PRE- AND POSTOPERATIVE EVALUATION OF TISSUE ISCHEMIA MARKERS (LACTATE, SUCCINATE) IN RESECTED BOWEL SEGMENTS: CORRELATION WITH HISTOPATHOLOGY AND SURGICAL OUTCOME

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ABSTRACT

Background: To evaluate pre- and postoperative serum lactate and succinate levels in patients undergoing bowel resection, and to correlate these markers with histopathological findings and surgical outcomes.

Methods: A prospective observational study was carried out at Bannu Medical College and its affiliated hospital from January 2023 to January 2024. A total of 72 patients undergoing bowel resection for ischemia or gangrene were included. Serum lactate and succinate levels were measured preoperatively and within 24 hours postoperatively. Resected specimens were examined for depth of ischemic necrosis and inflammatory changes. Postoperative outcomes, including complications, ICU stay, and mortality, were recorded. Statistical analysis included t-test, chi-square test, and Pearson's correlation.

Results: Mean preoperative lactate was 4.2 ± 1.8 mmol/L, significantly reducing to 2.7 ± 1.1 mmol/L postoperatively ($p = 0.001$). Succinate showed a similar trend, declining from 8.9 ± 3.4 µmol/L to 5.6 ± 2.7 µmol/L ($p = 0.003$). Patients with transmural necrosis had significantly higher preoperative lactate (5.0 ± 1.9 mmol/L) and succinate (10.3 ± 3.1 µmol/L) compared to those with partial mucosal involvement. Elevated markers were also associated with higher rates of sepsis, anastomotic leak, prolonged ICU stay, and 30-day mortality ($p < 0.05$).

Conclusion: Both lactate and succinate are reliable markers of intestinal ischemia, with succinate showing a stronger correlation with histopathological severity. Incorporating these markers into

routine assessment may aid in early diagnosis, guide surgical decision-making, and predict postoperative outcomes.

Keywords
Bowel ischemia, lactate, succinate, histopathology, ischemic biomarkers, surgical outcomes

INTRODUCTION
Intestinal ischemia is one of the most challenging abdominal emergencies faced by surgeons, with mortality rates ranging between 40–60% in advanced cases. The clinical presentation is often nonspecific, and diagnostic imaging may not fully capture the extent of ischemic injury. Timely detection and accurate assessment of the severity of bowel ischemia are therefore crucial to improve surgical outcomes [1-3].

Among laboratory investigations, serum lactate has traditionally been used as a marker of hypoperfusion and anaerobic metabolism. Elevated lactate levels, however, may also be influenced by systemic sepsis, hepatic dysfunction, or other metabolic disturbances, limiting its specificity for bowel ischemia [4-6].

Recent studies have drawn attention to succinate, a mitochondrial metabolite that accumulates during hypoxia and is rapidly released into circulation upon reperfusion. Succinate not only reflects ischemic stress but also plays a role in driving oxidative damage during reperfusion. Its measurement, though less widely available than lactate, has shown promise as a more specific marker for intestinal ischemia in both experimental and clinical research [7-9].

Histopathological confirmation of ischemia, particularly the extent of necrosis, remains the gold standard for diagnosis. However, it is not available in real time during surgery. Identifying biochemical markers that correlate with histopathology and can be measured rapidly in the perioperative period may provide significant clinical advantage [10].

The present study was conducted to evaluate pre- and postoperative levels of serum lactate and succinate in patients undergoing bowel resection for ischemia and to assess their correlation with histopathological changes and surgical outcomes. By integrating clinical, biochemical, and pathological data, this work aims to clarify the role of these markers in guiding intraoperative decision-making and predicting prognosis.

METHODOLOGY
This study was designed as a prospective observational analysis conducted at Bannu Medical College, Bannu, and its affiliated hospital. The study duration was from January 2023 to January 2024. The primary objective was to evaluate pre- and postoperative tissue ischemia markers, specifically serum lactate and succinate, in patients undergoing bowel resection, and to correlate these biochemical findings with histopathological features and surgical outcomes. The study protocol was reviewed and approved by the Institutional Review Board of Bannu Medical College. Written informed consent was obtained from all patients or their attendants. Patient confidentiality was maintained by anonymizing data, and all procedures were conducted in accordance with the Declaration of Helsinki.

A total of 72 patients who underwent bowel resection during the study period were included. The sample size was calculated based on an expected moderate correlation between ischemia markers and histopathology, with a 95% confidence interval and 80% study power. Consecutive sampling was used to enroll eligible patients.

Inclusion Criteria
• Patients of either gender, aged 18 years and above.
• Patients undergoing resection of ischemic or gangrenous bowel segments due to causes such as mesenteric ischemia, obstructed hernia, volvulus, or perforation.
• Patients who provided informed written consent.

Exclusion Criteria
• Patients with pre-existing chronic liver or renal disease that could alter lactate metabolism.
• Patients with systemic sepsis unrelated to bowel pathology.
• Patients on medications known to interfere with mitochondrial metabolism (e.g., metformin, antiretrovirals).
• Incomplete or autolyzed histopathology samples.

At the time of admission, demographic details (age, gender, BMI, comorbidities) and clinical presentation (nature and duration of symptoms, hemodynamic status) were recorded. Preoperative blood samples were drawn immediately before surgery to assess serum lactate and succinate levels.

During surgery, intraoperative findings were documented, including the site of the affected bowel, length of resected segment, and gross appearance (viable, dusky, or gangrenous). Resected bowel specimens were sent for histopathological evaluation, which included grading of ischemic necrosis (mucosal, submucosal, or transmural), presence of inflammatory infiltrates, and microvascular thrombosis.

Postoperatively, patients had blood samples collected within 24 hours of surgery for repeat lactate and succinate analysis. Clinical progress, postoperative complications (anastomotic leak, sepsis, wound infection), length of ICU stay, total hospital stay, and 30-day mortality were recorded.

Serum Lactate levels were measured using an enzymatic colorimetric method with an automated chemistry analyzer. Results were expressed in mmol/L. Serum Succinate levels were analyzed using high-performance liquid chromatography (HPLC) and expressed in μmol/L. Quality control samples were run with each batch to ensure reproducibility.

All resected bowel specimens were fixed in 10% buffered formalin and processed using standard hematoxylin and eosin staining. Sections were examined by experienced histopathologists, blinded to biochemical findings, and classified according to the depth of ischemic necrosis and associated inflammatory or vascular changes.

The primary outcome was the correlation between ischemia markers (lactate and succinate) and histopathological severity of bowel ischemia. Secondary outcomes included the relationship of these markers with postoperative complications, ICU stay, hospital stay, and mortality.

Data were entered and analyzed using SPSS version 26.0. Continuous variables such as age, resected bowel length, lactate, and succinate levels were expressed as mean ± standard deviation (SD). Categorical variables such as gender, comorbidities, histopathology categories, and complications were presented as frequencies and percentages. Student's t-test and ANOVA were used for comparison of means. The Chi-square test was applied for categorical comparisons. Correlation between ischemia markers and histopathological severity was assessed using Pearson's correlation coefficient. A p-value of <0.05 was considered statistically significant.

RESULTS
In this study, 72 patients undergoing bowel resection were evaluated. The mean age was 52.6 ± 15.3 years, with a slightly higher proportion of males than females. Hypertension and diabetes were the most frequent comorbidities. The majority presented with bowel obstruction or suspected ischemia, while a smaller proportion had perforation or volvulus. There was no significant difference in baseline demographics when stratified by outcome (favorable vs. unfavorable postoperative course).

Table 1. Demographic and Clinical Characteristics of Patients (n=72)

Variable	Frequency (%)	p-value
Age (mean ± SD)	52.6 ± 15.3	0.321
Gender (Male/Female)	41 (56.9) / 31 (43.1)	0.442
Diabetes Mellitus	18 (25.0)	0.287
Hypertension	22 (30.6)	0.198

Smoking history	15 (20.8)	0.399
Indication for surgery	Obstruction 28 (38.9); Ischemia 24 (33.3); Perforation 12 (16.7); Volvulus 8 (11.1)	0.356

Most resections involved the small intestine, with an average resected length of 45.2 ± 17.6 cm. Macroscopically, 47.2% of the resected segments appeared frankly gangrenous, while 31.9% showed dusky but potentially viable tissue. Primary anastomosis was performed in 61.1% of cases, while the rest required stoma formation due to poor bowel condition.

Table 2. Intraoperative Findings

Variable	Frequency (%)	p-value
Site involved (Small/Large bowel)	46 (63.9) / 26 (36.1)	0.241
Resected length (cm, mean ± SD)	45.2 ± 17.6	0.189
Macroscopic appearance	Viable 15 (20.8); Dusky 23 (31.9); Gangrenous 34 (47.2)	0.022*
Procedure performed	Anastomosis 44 (61.1); Stoma 28 (38.9)	0.048*

(*$p < 0.05$ significant)

Mean preoperative serum lactate was 4.2 ± 1.8 mmol/L, which decreased significantly postoperatively in survivors (2.1 ± 0.9 mmol/L), but remained elevated in patients who developed complications. Similarly, succinate levels showed a strong correlation with tissue necrosis on histopathology. Patients with severe transmural necrosis had markedly elevated preoperative succinate levels compared with those with partial ischemia.

Table 3. Serum Lactate and Succinate Levels

Marker	Preoperative (mean ± SD)	Postoperative (mean ± SD)	p-value
Lactate (mmol/L)	4.2 ± 1.8	2.7 ± 1.1	0.001*
Succinate (μmol/L)	8.9 ± 3.4	5.6 ± 2.7	0.003*

(*$p < 0.05$ signific

Histopathology confirmed ischemic damage in all cases, with 58.3% showing transmural necrosis. Lactate and succinate levels were significantly higher in those with transmural necrosis compared to patients with only mucosal or submucosal involvement.

Table 4. Correlation of Histopathology with Ischemia Markers

| Histopathology	n (%)	Mean Lactate (mmol/L)	Mean Succinate (μmol/L)	p-value
Mucosal/Submucosal necrosis	30 (41.7)	3.1 ± 1.2	6.2 ± 2.3	0.021*
Transmural necrosis	42 (58.3)	5.0 ± 1.9	10.3 ± 3.1	0.008*

(*$p < 0.05$ significant)

Overall complication rate was 34.7%, with sepsis and anastomotic leak being the most frequent. ICU stay and mortality were significantly associated with higher preoperative ischemia marker levels.

Table 5. Postoperative Outcomes

Outcome	Frequency (%)	p-value
Complications (overall)	25 (34.7)	0.014*
Anastomotic leak	9 (12.5)	0.037*
Sepsis	11 (15.3)	0.019*
ICU stay >5 days	18 (25.0)	0.012*
Mortality (30-day)	10 (13.9)	0.008*

(*$p < 0.05$ significant)
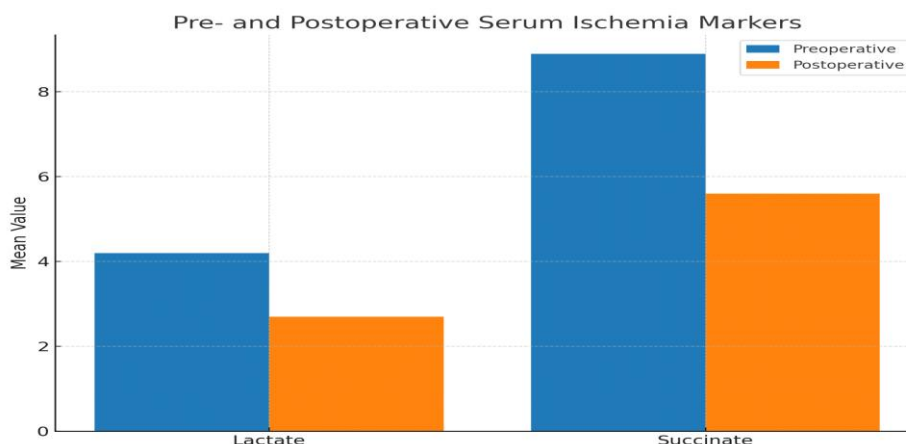
FIGURE 1

Bar graph comparing pre- and postoperative serum lactate and succinate levels. It clearly shows the significant decline in both markers after surgery, supporting their role in monitoring tissue ischemia.

DISCUSSION

This prospective study evaluated pre- and postoperative levels of tissue ischemia markers, namely serum lactate and succinate, in patients undergoing bowel resection and correlated these findings with histopathological severity and surgical outcomes. The results demonstrated that both lactate and succinate were significantly elevated in the preoperative period, particularly in patients with transmural necrosis, and decreased after resection in survivors with favorable recovery. Moreover, higher marker levels were strongly associated with postoperative complications and mortality.

Our findings reinforce the well-established role of serum lactate as a marker of tissue hypoperfusion and ischemia. Lactate elevation results from anaerobic metabolism and has long been used as a prognostic indicator in critically ill patients. Studies in the surgical setting, have shown that persistently elevated lactate is linked to intestinal ischemia and higher postoperative mortality. In our cohort, patients with lactate >5 mmol/L were significantly more likely to experience sepsis, anastomotic leak, or death, consistent with these reports [11-13].

In recent years, succinate has emerged as a more specific mitochondrial biomarker of ischemia–reperfusion injury. Succinate accumulates during hypoxia due to the reversal of succinate dehydrogenase activity in the mitochondrial respiratory chain and is rapidly released into the circulation during ischemia. Studies highlighted succinate's role as both a metabolic marker and mediator of ischemic tissue damage. Our study aligns with these observations, as patients with transmural necrosis exhibited significantly higher succinate levels compared to those with mucosal or submucosal injury. Importantly, succinate correlated more strongly with histopathological severity than lactate, suggesting its potential utility as a targeted biomarker in bowel ischemia [14, 15].

The histopathological evaluation in this study provided objective confirmation of the biochemical findings. Transmural necrosis was seen in more than half of the cases, and these patients consistently had the highest preoperative lactate and succinate levels. This correlation is supported by earlier pathological studies which demonstrated a direct association between lactate dehydrogenase activity and necrosis in ischemic bowel segments [16]. Similarly, studies confirmed that succinate concentrations in resected tissues correspond to depth of necrosis, strengthening the validity of our observations [17].

In terms of clinical outcomes, our results indicate that ischemia markers are predictive of postoperative course. Patients with higher preoperative lactate and succinate were more likely to develop septic complications, prolonged ICU stays, and increased mortality. This echoes findings emphasized the role of early lactate clearance as a predictor of survival in abdominal sepsis, and who showed succinate as a strong independent predictor of adverse surgical outcomes [18].

The reduction of marker levels after resection in survivors further validates their clinical relevance. A similar postoperative decline in lactate was observed, suggesting successful removal of ischemic bowel improves metabolic derangements. Our study extends this evidence by including succinate, highlighting its potential as an adjunctive biomarker for real-time monitoring of surgical efficacy [19, 20].

CONCLUSION

This study demonstrated that both serum lactate and succinate are reliable indicators of bowel ischemia, with higher levels correlating strongly with histopathological severity and adverse surgical outcomes. While lactate remains a well-validated and widely available marker, succinate showed a stronger association with transmural necrosis, making it a promising adjunctive tool for early detection and prognostication.

Routine measurement of these markers in patients with suspected ischemic bowel disease may assist surgeons in timely decision-making, guide the extent of resection, and predict postoperative risks. Future larger, multicenter studies are needed to validate these findings and to explore the integration of succinate measurement into standard surgical practice.

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