ISSN: 0975-3583, 0976-2833 VOL15, ISSUE6, 2024

# A study of predictive and prognostic value of Triple L (Leucocytosis LDH, Lactic Acid) biomarkers in patients of Acute Mesenteric Ischemia in Tertiary Care Center.

**Authors: Dr. Sakshi Choudhury[1] (PG Resident), Dr. Shweta Vaskale[2] (Assistant Professor) Dr. Divya Sengar[3] (Assistant Professor) & Dr. Abhishek Kansal[4] (Professor)**

**Dept. of General Surgery, Sri Aurobindo Institute of Medical Science and PGI, Indore, M.P.[1,2,3&4]**

**Corresponding Author: Dr. Shweta Vaskale**

## Abstract

**Background & Methods:** The aim of the study is to study of predictive and prognostic value of Triple L (Leucocytosis LDH, Lactic Acid) biomarkers in patients of Acute Mesenteric Ischemia/ Approximately 10-15 lower abdominal and/ or pelvic surgeries per month are performed on adults at the institution. A pilot study was conducted for a month and it was found that 5-8 patients will be meeting my inclusion criteria. So, the tentative sample size for my study was (5 multiplied by 12), 60 patients with 30 patients in GROUP A and 30 patients in GROUP B during the period of study were studied and analyzed prospectively.

**Results:** Among the subjects with ischaemic necrosis (Group 1), 45.3% had high LDH levels whereas among those without ischaemic necrosis (Group 2), 9.7% had high LDH levels. The difference between the groups was statistically significant (p-value <.05). This indicated that there was a significant association between the presence of acute mesenteric ischemia and high plasma lactate dehydrogenase (p-value <.05). The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of plasma lactate dehydrogenase in diagnosing acute mesenteric ischaemia.

**Conclusion:** In clinical practice, a combination of clinical symptoms and biochemical markers should be used for diagnosing AMI. High serum lactate levels and elevated LDH levels can be indicative of AMI but should be complemented by clinical evaluation and imaging studies for accurate diagnosis.

**Keywords:** prognostic, Leucocytosis, LDH, Lactic Acid, Acute, Mesenteric & Ischemia.

**Study Design:** Observational Study.

## Introduction

Acute mesenteric ischemia (AMI) is a critical medical condition characterized by a sudden blockage of blood flow to a portion of the small intestine and the surrounding vessels, resulting in reduced blood supply, tissue damage, and potential death if not promptly treated.

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[1] AMI can manifest as non-occlusive (NOMI) or occlusive types, with specific causes being acute mesenteric arterial embolism (AMAE) accounting for 50%, acute mesenteric arterial thrombosis (AMAT) ranging from 15-25%, and mesenteric venous thrombosis (MVT) representing 5-15% of cases. [2].

The prevalence of acute mesenteric ischemia (AMI) in emergency departments is relatively low, accounting for only 0.09 to 0.2% of all acute admissions. Despite its rarity as a cause of abdominal pain, AMI carries a high mortality rate varying from 50% to 80%. [3] Timely and accurate identification, along with the utilization of suitable emergency resources, can help mitigate the lasting effects of AMI. This is crucial for improving quality of life and decreasing mortality rates associated with this condition.[4]

Intestinal ischemia is observed in anecdotal reports when there is a decrease of over 50% in the blood supply or if the patient's mean arterial pressure falls below 45 mmHg. [5,6] The small intestine can adapt to a reduction of up to three-quarters in blood supply for about 12 hours. [7]

AMI is the result of a variety of pathologies and their underlying factors. AMAE is caused by a variety of conditions, such as valvular heart disease, atrial fibrillation or flutter, myocardial infarction, cardiac valvular vegetation, mechanical valve prostheses, and cardiomyopathies, which can all result in arterial embolism. AMAT can be caused by atherosclerotic disease, congestive heart failure, vasculitis, conditions that result in reduced cardiac output, procoagulative status, and iatrogenic causes (cardiac catheterization-related emboli and angiography). NOMI may be the consequence of a shock, such as that caused by heart failure, inadequately controlled vasopressors, or excessive diuretic-associated volume depletion. Conversely, MVT is predominantly caused by conditions that result in a hypercoagulable state, intra-abdominal infections, portal hypertension, elevated intra- abdominal pressure, and venous trauma. [8].

The ischemic damage in the intestinal mucosa is mostly reversible, unless there is a transmural injury, which can result in inflammation, necrosis, sepsis, and multiple organ failure (MOF). [9]. Patients with acute myocardial infarction (AMI) may exhibit nonspecific and ambiguous symptoms, which can manifest as moderate to severe diffuse abdominal pain, nausea, vomiting, loss of appetite, and diarrhea. These initial symptoms can then escalate to obstipation, abdominal distention, and gastrointestinal bleeding in some cases. As the intestinal necrosis advances, signs of sepsis may emerge, including tachycardia, rapid breathing, low blood pressure, fever, and changes in mental status. [2].

## Material and Methods

84 Patients of age more than 18 years admitted in SAIMS and PG institute in the Department of Gen. Surgery suspected of Acute Mesenteric Ischemia. Surgery suspected of Acute Mesenteric Ischemia during the study period was included in the study. Each patient fulfilling the inclusion criteria was included in the study. After taking pre-informed written consent from the patient, a prestructured proforma was used to collect the desired baseline data. Detailed clinical history, general physical examination, laboratory and other investigations were done on all patients as per the protocol. The patients were recruited from the ward and pre anaesthetic check-up was done.

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Patients fulfilling inclusion and exclusion criteria were enrolled for the study. An informed written consent was taken from all selected patients after the approval of institutional ethical committee. The data was recorded on the pre- structured proforma.

Group allocation was done by basis drug administered and patients were divided into 2 groups

- GROUP A included patients who had acute mesenteric ishaemia (n=53)
- GROUP B included patients who had any other pathology other than acute ischaemia (n=31)

**INCLUSION CRITERIA**

- Group A: All patient more than 18 years age admitted in SAIMS and PG institute in department of General surgery, suspected of acute mesenteric ischemia.
- Control group B: included all patient above 18 years of age admitted with complaint of Acute Abdominal Obstruction which were causes other than acute mesenteric ischemia

**EXCLUSION CRITERIA**

1. Patient not willing for admission.
2. Patients who do not continue complete treatment because of financial or social constraints.

**Result**

**Table 1. Distribution of Group 1 subjects based on diagnosis.**

| Diagnosis | Number of subjects | Percentage |
|---|---|---|
| SMA thrombosis | 39 | 73.6 |
| SMV thrombosis | 9 | 17.0 |
| SMA+SMV thrombosis | 5 | 9.4 |
| Total | 53 | 100.0 |

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The present study included 84 subjects. Of these, 53 subjects had ischemic necrosis and 31 subjects had other pathologies not involving ischemic necrosis. In group 1, the majority of the subjects had SMA thrombosis (73.6%), followed by those having SMV thrombosis (17.0%), followed by those having both SMA + SMV thrombosis (9.4%).

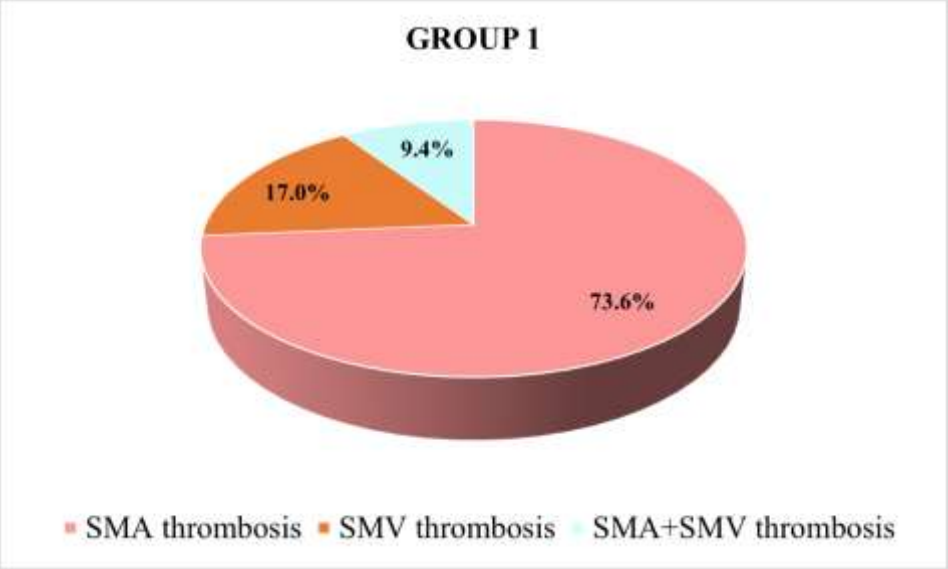


**Table 2. Inter-group comparison of the presenting signs and symptoms of the subjects.**

| Presenting signs and symptoms | | Group 1 (n=53) | Group 2 (n=31) | Total (n=84) | Chi-square value | Df | p-value |
|---|---|---|---|---|---|---|---|
| Pain | Number | 53 | 31 | 84 | - | - | - |
| | Percentage | 100.0% | 100.0% | 100.0% | | | |
| Distension | Number | 34 | 8 | 42 | 11.503 | 1 | .001* |
| | Percentage | 64.2% | 25.8% | 50.0% | | | |
| Tenderness | Number | 53 | 31 | 84 | - | - | - |
| | Percentage | 100.0% | 100.0% | 100.0% | | | |
| Vomiting | Number | 39 | 16 | 55 | 4.177 | 1 | .041* |
| | Percentage | 73.6% | 51.6% | 65.5% | | | |
| Fever | Number | 42 | 22 | 64 | .739 | 1 | .390 |
| | Percentage | 79.2% | 71.0% | 76.2% | | | |
| Constipation | Number | 49 | 0 | 49 | 68.785 | 1 | <.001* |

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| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | Percentage | 92.5% | 0.0% | 58.3% | | | |
| Jaundice | Number | 3 | 3 | 6 | .476[a] | 1 | .490 |
| | Percentage | 5.7% | 9.7% | 7.1% | | | |
| Effusion | Number | 0 | 0 | 0 | - | - | - |
| | Percentage | 0.0% | 0.0% | 0.0% | | | |
| Ascites | Number | 2 | 3 | 5 | 1.218 | 1 | .270 |
| | Percentage | 3.8% | 9.7% | 6.0% | | | |

Chi-square test. *p-value <.05 was considered statistically significant.

Pain and tenderness were universal signs and symptoms, present in all subjects.

In group 1, pain, distention, tenderness, vomiting, fever, constipation, jaundice, effusion, and ascites were present in 100.0%, 64.2%, 100.0%, 73.6%, 79.2%, 92.5%, 5.7%, 0.0%, and 3.8% of the subjects respectively. In group 2, pain, distention, tenderness, vomiting, fever, constipation, jaundice, effusion, and ascites were present in 100.0%, 25.8%, 100.0%, 51.6%,

71.0%, 0.0%, 9.7%, 0.0%, and 9.7% of the subjects respectively. The prevalence of distension, vomiting, and constipation was significantly greater in Group 1 compared to Group 2 (p-value <.05).

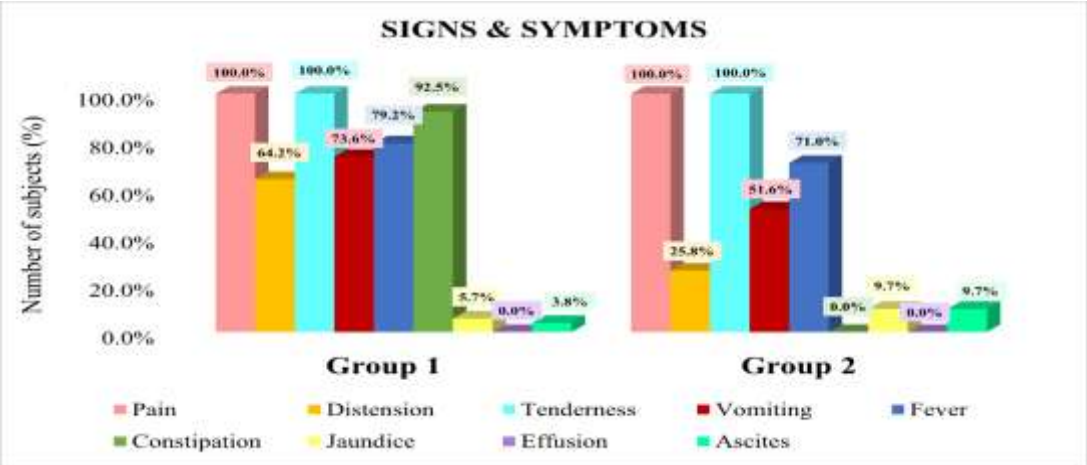


**Table 3. Inter-group comparison of the comorbidities among the subjects.**

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| Comorbidities | | Group 1 (n=53) | Group 2 (n=31) | Total (n=84) | Chi-square value | Df | p-value |
|---|---|---|---|---|---|---|---|
| Diabetes | Number | 22 | 11 | 33 | .298 | 1 | .585 |
| | Percentage | 41.5% | 35.5% | 39.3% | | | |
| Hypertension | Number | 35 | 7 | 42 | 14.775 | 1 | <.001* |
| | Percentage | 66.0% | 22.6% | 50.0% | | | |
| Coronary artery disease | Number | 7 | 3 | 10 | .232 | 1 | .630 |
| | Percentage | 13.2% | 9.7% | 11.9% | | | |

Chi-square test. *p-value <.05 was considered statistically significant.

In Group 1 and Group 2, diabetes was present in 41.5% and 35.5% of the subjects respectively, hypertension was present in 66.0% and 22.6% of the subjects respectively, and CAD was present in 13.2% and 9.7% of subjects respectively.

The hypertension was seen in significantly more subjects in Group 1 compared to Group 2 (p-value <.05).

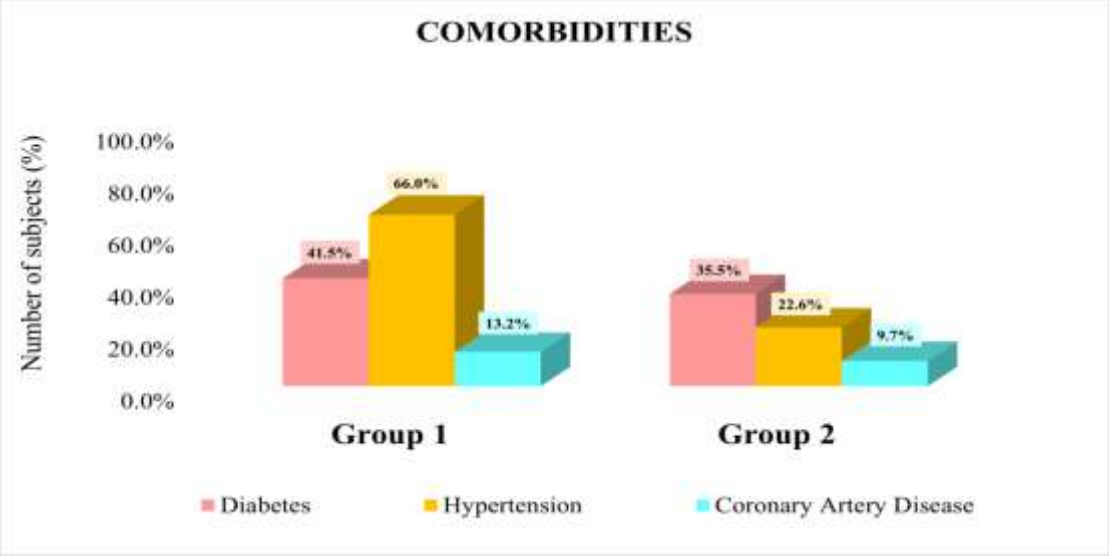

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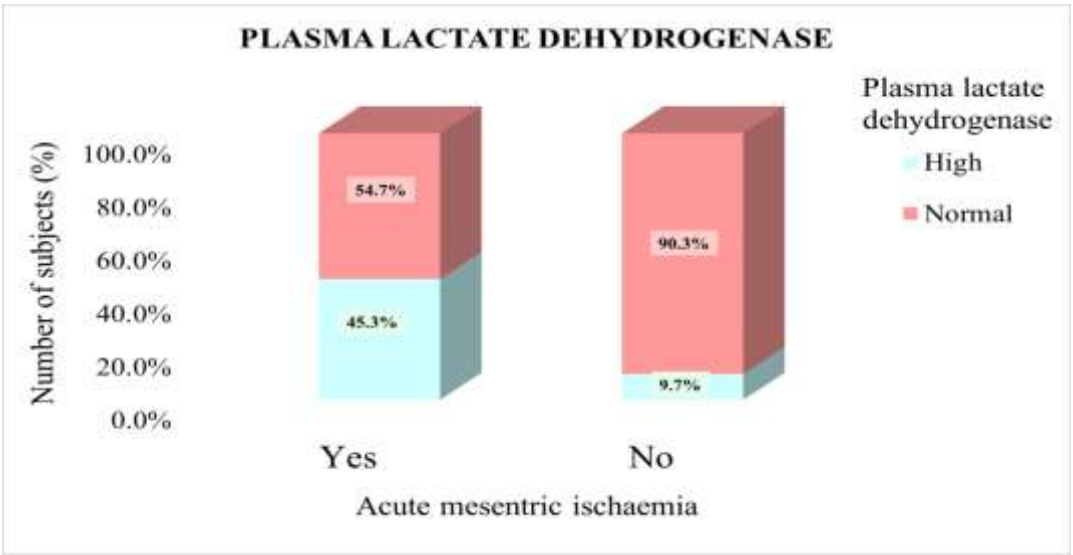
**Table 4. Sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of plasma lactate dehydrogenase in diagnosing acute mesenteric ischaemia.**

| Statistic | Value | 95% CI |
|---|---|---|
| Sensitivity | 45.28% | 31.56% to 59.55% |
| Specificity | 90.32% | 74.25% to 97.96% |
| Positive Predictive Value | 88.89% | 72.39% to 96.06% |
| Negative Predictive Value | 49.12% | 42.41% to 55.86% |
| Accuracy | 61.90% | 50.66% to 72.29% |

Among the subjects with ischaemic necrosis (Group 1), 45.3% had high LDH levels whereas among those without ischaemic necrosis (Group 2), 9.7% had high LDH levels. The difference between the groups was statistically significant (p-value <.05). This indicated that there was a significant association between the presence of acute mesenteric ischemia and high plasma lactate dehydrogenase (p-value <.05). The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of plasma lactate dehydrogenase in diagnosing acute mesenteric ischaemia.



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**Discussion**

Acute mesenteric ischemia (AMI) is a life-threatening vascular emergency and a diagnostic challenge for physicians. It represents a group of pathophysiologic processes that have a common end point, that is, bowel infarction, and has a nonspecific clinical picture and a high mortality rate[9]. The most common underlying etiologies are arterial embolism, arterial thrombosis, nonocclusive mesenteric ischemia (NOMI), and mesenteric venous thrombosis. NOMI is caused by prolonged functional vasoconstriction of the visceral arterial vessels, leading to progressive intestinal ischemia, and could be defined by the absence of atherosclerotic thrombotic or embolic occlusion of the mesenteric arteries[10].

Computed tomography angiogram (CTA) is the most effective diagnostic method for acute mesenteric ischemia (AMI), with a sensitivity of 85% to 98% and a specificity of 91% to 100%. However, plain abdominal radiography has limited diagnostic efficacy in AMI, showing positive results only when perforation occurs. Research has led to the discovery of several potential markers for this condition, such as serum lactate levels, D-dimer, amylase, I-FABP, and alpha-GST. L-lactate, a natural enantiomer of 2-hydroxypropanoate, has potential as a biomarker for intestinal ischemia[11]. A combination of Triple "L" markers (Leukocytosis, Lactate dehydrogenase, Lactic Acid) with increased plasma concentrations provides more precise indications of mesenteric ischemia.

A total of 84 subjects were evaluated consisting of 53 subjects who had ischemic necrosis and 31 subjects had other pathologies not involving ischemic necrosis. In patients with ischemic necrosis, the majority of the subjects had SMA thrombosis (73.6%), followed by those having SMV thrombosis (17.0%), followed by those having both SMA + SMV thrombosis (9.4%). Whereas in patients with other pathologies not involving ischemic necrosis the most common diagnosis was Koch Abdomen (32.3%), followed by Intestinal Stricture (22.6%), followed by Intestinal diverticuli (12.9%).

In the present study, pain and tenderness were universal signs and symptoms, present in all subjects. In patients with ischemic necrosis, pain, distention, tenderness, vomiting, fever, constipation, jaundice, effusion, and ascites were present in 100.0%, 64.2%, 100.0%, 73.6%, 79.2%, 92.5%, 5.7%, 0.0%, and 3.8% of the subjects respectively[12]. Whereas in patients Whereas in patients with other pathologies not involving ischemic

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necrosis pain, distention, tenderness, vomiting, fever, constipation, jaundice, effusion, and ascites were present in 100.0%, 25.8%, 100.0%, 51.6%, 71.0%, 0.0%, 9.7%, 0.0%, and 9.7% of the

subjects respectively. The prevalence of distension, vomiting, and constipation was significantly greater in Group 1 compared to Group 2 (p-value <.05).

This was in concurrence with results reported by Mishra K P et al. who reported that All 30 patients were symptomatic at presentation, with abdominal pain (100%), abdominal distension, and vomiting, alone, or in combination. The classical description of gastrointestinal bleeding was present in eight patients. 20% of the patients presented with shock, with a systolic blood pressure below 100 mm of Hg. On examination, localized abdominal tenderness was elicited in 60% of patients without any features of peritonism, and 40% of the cohort showed signs of localized or generalized peritonitis.[13]

In the present study, hypertension was the most common comorbidity present in 66.0% and 22.6% of the subjects respectively for Group 1 and Group 2, followed by diabetes which was present in 41.5% and 35.5% of the subjects respectively, and CAD was present in 13.2% and 9.7% of subjects respectively. The hypertension was seen in significantly more subjects in Group 1 compared to Group 2 (p-value <.05).

In a similar study done by Mishra K P et al. Hypertension, ischemic heart disease, and diabetes mellitus were the three most commonly associated medical conditions. This was comparable to our study. [14]

In a study done by Moncy A et al diabetes was the most common comorbidity followed by hypertemsion. [13]

**Conclusion**

In clinical practice, a combination of clinical symptoms and biochemical markers should be used for diagnosing AMI. High serum lactate levels and elevated LDH levels can be indicative of AMI but should be complemented by clinical evaluation and imaging studies for accurate diagnosis. Group 1 (Ischemic Necrosis): Predominantly had SMA thrombosis as the underlying cause, with pain and tenderness being universal symptoms. Additional symptoms such as distention, vomiting, and constipation were significantly more prevalent in Group 1 compared to Group 2. Group 2 (Other Pathologies): Most common diagnoses included Koch abdomen and intestinal stricture, with symptoms like distention, vomiting, and constipation occurring less frequently. Hypertension was significantly more common in Group 1,

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indicating a potential risk factor for AMI. Diabetes and CAD were present in both groups, but their prevalence did not show significant differences between the groups.

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