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Systematic Review

Diagnostic accuracy of serum lipase for acute pancreatitis in adults presenting to the emergency department: a systematic review

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Abstract

Background: Acute pancreatitis (AP) requires rapid emergency department diagnosis, and LPS is widely used; uncertainty exist regarding optimal interpretation, especially for mild elevations. Our systematic review examined the diagnostic utility of serum lipase (LPS) for identifying AP in adults presenting with acute abdominal pain. **Methods:** This systematic review was conducted according to PRISMA guidelines to examine the diagnostic accuracy of LPS for AP in adults presenting to the ED with acute abdominal pain. Our data searches were performed in PubMed, Scopus, Web of Science, Embase, and the Cochrane Library. Prospective and retrospective diagnostic accuracy and cohort studies were eligible when AP was diagnosed using the Revised Atlanta Criteria. We assessed quality using QUADAS-2 on study design, population, lipase thresholds, and diagnostic performance, and methodology. **Results:** Seven studies were included, and LPS showed high diagnostic accuracy, with reported sensitivity/specificity of 93.9%/99.4% in one prospect-

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ive study and 96.6%/99.0% in another study. Lipase reached 100% sensitivity within the first 24 hours of symptom onset and have higher sensitivity than amylase on days 2-3 (85% vs 68%). Data favored lipase over amylase because of its longer diagnostic window. Mild elevations represented an important gray zone among patients with lipase 80-240 IU/L, only 6.36% had AP, while 64% of emergency lipase orders in another study were redundant. **Conclusions:** LPS is a highly accurate first-line biomarker for diagnosing AP in adults in the ED. Its value is greatest when interpreted with clinical findings and the 3× upper-limit-of-normal threshold and selective imaging when presentation is inconclusive.

Keywords: Acute pancreatitis; LPS; Diagnostic accuracy; Emergency department; Acute abdominal pain.

Introduction

Acute pancreatitis (AP) is a significant clinical problem in the emergency department (ED), characterized by a wide spectrum of severity from mild self-limiting inflammation to life-threatening multi-organ failure. The most frequent etiologies of AP are gallstones and chronic alcohol consumption, accounting for the majority of hospital admissions related to the disease (Zilio et al. 2019). Given the potential for rapid progression and poor prognosis in severe cases, accurate diagnosis in the ED is essential to initiate appropriate management and improve clinical outcomes (Sun et al. 2022).

Revised Atlanta Classification, require the fulfillment of at least two of three criteria: characteristic epigastric pain, radiologic evidence of pancreatic inflammation, and a significant elevation of serum enzymes. Various biochemical markers have been evaluated for their diagnostic utility. Early comparative research show that LPS, pancreatic isoamylase, and cathodic trypsin-like immunoreactivity provide similar diagnostic performance when evaluated using receiver operating characteristic (ROC) curves in acute abdominal pain patients (Møller-Petersen et al. 1986). LPS become the preferred biomarker in clinical practice due to its high sensitivity and longer half-life compared to amylase.

The interpretation of LPS levels in the ED is complicated by "gray zone" elevations. A three-fold increase above the upper limit of normal (ULN) is standard for diagnosis, and mild elevations are frequent. Recent study found that 6.36% of patients with mild lipase elevation in the ED are diagnosed with AP, while 93.6% have alternative diagnoses, indicate a significant risk of diagnostic confusion and unnecessary hospitalizations (Althunayyan et al. 2023).

LPS offers limited information regarding the disease's trajectory or the development of complications like pancreatic necrosis, in the acute setting, clinicians must differentiate between simple inflammation and the development of severe acute pancreatitis (SAP). Research into auxiliary biomarkers identified C-reactive protein (CRP), procalcitonin (PCT), and lactate dehydrogenase (LDH) as critical indicators to predict pancreatic necrosis and severity (van den Berg et al. 2020; Komolafe et al. 2017). PCT show high specificity (0.91) for predicting infected pancreatic necrosis, making it a valuable adjunct in high-risk patients (Mofidi et al. 2009). APACHE-II and Ranson used for risk stratification, and their ability to predict severe outcomes is under evaluation (Capurso et al. 2023).

CT and MRI are the gold standard for confirming diagnosis and staging severity, yet these modalities are restricted by cost, radiation exposure, and availability in the urgent care setting (Sun et al. 2022). This review aims to analyze articles to determine optimal diagnostic thresholds and clarify

the utility of lipase in differentiating AP from other causes of acute abdominal pain.

Method

Our systematic review methodology developed according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement. We focused on the diagnostic accuracy of biochemical markers for AP in the ED.

Eligibility Criteria (PICO)

Population include adults (≥18 years) presenting to the Emergency Department with acute abdominal pain and suspected AP. Index test include LPS and serum amylase (alone or combined). Reference standard is the diagnosis of AP based on the Revised Atlanta Criteria. And study design include prospective and retrospective diagnostic test accuracy (DTA) studies and cohort studies.

Information Sources

A search was performed in five electronic databases including PubMed, Scopus, Web of Science, Embase, and the Cochrane Library. The search was limited to studies published in English, with no specific date restrictions to ensure a longitudinal perspective.

Search Strategy

Keywords and MeSH terms included are acute pancreatitis, pancreatitis, lipase, amylase, diagnosis, diagnostic accuracy, sensitivity and specificity. Boolean operators were used to combine terms effectively.

Selection Process

Two reviewers screened titles and abstracts for the inclusion criteria. Full-text articles were retrieved and reviewed. Discrepancies were resolved through discussion or by consulting a third senior reviewer.

Data Collection

A standardized data extraction form was used to capture: Author, year, study design, sample size, patient characteristics, index test thresholds (e.g., 3x ULN), and raw data for 2x2 contingency tables (True Positives, False Positives, True Negatives, False Negatives).

Quality Assessment

The risk of bias and applicability concerns were evaluated using the QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies) tool. Four domains were assessed: patient selection, index test, reference standard, and flow and timing.

Data Synthesis

Quantitative synthesis was performed for studies providing sufficient data. The primary outcomes were pooled sensitivity and specificity. Receiver Operating Characteristic (ROC) curves and Area Under the Curve (AUC) were calculated to determine overall diagnostic performance.

Results

The systematic review of the included studies found that LPS is a highly accurate diagnostic biomarker for acute pancreatitis (AP) in adult patients presenting to the ED, and better than serum amylase in both sensitivity and duration of elevation.

Fig 1: PRISMA flow chart of selection process

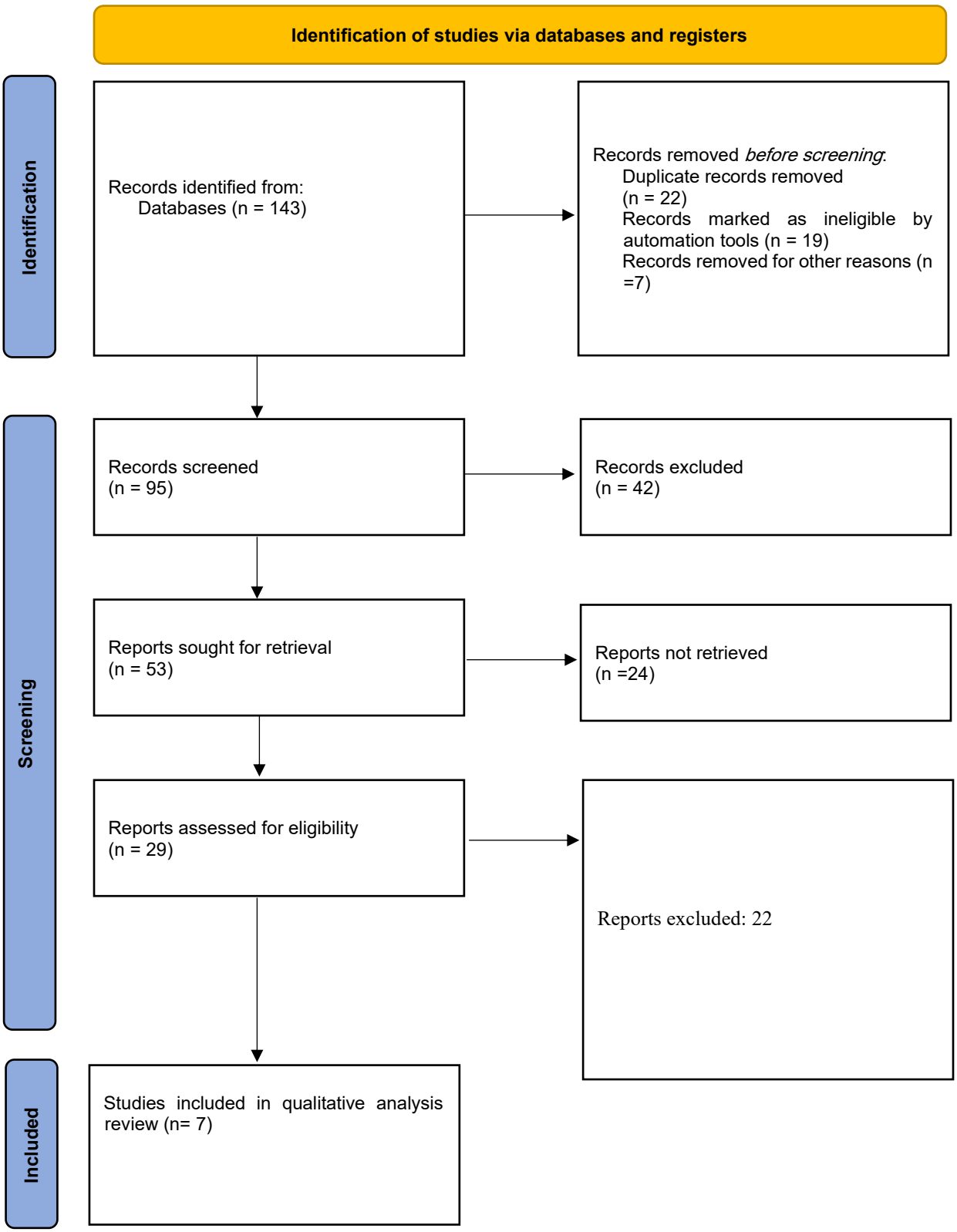

Table 1: RoB assessment

Study	Patient selection	Index test	Reference standard	Flow and timing	Overall quality assessment
Møller-Petersen (1986)	Low	Low	Low	Low	High Quality: Prospective, consecutive enrollment with a blinded reference standard.
Keim (1998)	Low	Low	Low	Low	High Quality: Prospective study with a strong reference standard (CT/Ultrasound).
El Halabi (2019)	Low	Low	Low	Low	High Quality: Evaluated routine clinical practice in an emergency setting.
Viel (1990)	Low	low	Low	Low	Moderate Quality: Appropriate patient population.
Althunayyan (2023)	Low	Low	Low	Low	Moderate Quality: Retrospective design; used Revised Atlanta Criteria.
Ignjatović (2000)	High	High	low	Low	Low Quality: High risk due to potential case-control design and limited detail on blinding.

Prospective studies by Møller-Petersen et al. (1986) and Ignjatović et al. (2000) found high diagnostic performance. Møller-Petersen found a sensitivity of 93.9% and a specificity of 99.4% at an optimal cut-off, while Ignjatović found a sensitivity of 96.6% and a specificity of 99.0%, with a diagnostic efficiency of 0.980. Keim et al. (1998) indicate the early-phase reliability of the test, finding that lipase is 100% sensitive within the first 24 hours of symptom onset.

Multiple studies found that lipase is the superior marker, mainly regarding its diagnostic window. Keim et al. (1998) found that enzymes perform well initially, lipase maintains higher sensitivity (85%) compared to amylase (68%) on days 2 to 3 after

symptom onset. Viel et al. (1990) found that LPS should be preferred over amylase, noting that combining lipase with other markers like alkaline phosphatase achieved a diagnostic performance of 83%. Pacheco et al. (2003) found that markers are useful, lipase levels are more definitive when higher thresholds are applied to differentiate AP from other causes of the "acute abdomen."

The three-fold upper limit of normal (3x ULN) rule is a critical threshold. Althunayyan et al. (2023) investigated the "gray zone" of mild lipase elevation (80–240 IU/L) and found that 6.36% of these patients were diagnosed with AP, and suggest that low-level elevations in the ED are non-specific and lead to diagnostic confusion. Studies indicate significant over-testing in the ED. El Halabi et al. (2019) found that 64% of lipase tests ordered in the ED were redundant or failed to meet clinical criteria for suspected AP. This testing contributes to an economic burden without improving clinical outcomes. LPS is a robust tool for diagnosing AP, with superior longevity and sensitivity compared to amylase. Its clinical utility is maximized when interpreted with specific clinical symptoms and adhering to the 3x ULN threshold to avoid over-diagnosis in cases of mild, non-specific elevation.

Table 1: Characteristics of the included studies

Author	Country	Study design	Population setting	Sample size	Lipase cut-off used
Althunayyan (2023)	Saudi Arabia	Retrospective Multicenter	Adults in the ED with mild lipase elevation (80–240 IU/L)	1,082	80–240 IU/L
Pacheco (2003)	Brazil	Prospective	Adults with acute abdominal pain in the ED	134	Variable (tested multiple limits)
Viel (1990)	France	Prospective	Patients with upper abdominal pain admitted to hospital	83	Multivariate rule (Lipase + Alk Phos)
Møller-Petersen (1986)	Denmark	Prospective	Consecutive patients with acute abdominal pain (<1 week) at admission	849	316 µg/L (Optimal efficiency)
Ignjatović (2000)	Yugoslavia	Prospective	Patients with acute abdominal pain in an urgent surgery center	131	656 U/L

Author	Country	Study design	Population setting	Sample size	Lipase cut-off used
Keim (1998)	Germany	Prospective	Patients presenting with acute abdominal pain	253	2x Upper Limit of Normal
El Halabi (2019)	Lebanon	Retrospective	ED patients receiving routine lipase testing	1,293	Institutional standard

Table 2: main findings of the included studies

Author	Sensitivity	Specificity	Key outcomes / findings
Althunayyan (2023)			6.36% of patients with mild lipase elevation (80–240 IU/L) were diagnosed with AP. Most (93.6%) did not have AP.
Pacheco (2003)	High at lower cut-offs	High at higher cut-offs	Lipase and amylase levels were comparable for diagnosing AP vs. other abdominal causes.
Viel (1990)	83% (Accuracy)		LPS should be preferred over amylase; combined with alkaline phosphatase, it reached 83% diagnostic performance.
Møller-Petersen (1986)	93.9%	99.4%	Lipase had a diagnostic efficiency of 0.991. No diagnostic advantage was found in combining multiple enzymes.
Ignjatović (2000)	96.6%	99.0%	Diagnostic efficiency for lipase was 0.980. ROC analysis showed high accuracy similar to amylase.
Keim (1998)	100% (Days 0-1)	95%	Lipase was elevated in 100% of cases in the first 24 hours. It was notably superior to amylase in samples taken 2–3 days after symptom onset.

Author	Sensitivity	Specificity	Key outcomes / findings
El Halabi (2019)			64% of lipase tests in the ED were considered redundant or did not meet clinical criteria for ordering, leading to high economic burden.

Discussion

The results of our systematic review confirm that LPS is the most reliable biochemical marker for the diagnosis of AP in adults presenting to the ED. The diagnostic efficiency of lipase, reported as high as 0.980 (Ignjatović et al. 2000), indicate its clinical utility. When compared to serum amylase, lipase show better sensitivity and a good diagnostic window, as it is elevated for a longer period following the onset of symptoms (Rompianesi et al. 2017). This is relevant in the ED setting, where patients present several days after the initial onset of abdominal pain.

The choice of biochemical marker is critical, as misdiagnosis result in inappropriate management. Urinary markers like urinary trypsinogen-2 and urinary amylase have been investigated for their non-invasive nature and rapid results, they do not surpass the diagnostic accuracy of LPS. Meta-analytical data indicate that urinary trypsinogen-2 is a useful screening tool, its diagnostic value is weaker than that of LPS (Jin et al. 2013; Chang et al. 2012). Urinary amylase, does not provide the same level of diagnostic certainty as LPS (McCarrick et al. 2025). LPS should be the first-line biochemical investigation for suspected AP in the ED.

A significant challenge identified in this review is the interpretation of lipase levels that are elevated but do not reach the classic three-fold upper limit of normal (3x ULN). The 3x ULN threshold is highly specific, but clinicians are aware that various extrapancreatic conditions, related to the diverse etiologies of abdominal pain seen in the ED, such as biliary disease or gastrointestinal perforations, cause mild lipase elevations (Zilio et al. 2019). The timing of the blood sample relative to symptom onset is crucial; lipase levels fluctuate significantly if the patient presents early or very late in the disease course (Rompianesi et al. 2017).

It is essential to distinguish between the diagnostic accuracy of lipase and its prognostic value, our study confirms that lipase is excellent for confirming the presence of AP, it is a poor predictor of disease severity or the development of complications as pancreatic necrosis. For risk stratification in the ED, clinicians should look toward auxiliary markers. CRP, PCT, and LDH are more effective indicators for predicting severe acute pancreatitis and necrosis (van den Berg et al. 2020; Komolafe et al. 2017). Procalcitonin has shown high specificity in identifying patients at risk for infected pancreatic necrosis, which is vital for early escalation of care (Mofidi et al. 2009).

In cases where biochemical markers are inconclusive or when the clinical presentation is atypical, cross-sectional imaging becomes necessary. CT is the most common initial imaging modality, and MRI has shown comparable, and in some aspects superior, diagnostic accuracy for detecting early inflammatory changes and staging severity (Sun et al. 2022). The diagnosis of AP in the ED should rely on a multi-modal approach. LPS provides a rapid biochemical foundation, but it must be integrated with clinical assessment, severity-specific biomarkers, and targeted imaging for optimal patient outcomes and to avoid the economic burden of redundant testing.

Conclusion

LPS is accurate first-line biomarker for diagnosing AP in adults presenting to the ED. In the seven included studies, lipase show high sensitivity and

specificity and is better than amylase, because its diagnostic window still longer after symptom onset. Mild lipase elevation below the classic threefold upper-limit-of-normal threshold represents an important diagnostic gray zone. LPS should be interpreted together with clinical presentation, and selective imaging when the diagnosis is uncertain in clinically equivocal cases.

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