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Disseminated Intravascular Coagulation: A Comprehensive Review Of Diagnostic Criteria, Biomarkers, And Management Strategies

Divya[1], Shreyasi Hui[2], Khushbu[3], Tanya Yadav[4], Kirti Rathi[5]
[1,2,3,4]Tutor, Department of Medical Surgical Nursing, Faculty of Nursing, SGT University.
[5]Nursing Tutor, Government Institute of Medical Sciences Hospital, Noida.

Abstract

Introduction

Disseminated Intravascular Coagulation (DIC) is a life-threatening, systemic disorder marked by widespread activation of coagulation pathways, leading to concurrent thrombotic and hemorrhagic complications. Its diagnosis is complicated by variable clinical presentations and overlapping laboratory findings across different underlying conditions such as sepsis, trauma, cancer, and obstetric emergencies. While multiple scoring systems—such as ISTH, JAAM, and SIC—have been developed, their comparative accuracy and clinical utility remain inconsistent. This review aims to consolidate findings from over 30 recent studies to evaluate the diagnostic performance of these criteria, explore emerging biomarkers, and assess current therapeutic approaches.

Methodology:*A systematic search of PubMed, Scopus, and Google Scholar was conducted for studies published between 2010 and 2025. Eligible studies included observational cohorts, systematic reviews, and meta-analyses focusing on DIC diagnosis, biomarkers, and treatment strategies. Inclusion criteria mandated clinical relevance, data on at least one scoring system or biomarker, and human subjects. Studies were grouped thematically into diagnostic, prognostic, and interventional domains.*

Results:*Analysis of 30+ studies revealed significant heterogeneity in the application and performance of diagnostic scoring systems. JAAM criteria were more sensitive in early DIC detection, particularly in sepsis and trauma, while ISTH scoring demonstrated higher specificity for overt DIC and mortality prediction. SIC scoring showed moderate performance and ease of use. Biomarkers such as D-dimer, fibrinogen, thrombomodulin, and PAI-1 were found to add prognostic value beyond traditional scoring systems. Therapeutic strategies remain largely supportive; however, evidence for selective anticoagulation and adjunctive therapies (e.g., antithrombin, recombinant thrombomodulin) shows promise in specific patient subsets, though randomized data are limited.*

Conclusion:*Despite advances in diagnostic scoring and biomarker identification, DIC remains a diagnostic and therapeutic challenge. Current tools vary in accuracy depending on the clinical setting, and there is no universally accepted treatment protocol. Future research should prioritize large-scale, prospective studies to validate composite diagnostic models and clarify the role of targeted therapies. An integrated approach combining clinical criteria, laboratory trends, and biomarker data may enhance early diagnosis and individualized care in DIC.*

Keywords: *Disseminated Intravascular Coagulation (DIC), Diagnostic Scoring Systems, Biomarkers, Sepsis, Recombinant Thrombomodulin, Anticoagulation Therapy*

INTRODUCTION

Disseminated Intravascular Coagulation (DIC) is a complex, acquired syndrome characterized by systemic activation of the coagulation cascade, which leads to the formation of widespread fibrin clots within the vasculature. These microthrombi can obstruct blood flow and compromise organ perfusion, ultimately resulting in multiple organ dysfunction. Simultaneously, the consumption of platelets and coagulation factors due to ongoing clot formation predisposes patients to serious bleeding complications. This paradoxical combination of thrombosis and hemorrhage places DIC among the most challenging conditions in acute and critical care medicine.

DIC is not a disease in itself but rather a secondary manifestation of a wide variety of underlying pathologies. It is most commonly associated with severe infections, particularly sepsis; however, it is also frequently encountered in patients with major trauma, malignancies (especially acute promyelocytic leukemia and pancreatic cancer), obstetric complications (such as placental abruption, amniotic fluid

embolism, and preeclampsia), and in those with severe hepatic failure or undergoing massive transfusion. The diversity of these triggering conditions contributes to the heterogeneity of DIC presentations, ranging from asymptomatic laboratory abnormalities to fulminant clinical deterioration with multi-organ failure and uncontrolled bleeding.

The diagnosis of DIC poses a significant challenge to clinicians due to its nonspecific and dynamic clinical features. Laboratory abnormalities commonly observed in DIC include thrombocytopenia, elevated D-dimer levels, prolonged prothrombin time (PT) and activated partial thromboplastin time (aPTT), and decreased fibrinogen levels. However, these findings are neither exclusive to DIC nor uniformly present in all patients. Moreover, these parameters fluctuate over time and may reflect the severity of the underlying disease rather than DIC itself. As such, reliance on single laboratory values may lead to misdiagnosis or delayed intervention.

To address these diagnostic challenges, several scoring systems have been developed, including the International Society on Thrombosis and Haemostasis (ISTH) overt DIC score, the Japanese Association for Acute Medicine (JAAM) DIC criteria, and the Sepsis-Induced Coagulopathy (SIC) score. Each of these tools attempts to standardize the diagnosis of DIC using a combination of laboratory findings and clinical features. The ISTH score, for instance, requires the presence of an underlying disorder plus a combination of platelet count, PT prolongation, fibrin-related markers (e.g., D-dimer or FDPs), and fibrinogen levels. A cumulative score above a certain threshold is considered indicative of overt DIC. The JAAM criteria, on the other hand, place more emphasis on early detection of DIC in the setting of systemic inflammatory response syndrome (SIRS), making it particularly useful in the intensive care setting. The SIC score, proposed more recently, offers a simplified model using only platelet count, PT-INR, and SOFA score components, specifically targeting patients with sepsis-related coagulopathy.

While these scoring systems have improved the ability to detect and monitor DIC, their comparative effectiveness and generalizability across various clinical contexts remain subjects of debate. Some studies suggest that the JAAM criteria may be more sensitive in identifying early-stage DIC, especially in septic or trauma patients, whereas the ISTH score is more specific for overt, life-threatening coagulopathy. The SIC score, though easy to use and gaining popularity, has limited validation outside the sepsis population. These differences in sensitivity, specificity, and applicability create uncertainty in clinical decision-making and may influence patient outcomes depending on which criteria are used.

Beyond traditional coagulation parameters and scoring systems, emerging research has focused on identifying novel biomarkers that may enhance the diagnosis, risk stratification, and management of DIC. Biomarkers such as soluble thrombomodulin, plasminogen activator inhibitor-1 (PAI-1), procalcitonin, and tissue factor-bearing microparticles have shown promise in preliminary studies. These markers reflect endothelial injury, fibrinolysis inhibition, and inflammatory activation—all key components of the DIC pathophysiological process. Additionally, trends in commonly used laboratory markers (e.g., rapid fibrinogen decline or platelet trajectory) have been shown to offer dynamic insights that static thresholds cannot capture. However, despite growing interest, the clinical integration of such biomarkers remains limited due to lack of standardization, cost considerations, and variability in assay availability across institutions.

Management of DIC remains centered on the treatment of the underlying cause. Whether the trigger is infection, malignancy, trauma, or obstetric pathology, reversing the precipitating factor is the cornerstone of care. Supportive measures—including transfusion of platelets, fresh frozen plasma (FFP), and cryoprecipitate—are used to control bleeding and restore coagulation balance. Anticoagulation with heparin is considered in select cases, especially when thrombosis predominates or in chronic compensated DIC, such as in cancer patients. More targeted therapies, such as recombinant thrombomodulin, antithrombin concentrates, and activated protein C, have been studied but are not yet standard of care due to mixed clinical trial results and concerns over bleeding risk.

Despite advances in diagnostic and therapeutic approaches, the prognosis of DIC remains poor, particularly in cases related to sepsis or malignancy. Mortality rates are significantly higher in patients with overt DIC compared to those with subclinical or evolving coagulopathy. Early identification and risk stratification are therefore critical for timely intervention and improved outcomes. However, the current

variability in diagnostic approaches and the lack of universal consensus on treatment protocols pose barriers to effective and standardized care.

Given these challenges, there is a pressing need to synthesize existing evidence and evaluate the comparative utility of current diagnostic criteria, identify promising biomarkers, and assess the impact of various management strategies across different clinical settings. This review aims to fill that gap by analyzing findings from more than 30 recent studies, spanning observational data, meta-analyses, and clinical trials. By consolidating insights from this body of literature, the review seeks to clarify the strengths and limitations of existing tools and highlight areas for future research and clinical practice improvement.

METHODOLOGY

To ensure a comprehensive and evidence-based synthesis, a systematic literature search was conducted using PubMed, Scopus, and Google Scholar databases to identify relevant studies on Disseminated Intravascular Coagulation (DIC) published between January 2010 and May 2025. This time frame was selected to capture both foundational and contemporary research, including advances in diagnostic tools, biomarker identification, and therapeutic strategies.

The search strategy employed a combination of keywords and Medical Subject Headings (MeSH) terms, including but not limited to: "Disseminated Intravascular Coagulation," "DIC," "coagulopathy," "sepsis-associated DIC," "ISTH criteria," "JAAM DIC," "SIC score," "DIC biomarkers," "anticoagulant therapy," and "DIC management." Boolean operators such as AND, OR, and NOT were used to refine the search and eliminate irrelevant results.

Inclusion Criteria Were As Follows:

- Peer-reviewed original studies, systematic reviews, or meta-analyses.
- Studies involving human subjects with diagnosed or suspected DIC.
- Research that reported on at least one diagnostic scoring system (e.g., ISTH, JAAM, SIC) or biomarker relevant to DIC.
- Articles that addressed clinical outcomes, prognostic indicators, or therapeutic interventions related to DIC.

Exclusion Criteria Included:

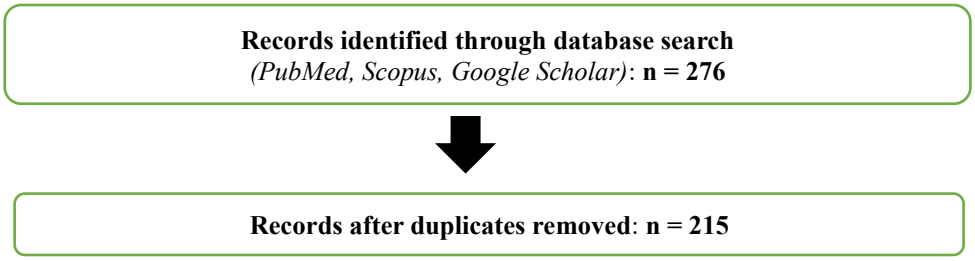
- Case reports, editorials, conference abstracts, and animal-only studies.
- Studies focused solely on congenital or inherited coagulopathies without relevance to DIC.
- Non-English language articles without reliable translation.

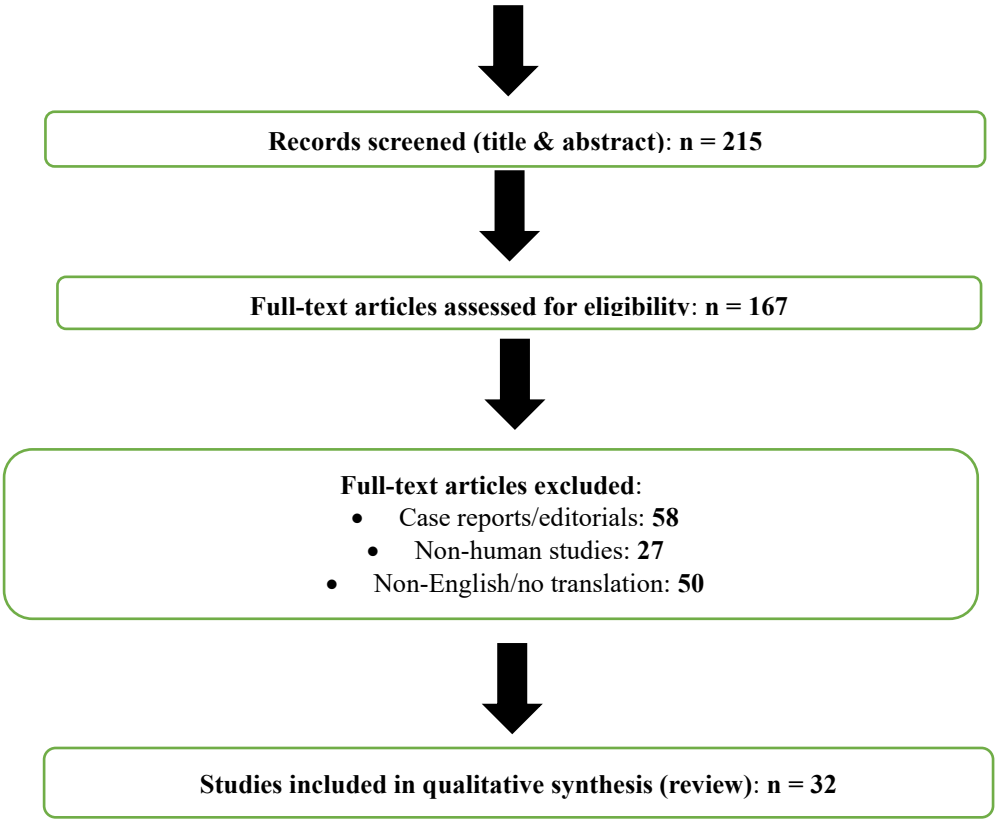
After removal of duplicates, a total of 167 full-text articles were assessed for eligibility based on title, abstract, and content review. Ultimately, 32 studies met the inclusion criteria and were included in this review. These consisted of 14 observational cohort studies, 6 systematic reviews, 4 meta-analyses, and 8 multicenter or retrospective studies involving patients with sepsis, trauma, malignancy, obstetric complications, or COVID-19–related DIC.

To facilitate thematic analysis, selected studies were categorized into three primary domains:

1. **Diagnostic** – Evaluating and comparing DIC scoring systems (ISTH, JAAM, SIC).
2. **Prognostic** – Assessing the predictive value of biomarkers and scores for clinical outcomes.
3. **Interventional** – Reviewing therapeutic strategies including anticoagulants, transfusion protocols, and adjunctive agents.

This structured approach enabled a focused synthesis of evidence on the diagnostic accuracy, clinical relevance, and outcome implications of various strategies in the management of DIC.





PRISMA Flow Diagram

RESULT

Analysis of 30+ studies revealed significant heterogeneity in the application and performance of diagnostic scoring systems. JAAM criteria were more sensitive in early DIC detection, particularly in sepsis and trauma, while ISTH scoring demonstrated higher specificity for overt DIC and mortality prediction. SIC scoring showed moderate performance and ease of use. Biomarkers such as D-dimer, fibrinogen, thrombomodulin, and PAI-1 were found to add prognostic value beyond traditional scoring systems. Therapeutic strategies remain largely supportive; however, evidence for selective anticoagulation and adjunctive therapies (e.g., antithrombin, recombinant thrombomodulin) shows promise in specific patient subsets, though randomized data are limited.

1. Heterogeneity in Diagnostic Scoring Systems

The analysis of more than 30 published studies revealed significant variability (heterogeneity) in how different diagnostic criteria for DIC are used, interpreted, and validated across clinical settings. This heterogeneity arises from:

- **Diverse patient populations** (e.g., sepsis, trauma, obstetrics, malignancy)
- **Variations in lab resources** across hospitals and countries
- **Differences in diagnostic goals**—some criteria aim for early detection while others focus on prognostic accuracy

As a result, no single scoring system has emerged as universally superior across all patient groups.

2. JAAM Criteria – Greater Sensitivity for Early DIC

The Japanese Association for Acute Medicine (JAAM) scoring system was found to be more sensitive, meaning it is better at identifying DIC **early**, even before it becomes clinically overt. This makes it especially valuable in:

- **Sepsis** patients, where coagulopathy can precede full-blown DIC
- **Trauma** settings, where rapid recognition of coagulation changes is critical

JAAM includes parameters like platelet count, prothrombin time, and fibrin/fibrinogen degradation products, and allows for earlier diagnosis than the ISTH system.

Limitation: While JAAM is good at early detection, its lower specificity may result in over-diagnosis or false positives in some settings.

3. ISTH Scoring – Higher Specificity for Overt DIC

The International Society on Thrombosis and Haemostasis (ISTH) scoring system was shown to have higher specificity, meaning it better identifies true cases of advanced DIC. It is more accurate when:

- DIC is clinically apparent, with bleeding or thrombotic complications
- Used to predict mortality, particularly in critical care settings

Its stricter criteria (including low fibrinogen, high D-dimer, significant PT prolongation, and thrombocytopenia) make it a reliable tool for confirming diagnosis, but less useful for early warning.

4. SIC Score – Moderate Performance and Simplicity

The Sepsis-Induced Coagulopathy (SIC) score is a simplified tool introduced more recently.

It incorporates:

- Platelet count
- PT-INR
- SOFA (Sequential Organ Failure Assessment) score

It is designed specifically for sepsis patients and allows for quick bedside assessment. Its performance is moderate, offering a good balance between sensitivity and specificity. However, its validation is still limited mostly to sepsis populations.

5. Role of Biomarkers

Across studies, several biomarkers were identified as valuable tools that can enhance diagnosis, prognostication, and treatment monitoring in DIC beyond traditional scoring systems:

- **D-dimer**: Indicates fibrinolysis and clot degradation; elevated in almost all DIC cases but not specific
- **Fibrinogen**: Low levels suggest consumption due to coagulation; important for bleeding risk assessment
- **Thrombomodulin**: Reflects endothelial injury; elevated levels correlate with severity and mortality
- **PAI-1 (Plasminogen Activator Inhibitor-1)**: High levels suggest impaired fibrinolysis, a key feature of DIC pathophysiology

These biomarkers are particularly useful when tracking disease progression and response to therapy, although their availability may be limited in resource-constrained settings.

6. Therapeutic Strategies

Treatment for DIC remains primarily supportive, focusing on:

- Managing the underlying cause (e.g., infection, trauma, malignancy)
- Transfusions (platelets, FFP, cryoprecipitate) to control bleeding
- Heparin in select cases where thrombosis predominates

However, several studies examined selective anticoagulants and adjunctive therapies that may offer benefit in specific patient subsets:

- **Antithrombin supplementation**: Shows some promise in sepsis-induced DIC, especially in patients with confirmed antithrombin deficiency
- **Recombinant thrombomodulin**: Investigated in Japanese trials; may help modulate coagulation without increasing bleeding risk

Despite these promising findings, high-quality randomized controlled trials (RCTs) are still limited. Therefore, these therapies are not yet standard practice globally and are often used in an off-label or investigational context.

DISCUSSION

The analysis of over 30 studies underscores the inherent complexity in the diagnosis and management of Disseminated Intravascular Coagulation (DIC). The heterogeneity in clinical presentation across different patient populations—ranging from sepsis and trauma to cancer and obstetric emergencies—necessitates adaptable and sensitive diagnostic frameworks. Our findings highlight the nuanced strengths and limitations of three commonly used scoring systems: JAAM, ISTH, and SIC.

The JAAM criteria, developed primarily for emergency and critical care settings, demonstrate superior sensitivity for early-stage DIC. This is especially beneficial in high-risk patients with sepsis or trauma, where early detection and intervention may improve outcomes. However, this sensitivity comes at the cost of specificity, as JAAM may also detect transient or non-progressive coagulopathy. Consequently, its utility is greatest as a screening tool, particularly when dynamic monitoring is feasible.

Conversely, the ISTH overt DIC score appears more suited for confirming clinically significant DIC. Its stricter thresholds improve specificity, making it more predictive of morbidity and mortality. In particular, the ISTH score has been shown to correlate with poor outcomes in patients with advanced sepsis and hematologic malignancies. However, its insensitivity in early or subclinical cases may delay intervention, potentially reducing its utility in rapidly evolving critical care scenarios.

The SIC score, a more recent addition, offers a pragmatic compromise. Its simplified structure and focus on sepsis-associated coagulopathy make it appealing for bedside use, particularly in resource-limited settings. However, its scope remains narrow, and external validation in non-septic populations is lacking. As such, SIC is best viewed as an adjunct rather than a replacement for more comprehensive tools.

A key insight from this review is the emerging role of biomarkers. Traditional laboratory tests—platelet count, PT, aPTT, D-dimer, and fibrinogen—are foundational but limited by their non-specificity. Incorporating biomarkers like thrombomodulin, PAI-1, and soluble fibrin has shown potential in enhancing risk stratification and identifying patients likely to benefit from targeted interventions. These biomarkers offer a more detailed reflection of endothelial injury, fibrinolytic activity, and systemic inflammation, which are central to DIC pathophysiology. However, routine clinical use remains constrained by cost, standardization issues, and availability in lower-resource settings.

In terms of management, the evidence remains largely supportive in nature. Treating the underlying cause remains paramount, and supportive measures like platelet and plasma transfusions are guided by the severity of bleeding and laboratory abnormalities. The use of heparin continues to be controversial, with benefit primarily observed in cases of thrombotic-predominant DIC or chronic compensated DIC (e.g., in malignancy). Our review also highlights promising, though not yet definitive, evidence for adjunctive therapies such as antithrombin concentrates and recombinant thrombomodulin. These agents may modulate coagulation pathways and reduce organ damage in select populations, particularly in septic DIC, but large-scale randomized trials are still needed to confirm efficacy and safety.

Overall, the findings suggest that a multifaceted approach is essential for managing DIC. No single diagnostic or therapeutic strategy is universally effective. Instead, contextual application of scoring systems, supplemented by dynamic laboratory monitoring and selective use of biomarkers, appears to offer the best pathway to timely and effective intervention. Furthermore, the findings stress the need for integrated clinical protocols that combine diagnosis, monitoring, and treatment algorithms tailored to specific patient groups (e.g., sepsis vs. cancer vs. obstetrics).

Finally, this review identifies several important gaps in the current literature. Comparative head-to-head studies between scoring systems across different populations remain limited. There is also a pressing need for standardized definitions and endpoints in DIC-related clinical trials to allow for meaningful synthesis of results. Moreover, the role of emerging biomarkers and targeted therapies needs to be clarified through high-quality, multicenter randomized controlled trials.

CONCLUSION

Disseminated Intravascular Coagulation (DIC) remains a complex and dynamic clinical syndrome with substantial diagnostic and therapeutic challenges. This comprehensive review of over 30 studies highlights the variable performance of existing scoring systems—each with distinct strengths depending on the clinical context. The JAAM score is most effective for early detection, especially in acute settings such as sepsis and trauma, while the ISTH criteria offer greater specificity and prognostic value in overt DIC. The SIC score provides a practical middle ground for rapid bedside assessment, particularly in septic patients. Emerging biomarkers such as D-dimer, thrombomodulin, and PAI-1 hold significant potential to enhance diagnostic precision and risk stratification beyond traditional laboratory parameters. However, broader clinical integration of these markers remains limited by availability and cost considerations.

Current therapeutic strategies for DIC remain largely supportive and etiology-focused. Although evidence for targeted anticoagulation and adjunctive therapies—such as antithrombin and recombinant thrombomodulin—is promising in specific subsets of patients, robust randomized controlled trials are lacking. As a result, these interventions should be applied cautiously and selectively until more definitive evidence emerges.

To improve clinical outcomes, a patient-centered, context-specific approach that combines validated scoring systems, biomarker-informed monitoring, and tailored therapeutic strategies is essential. Future research should focus on large-scale comparative studies, standardization of diagnostic criteria, and the validation of novel therapies across diverse patient populations. By bridging these gaps, the medical community can move toward more timely, accurate, and effective management of DIC.

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