International Journal of Research in Medical Sciences
Rajak RK et al. Int J Res Med Sci. 2026 Nov;14(11):5103-5109
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20263708

Original Research Article

Early postoperative serum albumin decline as a predictor of complications following emergency exploratory laparotomy for duodenal perforation

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Received: 21 September 2026
Revised: 07 October 2026
Accepted: 08 October 2026

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ABSTRACT

Background: Emergency laparotomy for duodenal perforation carries substantial postoperative morbidity and mortality. Serum albumin falls after surgery because of inflammation-driven suppression of hepatic synthesis, capillary leak, and catabolism. We examined whether early postoperative changes in serum albumin are associated with complications and mortality after emergency surgery for duodenal perforation.

Methods: This single-centre prospective observational study was conducted over 18 months in the Department of General Surgery, Rajendra Institute of Medical Sciences (RIMS), Ranchi, India. A total of 125 patients undergoing emergency exploratory laparotomy for duodenal perforation were enrolled. Serum albumin was measured preoperatively and on postoperative days (POD) 2 and 5. The outcomes were surgical site infection (SSI), wound dehiscence, burst abdomen, bile leak, intensive care unit (ICU) requirement, and in-hospital mortality. Albumin was compared across time points and between survivors and non-survivors, and survival was analysed by albumin category (<2.5 versus ≥2.5 g/dl). A p value <0.05 was considered statistically significant.

Results: The mean age was 39.30±12.05 years, and 75 patients (60%) were male. Mean serum albumin was 2.80±1.09 g/dl preoperatively, 2.44±1.09 g/dl on POD 2, and 2.60±1.09 g/dl on POD 5 (repeated-measures ANOVA, p=0.034); the preoperative-to-POD 2 decline of 0.36 g/dl was significant on pairwise comparison (p=0.026). SSI and wound dehiscence each occurred in 66 patients (52.8%), burst abdomen in 38 (30.4%), and bile leak in 12 (9.6%). In-hospital mortality was 9.6% (12/125). Survivors had significantly higher albumin than non-survivors at all three time points (p<0.001). Survival was 100% in patients with albumin ≥2.5 g/dl and 79.3% in those with albumin <2.5 g/dl. In multiple linear regression, only length of hospital stay was an independent predictor of mortality.

Conclusions: Serum albumin fell significantly within 48 hours of emergency laparotomy for duodenal perforation, and low albumin levels, both before and after surgery, were associated with in-hospital mortality. Serial albumin measurement is a simple and inexpensive adjunct for postoperative risk stratification. However, albumin was not an independent predictor of mortality in multivariable analysis, and larger studies are needed to establish the prognostic value of the albumin decline itself.

Keywords: Postoperative albumin decline, Duodenal perforation, Emergency laparotomy, Hypoalbuminemia, ΔAlb

INTRODUCTION

Duodenal perforation is less frequent than gastric perforation but is associated with considerable morbidity, largely because of the volume and enzymatic activity of the escaping duodenal contents. Once the wall is breached, gastric acid, bile, pancreatic secretions, and enteric bacteria enter the peritoneal cavity within hours, causing

chemical and bacterial peritonitis that can progress rapidly to systemic sepsis.[1,2] Patients commonly present dehydrated, acidotic, and hemodynamically unstable, leaving little time for preoperative optimization. Emergency laparotomy for duodenal perforation is therefore among the highest-risk abdominal operations in routine surgical practice.[1,3]

Despite advances in anesthesia, perioperative antibiotic prophylaxis, and critical care, adverse events after this operation remain frequent. Wound complications, intra-abdominal collections, prolonged ileus, respiratory failure, and multi-organ dysfunction affect a substantial proportion of patients, increasing intensive care unit (ICU) admission and prolonging hospital stay.[3,4] Many of these complications become clinically apparent only after a delay of several days, when the opportunity for pre-emptive intervention may already be limited. An ideal early biomarker should therefore become abnormal within the first 24-48 hours, before overt clinical deterioration occurs.

Several biomarkers have been evaluated for this purpose. C-reactive protein (CRP) is widely available and inexpensive, but it peaks only on the second or third postoperative day, which limits its use as an early warning signal.[5] Procalcitonin is more specific for bacterial sepsis but is costly and often unavailable in resource-limited settings.[6] Interleukins and cytokine panels remain largely confined to research laboratories, and the leukocyte count is raised non-specifically by surgical trauma and has limited discriminatory power early after surgery.[6] A marker that is inexpensive, routinely measured, and responsive within 24-48 hours of surgery is therefore needed.

Albumin is the most abundant plasma protein, accounting for more than half of total plasma protein, and has a circulating half-life of about three weeks. It contributes to oncotic pressure, ligand transport, antioxidant defense, and immune modulation.[7,8] Although its long half-life once raised doubts about its sensitivity to acute events, albumin behaves as a negative acute-phase reactant: pro-inflammatory cytokines such as interleukin-6 and tumor necrosis factor-α suppress its hepatic synthesis, while increased microvascular permeability moves albumin from the intravascular to the interstitial compartment.[6,9] Fluid resuscitation, which is unavoidable in hemodynamically compromised patients, further dilutes the circulating pool. The postoperative fall in albumin (ΔAlb) is therefore thought to reflect the combined effect of the inflammatory response, capillary leak, and metabolic stress.

Preoperative hypoalbuminemia has been studied extensively in colorectal, hepatobiliary, vascular, and emergency abdominal surgery and is consistently associated with more complications, longer hospital stay, and higher mortality.[10-12] More recently, attention has turned from the static preoperative value to the dynamic postoperative decline, which may capture the physiological insult of surgery better than a single baseline measurement.[6,13] In elective major abdominal surgery, a fall in albumin of 10 g/l or more on POD 1 was associated with a threefold higher risk of overall postoperative complications.[6] A greater ΔAlb was likewise associated with complications after laparoscopic intestinal resection for Crohn's disease, where it outperformed absolute albumin values.[14] A systematic review of gastrointestinal surgery likewise identified ΔAlb as a promising early predictor of complications, with sensitivity of 63-84% and specificity of 61-86%.[15]

However, nearly all data on ΔAlb as a predictor of outcome come from elective procedures or heterogeneous emergency cohorts. Emergency laparotomy for duodenal perforation differs fundamentally from planned surgery because of pre-existing peritoneal inflammation, bacterial contamination, and systemic compromise. Whether ΔAlb retains, or even increases, its predictive value in this setting has not been adequately examined. We therefore measured early postoperative albumin changes prospectively in patients undergoing emergency exploration for duodenal perforation and examined their relationship with postoperative outcomes.

METHODS

Study design and setting

This single-centre, prospective, observational cohort study was conducted over 18 consecutive months in the Department of General Surgery, Rajendra Institute of Medical Sciences, Ranchi, a tertiary-care teaching hospital serving a predominantly rural and semi-urban population in Jharkhand, India. The study began after written approval from the institutional ethics committee.

Participant selection

All adult and adolescent patients who underwent emergency exploratory laparotomy with an intraoperatively confirmed diagnosis of duodenal perforation during the study period were eligible, irrespective of sex or of comorbidities such as type 2 diabetes mellitus, hypertension, ischemic heart disease, or chronic renal insufficiency. Patients were excluded if they had Child-Pugh class C liver disease or were pregnant, because these conditions independently alter albumin kinetics or distribution, or if informed consent was not obtained. Patients lost to follow-up before the POD 5 assessment were excluded from the final analysis.

Sample size estimation

The sample size was calculated using the formula give, assuming a reference event prevalence (p) of 95% from previously published work, a two-tailed 95% confidence level, and an absolute precision (d) of ±4%.

$N = z^2pq/d^2$

This gave a minimum of 114 participants; after adding 10% for anticipated attrition, the target sample was 125 participants.

Clinical and laboratory data collection

After informed consent, demographic data (age, sex, occupation), duration of symptoms from onset to hospital arrival, hemodynamic parameters, and comorbidities were recorded on a structured proforma. All patients underwent standard preoperative evaluation, including erect chest and abdominal radiographs, arterial blood gas analysis, and routine hematological and biochemical investigations. Serum albumin was measured by the bromocresol green colorimetric method at three predefined time points: immediately before induction of anesthesia (baseline), on the morning of POD 2, and on the morning of POD 5. The postoperative decline (ΔAlb) was calculated as the difference between the baseline and POD 2 values.

The operating surgeon documented the operative findings at the time of surgery, and the attending surgical team assessed the wound daily. Complications were recorded prospectively using predefined criteria. SSI was diagnosed according to the centers for disease control and prevention criteria, and wound dehiscence was graded using the world union of wound healing societies classification.

Burst abdomen was defined as full-thickness disruption of the abdominal wall requiring operative repair. Bile leak was diagnosed biochemically when the bilirubin concentration in drain fluid exceeded three times the serum bilirubin concentration. ICU requirement and in-hospital mortality were also recorded as outcomes.

Statistical methods

Data were analysed using IBM statistical package for the social sciences (SPSS) statistics version 21. Normally distributed continuous variables are presented as mean ± standard deviation (SD) and were compared between groups using the independent-samples t-test. Categorical variables are presented as counts and percentages and were compared using Pearson's Chi-square test or Fisher's exact test, as appropriate.

Changes in albumin across the three time points were analysed by one-way repeated-measures ANOVA, with Bonferroni-corrected pairwise comparisons. Multiple linear regression was used to identify independent predictors of mortality after adjustment for confounders. Survival according to albumin category was estimated by the Kaplan-Meier method and compared using the log-rank test.

A two-tailed p value <0.05 was considered statistically significant.

RESULTS

Sociodemographic characteristics

A total of 125 patients met the eligibility criteria and completed the observation period, and all were included in the final analysis. The largest age group was ≤30 years (38 patients, 30.4%), followed by 51-60 years (31 patients, 24.8%), with 28 patients (22.4%) each in the 31-40- and 41-50-year groups. The mean age was 39.30±12.05 years. There were 75 males (60%) and 50 females (40%), a ratio of 3:2. The interval from symptom onset to presentation was 1-2 days in 52 patients (41.6%), 3-4 days in 52 patients (41.6%), and 5 days or more in [22 patients (17.6%)] (Table 1).

Table 1: Sociodemographic and clinical profile of study participants (n=125).

Characteristic	N	% or mean±SD
Age group (years)		
≤30	38	30.4
31-40	28	22.4
41-50	28	22.4
51-60	31	24.8
Mean age	-	39.30±12.05 years
Sex		
Male	75	60.0
Female	50	40.0
Symptom duration before admission (days)		
1=2	52	41.6
3=4	52	41.6
≥5	22	17.6

Postoperative complications, ICU requirement, and mortality

Wound-related complications were common. SSI and wound dehiscence, which frequently co-occurred, were each recorded in 66 patients (52.8%). Burst abdomen requiring operative repair occurred in 38 patients (30.4%), and bile leak in 12 patients (9.6%). ICU care was required in 38 patients (30.4%) overall, rising to 57.6% (38/66) among patients who developed any complication. Twelve patients (9.6%) died before discharge, and all deaths occurred among the 66 patients with at least one postoperative complication (p=0.002), giving a mortality of 18.2% in that subgroup (Table 2).

Temporal pattern of serum albumin

Serum albumin fell from the preoperative baseline to a nadir on POD 2 and recovered partially by POD 5 without returning to the baseline level. Mean albumin was 2.80±1.09 g/dl preoperatively, 2.44±1.09 g/dl on POD 2, and 2.60±1.09 g/dl on POD 5. Repeated-measures ANOVA showed a significant overall change across the three time points (F=3.41, p=0.034). On pairwise comparison, the decline of 0.36 g/dl from baseline to POD

2 was significant (p=0.026), whereas the difference between baseline and POD 5 (0.20 g/dl, p=0.319) and the increase of 0.16 g/dl between POD 2 and POD 5 (p=0.478) were not (Table 3).

Table 2: Postoperative outcomes in the study cohort (n=125).

Outcome variable	Frequency (N)	Percentage (%)
Surgical site infection	66	52.8
Wound dehiscence	66	52.8
Burst abdomen	38	30.4
Bile leak	12	9.6
ICU admission (overall)	38	30.4
ICU admission (among complicated cases)	38/66	57.6
In-hospital mortality (overall)	12	9.6
In-hospital mortality (among complicated cases)	12/66	18.2

Table 3: Serial serum albumin measurements and statistical comparisons.

Time point	Mean albumin± SD (g/dl)	F (ANOVA)	P value
Preoperative (baseline)	2.80±1.09	-	-
Postoperative day 2	2.44±1.09	-	-
Postoperative day 5	2.60±1.09	-	-
Overall change (repeated-measures ANOVA)	-	3.41	0.034*
Preop versus POD 2 (pairwise)	Δ=0.36 g/dl	-	0.026*
Preop versus POD 5 (pairwise)	Δ=0.20 g/dl	-	0.319
POD 2 versus POD 5 (pairwise)	Δ=0.16 g/dl	-	0.478

*Statistically significant SD=standard deviation; POD=postoperative day

Albumin levels according to survival outcome

Albumin differed markedly between survivors and non-survivors at every time point. Among the 113 survivors, mean albumin was 2.97±1.01 g/dl at baseline, 2.61±1.01 g/dl on POD 2, and 2.77±1.01 g/dl on POD 5, compared with 1.23±0.11, 0.84±0.11, and 1.04±0.11 g/dl, respectively, in the 12 non-survivors (independent-samples t-test: t =5.96, 6.06, and 5.90; p<0.001 for all comparisons) (Table 4).

Kaplan-Meier analysis stratified by albumin category (<2.5 versus ≥2.5 g/dl) showed that all patients with albumin ≥2.5 g/dl survived to discharge (100%), whereas survival was 79.3% in the group with albumin <2.5 g/dl ([log-rank p value to be inserted]).

Regression analysis and sex-mortality association

Multiple linear regression with age, symptom duration, preoperative albumin, POD 2 albumin, POD 5 albumin, and length of hospital stay as predictors identified hospital stay as the only significant variable (B=0.047; 95% CI 0.031-0.063; t=5.807; p<0.001). Albumin at none of the time points was an independent predictor of mortality. Chi-square analysis showed a significant association between male sex and mortality (p=0.002), as all 12 deaths occurred in male patients and no female patient died.

Table 4: Comparison of serum albumin levels between survivors and non-survivors.

Time point	Survivors (n=113), mean±SD	Non-survivors (n=12), mean±SD	t	P value
Preoperative	2.97±1.01	1.23±0.11	5.96	<0.001
POD 2	2.61±1.01	0.84±0.11	6.06	<0.001
POD 5	2.77±1.01	1.04±0.11	5.90	<0.001

POD=postoperative day; SD=standard deviation

DISCUSSION

In this prospective study of patients undergoing emergency laparotomy for duodenal perforation, serum albumin fell significantly within 48 hours of surgery and recovered only partially by POD 5. Albumin concentrations were consistently lower in patients who died than in survivors, at baseline and at both postoperative time points, and the mean values in non-survivors were less than half of those in survivors. These findings suggest that serial albumin measurement may provide useful prognostic information in this high-risk group. However, because non-survivors already had markedly low albumin before surgery, the difference between the groups appears to reflect baseline depletion at least as much as the postoperative fall.

The demographic profile of our cohort, predominantly young to middle-aged men presenting within four days of symptom onset, is consistent with the epidemiology of peptic ulcer perforation on the Indian subcontinent, where complications of peptic ulcer disease disproportionately affect working-age men. The mean age of 39.30±12.05 years and the male proportion of 60% are comparable to those reported by Rohith et al in an emergency laparotomy cohort (mean age 34.2 years; 61.7% male).[16] The male predominance is usually attributed to higher rates of alcohol use, smoking, and substance abuse among men.[16] In contrast, Mazia et al reported an equal number of men and women in a series of patients undergoing emergency laparotomy for non-traumatic acute abdomen.[17]

The wound complication rate in our study was high: SSI and wound dehiscence each affected 52.8% of patients, and burst abdomen occurred in nearly one-third. These

rates reflect the unfavorable wound-healing environment created by peritoneal contamination, systemic inflammation, and poor nutritional status at presentation. Similarly, Kumar and Sivakumar, studying emergency laparotomy, identified wound-related events as the most frequent complications.[18] The high complication burden in our patients underscores the need for tools that identify risk early.

The postoperative fall in albumin in our patients is consistent with the acute-phase response to major surgical trauma. Pro-inflammatory mediators, chiefly interleukin-6, tumor necrosis factor-α, and interleukin-1β, suppress albumin gene transcription in hepatocytes while upregulating positive acute-phase proteins such as CRP and fibrinogen.[6,9] In addition, disruption of the endothelial glycocalyx increases microvascular permeability and allows albumin to move from the plasma into the interstitium.[6] Where pre-existing peritonitis amplifies endothelial injury, as in duodenal perforation, this loss may be greater than in elective surgery. In a prospective study of elective major abdominal surgery, Labgaa et al showed that the albumin decrease on POD 1 correlated with the rise in CRP ($r=0.536$, $p<0.001$) and with postoperative complications ($r=0.485$, $p<0.001$), supporting the use of albumin as a marker of surgical stress.[6] Our study extends this observation to emergency surgery. A significant albumin fall from POD 1 to POD 5 relative to preoperative values was also reported in a mixed elective and emergency laparotomy cohort.[19]

The difference in albumin between survivors and non-survivors was large. Preoperative albumin averaged 1.23 g/dl in non-survivors, a level indicating severe pre-existing protein depletion, compared with 2.97 g/dl in survivors, and it fell further to 0.84 g/dl on POD 2. At such concentrations, loss of oncotic pressure, immune impairment, and altered drug pharmacokinetics may be expected to contribute to clinical deterioration. The absolute fall from baseline to POD 2 was similar in the two groups (0.39 g/dl in non-survivors and 0.36 g/dl in survivors, calculated from the mean values), which suggests that the prognostic signal in our cohort lay mainly in the low albumin level itself rather than in the size of the early decline. Liu et al reported complications in 46.7% of patients whose albumin fell by 14% or more after gastrectomy, compared with 5.0% of those with smaller declines.[20] Ahmed and Sarma observed complications in 44.6% of hypoalbuminemic patients undergoing emergency abdominal surgery, compared with 17.5% of those with normal albumin.[21] Direct comparison is limited because these studies examined complications rather than mortality, but the large albumin gap in our cohort may reflect the greater inflammatory burden of duodenal perforation with peritonitis.

Kaplan-Meier analysis showed that all patients with albumin ≥2.5 g/dl survived to discharge, whereas survival was 79.3% in those with albumin <2.5 g/dl, which suggests a threshold effect. This is in line with the findings of Petch-in et al, who reported an adjusted odds ratio of 8.11 for in-hospital death among patients with severe preoperative hypoalbuminemia undergoing major gastrointestinal surgery, compared with patients with normal albumin.[22] Larsen et al likewise found that preoperative hypoalbuminemia predicted early mortality after open abdominal surgery in patients older than 60 years.[23] The consistency of the association between low albumin and mortality across different surgical populations and study designs supports its biological plausibility.

In a systematic review of gastrointestinal surgery, Joliat et al. reported that ΔAlb predicted postoperative complications with a sensitivity of 63-84% and a specificity of 61-86%, with optimal cut-offs of 5-11 g/l for the absolute decline and 14-27% for the percentage decline.[15] Reddy et al, studying emergency laparotomy for gastrointestinal conditions, identified a POD 1 albumin fall of 1 g/dl or more as a predictor of postoperative complications, with 71.1% sensitivity, 97.4% specificity, and 83.3% diagnostic accuracy.[24] We did not perform receiver operating characteristic (ROC) analysis and therefore could not derive a ΔAlb cut-off specific to duodenal perforation. Larger studies are needed to establish such a threshold.

A practical advantage of albumin monitoring is its availability. Unlike procalcitonin or cytokine assays, which require specialized reagents, trained personnel, and considerable expense, serum albumin is part of the standard liver function and protein panels offered by most hospitals, including district-level facilities. In India, where emergency surgical admissions often strain under-resourced hospitals, an inexpensive and widely available biomarker that can stratify risk within 48 hours of surgery has clear practical value. Mishra et al likewise found larger postoperative albumin drops in patients with surgical site infection and delayed wound healing after exploratory laparotomy, and recommended preoperative nutritional optimization.[25]

Although albumin distinguished survivors from non-survivors in unadjusted comparisons, hospital stay, rather than any albumin measurement, was the only independent predictor of mortality in the multivariable model. Hospital stay may be both a consequence of complications driven by low albumin and a marker of cumulative clinical deterioration, so the relationship is probably bidirectional. Albumin may act earlier in the causal pathway by predisposing patients to complications that prolong hospital stay and ultimately affect survival. Testing this hypothesis would require a longitudinal design with repeated albumin measurements and formal mediation analysis. Moreover, hospital stay is known only after the outcome has occurred and therefore cannot be used for prospective risk stratification, and the small number of deaths (n=12) relative to the number of covariates (six) limits the stability of the regression estimates.

This study has several limitations. First, it was conducted at a single tertiary centre, which may limit generalizability to settings with different patient populations or surgical volumes. Second, comparative biomarkers such as CRP, procalcitonin, and the neutrophil-to-lymphocyte ratio were not measured, so head-to-head comparison of predictive accuracy was not possible. Third, follow-up was limited to the in-hospital period, and 30-day and 90-day outcomes after discharge were not assessed. Fourth, nutritional assessment tools such as the malnutrition universal screening tool or the prognostic nutritional index were not applied, so the contribution of pre-existing malnutrition to the observed albumin patterns could not be quantified. Fifth, all 12 deaths occurred in men; given the small number of deaths, this association may be due to chance and should be interpreted cautiously. A larger, adequately powered multicentre study is warranted.

CONCLUSION

Serum albumin fell significantly within 48 hours of emergency exploratory laparotomy for duodenal perforation and recovered only partially by POD 5. Low albumin concentrations, both before and after surgery, were strongly associated with in-hospital mortality, and no deaths occurred among patients with albumin ≥2.5 g/dl. However, albumin was not an independent predictor of mortality in multivariable analysis, and this study did not show that the size of the early decline itself predicts outcome. Serial measurement of serum albumin, at baseline and on POD 2 at a minimum, is a simple and inexpensive adjunct that may help identify patients who need closer monitoring, intensive wound care, and nutritional support. Larger multicentre studies should test whether such an approach improves surgical outcomes.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Rajak RK, Kamal AK, Gaurav K, Madhu. Early postoperative serum albumin decline as a predictor of complications following emergency exploratory laparotomy for duodenal perforation. Int J Res Med Sci 2026;14:5103-9.