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ELEVATED SERUM LACTATE LEVELS AS INDEPENDENT PREDICTOR OF POOR OUTCOMES IN SEVERE ACUTE BILIARY PANCREATITIS

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Abstract

Objective: *To evaluate the association between elevated admission serum lactate and poor clinical outcomes in patients with severe acute biliary pancreatitis (SABP).*

Study Design: *Prospective observational cohort study.*

Place and Duration of Study: *Department of Surgery, Combined Military Hospital Kohat from Jun 2023 to Jun 2025.*

Methodology: *Sixty-four consecutive patients with SABP were enrolled and grouped by admission serum lactate: normal (<2 mmol/L, n=22) and elevated (≥2 mmol/L, n=42). The primary endpoint was composite poor outcome, defined as death, septic shock, or pancreatic infection. Clinical parameters, severity scores, and outcomes were compared. Binary logistic regression and receiver operating characteristic (ROC) curve analyses assessed the predictive value of serum lactate.*

Results: *Composite poor outcome occurred in 21/42 (50.0%) patients with elevated lactate versus 4/22 (18.2%) with normal lactate (p=0.016). The elevated lactate group showed higher rates of multiple organ failure (38.1% vs 9.1%, p=0.019), pancreatic necrosis (73.8% vs 40.9%, p=0.021), and longer hospital stay (median 19.5 vs 10.5 days, p<0.001). Elevated lactate was a significant univariate predictor of poor outcome (OR 4.5, 95% CI 1.3–15.6, p=0.018). The area under the ROC curve was 0.72.*

Conclusion: *Elevated admission serum lactate is significantly associated with adverse outcomes in SABP and can serve as a practical bedside marker for early risk stratification.*

INTRODUCTION

Acute pancreatitis is among the most frequent gastrointestinal emergencies requiring surgical admission, and its global burden continues to rise, with reported incidence between 13 and 45 cases per 100,000 population per year [1,2]. Gallstones are the single commonest cause worldwide, and this biliary predominance is more marked across South Asia, where cholelithiasis is prevalent and access to early cholecystectomy is limited. In Pakistan, a recent cross-sectional study from a university hospital in Karachi identified biliary etiology in nearly 69% of all acute pancreatitis admissions [3]. While most episodes settle with conservative management, roughly 15% to 20% progress to severe disease, defined by persistent organ failure lasting beyond 48 hours under the revised Atlanta classification [1]. Mortality in this severe subgroup is reported between 15% and 30%, and rises sharply once more than one organ system is involved [2,4].

The central difficulty at the bedside is separating, within the first hours of admission, the patient who will settle from the one drifting toward organ failure. Established scores carry practical drawbacks: Ranson cannot be completed before 48 hours, APACHE II depends on variables not reliably available in every district hospital, and none has shown consistent superiority head to head [5]. In resource-limited units across Pakistan, where intensive care beds are scarce and transfer takes time, a rapid and inexpensive bedside marker of early physiological derangement would carry real value.

Serum lactate reflects the shift toward anaerobic glycolysis that accompanies tissue hypoperfusion, and its measurement is rapid and inexpensive [6]. Updated sepsis management guidelines endorse serial lactate monitoring as a core resuscitation target [7]. In acute pancreatitis — where hypovolaemia, vasodilatation, and microcirculatory dysfunction converge — elevated lactate carries strong biological plausibility as a prognostic indicator. Shu and colleagues found that arterial lactate above 4 mmol/L independently predicted organ failure and death in a mixed-etiology cohort of severe acute pancreatitis (SAP) [8], and lactate clearance kinetics have shown similar value in grading disease severity [9].

What remains unaddressed is whether this relationship holds in biliary disease specifically. Published cohorts have almost uniformly pooled alcoholic, biliary, hypertriglyceridaemic and idiopathic cases, yet biliary disease carries a distinct physiological burden: ductal obstruction, the risk of ascending cholangitis, and hepatic dysfunction that may impair lactate clearance independently of tissue perfusion. No prospective study from Pakistan has examined admission lactate in an exclusively biliary cohort. We therefore designed this study to evaluate whether elevated admission serum lactate (≥2 mmol/L) is associated with composite poor outcome (death, septic shock, or pancreatic infection) in a prospective cohort of patients with SABP at a tertiary surgical centre in Pakistan.

METHODOLOGY

This prospective observational cohort study was conducted at the Department of Surgery, Combined Military Hospital, Kohat, from Jun 2023 to Jun 2025. The hospital has a surgical facility handling approximately 170 major procedures per month and serves as the receiving centre for complicated pancreatobiliary disease referred from peripheral hospitals and medical facilities across the region. Ethical clearance was obtained from the Ethical Review Committee of Combined Military Hospital Kohat (ERC No. E-2005/A/11) prior to commencement of data collection. Written informed consent was obtained from every participant or from the next of kin where the patient was unable to consent.

Sample size was estimated using the WHO single-proportion formula ($n = Z^2P(1-P)/d^2$) ($Z = 1.96$, $P = 0.50$, $d = 0.15$), yielding a minimum of 43 patients [8]; 64 were enrolled. Non-probability consecutive sampling was used. All patients admitted directly with acute pancreatitis, and all patients referred from peripheral hospitals with established severe acute biliary pancreatitis, were screened. Acute biliary pancreatitis was diagnosed when at least two of the following were present: characteristic abdominal pain, serum amylase or lipase exceeding three times the upper limit of normal, or compatible findings on contrast-enhanced CT (CECT) [8]. Biliary etiology was confirmed by gallstones or sludge on ultrasonography, elevated liver enzymes (above three times normal), or imaging evidence of common bile duct stones. Severe disease was classified as persistent organ failure — modified Marshall score ≥2 in at least one organ system — lasting beyond 48 hours [1].

Inclusion Criteria

First episode of severe acute biliary pancreatitis, age 18 to 75 years, symptom onset to admission within 72 hours, serum lactate measured within 2 hours of admission and informed consent obtained.

Exclusion Criteria

Non-biliary etiology, pancreatitis in pregnancy, incomplete laboratory workup, transfer to another facility within 48 hours, or refusal to consent.

Data were recorded at enrollment and throughout hospitalisation: demographics, admission laboratory values (full blood count, renal and hepatic panels, glucose, calcium, albumin, CRP, base excess, lactate, amylase, lipase, LDH), severity scores (APACHE II, SIRS, Ranson), and clinical outcomes (death, septic shock, pancreatic infection, organ failure pattern, necrosis, ventilator support, cholangitis, hospital and ICU stay). Serum lactate was measured from venous blood within 2 hours of presentation and daily for seven days. Follow-up extended to 30 days via inpatient monitoring and telephone or outpatient contact.

Patients were allocated into Group A (normal lactate: <2 mmol/L) and Group B (elevated lactate: ≥2 mmol/L). The primary endpoint was composite poor outcome, defined as the occurrence of any one or more of death within 30 days, septic shock (sepsis-induced hypotension persisting despite adequate fluid resuscitation), or pancreatic infection (gas in collections on CECT, or positive culture from aspiration/drainage). Data were analysed using IBM SPSS version 26.0. Continuous variables were reported as mean ± SD or median (IQR) and compared using the independent-samples t-test or Mann-Whitney U test. Categorical data were expressed as frequencies and percentages and compared with the chi-square or Fisher exact test. Univariate and multivariate binary logistic regression identified predictors of poor outcome, reported as odds ratios (OR) with 95% CI. The multivariate model was restricted to three variables based on the ten-events-per-variable convention [10]. ROC curves evaluated discriminative performance. A two-tailed $p \leq 0.05$ was considered significant. Reporting followed the STROBE guidelines for observational studies.

RESULTS

During the study period, 187 patients with acute pancreatitis of any etiology were admitted directly to the surgical department, of whom 129 (69.0%) had a biliary cause. Thirty of these 129 patients (23.3%) met criteria for severe disease. A further 46 patients with established severe acute biliary pancreatitis were referred from peripheral military and civil hospitals within 72 hours of symptom onset, giving 76 patients assessed for eligibility. Twelve were excluded (incomplete laboratory workup n=4, transfer within 48 hours n=3, recurrent episode n=3, consent declined n=2), leaving 64 patients for analysis: 22 in Group A and 42 in Group B (Figure 1).

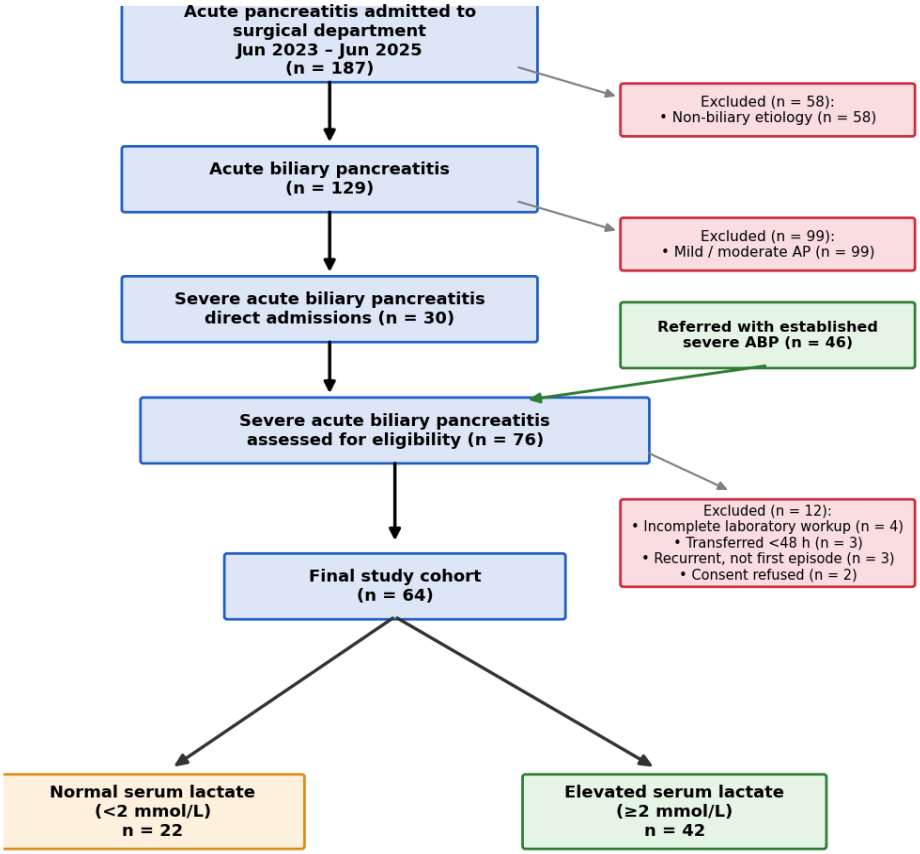

Figure 1. Patient selection flow diagram

The groups were broadly comparable in age (43.9 ± 13.3 vs 50.9 ± 13.5 years, p=0.053), sex distribution (55% vs 64% male, p=0.62), and BMI (p=0.55). Laboratory derangements were more pronounced in the elevated lactate group: white cell count 17.2 ± 5.1 vs 14.3 ± 3.8 $\times 10^9$/L (p=0.023), serum glucose median 10.4 vs 8.0 mmol/L (p=0.006), serum urea median 8.9 vs 5.3 mmol/L (p=0.015), haematocrit median 46.5% vs 43.5% (p=0.048), and serum creatinine ≥1.9 mg/dL in 26% vs 0% (p=0.011). Inflammatory markers were also disturbed: CRP ≥150 mg/L in 74% vs 36% (p=0.008), procalcitonin ≥3.8 ng/mL in 71% vs 41% (p=0.035), base excess ≥|4| mmol/L in 76% vs 18% (p<0.01). Severity scores were worse in Group B: APACHE II ≥15 in 29% vs 0% (p=0.005), SIRS ≥3 in 62% vs 32% (p=0.043), median Ranson 4.5 vs 2.5 (p<0.01). Total bilirubin was higher in Group B (median 4.0 vs 1.9 mg/dL, p=0.017), while amylase, lipase, and ALT showed no significant difference (Table I).

Table I: Baseline Characteristics by Serum Lactate Group

Variable	All (N=64)	Normal (n=22)	Elevated (n=42)	p-value
Age, years, mean ± SD	48.5 ± 13.8	43.9 ± 13.3	50.9 ± 13.5	0.053
Sex (male), n (%)	39 (61%)	12 (55%)	27 (64%)	0.62
BMI, kg/m², mean ± SD	24.9 ± 3.6	24.6 ± 3.1	25.1 ± 3.8	0.55
WBC, ×10⁹/L, mean ± SD	16.2 ± 4.9	14.3 ± 3.8	17.2 ± 5.1	**0.023**
Hematocrit, %, median (IQR)	45.1 (40.0–49.0)	43.5 (37.1–46.9)	46.5 (42.6–49.7)	**0.048**
Serum glucose, mmol/L, median (IQR)	9.8 (6.8–11.9)	8.0 (6.2–9.9)	10.4 (8.0–13.4)	**0.006**
Serum urea, mmol/L, median (IQR)	7.6 (3.4–11.6)	5.3 (2.8–8.0)	8.9 (5.7–12.5)	**0.015**
Serum creatinine ≥1.9 mg/dL, n (%)	11 (17%)	0 (0%)	11 (26%)	**0.011**
Serum albumin, g/L, mean ± SD	32.7 ± 5.2	33.6 ± 5.2	32.3 ± 5.3	0.35
CRP ≥150 mg/L, n (%)	39 (61%)	8 (36%)	31 (74%)	**0.008**
Procalcitonin ≥3.8 ng/mL, n (%)	39 (61%)	9 (41%)	30 (71%)	**0.035**
Base excess ≥|4| mmol/L, n (%)	36 (56%)	4 (18%)	32 (76%)	**<0.01**
Serum calcium, mmol/L, median (IQR)	1.8 (1.7–2.0)	1.8 (1.8–2.0)	1.8 (1.7–2.0)	0.34
Total bilirubin, mg/dL, median (IQR)	3.2 (1.5–5.1)	1.9 (0.9–3.7)	4.0 (2.5–5.2)	**0.017**
ALT, U/L, median (IQR)	162.6 (103.9–305.1)	173.3 (132.6–297.6)	155.3 (96.7–313.5)	0.66
Amylase, U/L, median (IQR)	837.1 (523.3–1259.6)	845.2 (337.7–1333.1)	837.1 (632.0–1221.9)	0.69
Lipase, U/L, median (IQR)	1224.7 (810.7–1527.4)	1246.9 (963.1–1566.9)	1157.0 (725.0–1453.1)	0.45
SIRS ≥3, n (%)	33 (52%)	7 (32%)	26 (62%)	**0.043**
APACHE II, median (IQR)	12.0 (8.0–14.0)	9.0 (6.0–12.0)	13.0 (10.2–15.8)	**<0.01**
APACHE II ≥15, n (%)	12 (19%)	0 (0%)	12 (29%)	**0.005**
Ranson score, median (IQR)	4.0 (2.0–5.0)	2.5 (2.0–4.0)	4.5 (3.0–6.0)	**<0.01**

Data are mean ± SD, median (IQR), or n (%). WBC, white blood cell count; CRP, C-reactive protein; ALT, alanine aminotransferase; SIRS, systemic inflammatory response syndrome; APACHE, Acute Physiology and Chronic Health Evaluation

Multiple persistent organ failure was significantly more common in Group B (38.1% vs 9.1%, p=0.019). Single-organ failure, almost always respiratory, predominated in Group A (90.9%). In the elevated lactate group, combined respiratory and renal failure was the dominant multiple-organ pattern (21.4%), with respiratory and cardiovascular failure in 7.1% and triple-system involvement (respiratory, cardiovascular, renal) in 9.5%.

Composite poor outcome occurred in 25/64 patients overall (39.1%): 4/22 (18.2%) in Group A versus 21/42 (50.0%) in Group B (p=0.016). Each component trended toward worse outcomes in the elevated lactate group: death 16.7% vs 4.5%, septic shock 23.8% vs 4.5%, and pancreatic infection 33.3% vs 13.6%, without any

component individually reaching significance. Pancreatic necrosis (74% vs 41%, p=0.021), ventilator requirement (62% vs 27%, p=0.018), median hospital stay (19.5 vs 10.5 days, p<0.001), and median ICU stay (10.0 vs 4.0 days, p<0.001) were all significantly worse in Group B (Table II).

Table II: Clinical Outcomes by Serum Lactate Group

Variable	All (N=64)	Normal (n=22)	Elevated (n=42)	p-value
Primary Endpoint				
Composite poor outcome	25 (39%)	4 (18%)	21 (50%)	**0.016**
Death	8 (13%)	1 (5%)	7 (17%)	0.25
Septic shock	11 (17%)	1 (5%)	10 (24%)	0.081
Pancreatic infection	17 (27%)	3 (14%)	14 (33%)	0.14
Organ Failure Pattern				
Single-organ POF	46 (72%)	20 (91%)	26 (62%)	—
Multiple-organ POF	18 (28%)	2 (9%)	16 (38%)	**0.019**
Secondary Outcomes				
Pancreatic necrosis	40 (63%)	9 (41%)	31 (74%)	**0.021**
Walled-off necrosis	9 (14%)	1 (5%)	8 (19%)	0.15
Ventilator support	32 (50%)	6 (27%)	26 (62%)	**0.018**
Cholangitis	17 (27%)	4 (18%)	13 (31%)	0.38
Hospital stay, days, median (IQR)	16.0 (10.0–22.0)	10.5 (9.2–16.0)	19.5 (13.0–25.5)	**<0.001**
ICU stay, days, median (IQR)	8.0 (5.0–10.0)	4.0 (3.2–5.0)	10.0 (8.0–11.0)	**<0.001**

On univariate logistic regression, elevated admission lactate was a significant predictor of composite poor outcome (OR 4.5, 95% CI 1.3–15.6, p=0.018). Procalcitonin ≥3.8 ng/mL (OR 4.2, p=0.016) and APACHE II ≥15 (OR 4.1, p=0.038) were also significant. Multivariate analysis with these three variables yielded an adjusted OR of 2.6 for lactate (95% CI 0.7–10.2, p=0.16), with procalcitonin showing a near-significant trend (OR 3.3, p=0.059). The loss of significance likely reflects collinearity among markers of systemic illness severity and limited statistical power with 25 events across 3 covariates (Table III).

Table III: Logistic Regression Analysis for Composite Poor Outcome

Variable	Univariate OR (95% CI)	p-value	Multivariate OR (95% CI)	p-value
Elevated lactate (≥ 2 mmol/L)	4.5 (1.3–15.6)	0.018	2.6 (0.7–10.2)	0.16
Procalcitonin ≥ 3.8 ng/mL	4.2 (1.3–13.5)	0.016	3.3 (1.0–11.2)	0.059
APACHE II ≥ 15	4.1 (1.1–15.6)	0.038	2.6 (0.6–11.2)	0.19
Serum creatinine ≥ 1.9 mg/dL	3.4 (0.9–13.2)	0.076	-	-
Hematocrit ≥ 44	1.9 (0.7–5.2)	0.23	-	-

OR, odds ratio; CI, confidence interval. Multivariate model limited to 3 variables based on events-per-variable rule [10].

The AUC for continuous serum lactate in predicting composite poor outcome was 0.72 (95% CI 0.59–0.85), with a sensitivity of 84% and specificity of 46% at the ≥2 mmol/L threshold. APACHE II had an AUC of 0.76 and serum creatinine 0.77 (Figure 2).

Serial lactate measurements over seven days showed that survivors demonstrated a steady decline toward normal by day 4 to 5, while non-survivors exhibited a secondary rise beginning around day 3, consistent with failed resuscitation and progressive microcirculatory failure [11].

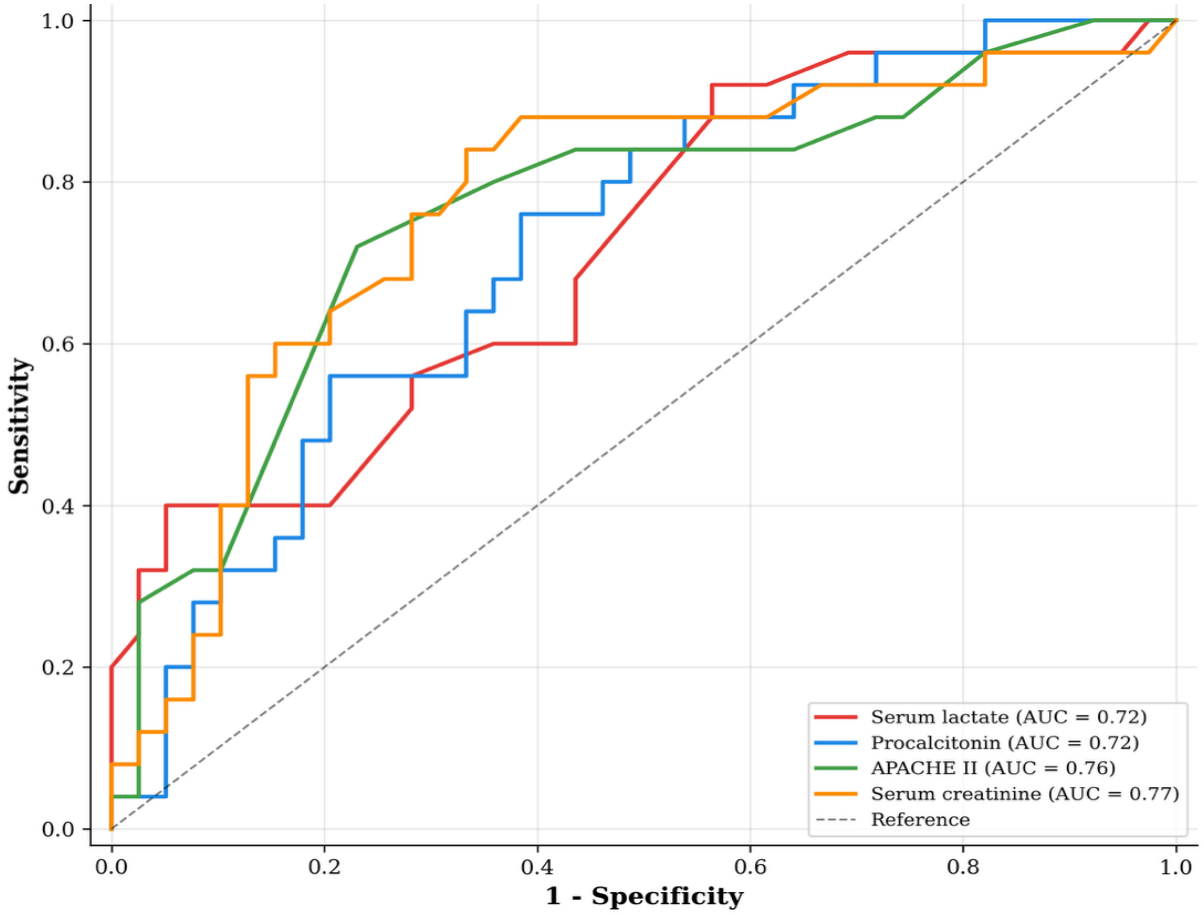

Figure 2. ROC curves for serum lactate, procalcitonin, APACHE II, and serum creatinine in predicting composite poor outcome

DISCUSSION

The principal finding is that a single measurement taken at admission separated patients with severe acute biliary pancreatitis into groups whose subsequent courses differed substantially. The value of this lies less in the strength of the association than in its timing and cost: the result is available within minutes of arrival, well before any score requiring 48 hours of observation can be completed.

Our findings are broadly consistent with those of Shu et al., who reported that arterial lactate above 4 mmol/L predicted organ failure and mortality in a mixed-etiology SAP cohort [8]. Two methodological differences deserve comment. We sampled peripheral venous rather than arterial blood; venous values run marginally higher than simultaneous arterial samples, with agreement adequate for screening, so a venous threshold should sit at or slightly above its arterial equivalent rather than below it [20]. Our cutoff of 2 mmol/L was chosen to favour sensitivity, whereas 4 mmol/L identifies a smaller group already in overt shock. That the association holds across both thresholds suggests a graded relationship rather than dependence on a single cut point. Kayhan et al. similarly found that lactate correlated with hospitalisation duration and mortality, and that

adding it to the Ranson score improved accuracy [12]—an argument for using lactate to supplement rather than replace established scores. Work on lactate-derived indices [13] and wider biomarker panels and multivariable models [14,15] points the same way.

What distinguishes this study is the exclusive focus on biliary disease. Biliary obstruction, with or without cholangitis, layers a haemodynamic insult onto the systemic inflammatory cascade of pancreatic injury, so lactate production may be amplified by deeper tissue hypoperfusion while its clearance is impaired by hepatic dysfunction. The higher total bilirubin in our elevated lactate group (median 4.0 vs 1.9 mg/dL, p=0.017) is circumstantial evidence for this dual mechanism, though direct measurement of hepatic lactate extraction would be needed to confirm it.

The substantially higher rate of multiple organ failure in the elevated lactate group (38.1% vs 9.1%, p=0.019) deserves attention; all eight deaths in this cohort occurred among the 18 patients with multiple-organ involvement. Multi-organ failure is the principal driver of early death in severe pancreatitis [4,16]. A Pakistani surgical series of severe necrotising pancreatitis reported a 12.3% mortality concentrated almost entirely in patients with multi-organ involvement [17]. Our data suggest that a simple lactate measurement at admission can flag this deteriorating trajectory early enough to influence ICU referral and the timing of biliary intervention.

A composite primary endpoint was used to address the limitations of a 64-patient cohort. Pooling death, septic shock and pancreatic infection yielded 25 events, permitting logistic regression with three predictors [10]. The significant univariate result (p=0.018) was attenuated on multivariate analysis (OR 2.6, p=0.16), as expected when correlated markers of illness severity compete in a limited sample; separating their independent contributions requires a larger dataset.

The AUC of 0.72 represents moderate but clinically useful discrimination. At the ≥2 mmol/L cutoff, 84% sensitivity identifies most patients who will deteriorate, while 46% specificity means many flagged patients recover. That trade-off is acceptable for a test whose role is to prompt closer monitoring rather than dictate management. Comparable discrimination has been reported from larger cohorts using lactate in nomogram-based prediction of organ failure and mortality [14,18].

The serial lactate data, limited by few non-survivors (n=8), showed the characteristic biphasic pattern — initial decline then rebound in those who died — mirroring observations in septic patients where failed lactate clearance predicted high ICU mortality [11,19]. A secondary rise in lactate after initial improvement should prompt urgent reassessment and search for septic foci.

Several questions follow. A multicentre cohort with sufficient events would permit mortality-specific modelling and a formal test of whether lactate adds discrimination beyond APACHE II. Whether the lactate trajectory over the first 24 to 48 hours outperforms a single admission value warrants evaluation, which our serial data suggest but cannot demonstrate. The interaction between biliary obstruction, hepatic lactate clearance and measured lactate merits direct study alongside the timing of biliary decompression.

Strengths include the prospective design, homogeneous biliary etiology, serial lactate measurements, and biliary-specific parameters relevant to surgical practice. Several limitations apply. The study was conducted at a single centre with 64 patients. Because the unit receives referrals of established severe disease, the cohort is enriched for severity and its case mix does not reflect that of an unselected population presenting with acute biliary pancreatitis. Only eight deaths occurred, precluding mortality-specific regression and leaving the multivariate model marginally powered. Pre-hospital fluid resuscitation, particularly in referred patients, may have lowered admission lactate and biased the association toward the null.

CONCLUSION

Elevated serum lactate at admission (≥2 mmol/L) is significantly associated with composite poor outcomes in patients with severe acute biliary pancreatitis, with a univariate odds ratio of 4.5 (95% CI 1.3–15.6, p=0.018). Patients with

elevated lactate also showed higher rates of multiple organ failure, pancreatic necrosis, ventilator requirement, and prolonged hospital and ICU stay. As a low-cost and rapidly available test, serum lactate provides meaningful prognostic information that can complement established severity scoring tools in the early assessment of this condition.

CONFLICT OF INTEREST

"We declare that there was no conflict of interest."

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AUTHORS CONTRIBUTIONS

UN: Substantial contributions to study design, acquisition of data, manuscript drafting, has given final approval of the version to be published.
HJ: Substantial contributions to concept, study design, critical review, has given final approval of the version to be published.
MI: Substantial contributions to analysis and interpretation of data, Critical review, Has given final approval of the version to be published.
MA: Substantial contributions to analysis and interpretation of data, Critical review, Has given final approval of the version to be published.
WR: Substantial contributions to acquisition of data and patient follow-up, critical review, has given final approval of the version to be published.
MN: Substantial contributions to acquisition of data and statistical analysis, critical review, has given final approval of the version to be published.
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