Section: General Surgery

Original Research Article

A STUDY IN CORRELATION OF PREOPERATIVE SERUM LDH AND C-REACTIVE PROTEIN IN PREDICTING BOWEL NECROSIS – A CROSS-SECTIONAL STUDY AMONG PATIENTS PRESENTING TO A TERTIARY CARE HOSPITAL IN SALEM

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Received : 12/03/2024
Received in revised form : 20/05/2024
Accepted : 04/06/2024

Keywords:
Bowel obstruction, CRP, LDH, Necrosis, Strangulation.

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DOI: 10.47009/jamp.2024.6.3.105

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (3); 511-516

Abstract

Background: Intestinal obstruction represents a prevalent pathological condition encountered in surgical practice, giving rise to notable complications such as strangulation. Various studies suggests that preoperative serum CRP & LDH levels can serve as a valuable biomarker in predicting bowel necrosis by reflecting the extent of tissue damage and inflammation. Hence this study aims to investigate the correlation between preoperative serum LDH and C-reactive protein in predicting bowel necrosis in patients presenting to a tertiary care hospital in Salem. **Materials and Methods:** It is a cross-sectional study conducted on 66 patients who presented with clinical indications suggestive of acute intestinal obstruction at the Vinayaka Mission's Kirupananda Variyar Medical College and Hospital in Salem. The patients were divided into two groups based on intraoperative findings: those with simple bowel obstruction and those with strangulated bowel obstruction. **Result:** The study showed a significant correlation between preoperative serum LDH and C-reactive protein levels and the presence of bowel necrosis. C-reactive protein (CRP) and lactate dehydrogenase (LDH) positively correlated ($r_s = 0.726$, $p < 0.001$) and were significantly elevated in strangulated necrotic bowel, emphasizing their diagnostic value. Significant associations included a strangulated abdomen with younger age, shock, and duration of symptoms. **Conclusion:** C-reactive protein (CRP) and lactate dehydrogenase (LDH) demonstrated a strong positive correlation and were notably heightened in cases of strangulated necrotic bowel, emphasizing their diagnostic significance. The study also suggests the combination of these two biomarkers can provide valuable insights into the presence and extent of tissue damage, including in the context of bowel necrosis.

INTRODUCTION

Intestinal obstruction represents a prevalent pathological condition encountered in surgical practice, giving rise to notable complications such as strangulation, necessitating emergent celiotomy for intervention. Acute mesenteric ischemia (AMI) represents a critical gastrointestinal and vascular emergency, with its occurrence exhibiting an exponential rise in tandem with advancing age.

The immediate fatality rates associated with AMI are considerable, primarily attributable to the onset of intestinal necrosis. This frequently necessitates extensive surgical interventions involving substantial intestinal resections. Consequently, survivors of AMI are frequently afflicted with short bowel syndrome, further exacerbating the challenges in their postoperative recovery.[1]

The concomitant occurrence of ischemia in 7 to 42% of instances of bowel obstructions markedly amplifies the associated mortality. Temporal considerations are paramount, as expedited diagnosis of strangulation correlates with enhanced patient survival. Clinical discernment remains central to the diagnostic process, characterized by abrupt onset of continuous pain, early manifestation of shock, pyrexia, tachycardia, pronounced abdominal tenderness, guarding, rebound tenderness, and the presence of a tender abdominal mass.

Additionally, a spectrum of biochemical markers, including serum tumor necrosis factor α, C-reactive protein, interleukin-6, D-lactate, D-dimer, alpha

ISSN (O): 2687-5365; ISSN (P): 2753-6556

glutathione S-transferase, intestinal fatty acid binding protein, creatine kinase B, lactate dehydrogenase isoenzymes, procalcitonin, alkaline liver phosphatase, and urinary phosphate, has been investigated, predominantly in animal models and to a limited extent in clinical contexts.[2-4]

Despite these efforts, a comprehensive understanding of the utility of biomarkers in predicting strangulation in cases of acute bowel obstruction remains elusive. Further dedicated research, particularly in human clinical settings, is imperative to elucidate the precise role and efficacy of biomarkers in preoperative prognostication of strangulation in acute bowel obstruction patients.

In the context of predicting bowel necrosis, the correlation between preoperative serum lactate dehydrogenase (LDH) and C-reactive protein (CRP) levels has been a subject of interest in various medical studies. LDH is an enzyme that is released from damaged cells, including those in the bowel, and elevated levels can indicate tissue damage or necrosis.[5] On the other hand, CRP is a marker of inflammation and has been studied in various medical conditions to assess the severity of inflammation and tissue damage.[6-10]

The combination of these two biomarkers, LDH and CRP, can provide valuable insights into the presence and extent of tissue damage, including in the context of bowel necrosis. Studies have shown that CRP levels can be indicative of the severity of tissue damage and inflammation in various conditions, such as hepatocellular carcinoma,[6] heart failure,[11] ulcerative colitis,[7] breast cancer surgery,[8] and upper urinary tract urothelial carcinoma.[9] Additionally, the correlation between CRP and various inflammatory markers like interleukin-1β, interleukin-6, and tumour necrosis factor-α has been investigated in colorectal cancer,[12] further emphasizing the role of CRP in reflecting inflammatory processes.

Moreover, the prognostic value of CRP has been explored in different malignancies, including bladder cancer,[13] myeloma bone disease,[14] and malignant fibrous histiocytoma,[15] indicating its potential as a predictive biomarker for outcomes in cancer patients. Furthermore, the association between CRP and other factors like serum retinol, systemic inflammatory response, and lympho-vascular invasion in non-small cell lung cancer has been studied, highlighting the diverse applications of CRP in assessing disease severity and prognosis.[14-18]

The synthesis of these studies suggests that preoperative serum CRP levels can serve as a valuable biomarker in predicting bowel necrosis by reflecting the extent of tissue damage and inflammation. Hence assessing correlation between CRP and other biomarkers like LDH can provide a comprehensive assessment of the pathological processes underlying bowel necrosis, aiding in early detection and management of this critical condition.

MATERIALS AND METHODS

Study design, area and duration: After obtaining Ethical clearance from the Institutional Ethical Committee, this observational cross sectional study was conducted with 66 consecutively selected adult patients who presented at the casualty of the Vinayaka Mission's Kirupananda Variyar Medical College and Hospital, Salem during the period from October 2023 to September 2024, exhibiting clinical indications suggestive of acute intestinal obstruction and subsequently undergoing emergency surgical procedures. The cohort was divided into two groups based on intraoperative findings: those with simple bowel obstruction and those with strangulated bowel obstruction.

Study population: Exclusion criteria comprised individuals with concomitant medical conditions, specifically chronic kidney diseases, cardiac ailments, diabetes mellitus, and coagulopathy, as these conditions have the potential to influence the progression of obstruction-strangulation dynamics in patients with acute intestinal obstruction. This was done as a measure of avoiding bias, as these medical comorbidities could introduce confounding factors, particularly in the cases of diabetes and chronic kidney disease, leading to erroneous positive outcomes. Furthermore, patients presenting with intraoperative findings beyond simple or strangulated bowel obstruction were also excluded.

Sampling and inclusion strategy: Consecutively, 66 individuals presenting with symptoms indicative of acute abdominal issues were initially considered for potential bowel obstruction. Subsequently, 11 patients undergoing conservative management for bowel obstruction and an additional 12 individuals concurrently affected by other medical conditions were excluded from the study. Consequently, a cohort of 43 patients diagnosed with bowel obstruction underwent surgical intervention. Eight patients exhibiting intraoperative findings beyond the scope of obstruction and/or strangulation were further excluded, resulting in the inclusion of a final sample size of 35 patients.

Upon surgical examination, the participants were categorized into two distinct groups based on their pathology: those presenting with strangulated bowel obstruction - necrosis (n = 14) and those manifesting simple bowel obstruction (n = 21). This methodology ensured a more refined analysis and classification of the cohort in accordance with the surgical findings. Measures were taken to uphold academic standards and prevent any instances of plagiarism.

Data collection: The proforma for this study was derived from a study conducted by Ajay K Pal et al in Uttar Pradesh (An open access article). Demographic parameters, including age and gender, along with clinical manifestations such as duration of symptoms, diffuse pain, generalized abdominal distension, vomiting, fever, obstipation, history of prior abdominal surgery, shock (defined as systolic blood pressure <90 mm Hg), tenderness, guarding or

ISSN (O): 2687-5365; ISSN (P): 2753-6556

rigidity, and exaggeration of bowel sounds, constituted the variables analysed in this investigation. Informed consent was obtained from all participating patients to ensure adherence to ethical standards.

Blood samples were obtained from 66 patients upon their initial presentation to the emergency department within a timeframe of 20 minutes from arrival. All individuals were under investigation for suspected acute intestinal obstruction. Subsequently, venous blood specimens were procured and dispatched to the Department of Biochemistry for the assessment of total leukocyte count (TLC), serum C-reactive protein (CRP) levels, and serum lactate dehydrogenase (LDH) levels.

Measures taken to avoid Inter-observer bias: All cases were overseen by a singular Surgery Resident, who also conducted the subsequent patient follow-up. The attending surgeon was apprised of the study, and the identical Surgery Resident provided assistance during the surgical procedures. This approach seeks to minimize variability in observations and interpretations of data that may arise from different observers, thereby enhancing the internal validity of the study.

Statistical analysis: The dataset was subjected to a comprehensive analysis encompassing demographic attributes, clinical manifestations, blood parameters (specifically white blood cell count, serum C-reactive protein, and serum lactate dehydrogenase levels) obtained at the time of admission, and operative findings. Tabular presentations were constructed utilizing Pearson's chi-square test for the comparative assessment of clinical characteristics, operative findings, and blood investigations between patients with strangulation and those without. Statistical significance was determined based on p-values below 0.05. Furthermore, a Receiver Operating Characteristic (ROC) analysis was conducted for serum C-reactive protein and D-lactate, with subsequent acquisition of the area under the ROC curve. All analytical procedures were executed utilizing Jamovi software.

RESULTS

In the investigation of a cohort comprising 35 individuals subjected to bowel obstruction, a noteworthy observation revealed the presence of necrosis / strangulated abdomen in 14 patients. This study reveals a higher incidence of bowel necrosis in females (42.1%) compared to males (37.5%) following strangulation, suggesting a potential gender-related susceptibility. Younger age emerges as a prominent factor in strangulation incidents. Alcohol consumption (75%) and tobacco use (63.6%) associate with simple obstruction. Hypertensive patients exhibit a higher prevalence of necrosis (53.3%), while diabetics (57.1%), those with cardiovascular history (58.8%), and prior abdominal surgeries tend toward simple obstruction.

Timely hospital presentation differs significantly; 71.4% of strangulation cases seek medical attention within 12 hours, whereas 86.7% of simple obstruction cases present after 24 hours. Clinical manifestations distinguish the cohorts, with simple obstruction displaying diffuse pain (52.9%), abdominal distension (72.2%), obstipation (52.4%), gastrointestinal bleeding (58.8%), tenderness (54.2%), and accentuated bowel sounds (64.7%). Conversely, strangulated bowel patients present with shock (60%) and guarding and rigidity (52.6%). [Table 1]

Statistically significant findings include the association of a strangulated abdomen with younger age, shock, and duration of symptoms. These insights contribute to a more refined understanding of the complex interplay between demographic factors, clinical presentations, and temporal dynamics in bowel strangulation. Findings from this study contribute to a more nuanced understanding of the clinical characteristics associated with strangulation-induced necrosis, shedding light on gender-specific patterns, age considerations, comorbidities, and temporal aspects of presentation. The identification of shock and specific clinical signs further underscores the complexity of the pathophysiological responses to strangulation of intestine.

A robust positive correlation was observed between C-reactive protein (CRP) and lactate dehydrogenase (LDH) levels ($r_s = 0.726$, $p < 0.001$). Additionally, both CRP and LDH exhibited a positive correlation with the diagnosis of bowel necrosis, as elucidated in [Table 2]. Notably, patients presenting with strangulated necrotic bowel displayed an elevation exceeding threefold in these biomarker values compared to individuals with simple bowel obstruction. Importantly, this discrepancy reached a high level of statistical significance, underscoring the diagnostic utility of CRP and LDH in discerning between these distinct pathological entities.

Table 1: Presentation characteristics of the patients (n =35).

Characteristic feature	S.NO	Variable	n	Simple bowel obstruction	Bowel obstruction with necrosis	p
Demography	1	Female Gender	19	11 (57.9%)	8 (42.1%)	0.782
	2	#Age (mean ± SD)	35	53.6 ± 3.16	38.6 ± 3.84	<0.001*
Addictions	1	H/O Alcoholism	8	6 (75%)	2 (25%)	0.324
	2	H/O Tobacco use	11	7 (63.6%)	4 (36.4%)	0.766
Co-morbidities	1	H/O Hypertension	15	7 (46.7%)	8 (53.3%)	0.163
	2	H/O Diabetes	21	12 (57.1%)	9 (42.9%)	0.673
	3	H/O CVD	17	10 (58.8%)	7 (41.2%)	0.890

ISSN (O): 2687-5365; ISSN (P): 2753-6556

Additional information	1	H/O Previous Abdominal surgeries	11	9 (81.8%)	2 (18.2%)	0.074
Presenting symptoms & signs	1	Duration of symptoms < 12 hours	7	2 (28.6%)	5 (71.4%)	0.015*
	2	Diffuse pain	17	9 (52.9%)	8 (47.1%)	0.407
	3	Abdominal distension	18	13 (72.2%)	5 (27.*%)	0.129
	4	Vomiting	20	10 (50%)	10 (50%)	0.163
	5	Obstipation	21	11 (52.4%)	10 (47.6%)	0.260
	6	Gastrointestinal haemorrhage	17	10 (58.8%)	7 (41.2%)	0.890
	7	Shock	20	8 (40%)	12 (60%)	0.005*
	8	Tenderness	24	13 (54.2%)	11 (45.8%)	0.298
Examination findings	1	Guarding and Rigidity	19	9 (47.4%)	10 (52.6%)	0.096
	2	Exaggeration of bowel sounds	17	11 (64.7%)	6 (35.3%)	0.581

*Statistical significance, #Independent t test, CVD – Cardio Vascular Diseases.

Table 2: Correlation Matrix

Variables	Statistics	CRP	LDH	Diagnosis
CRP	Spearman rho (rs)	-	0.726	0.851
	df	-	33	33
	p	-	< .001*	< .001*
LDH	Spearman rho (rs)	0.726	-	0.849
	df	33	-	33
	p	< .001*	-	< .001*
Bowel necrosis	Spearman rho (rs)	0.851	0.849	-
	df	33	33	-
	p	< .001*	< .001*	-

*Statistical significance

Table 3: Difference in CRP and LDH values in patients with Simple bowel obstruction as well as strangulated bowel obstruction

Variables	Group	N	Mean	Median	SD	SE	df	p
CRP	Simple bowel obstruction	21	0.614	0.600	0.274	0.0599	33	<0.001*
	Strangulated bowel obstruction	14	9.64	9.60	3.14	0.839		
LDH	Simple bowel obstruction	21	166.952	165.000	49.010	10.6948	33	<0.001*
	Strangulated bowel obstruction	14	971.21	946.50	319.30	85.336		

DISCUSSION

This study investigated a cohort of 35 individuals with bowel obstruction, revealing a higher incidence of bowel necrosis in females (42.1%) compared to males (37.5%). Strangulation was associated with younger age, alcohol consumption (75%), and tobacco use (63.6%). Hypertensive patients had a higher prevalence of necrosis (53.3%), while diabetics (57.1%) and those with cardiovascular history (58.8%) leaned towards simple obstruction.

Strangulation cases sought medical attention promptly (71.4% within 12 hours), while simple obstruction cases presented later (86.7% after 24 hours). Clinical manifestations differed, with simple obstruction displaying characteristic symptoms, and strangulated bowel patients presenting with shock (60%) and guarding/rigidity (52.6%).

Significant associations included a strangulated abdomen with younger age, shock, and duration of symptoms. These findings contribute to a nuanced understanding of clinical characteristics associated with strangulation-induced necrosis. C-reactive protein (CRP) and lactate dehydrogenase (LDH) positively correlated ($rs = 0.726$, $p < 0.001$) and were significantly elevated in strangulated necrotic bowel, emphasizing their diagnostic value. This study enhances comprehension of the intricate interplay between demographic factors, clinical presentations, and biomarker dynamics in bowel strangulation.

In the realm of serum C-reactive protein (CRP), an array of investigations involving both animal and human subjects consistently indicates heightened levels in instances of mesenteric ischemia and strangulation. One noteworthy study by Demir et al. aimed at elucidating factors predictive of the imperative need for surgical intervention, thereby illuminating a significant correlation between elevated CRP levels and the incidence of bowel gangrene. Correspondingly, in an extensive analysis conducted by Lin et al., focusing on risk factors for intestinal gangrene specifically among a cohort of 49 children with volvulus, an elevated serum CRP emerged as a salient marker intricately associated with the onset of bowel gangrene. Collectively, these findings not only underscore the potential of elevated CRP as a predictive indicator but also emphasize the imperative for additional clinical scrutiny and the contemplation of surgical intervention in cases where such elevation is observed.[20,21]

The examination of serum lactate dehydrogenase (LDH) as a predictive marker for bowel necrosis is a longstanding and pertinent area of research, necessitating ongoing exploration due to the existing ambiguity in results. An observational study conducted by Dhiman et al. in 1988 encompassed 80 patients grappling with bowel obstruction. The study's conclusion emphasized that a serum LDH level surpassing 300 I.U./litre within the initial 24 to 72 hours significantly indicates strangulated intestinal obstruction. The investigation effectively

ISSN (O): 2687-5365; ISSN (P): 2753-6556

differentiated between the 28 cases of strangulated and 52 cases of non-strangulated intestinal obstruction.[22]

In a study focusing on 40 patients diagnosed with strangulated bowel, Keiichiro Tanaka et al. highlighted that, in terms of diagnostic efficiency, lactate levels emerged as the sole laboratory parameter significantly associated with viability ($P < 0.01$, Mann-Whitney test). Conversely, other laboratory metrics, such as white blood cell count and serum levels of creatine phosphokinase, amylase, and C-reactive protein, did not manifest statistically significant associations.[23]

Moreover, Ananth Kumar Nateson et al. conducted a comprehensive investigation involving 45 cases of acute intestinal obstruction. Their findings underscored that ischemic alterations in any segment of the bowel could trigger an elevation in serum LDH levels. Importantly, a higher threshold of >1000 IU/L was strongly indicative of an underlying gangrenous change. This diagnostic approach, marked by its minimal invasiveness, cost-effectiveness, and widespread availability, emerges as a pragmatic and valuable tool for the precise diagnosis of bowel ischemia and gangrene. The amalgamation of these diverse research findings not only contributes to the existing body of knowledge but also emphasizes the ongoing significance and need for nuanced exploration in this critical medical domain.[24]

C-reactive protein (CRP) stands as a well-established acute-phase reactant, serving as a reliable marker of systemic inflammation. Extensive investigations have elucidated the association between elevated CRP levels and a spectrum of medical conditions, encompassing bowel obstruction. In instances of small bowel obstruction, heightened CRP levels have been identified as a noteworthy predictive factor for the necessity of bowel resection. Furthermore, empirical evidence derived from studies on Crohn's disease patients substantiates the correlation between elevated CRP levels, disease progression, and the ability to prognosticate a more severe clinical course.[25,26]

The applicability of CRP in both diagnosing and prognosticating outcomes in the context of bowel obstruction has been a focal point of research. Pal A et al. proposed a comprehensive approach, suggesting the amalgamation of CRP with other markers, such as D-lactate, to enhance the predictive capability for identifying strangulation in cases of intestinal obstruction. Additionally, in the realm of post-surgery small bowel pseudo-obstruction, the augmentation of CRP levels has been posited as a diagnostic indicator by Salehi F et al. Whereas Broek R et al. concluded that, particularly in the context of adhesive small bowel obstruction, CRP levels assume significance in both the diagnostic and therapeutic dimensions of the condition. Consequently, C-reactive protein (CRP) levels emerge as pivotal in the comprehensive evaluation, diagnosis, and treatment of bowel obstruction and allied medical conditions. The observed association between elevated CRP levels and the severity, progression, and outcomes of various pathological conditions underscores the pivotal role of CRP as a biomarker of considerable importance in clinical practice.[27-29]

This study contributes valuable insights to the extant body of knowledge concerning the association between C-reactive protein (CRP) and bowel obstruction. Furthermore, it elucidates the potential utility of combining lactate dehydrogenase (LDH) and CRP as predictive factors and markers specifically for strangulated bowel obstruction leading to necrosis. The integration of these biomarkers enhances the prognostic capability and diagnostic precision in the context of bowel obstruction, thereby augmenting our understanding of the pathophysiological processes involved in cases characterized by strangulation-induced necrosis.

The principal constraint in this study pertains to the limited sample size, a limitation observed in numerous relevant literature sources consulted during the investigation. This limitation may be attributed to the relatively infrequent occurrence of bowel obstruction compared to more prevalent conditions encountered within surgical departments. Given the rarity of this phenomenon, a systematic review and meta-analysis encompassing all available literature on the correlation between C-reactive protein (CRP) and lactate dehydrogenase (LDH) with strangulated bowel obstruction would significantly enhance the robustness and generalizability of findings in this domain. Such an integrative analysis would provide a comprehensive synthesis of existing evidence, mitigating the impact of individual study limitations and fostering a more nuanced understanding of the relationship between these biomarkers and strangulated bowel obstruction.

CONCLUSION

In this study involving 35 individuals with bowel obstruction, a higher incidence of bowel necrosis was observed in females compared to males, with strangulation correlating with younger age, alcohol consumption, and tobacco use. Hypertensive patients exhibited a greater prevalence of necrosis, while diabetics and those with a cardiovascular history leaned towards simple obstruction. Strangulation cases sought prompt medical attention, contrasting with simple obstruction cases presenting later. Clinical manifestations differed, with simple obstruction displaying characteristic symptoms, and strangulated bowel patients presenting with shock and guarding/rigidity. Noteworthy associations included a strangulated abdomen with younger age, shock, and duration of symptoms. C-reactive protein (CRP) and lactate dehydrogenase (LDH) exhibited a robust positive correlation and were significantly elevated in strangulated necrotic bowel, underscoring their diagnostic value. This study contributes nuanced insights into the interplay of demographic,

ISSN (O): 2687-5365; ISSN (P): 2753-6556

clinical, and biomarker dynamics in bowel strangulation.

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ISSN (O): 2687-5365; ISSN (P): 2753-6556