Original Article

DOI: 10.7860/JCDR/2026/79868.22484

Assessing the Predictive Value of D-dimer in Acute Pancreatitis: A Systematic Review and Meta-analysis

Internal Medicine Section

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ABSTRACT

Introduction: Acute Pancreatitis (AP) often leads to multi-organ dysfunction with high morbidity and mortality necessitating early identification for optimal management. Traditional severity scores have limitations, prompting exploration of biomarkers like D-dimer.

Aim: To evaluate D-dimer's accuracy as a severity marker in AP when compared to theother biomarkers.

Materials and Methods: The present comprehensive search was conducted on multiple databases. The authors included randomised clinical trials, cohort, cross-sectional, and case-control studies with adults diagnosed with AP and D-dimer measurements. Non-human studies, case reports, and non-English articles were excluded. Risk of bias was assessed using the Newcastle-Ottawa Scale. Data were analysed with R software focusing on diagnostic accuracy.

Results: Nineteen studies met the inclusion criteria. Most were retrospective with predominantly male participants. The pooled sensitivity for D-dimer in identifying Severe AP (SAP) was 0.85 (95% CI: 0.78-0.91), and specificity was 0.58 (95% CI: 0.31-0.85). The AUC for diagnostic accuracy was 0.75 (95% CI: 0.66-0.83). For severity assessment, sensitivity was 0.77 (95% CI: 0.71-0.83), specificity was 0.75 (95% CI: 0.67-0.83), and AUC was 0.78 (95% CI: 0.73-0.83). D-dimer had 0.86 sensitivity for organ failure detection (AUC 0.72, 95% CI: 0.63-0.81).

Conclusion: D-dimer shows moderate-to-high accuracy in identifying SAP and predicting organ failure. It is a promising, cost-effective, and easily accessible biomarker for early severity assessment. Further research is needed to confirm its clinical role and integration into severity models.

Keywords: Biomarkers, Disease progression, Fibrin degradation product, Inflammatory mediators

INTRODUCTION

The AP exhibits a wide spectrum of severity, ranging from mild edematous disease with minimal risk of death to necrotising pancreatitis, which carries a significantly higher mortality [1]. In a meta-analysis, the mortality rate for sterile necrosis was reported at 13%, increasing to 28% in cases of infected necrosis, and reaching 35% when organ failure was also present [2]. AP is classified into three severity levels: Mild (MAP), Moderately Severe (MSAP), And Severe (SAP), with severity often exacerbated by comorbid conditions and demographic factors, including obesity, type 2 diabetes, cardiovascular and renal disorders, alcoholism, and advanced age (over 45 years) [3]. SAP is often characterised by pancreatic necrosis, systemic inflammation, and multi-organ dysfunction or failure, with a mortality rate of 20% to 40%, substantially greater than that found in MAP and MSAP [4]. Early identification of patients at risk for SAP is essential for the implementation of appropriate and timely management. Traditional severity scoring systems, such as Acute Physiology and Chronic Health Evaluation II (APACHE II), Ranson's criteria, and Bedside index of severity in acute pancreatitis (BISAP), rely on clinical and laboratory data collected over 24-48 hours [5]. However, these scoring systems are hampered by their complexity, delayed result availability, and inconsistent predictive accuracy. To overcome these limitations, researchers have explored novel biomarkers that are widely accessible, cost-effective, and time-efficient.

D-dimer, a Fibrin Degradation Product (FDP), is released into the bloodstream when a blood clot dissolves by fibrinolysis [6]. It is routinely used for the exclusion of Venous Thromboembolism (VTE), assessment of VTE recurrence risk, and to guide the duration of anticoagulation therapy. In addition to VTE, elevated D-dimer levels may be caused by factors such as ageing, pregnancy, and intense physical activity. D-dimer has also been implicated in conditions such as cancer, infections, and disseminated intravascular coagulation [7]. Recent studies have found a robust link between D-dimer levels and the severity of pancreatitis. An observational study in India discovered that individuals with pancreatic necrosis, those requiring mechanical ventilation, those with organ dysfunction, and those who died exhibited significantly higher peak D-dimer levels ($p<0.0001$) [5]. A 2023 study further substantiated the involvement of D-dimer and FDPs as independent risk variables with a high predictive value for splanchnic vein thrombosis in patients with severe AP [8]. Moreover, a retrospective study from 2019 demonstrated that 1205 patients with serum D-dimer levels exceeding 2.5 mg/L had a worse prognosis compared to 1237 patients with levels below this threshold [9]. Furthermore, a 2019 retrospective cohort study by Zhang GQ et al., involving 334 patients revealed a significant correlation between D-dimer levels and the development of MSAP and SAP with sensitivity of 81.3% and specificity of 91%, indicating its potential as an early marker for severity stratification in AP [10]. In addition to its prognostic value in SAP, D-dimer has been linked to systemic complications, including necrosis and organ failure. A 2022 retrospective investigation of 238 patients discovered that a D-dimer level of more than 1.805 mg/L within 48 hours of admission was an independent predictor of Multi-organ Dysfunction Syndrome (MODS) and mortality. The ROC analysis produced an AUC of 0.78, validating the diagnostic accuracy of D-dimer in detecting high-risk patients [11]. Furthermore, a prospective cohort study by Garcia Borobia F in 2023, involving 346 patients, demonstrated that D-dimer could effectively discriminate between pancreatic and peripancreatic necrosis, with an AUC of 0.763 [12]. Despite these promising findings, further large-scale, prospective research is needed to validate the role of D-dimer in assessing AP severity. The incorporation of D-dimer into predictive models alongside existing

severity scoring systems is supported by current evidence. This review aims to critically evaluate the existing literature on D-dimer as a severity marker in AP, focusing on its potential applications in clinical practice, its predictive accuracy relative to other biomarkers, and its relationship with clinical outcomes.

MATERIALS AND METHODS

The systematic review followed the principles indicated in the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) [13]. The review protocol was prospectively registered with the International Prospective Register of Systematic Reviews (PROSPERO), under the registration ID-CRD42024619346.

Search Strategy and Data Sources

A comprehensive systematic search was undertaken in three databases: PubMed, Web of Science, and Medline; in addition, Google Scholar was searched for pertinent studies. The literature search approach included both text words and medical topic headings (MeSH) keywords (all fields). Key terms such as (D-dimer OR "FDP") AND ("AP" OR "severe pancreatitis") were used to develop a search strategy [Table/Fig-1].

Database	Search strategy	Search results
PubMed	("D-dimer" OR "FDP" OR "fibrin fragments") AND ("AP" OR "pancreatic inflammation" OR "severe pancreatitis") AND ("severity" OR "prognosis" OR "biomarker" OR "severity marker" OR "risk assessment")	64
Google Scholar	"D-dimer" "AP" -review -paediatric -COVID-19	730
Web of Science	TS= ("D-dimer" OR "FDP" OR "fibrin fragments") AND TS= (" AP " OR "pancreatic inflammation") AND TS= ("severity" OR "prognosis" OR "biomarker" OR "severity marker" OR "risk assessment") AND LA=(English)	70
Medline	"D-dimer" [Title/Abstract] AND " AP " [Title/Abstract] AND severity [Title/Abstract] AND medline [sb] AND English [lang]	33

[Table/Fig-1]: Search strategies and the number of results retrieved from each database.

The literature was searched from inception until November 2024 without time frame limitations. The PICOS for the systematic review included population (P): Adults diagnosed with AP, interventions (I): Measurement of D-Dimer levels at admission or during hospitalisation, comparators (C):, no measurements of D-dimer or different markers (e.g., Computed Tomography (CT), C-reactive Protein (CRP), Ranson criteria), outcomes (O): Association of D-dimer level with clinical outcomes such as pancreatitis severity, complications (e.g., necrosis, organ failure), or mortality, study design (S): randomised controlled trials, prospective and retrospective cohort studies, cross-sectional studies and case-control studies. The exclusion criteria included studies not reporting outcomes related to AP. Furthermore, non-human studies, case reports, reviews, and opinion articles were also excluded. Non-English language studies without available translations were also excluded.

Data Collection Process

The results of electronic database searches were transmitted to Rayyan Software for screening and selection. Before the screening procedure, duplicates were deleted. To identify potentially suitable research, the first and second authors independently reviewed the titles and abstracts of all papers found in the database search. We obtained full-text papers for studies that met the inclusion criteria, and the first and second authors independently assessed all full-text publications to determine eligibility. After the included studies were finalised, the data was retrieved and stored in an Excel file. Study parameters such as author, year of publication, country, study design, sample size, follow-up time, and outcome measures were collected from the included studies. The primary outcome of the systematic review was the accuracy of D-dimer in the evaluation of AP measured by the sensitivity, specificity and Area Under Curve (AUC). The secondary outcomes were to identify any factors that may influence the reliability of D-dimer as a marker of severity in AP, such as the assay method used the timing of measurement, and patient-specific characteristics. The level of evidence was determined by the Newcastle-Ottawa Scale.

Quality Assessment

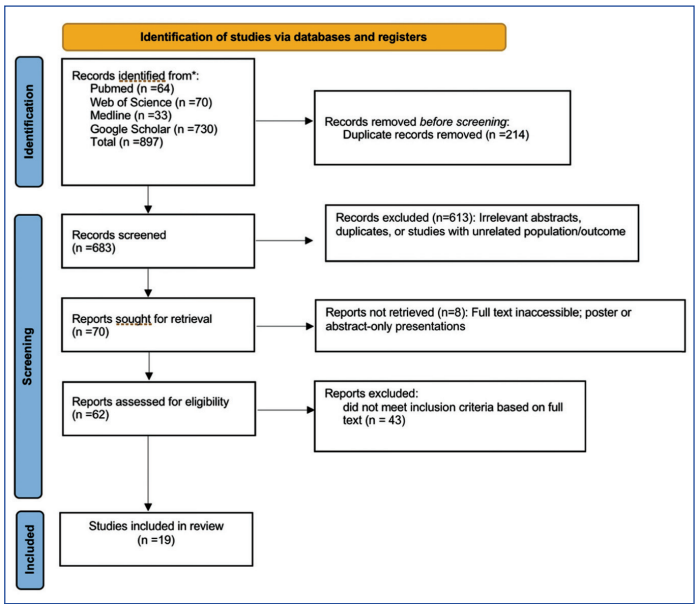
The risk of bias assessment was conducted using the Newcastle-Ottawa Scale, which evaluates studies across three domains. Two reviewers (the first and second authors) independently assessed each study using the NOS. Discrepancies in scoring were resolved through discussion until consensus was reached. No automation tools were used in the risk of bias assessment process. A total score of ≥7 was considered high quality, while ≤6 indicated a moderate-to-high risk of bias.

STATISTICAL ANALYSIS

We conducted the meta-analysis using R version 4.4. A random-effect model was used to compute the pooled effect size and 95% Confidence Intervals (CIs) for outcomes. The Chi-square test and I^2 statistic were employed to analyse heterogeneity, with p-values <0.05 indicating significance.

RESULTS

The literature search yielded 897 studies from PubMed (64), Web of Science (70), Medline (33), and Google Scholar (n=730). Before the screening process began, 214 duplicates were deleted. During screening, 613 records were deleted based on the title and abstract. The full-length screening comprised 70 pieces. After a comprehensive evaluation of full-length publications, 19 articles were selected, as indicated in [Table/Fig-2] [5,9-12,14-27].



[Table/Fig-2]: The PRISMA flow diagram of included studies.

This review included 19 studies [5,9-27]. The studies were from multiple countries, the majority were from China. Retrospective study designs were the most frequent. Seven studies were prospective [12,15,17,18,22,26,27]. Sample sizes ranged from 30 patients in Newton MV (2024) to 3,451 in Wan J et al., (2019) [7,13]. Gender distribution showed male predominance in most studies. The reported D-dimer cut-off values varied, with the highest being 7.267 mg/L (Zhang GQ et al., 2019) and the lowest at 0.0005 mg/L (Sternby H et al.,, 2016) [Table/Fig-3] [5,9-12,14-27].

Study ID	Country	Study Design	No. of Patients	Male	Female	D-dimer Cutoff	Standardised cutoff (mg/L)	Results
Kumar A and Kothagattu R (2017) [5]	India	Retrospective	60	53	7	N/A	N/A	Both the maximum and mean levels of D-dimer were significantly different between patients with and without clinical variables such as Multiple-organ Dysfunction Syndrome (MODS), need for surgical intervention, and the mortality.
Wan J et al., (2019) [9]	China	Retrospective	3451	N/A	N/A	>2.5 mg/L	>2.5	D-dimer >2.5 mg/L linked to higher incidences of SAP, APFC, ANC, PN, IPN, OF, POF, ICU, and mortality; higher D-dimer associated with poorer prognoses over time; useful for risk stratification.
Zhang GQ et al., (2019) [10]	China	Retrospective	334	220	114	7.268 mg/L	7.268	D-dimer at admission and average D-dimer distinguish MAP from MSAP/SAP; specific cut-offs provided. Average D-dimer useful predictor of AP severity.
He Q et al., (2022) [11]	China	Retrospective	238	137	101	1.805 mg/L	1.805	D-dimer was an independent predictor of severe acute pancreatitis (SAP) and persistent organ failure (POF); AUC for D-dimer in predicting SAP was 0.82; its predictive power was comparable to BISAP and less than APACHE II.
Garcia Borobia F et al., (2023) [12]	Spain	Prospective	346	154	192	1405.5 ng/mL	1.4055	D-dimer at 24 hours had an AUC of 0.77 (95% CI: 0.70-0.83) for predicting MSAP/SAP, with an optimal cut-off of 0.56 mg/L, achieving 75.0% sensitivity and 75.3% specificity.
Liu C et al., (2019) [14]	China	Retrospective	273	167	106	>2 mg/L	>2	D-dimer, APTT, TT, FDP, platelet, and PT are predictors of AP-related mortality and organ failure
Newton MV (2024) [15]	India	Prospective	30	24	6	N/A	N/A	D-dimer significantly higher in CAP, abnormal CT, and organ failure; increased with OF severity and in ICU. Correlated with APACHE II. Optimal cut-offs identified for CAP (>933.5 ng/L), positive CT findings (>827.5 ng/L), and organ failure development (>1060.5 ng/L).
Xu T-T et al., (2024) [16]	China	Retrospective	84	36	48	N/A	N/A	D-dimer levels in patients with severe pancreatitis were markedly higher than in control groups ($p<0.05$). D-dimer levels were also significantly higher in the death group compared to the survival group ($p<0.05$).
Badhal SS et al., (2012) [17]	India	Prospective	38	23	15	200 ng/mL	0.2	D-dimer >400-800 ng/mL at admission linked to high mortality (OR 11.2, AUROC 0.70) and predicted organ failure; useful for assessing severity and predicting outcomes.
Gomercic C et al., (2016) [18]	France	Prospective	71	48	23	500 ng/mL	0.5	D-dimer >1474 ng/mL at 36-48 hr predictive of complications (AUC 0.75-0.76); combining D-dimer + CRP at 48 hr improved prediction (AUC 0.83).
He S-S et al., (2022) [19]	China	Retrospective	469	288	181	N/A	N/A	D-dimer is an independent prognostic risk factor for MSAP/SAP; levels significantly higher in MSAP+SAP (median 2.990 mg/L) vs. MAP (median 1.670 mg/L). Optimal cut-off >2.23 mg/L. AUC 0.679 (Sens 65.17%, Spec 65.35%). Incorporated into new superior predictive models (unwScore AUC=0.854, wScore AUC=0.837).
Yang N et al., (2015) [20]	China	Retrospective	106	72	34	N/A	N/A	D-dimer increased with AP severity, positively correlated with LDL-C. Sensitive/specific predictor of severity, especially in hyperlipidemia-induced AP. The study included 106 AP patients.
Ke L et al., (2011) [21]	China	Retrospective	45	29	16	500	0.5	D-dimer significantly higher in AP with MODS/surgical need/pancreatic infection, correlated with APACHE II/CRP. High precision for predicting MODS/secondary infection. Useful early prognostic marker for SAP evolution/complications.
Salomone T et al., (2003) [22]	Italy	Prospective	30	14	16	>500	>0.5	D-dimer levels increased approximately 1.5 times over the normal limit in uncomplicated AP, and were "more consistently and significantly increased" in patients with complicated and severe AP
Yang N et al., (2017) [23]	China	Retrospective	95	65	30	N/A	N/A	D-dimer at admission and its dynamic change are independent risk factors for predicting AP severity (OR: 4.098 and 1.838 respectively). Optimal cut-off for D-dimer was 1.15 mg/L, with an AUROC of 0.817.
Qin X et al., (2024) [24]	China	Retrospective	240	142	98	N/A	N/A	D-dimer levels at admission and 24h significantly higher in SAP ($p<0.001$); optimal cutoff 0.67 mg/L for SAP prediction (AUC 0.817, Sens 76.5%, Spec 87.1%); independent risk factor for organ failure, pancreatic necrosis, and death.
Ke L et al., (2014) [25]	China	Retrospective	173	105	68	0.67 mg/L	0.67	D-dimer (AUC 0.81, cutoff 0.67 mg/L) predicts Critical AP (CAP) with 83% sensitivity/68% specificity; improved accuracy when combined with CRP or IAP.
Maeda K et al., (2006) [26]	Japan	Prospective	139	96	43	6.1 µg/mL	6.1	D-dimer, as a DIC parameter, significantly associated with AP severity/prognosis, showing better AUC than CRP; implicated in predicting fatal outcomes.
Sternby H et al., (2016) [27]	Sweden	Prospective	232	121	111	0.5 µg/L	0.0005	D-dimer at >0.5 µg/L showed 75% sensitivity, 12% specificity for severity; low AUCs (0.516/0.422) indicated suboptimality for predicting severity in unselected AP; not predictive of mortality.

[Table/Fig-3]: Study characteristics [5,9-12,14-27].

Risk of Bias Assessment

Studies with 8 stars, such as Xu T-T et al., (2024) [16], Wan J et al., (2019) [9], He Q et al., (2022) [11], Yang N et al., (2015) [20], and Zhang GQ et al., (2019) [10], demonstrated a low-risk of bias. Conversely, studies with six stars, including Kumar A and Kothagattu R (2017) [5], Newton MV (2024) [15], Ke L et al., (2011) [21], Salomone T et al., (2003) [22] and Garcia Borobia F et al., (2023) [12] were classified as having a moderate risk of bias. No studies were classified as high-risk. [Table/Fig-4] [5,9-12,14-27].

Pooled Diagnostic Performance Estimates

Diagnostic Accuracy for Diagnosis (DAD): The pooled sensitivity for the diagnostic accuracy of D-dimer in identifying severe AP was 0.85 (95% CI: 0.78-0.91), indicating a high ability to detect severe cases. However, substantial heterogeneity was observed among the included studies ($\chi^2=26.35$, $p<0.001$; $I^2=84.8\%$) ([Table/Fig-5a]. The pooled specificity for the diagnostic accuracy of D-dimer in identifying severe AP was 0.58 (95% CI: 0.31-0.85), indicating moderate discriminative ability in correctly identifying

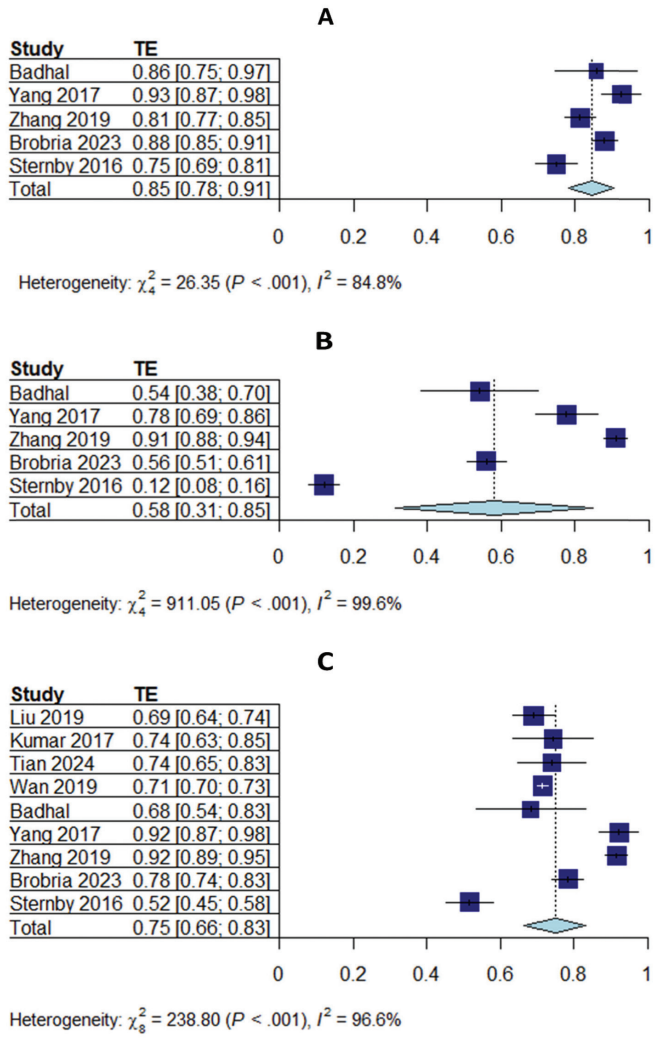
Study ID	Selection	Comparability	Outcome	Total stars	Final decision
Kumar A and Kothagattu R (2017) [5]	***	*	**	6	Moderate risk
Wan J et al., (2019) [9]	***	**	***	8	Low risk
Zhang GQ et al., (2019 [10]	***	**	**	7	Low risk
He Q et al., (2022) [11]	***	**	**	7	Low risk
Garcia Borobia F et al., (2023) [12]	***	*	**	6	Moderate risk
Liu C et al., (2019) [14]	***	**	**	7	Low risk
Newton MV (2024) [15]	***	*	**	6	Moderate risk
Xu TT et al., (2024) [16]	***	**	***	8	Low risk
Badhal SS et al., (2012) [17]	***	**	**	7	Moderate risk
Gomercic C et al., (2016) [18]	***	*	**	6	Moderate risk
He SS et al., (2019) [19]	***	**	**	7	Moderate risk
Yang N et al., (2015) [20]	***	**	**	8	Low risk
Ke L et al., (2011) [21]	***	*	**	6	Moderate risk
Salomone T et al., (2003) [22]	***	*	**	6	Moderate risk
Yang N et al., (2017) [23]	***	**	**	7	Moderate risk
Qin X et al., (2024) [24]	***	**	**	7	Moderate risk
Ke L et al., (2014) [25]	***	*	**	6	Moderate risk
Maeda K et al., (2006) [26]	***	**	**	7	Moderate risk
Sternby H et al., (2016) [27]	***	*	**	6	Moderate risk

[Table/Fig-4]: Risk of Bias Assessment using Newcastle-Ottawa Scale [5,9-12,14-27].

non-severe cases. However, high heterogeneity was observed (χ^2=911.05, p<0.001; I^2=99.6%) [Table/Fig-5b]. The pooled Area Under The Curve (AUC) for the diagnostic accuracy of D-dimer in assessing severe AP was 0.75 (95% CI: 0.66-0.83), indicating a fair overall diagnostic performance. The AUC value suggested that D-dimer had moderate accuracy in distinguishing between mild and severe cases. However, substantial heterogeneity was observed across the included studies (χ^2=238.80, p<0.001; I^2=96.6%) [Table/Fig-5c].

Diagnostic Accuracy for Severity (DAS): The pooled sensitivity for the diagnostic accuracy of D-dimer in assessing the severity of AP was 0.77 (95% CI: 0.71-0.83), indicating a good ability to correctly identify severe cases. However, substantial heterogeneity was observed among the included studies (χ^2=85.09, p<0.001; I^2=90.6%) [Table/Fig-6a]. The pooled specificity for the diagnostic accuracy of D-dimer in assessing the severity of AP was 0.75 (95% CI: 0.67-0.83), indicating a moderate ability to correctly identify non-severe cases. However, substantial heterogeneity was observed (χ^2=176.48, p<0.001; I^2=95.5%) [Table/Fig-6b]. The pooled AUC for the diagnostic accuracy of D-dimer in classifying the severity of AP was 0.78 (95% CI: 0.73-0.83), indicating good overall discriminative ability. The AUC value suggested that D-dimer had a moderate-to-high accuracy in distinguishing between mild and severe cases. However, significant heterogeneity was present across the included studies (χ^2=111.03, p<0.001; I^2=91.9%) [Table/Fig-6c].

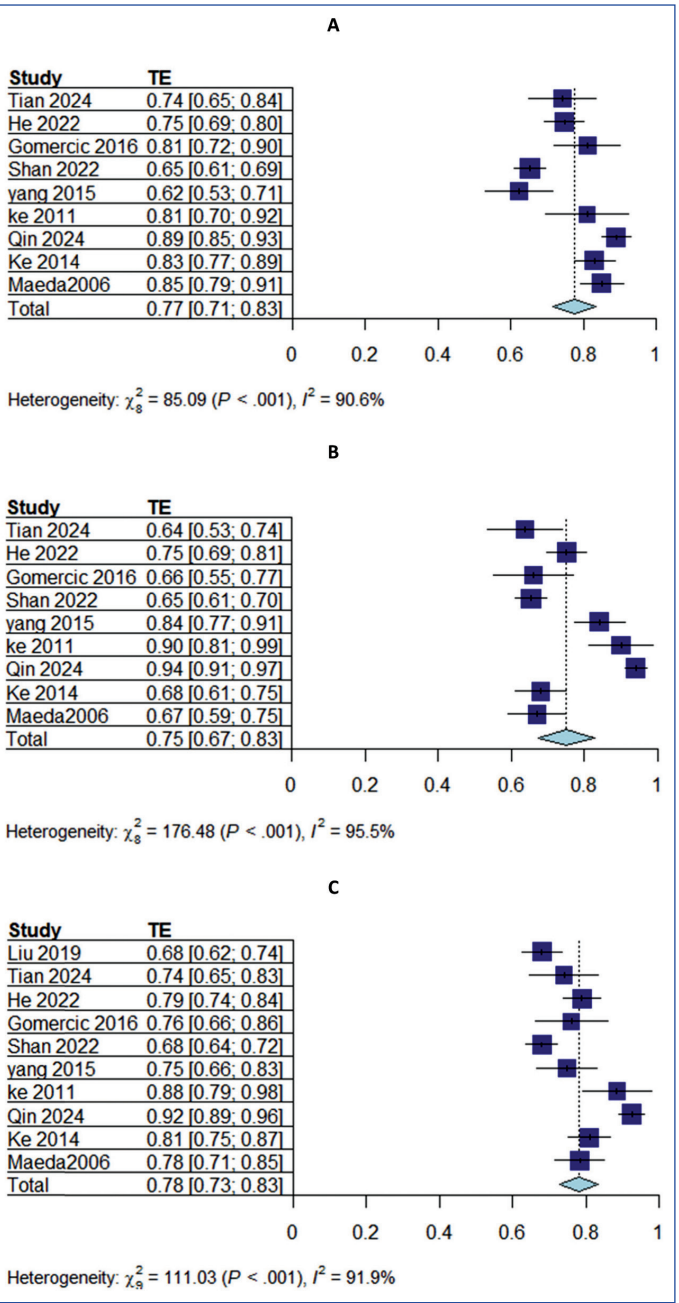
Diagnostic performance in detecting Organ Failure (OF): The pooled sensitivity for the diagnostic accuracy of D-dimer in detecting organ failure in AP was 0.86 (95% CI: 0.77-0.94), indicating a high ability to correctly identify cases with organ failure. Notably, no heterogeneity was observed across the included studies (χ^2=0.001, p>0.99; I^2=0.01%) [Table/Fig-7a]. The pooled specificity for the diagnostic accuracy of D-dimer in detecting organ failure in AP was 0.63 (95% CI: 0.45-0.82), indicating moderate ability to correctly identify patients without organ failure. Heterogeneity analysis showed moderate variability across the included studies (χ^2=2.62, p=0.11; I^2=61.8%) [Table/Fig-7b]. The pooled AUC for the diagnostic accuracy of D-dimer in detecting organ failure in AP was 0.72 (95% CI: 0.63-0.81), indicating moderate overall discriminative ability. The absence of heterogeneity across studies (χ^2=0.41, p=0.52; I^2=0.01%) [Table/Fig-7c].



[Table/Fig-5]: Diagnostic Accuracy for Diagnosis (DAD): a) Sensitivity; b) Specificity; c) AUC.

DISCUSSION

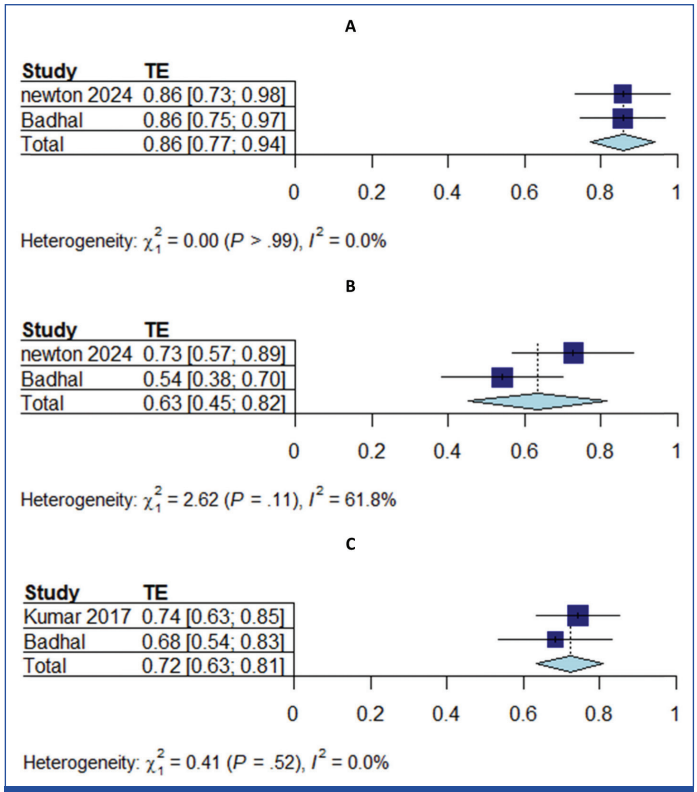
Early and accurate risk stratification enables timely intensive care support and interventions, which can improve patient outcomes in severe AP [15,28]. In this setting, the use of D-dimer as a predictive



[Table/Fig-6]: Diagnostic Accuracy for Severity (DAS): a) Sensitivity; b) Specificity; c) AUC.

biomarker has substantial clinical consequences. Elevated D-dimer levels during the initial days of AP may signal patients at risk of developing complications or organ failure before these issues fully manifest [12,15,18]. This review analysed 19 research studies to assess the utility of D-dimer in predicting the severity of AP. The findings indicate that D-dimer is highly effective in identifying severe cases, exhibiting good sensitivity. However, its specificity was moderate, and while it shows promise as an early warning tool for clinicians, there was some variability in the results across different studies.

When compared to C-Reactive Protein (CRP), D-dimer appears to perform similarly, with the advantage of rising earlier in the course of the illness. Studies have shown that within 48 hours, D-dimer's diagnostic accuracy for distinguishing mild from moderate-to-severe AP is comparable to CRP [11,29]. Importantly, D-dimer correlates with the systemic inflammatory response in AP, rising in parallel with other inflammatory markers and correlating with CRP levels [29,30] In one analysis, D-dimer levels showed significant correlation with AP severity indices and inflammatory markers, suggesting that combining D-dimer with CRP or Procalcitonin (PCT) could enhance its predictive power [31]. Unlike PCT or CRP (which peak later), D-dimer offers a readily available, rapid test that can augment early risk stratification when used alongside these other biomarkers.



[Table/Fig-7]: Diagnostic Performance for Organ Failure (OF): a) Sensitivity; b) Specificity; c) AUC.

D-dimer has several advantages as a severity marker in AP. It is widely available, inexpensive, and provides results within an hour, making it a practical tool for early risk stratification in diverse healthcare settings. Clinicians are familiar with D-dimer testing, easing its integration into pancreatitis care. Studies suggest good diagnostic accuracy for severe AP [21,32]. One study identified a D-dimer cut-off of ~1871 ng/L, with 87.5% sensitivity, 90.9% Negative Predictive Value (NPV), and 85% overall accuracy in predicting severe pancreatitis [33]. The high NPV is particularly valuable, as a low D-dimer level suggests a benign course, allowing for conservative management when other indicators are reassuring. Additionally, D-dimer correlates with organ dysfunction and pancreatic injury, rising with the number of failing organs and higher CT severity index scores [9,15]. This correlation with clinical endpoints underscores its physiological relevance in reflecting pancreatitis severity. The link to microthrombosis and disseminated intravascular coagulation in severe AP further supports its role in severity assessment [15].

The varied data on D-dimer in AP underscore the need for further research to clarify its role. Large-scale, multicenter trials are crucial for validating its prognostic utility across different patient populations and confirming initial findings. Research should also focus on determining optimal D-dimer cut-off levels and the timing for predicting severity, analysing levels at various time points-such as admission, 24 hours, and 48 hours. Reaching a consensus on clinically actionable thresholds and standardising assay units would aid in implementing guidelines.

Limitation(s)

This systematic review presents signifi cant limitations. A key issue was the variability in D-dimer cutoff values reported across studies, as different researchers suggest various thresholds for predicting severe AP and its complications. Additionally, differences in study populations and designs including limited patient numbers and specifi c etiologies can skew results. The timing of D-dimer measurements also varies, with levels taken at admission versus 48 hours having different predictive utilities. Moreover, the differing D-dimer assays complicate direct comparisons. This variability hinders the establishment of a universal cutoff value for clinical use.

CONCLUSION(S)

D-dimer shows promise as a diagnostic tool for assessing AP severity. It offers good sensitivity in identifying severe cases and predicting organ failure but has moderate specificity and variability in cutoff values. While it can complement, but not replace, existing gold-standard biomarkers, D-dimer is a valuable early indicator for risk stratification. Its availability, low cost, and rapid results make it especially useful in resource-limited settings. Future research should focus on defining optimal cutoff values and incorporating D-dimer into multi-marker predictive models.

REFERENCES

[1] Gapp J, Tariq A, Chandra S. Acute Pancreatitis. StatPearls. Treasure Island (FL): StatPearls Publishing Copyright © 2025, StatPearls Publishing LLC.; 2025.
[2] Werge M, Novovic S, Schmidt PN, Gluud LL. Infection increases mortality in necrotizing pancreatitis: A systematic review and meta-analysis. Pancreatology. 2016;16(5):698-707.
[3] Thapa R, Iqbal Z, Garikipati A, Siefkas A, Hoffman J, Mao Q, et al. Early prediction of severe acute pancreatitis using machine learning. Pancreatology. 2022;22(1):43-50.
[4] Lou D, Shi K, Li H-P, Zhu Q, Hu L, Luo J, et al. Quantitative metabolic analysis of plasma extracellular vesicles for the diagnosis of severe acute pancreatitis. J Nanobiotechnology. 2022;20(1):52-.
[5] Kumar A, Kothagattu R. D-dimer levels in predicting the severity of acute pancreatitis. International Surgery Journal. 2017;4(12):3993.
[6] Adam SS, Key NS, Greenberg CS. D-dimer antigen: Current concepts and future prospects. Blood. 2009;113(13):2878-87.
[7] Franchini M, Focosi D, Pezzo MP, Mannucci PM. How we manage a high D-dimer. Haematologica. 2024;109(4):1035-45.
[8] Zheng J, Han M, Chen J, Deng MM, Luo G. Predictive value of D-dimer and fibrinogen degradation product for splanchnic vein thrombosis in patients with severe acute pancreatitis: A single-center retrospective study. Scandinavian Journal of Gastroenterology. 2023;58(10):1166-72.
[9] Wan J, Yang X, He W, Zhu Y, Zhu Y, Zeng H, et al. Serum D-dimer levels at admission for prediction of outcomes in acute pancreatitis. BMC Gastroenterol. 2019;19(1):67.
[10] Zhang G-Q, Wang G, Li L, Hu J-S, Ji L, Li Y-L, et al. Plasma D-dimer level is an early predictor of severity of acute pancreatitis based on 2012 Atlanta Classification. Med Sci Monit. 2019;25:9019-27.
[11] He Q, Ding J, He S, Yu Y, Chen X, Li D, et al. The predictive value of procalcitonin combined with C-reactive protein and D dimer in moderately severe and severe acute pancreatitis. Eur J Gastroenterol Hepatol. 2022;34(7):744-50.
[12] Garcia Borobia F, Flores Clotet R, Bejarano Gonzalez N, Gonzalez Martinez S, Garcia Monforte N, Romaguera Monzonis A, et al. Predictive value of antithrombin III and d-Dimer in the development of moderate-to-severe acute pancreatitis. Pancreas. 2023;52(4):e241-e248.
[13] Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. Updating guidance for reporting systematic reviews: Development of the PRISMA 2020 statement. Journal of Clinical Epidemiology. 2021;134:103-12.
[14] Liu C, Zhou X, Ling L, Chen S, Zhou J. Prediction of mortality and organ failure based on coagulation and fibrinolysis markers in patients with acute pancreatitis: A retrospective study. Medicine (Baltimore). 2019;98(21):e15648.
[15] Newton MV. D-dimer as a marker of severity and prognosis in acute pancreatitis. Int J Appl Basic Med Res. 2024;14(2):101-07.
[16] Xu T-T, Chen S-B. The value of immature granulocyte percentage united with D-Dimer in the evaluation of severe pancreatitis and its prognosis. Clinics (Sao Paulo). 2024;79:100446.
[17] Badhal SS, Sharma S, Saraya A. Prognostic significance of D-dimer, natural anticoagulants and routine coagulation parameters in acute pancreatitis. Tropical Gastroenterology. 2012;33(2):193-99.
[18] Gomercic C, Gelsi E, Van Gysel D, Frin A-C, Ouvrier D, Tonohouan M, et al. Assessment of D-Dimers for the early prediction of complications in acute pancreatitis. Pancreas. 2016;45(7):980-85.
[19] He S-S, Li D, He Q-Y, Chen X-P, Lin Y-X, Yu Y-W, et al. Establishment of early multi-indicator prediction models of moderately severe acute pancreatitis and severe acute pancreatitis. Gastroenterol Res Pract. 2022;2022:5142473.
[20] Yang N, Zhang D-L, Hao J-Y. Coagulopathy and the prognostic potential of D-dimer in hyperlipidemia-induced acute pancreatitis. Hepatobiliary & Pancreatic Diseases International. 2015;14(6):633-41.
[21] Ke L, Ni Hb, Tong Zh, Li Wq, Li N, Li Js. <scp>d</scp>-dimer as a marker of severity in patients with severe acute pancreatitis. Journal of Hepato-Biliary-Pancreatic Sciences. 2011;19(3):259-65.
[22] Salomone T, Tosi P, Palareti G, Tomassetti P, Migliori M, Guariento A, et al. Coagulative disorders in human acute pancreatitis: Role for the D-Dimer. Pancreas. 2003;26(2):111-16.
[23] Yang N, Hao J, Zhang D. Antithrombin III and D-dimer levels as indicators of disease severity in patients with hyperlipidaemic or biliary acute pancreatitis. J Int Med Res. 2017;45(1):147-58.
[24] Qin X, Xiang S, Li W. Analysis of factors influencing onset and survival of patients with severe acute pancreatitis: A clinical study. Immun Inflamm Dis. 2024;12(6):e1267.
[25] Ke L, Tong Z-H, Li W-Q, Wu C, Li N, Windsor JA, et al. Predictors of critical acute pancreatitis: A prospective cohort study. Medicine (Baltimore). 2014;93(21):e108.
[26] Maeda K, Hirota M, Ichihara A, Ohmuraya M, Hashimoto D, Sugita H, et al. Applicability of disseminated intravascular coagulation parameters in the assessment of the severity of acute pancreatitis. Pancreas. 2006;32(1):87-92.
[27] Sternby H, Hartman H, Johansen D, Thorlacius H, Regnér S. Predictive capacity of biomarkers for severe acute pancreatitis. European Surgical Research. 2016;56(3-4):154-63.
[28] Silva-Vaz P, Abrantes AM, Castelo-Branco M, Gouveia A, Botelho MF, Tralhão JG. Multifactorial scores and biomarkers of prognosis of acute pancreatitis: Applications to research and practice. Int J Mol Sci. 2020;21(1):338.
[29] Gupta S, Shekhawat V, Kaushik G. D-dimer, a potential marker for the prediction of severity of acute pancreatitis. Clinical Laboratory. 2015;61(9):1187-95.
[30] Bao W, Qi X, Li HL, Hou F, Zhang X, Wang R, et al. Correlation of D-dimer level with the inflammatory conditions: A retrospective study. AME Medical Journal. 2017;2:27.
[31] Gao N, Yan C, Zhang G. Changes of Serum Procalcitonin (PCT), C-Reactive Protein (CRP), Interleukin-17 (IL-17), Interleukin-6 (IL-6), High Mobility Group Protein-B1 (HMGB1) and D-Dimer in patients with severe acute pancreatitis treated with Continuous Renal Replacement Therapy (CRRT) and its clinical significance. Med Sci Monit. 2018;24:5881-86.
[32] Talukdar M, Prashanth KR, Paul R. D-dimer - an essential marker in severity prediction of acute pancreatitis. International Journal of Scientific Research. 2021;9(10):78-82.
[33] Joseph A, Harikrishnan CP, Oommen AN, Nair A. D-dimer as a predictor of severity and outcome in acute pancreatitis. Journal of Medical and Scientific Research. 2024;12(4):275-80.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Apr 13, 2025
- Manual Googling: Aug 23, 2025
- iThenticate Software: Aug 26, 2025 (8%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? No
- Was informed consent obtained from the subjects involved in the study? No
- For any images presented appropriate consent has been obtained from the subjects. No

Date of Submission: **Apr 11, 2025**
Date of Peer Review: **Jun 14, 2025**
Date of Acceptance: **Aug 28, 2025**
Date of Publishing: **Mar 01, 2026**