2024); Zhuang et al., (2022c); Zhuang et al., (2022b); Ban et al., (2023)
Autonomic neuropathy; cognitive impairment in DPN	FAR and FPR; fibrinogen	Independent factors for cardiac autonomic neuropathy (prevalence 20.98%); fibrinogen predicted cognitive impairment (OR 2.674)	Zhao et al., (2023); Zhuang et al., (2022a)
Retinopathy	HbA1c, <i>D-dimer</i> , fibrinogen; FAR; FC-MLR; alpha angle and k value	All three rose from NDR to PDR; FAR independent (AUC 0.708); FC-MLR predicted occurrence (OR 6.123); alpha angle and k value AUC 0.897 and 0.859 but weaker for advanced stages	Zhao et al., (2021); Chen et al., (2023a); Huang et al., (2021); Zhuang et al., (2023)
Diabetic kidney disease (DKD)	FAR; fibrinogen with urinary α 1-MG/Cr; TAFI	FAR more discriminative than fibrinogen or albumin alone; combined biomarkers AUC 0.972 for overall DKD but 0.611 for advanced DKD; TAFI OR 15.72	Wang et al., (2021); Pan et al., (2022); Huang et al., (2023)
Diabetic foot	Fibrinogen, alpha angle, k value	All associated with occurrence and Wagner grade	Zhang et al., (2022)
Combined micro- and macrovascular complications	MPV, PDW, P-LCR; TEG-MA, velocity index, OHP	Platelet indices higher and independently associated; combined global assays C-statistic 0.82	Taderegew et al., (2021); Lim et al., (2021)

The most consistent associations involved fibrinogen and its derivatives: FAR was associated with retinopathy, diabetic kidney disease, peripheral and cardiac autonomic neuropathy, arterial stiffness, and post-PCI prognosis. D-dimer, factor XI, thrombin generation, and fibrin clot properties were mainly associated with cardiovascular outcomes, while the k value and alpha angle discriminated reasonably well in neuropathy and retinopathy. Although the overall direction supported a prothrombotic state, negative findings remained for TAFI by glycemic control, factor XI by HbA1c, FVIIa-AT complexes versus controls, and combined fibrinogen markers in advanced DKD.

Bibliometric Mapping Using VOSviewer

The network visualization placed T2DM at the center, linked to inflammation, coagulation indexes, fibrinogen, and microvascular complications, forming a T2DM–inflammation–fibrinogen axis that branches toward neuropathy, retinopathy, diabetic kidney disease, and cardiovascular outcomes. The cardiovascular branch connects through D-dimer, fibrinogen, factor XI, and platelet indicators, and the neuropathy branch is dense around DPN, the k value, fibrinogen, and platelet indices. The overlay visualization showed earlier themes (platelet indices, fibrinogen concentrations, D-dimer), a middle period centered on T2DM, inflammation, fibrinogen, k value, and DPN, and recent themes (diabetic kidney disease, baPWV, influencing factors, FVIIa-AT complexes) reflecting a shift toward biomarker ratios, arterial stiffness, genetic factors, and tissue factor activation. The density visualization showed three concentration areas: T2DM with inflammation and coagulation indexes; fibrinogen, k value, and DPN; and retinopathy with fibrinogen concentrations and D-dimer, with diabetic kidney disease forming a smaller area. Platelet indices sat at the periphery, and a separated FAR label indicates a need to harmonize terms in the thesaurus file.

Coagulopathy in Type 2 Diabetes Mellitus

The synthesis shows that coagulopathy in T2DM is not limited to prolonged clotting times but includes accelerated thrombin generation, increased fibrinogen, platelet activation, and impaired fibrinolysis. The PT- and aPTT-based prevalence of 26.6%, with shortened PT (12.3%) and aPTT (8.7%) more common than prolonged values (Getu et al., 2022), reflects only basic coagulation tests; global assays can detect increased thrombin generation even when routine tests are not abnormal in the same direction (Lim et al., 2021). The factor XI figure (18.8%) represents a specific procoagulant phenotype and cannot be added to this estimate (Paszek et al., 2023). Biologically, hyperglycemia increases tissue factor expression, enhances platelet reactivity, and suppresses fibrin breakdown, producing denser clots more resistant to lysis (Li et al., 2021), while fibrinogen glycation, insulin resistance, oxidative stress, and advanced glycation end products further alter clot structure and reduce endothelial antithrombotic function (Borghi et al., 2025; Gallo & Savoia, 2024). Reported prevalence therefore depends strongly on the operational definition and test used, and reliance on a single parameter risks underestimating the prothrombotic burden.

Glycemic Control, Fibrinogen, Platelets, and Impaired Fibrinolysis

Poor glycemic control was more consistently associated with markers of coagulation activation and impaired fibrinolysis than with the direction of PT or aPTT changes. PAI-1 was higher with poor control (Selleh et al., 2023), and higher HbA1c was independently associated with FVIIa–antithrombin complexes (Gastoł et al., 2024). Increased PAI-1 keeps fibrin in the circulation longer (Bryk-Wiązania & Undas, 2021), and chronic hyperglycemia promotes a hyperreactive platelet phenotype (Sharma et al., 2025), which helps explain why platelet indices, fibrinogen, D-dimer, and FAR often change with HbA1c even when platelet counts remain normal. Inconsistent PT and aPTT findings (Ebrahim et al., 2021; Habtu et al., 2024) may arise from diabetes duration, antithrombotic therapy, liver and kidney function, laboratory reagents, and HbA1c cutoffs; HbA1c also reflects only two to three months of average glucose and should be interpreted together with cardiovascular and renal factors and medications (Davies et al., 2022). Platelet indices are not yet suitable as stand-alone diagnostic tools (Zvetkova et al., 2024).

Hemostatic Biomarkers between Microvascular Damage and Cardiovascular Risk

In the cardiovascular domain, the highest D-dimer quartile, denser fibrin clots with slower lysis, higher peak thrombin, and elevated factor XI were associated with cardiovascular events or mortality (Cheng et al., 2022; Bryk et al., 2021; Paszek et al., 2023), supporting the view that vascular risk in T2DM arises from lysis-resistant fibrin and persistent coagulation activation as well as atherosclerosis. Guidelines nevertheless continue to emphasize control of blood pressure, lipids, glucose, and kidney function rather than D-dimer testing without a specific indication (American Diabetes Association Professional Practice Committee, 2024a). Among microvascular complications, fibrinogen was the most frequent link: the k value and alpha angle were associated with neuropathy and retinopathy (Zhuang et al., 2022; Zhuang et al., 2023), fibrinogen with the α_1 -microglobulin/creatinine ratio improved identification of DKD (Pan et al., 2022), and fibrinogen function was associated with diabetic foot severity (Zhang et al., 2022). Endothelial damage, platelet activation, and fibrinolytic imbalance integrate inflammation, ischemia, and microthrombosis and may aggravate impaired perfusion of the retina, nerves, and kidneys (Babel & Dandekar, 2021; Gallo & Savoia, 2024; Alsharidah, 2022).

Clinical Implications and Study Limitations

The results support a tiered approach to testing. PT, aPTT, platelet count, and fibrinogen may be considered in patients with poor glycemic control, kidney disease, vascular symptoms, prior thrombosis, foot ulcers, or planned invasive procedures, guided by clinical indications. D-dimer is better reserved for suspected thromboembolism or selected stratification because it rises with age, inflammation, and kidney dysfunction. FAR, TAFI, factor XI, FVIIa–antithrombin complexes, and thrombin generation are promising but not sufficiently standardized for routine use, and they do not replace eGFR and albuminuria monitoring or scheduled eye, neurological, and foot screening (Kidney Disease: Improving Global Outcomes Diabetes Work Group, 2022; American Diabetes Association Professional Practice Committee,

2024b).

The strengths of this review are the synthesis of 32 articles and the VOSviewer mapping. Its limitations are the dominance of cross-sectional designs, which limits causal inference, differing definitions of coagulopathy, overlap between two reports from the same 133-patient cohort (Bryk et al., 2021; Paszek et al., 2023), and regional concentration of evidence, so biomarker cutoffs should be applied cautiously to other populations. Future studies should use standardized definitions, multicenter cohorts, and measures of glucose variability alongside HbA1c, and should test whether fibrinogen, D-dimer, platelet indices, or global assays improve prediction beyond standard risk factors. Coagulopathy is relatively common and associated with glycemic control and T2DM complications, but its clinical use should rest on the patient's overall risk profile rather than a single laboratory result.

CONCLUSION

The synthesis of 32 articles indicated that patients with type 2 diabetes mellitus (T2DM) frequently exhibited a hypercoagulable state characterized by alterations in coagulation pathways, fibrinolytic activity, and platelet function. However, the prevalence of coagulopathy could not be expressed as a single pooled estimate because of substantial heterogeneity in diagnostic definitions, laboratory cutoff values, and hemostatic parameters across studies. One study reported a 26.6% prevalence of coagulation abnormalities, while elevated coagulation factor XI activity exceeding 120% was identified in 18.8% of patients. Alterations in prothrombin time (PT), activated partial thromboplastin time (aPTT), fibrinogen, D-dimer, thrombin generation, fibrinolytic inhibitors, and platelet indices were observed, with several markers showing more pronounced abnormalities among patients with poor glycemic control. These hemostatic disturbances were also associated with diabetic retinopathy, diabetic kidney disease, peripheral neuropathy, arterial stiffness, cardiovascular disease, and diabetic foot complications, suggesting potential links between coagulation dysfunction and diabetes-related vascular injury.

From a clinical perspective, these findings suggested that hemostatic biomarkers might provide supplementary information for identifying patients with T2DM at increased risk of vascular complications. Risk assessment should integrate glycemic control indicators, particularly glycated hemoglobin (HbA1c), with selected coagulation and fibrinolytic parameters, including fibrinogen, D-dimer, PT, aPTT, thrombin generation, and platelet indices, according to individual clinical circumstances. Nevertheless, the available evidence remained insufficient to support routine coagulation testing for all patients with T2DM. Selective testing may be considered when clinically indicated, particularly in patients with suspected thrombotic or hemostatic abnormalities, rather than solely on the basis of poor glycemic control or diabetes duration.

This review had several limitations, including the predominance of cross-sectional studies, geographical concentration of the available evidence, differences in participant characteristics, inconsistent definitions of coagulopathy, and variations in laboratory methods and diagnostic

thresholds. The absence of a meta-analysis also precluded the calculation of pooled prevalence estimates and effect sizes. Future research should prioritize prospective, multicenter cohort studies employing standardized diagnostic criteria, longitudinal hemostatic measurements, and comprehensive adjustment for potential confounding factors. Further investigations should also evaluate the predictive performance, incremental clinical utility, and cost-effectiveness of hemostatic biomarkers before their incorporation into routine risk stratification for diabetes-related complications.

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