ORIGINAL ARTICLE | ASIAN JOURNAL OF MEDICAL SCIENCES

Perioperative serum lactate as a predictor of post-operative length of hospital stay and in-hospital mortality in patients undergoing major emergency abdominal surgeries

Safura Riaz[1], Abdul Waheed Mir[2], Suhail Sidiq[3], Showkat Ahmed Gurcoo[4], Mohammad Akbar Shah[5], Falak Ara[6], Akif Mutahar Shah[7], Altaf Hussain Mir[8]

[1,6]Resident, [4]Professor, [8]Assistant Professor, Department of Anesthesiology, [2,5]Additional Professor, [3]Associate Professor, Department of Critical Care Medicine, Sher-Kashmir-Institute of Medical Sciences, [7]Consultant, National Rural Health Mission, JLNM Hospital, Srinagar, Jammu and Kashmir, India

Submission: 08-02-2024 Revision: 29-03-2024 Publication: 01-05-2024

ABSTRACT

Background: Major surgeries can develop metabolic acidosis during the perioperative period. Any clinical condition leading to decreased tissue oxygenation causes lactate levels to rise proportionally. **Aims and Objectives:** This study was aimed at evaluating perioperative serum lactate as a predictor of length of hospital stay and in-hospital mortality in patients undergoing emergency major abdominal surgeries. **Materials and Methods:** Adult patients posted for emergency abdominal surgical procedures were enrolled for 2 years. Patients were observed intraoperatively and lactate levels were measured. In post-operative period lactate levels were recorded for 24 h. Relationship of lactate with hospital length of stay and in-hospital mortality was analyzed. **Results:** Total of 93 patients were enrolled for 2 years. Mean age was 50.4 years. Mean baseline lactate was 2.95 mmol/L. Total in-hospital mortality was 16.1%. Thirteen patients had perioperative serum lactate level of ≤ 2 mmol/l, with a mean hospital length of stay of 8.6 days and no mortality. Fifty-one patients having perioperative serum lactate between 2 and 4 mmol/L, with a mean hospital length of stay of 11.2 days and mortality of 13.3%. Twenty-nine patients had serum lactate of >4 mmol/L, with a mean hospital length of stay of 17.3 days and mortality of 86.7%. Elevated serum lactate was associated with a longer length of hospital stay, with lactate at 12 h having the highest predictive value (area under curve 0.987). Similarly, lactate at 12 h had the highest accuracy at predicting mortality as per receiver operating characteristic (AUC 0.895). **Conclusion:** Serum lactate was associated with increased in-hospital mortality and longer length of hospital stay in emergency abdominal surgeries.

Key words: Serum lactate; In-hospital mortality; Length of hospital stay

Access this article online

Website:
http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v15i5.62619

E-ISSN: 2091-0576

P-ISSN: 2467-9100

INTRODUCTION

Lactate is the end product of pyruvate metabolism. Overburdening of compensatory mechanisms of the body, whether from long-term dysfunction or excessive production, leads to hyperlactatemia and metabolic acidosis ensue, commonly referred to as lactic acidosis.[1,2] In critically ill patients' lactic acidosis often correlates with the disease severity. Being of prognostic value, lactate is being widely used as a biomarker for screening, diagnosis, risk stratification, and monitoring of treatment response and predict outcome. Patients who undergo major abdominal surgeries, often develop metabolic acidosis during the perioperative period which continues in the post-operative period. Perioperative metabolic acidosis is usually normalized within a short period after surgery without any adverse clinical outcome. However, persistent metabolic acidosis in the post-operative period may result in

Address for Correspondence:
Dr. Suhail Sidiq, Associate Professor, Department of Critical Care Medicine, Sher-Kashmir-Institute of Medical Sciences, Srinagar, Jammu and Kashmir, India. **Mobile:** +91-9419408781. **E-mail:** sidiqsuhail@gmial.com

clinically significant changes such as myocardial depression, arrhythmias, diminished vascular tone, decreased response to catecholamines, platelet dysfunction, and coagulopathy.[3] Elevated serum lactate or hyperlactatemia is associated with increased rates of mortality in critically ill patients.[4] Elevated lactate has been postulated for risk stratification of critically ill non-surgical patients. Hyperlactatemia has an association with morbidity and post-operative complications following major non-abdominal surgeries.[5] Furthermore, by measuring the lactate levels, we can indirectly assess the effect of major surgery on tissue perfusion.[6]

Aims and objectives

To study the relationship of perioperative serial serum lactate with length of hospital stay and in-hospital mortality in patients undergoing major emergency abdominal surgeries.

MATERIALS AND METHODS

This was a hospital-based, prospective observational study, conducted for 2-year following approval by the Institutional Ethical Committee (RP 36/2021) and written informed consent. Adult patients (≥18 years) for emergency abdominal surgical procedures were enrolled. Patients undergoing neurosurgical, cardiac, and pediatric surgeries, patients with shock of any etiology pre-operatively, pre-operative acid-base imbalance, cirrhosis, impaired renal function, endocrine disorders, seizures, drugs known to cause lactic acidosis were excluded from the study. Patient's pre-operative characteristics and demographic data were assessed, such as: Age, sex, American Society of Anesthesiologists (ASA) physical status, medical illness, and drug history was noted. All baseline investigations were recorded. Baseline lactate level was recorded just before the induction of anesthesia. All vitals of the patient were recorded.

All patients were anesthetized as per institutional protocol under balanced general or regional anesthesia as indicated, with routine pre-operative medications and standard monitoring. Anesthetic drugs and techniques, intraoperative monitoring, and fluid management were selected by the attending anesthesiologist.

Intraoperative course of the patients was noted such as type and duration of surgery, type, and duration of anesthesia, episodes of hypotension, type and dose of inotropes or vasopressors used if any, type and amount of fluid used, blood loss, urine output, use of blood and blood products. Intraoperatively serum lactate was recorded hourly. Complication if any was recorded.

Patients shifted in post-operative period were observed for; Mechanical ventilation, duration of ventilation, inotropic support, and duration of intensive care unit (ICU) stay (if shifted to ICU). Patients shifted to the surgical ward were monitored as per standard protocol. Post-operative serum lactate was recorded on arrival and every 4 hourly for 24 h. Temperature on arrival, after 1 h, 2 h, 4 h, 6 h, 12 h, and 24 h was recorded. ICU length of stay and hospital length of stay was recorded. ICU mortality and in-hospital mortality were also recorded.

Statistical methods

Statistical software the SPSS (version 20.0) was used to carry out the statistical analysis of data. Continuous variables were expressed as mean±standard deviation and categorical variables were summarized as percentages. Analysis of variance was employed for comparison of continuous variables. The Chi-square test or Fisher's exact test, whichever is appropriate, was applied for the comparison of categorical variables. A $P<0.05$ was considered statistically significant. Receiver operating characteristics (ROC) were used to predict mortality and length of hospital stay.

RESULTS

A total of 93 patients were emergency abdominal surgical procedures for 2 years. Mean age of study patients was 50.4±14.98 (18–80) years. Majority of patients were in the age group of 51–60 years (28%). Fifty-five (59.1%) patients were males. Demographic data, including age, sex, ASA status, underlying comorbidities of study patients, type of anesthesia among study patients, duration of anesthesia, intraoperative ionotropic agents, and blood transfusion of study patients, is depicted in Table 1.

Serum lactate levels (mmol/L) at various intervals of study patients, Perioperative serum lactate levels with a length of hospital stay, and the association of perioperative serum lactate levels with in-hospital mortality is depicted in Table 2.

Out of 93 patients, 40 patients were shifted to the ICU in the post-operative period, and the remaining 53 patients were shifted to the post-operative ward. Length of hospital stays among study patients, ICU mortality of study patients, in-hospital mortality of study patients, and in-hospital mortality as depicted in Table 3.

Figure 1 shows ROC curve of serum lactate levels at four-time points following major surgeries to predict mortality.

Figure 2 shows ROC curve of serum lactate at 4 time points following major surgery to predict the length of hospital stay.

Table 1: Demographic data and perioperative characteristics

Age (years)	n	%
Age distribution of study patients		
21–30	14	15.1
31–40	12	12.9
41–50	21	22.6
51–60	26	28.0
61–70	12	12.9
>70	8	8.6
Total	93	100
Mean±SD (range)=50.4±14.98 (18–80)		
Gender distribution of study patients		
Male	55	59.1
Female	38	40.9
Total	93	
ASA status of study patients		
ASA I	16	17.2
ASA II	59	63.4
ASA III	17	18.3
ASA IV	1	1.1
Total	93	
Underlying comorbidities of study patients		
Hypertension	36	38.7
Hypothyroidism	12	12.9
Diabetes mellitus	11	11.8
COPD	7	7.5
Others	9	9.7
Type of anesthesia among study patients		
General anesthesia	81	87.1
Regional anesthesia	5	5.4
Combined	7	7.5
Total	93	
Duration of anesthesia		
<2 h	6	6.5
2–4 h	56	60.2
4–6 h	24	25.8
≥6 h	7	7.5
Total	93	
Mean±SD (range)=3.5±1.56		
Intraoperative ionotropic agents		
Not needed	46	49.5
Single	32	34.4
Multiple	15	16.1
Total	93	100
Blood transfusion among study patients		
Not needed	57	61.3
1 unit	14	15.1
2 unit	9	9.7
3 unit	4	4.3
4 unit	9	9.7
Total	93	100

SD: Standard deviation, ASA: American Society of Anesthesiologists, COPD: Chronic obstructive pulmonary disease

DISCUSSION

Tissue hypoperfusion causes a shift to anaerobic glycolysis and subsequent conversion of pyruvate to lactate. This causes a rise in serum lactate level, which normally ranges between 1 and 2 mmol/L.[4] Hyperlactemia is a marker of cellular damage and is associated with increased morbidity in critically ill patients.[7] Lactate can be increased during major surgeries due to multiple factors and can indirectly assess the effect of major surgery on tissue perfusion.[6] Prompt identification of the inciting factor may be needed.

In our study, the majority of the patients were between the age group (51–60) years (28.0%). It has been found that morbidity and mortality occur more commonly in elderly patients undergoing major surgical procedures.[8] Bou Chebl et al.,[4] and Veličković et al.,[9] also showed that patients with complications were significantly older and lactate levels were significantly higher in patients with complications. Majority of the patients were males as compared to females.

The ASA status of patients was comparable to that of Henry et al.,[7] majority of patients had ASA II and above. This makes sense that older patients with higher ASA class would need post-operative ICU care, and are more likely to have negative outcomes.

Majority of the patients (80%) had underlying co-morbidities such as, hypertension, hypothyroidism, diabetes, and chronic obstructed pulmonary disease. This is in contrast with a study by Henry et al.,[7] who did not find comorbidity in 74.4% of patients. Henry et al.,[7] included both elective and emergency cases; however, our study involved only emergency surgical procedures. Mean duration of surgery was 3.5 h. As per Veličković et al.,[9] major surgery was defined as a laparotomy with operative time of more than 2 h which was associated with higher lactate levels which resulted in increased risk of post-operative complications and mortality. A longer duration of anesthesia due to a major surgery causes greater physiologic stress and hence a greater likelihood of adverse outcomes.[5,6]

About 50.5% of our patients intraoperatively became hemodynamically unstable and required ionotropic support. (34.4%) required single support and (16.1%) required multiple inotropes.

Most of our patients were normothermic 88 (94.6%) and only 5 (5.3%) patients were hypothermic. Patients who received less frequent intraoperative warming developed higher lactate levels and post-operative complications.[4]

Mean baseline lactate level of our patients was 2.95 mmol/L. The mean lactate was elevated before surgery. This could be attributed to the fact that all these patients were in emergency surgical procedures and several factors such as hypotension, and hypoxia could have contributed to elevated lactate. This is not the case with elective patients where pre-operative status is relatively stable and patients

Table 2: Serum lactate in the perioperative period, length of hospital stay, and mortality

Intraoperative serum lactate levels (mmol/L) at various intervals of time

Time	Mean	SD	Min	Max
Baseline	2.95	2.59	0.6	6.9
1 h	3.07	2.55	0.68	16.6
2 h	3.32	2.61	0.8	16
3 h	3.64	3.08	0.62	16.8
4 h	3.68	2.49	1.2	9.3
5 h	5.56	2.39	2.8	10
6 h	5.22	2.06	3.2	8.4
7 h	4.57	1.16	3.8	5.9
8 h	4.50	2.12	3	6

Serum lactate levels (mmol/L) at various intervals of time in the post-operative period

Time	Mean	SD	Min	Max
0	3.91	3.14	0.56	17
2 h	3.61	2.85	0.58	15.2
4 h	3.26	2.81	0.56	11
8 h	3.16	3.15	0.23	15
12 h	2.92	3.05	0.35	12.5
16 h	2.96	3.37	0.35	16
20 h	2.74	2.96	0.24	13.5
24 h	2.46	2.43	0.47	10.5

Perioperative serum lactate levels of study patients

Serum lactate	n	%
≤2 mmol/L	13	14.0
2–4 mmol/L	51	54.8
>4 mmol/L	29	31.2
Total	93	100

Perioperative serum lactate levels with length of hospital stay (days)

Serum lactate	n	Mean	SD	95% CI	P-value
≤2 mmol/L	13	8.6	3.89	6.27–10.96	<0.001*
2–4 mmol/L	49	11.2	6.57	9.35–13.12	
>4 mmol/L	17	17.3	6.49	13.95–20.64	

Perioperative mortality among different lactate levels

Serum lactate	Mortality		No Mortality		P-value
	n	%	n	%	
≤2 mmol/L	0	0.0	13	16.7	
2–4 mmol/L	2	13.3	49	62.8	<0.001*
>4 mmol/L	13	86.7	16	20.5	
Total	15	100	78	100	

SD: Standard deviation, CI: Confidence interval, Data described as mean and standard deviation. *Statistically Significant (*P*<0.05)

are optimized before surgery. Furthermore, this study was done in a tertiary care center and some of the patients were referred (n=20), this could have led to delays in timely surgical interventions in these patients. Intraoperatively, there was an increasing trend in mean lactate levels with a maximum increase at the 5th h (5.56 mmol/L) after which lactate levels declined (4.50 mmol/L) at the 8th h. This decline was seen because patients who developed hyperlactemia intraoperatively due to hypotension, blood loss, and hypothermia were treated accordingly. Normal lactate was found only in 14% of patients. About 31% of patients had lactated more than 4 mmol/L. Overall 15 (16%) patients died. Maximum deaths (n=13) were found in patients with lactate more than 4 mmol/L. 86.6% of the patients who died had lactate >4 mmol/L. Abdominal surgeries can be accompanied by increased surgical stress, so post-operative hyperlactemia.[4] Veličković et al.,[9] indicated a significant effect of gastrointestinal surgery on the post-operative lactate levels and complications. ROC analysis indicated elevated lactate levels were accurate in predicting mortality and 12-h lactate level had the highest area under the curve (AUC) for predicting mortality (AUC 0.987, 95% CI: 0.938–0.998). This result was different from Henry et al.,[7] who found 24-h lactate levels had the best predictability for mortality. This difference could be attributed to different subsets of the population in their study, which included both elective and emergency patients. However, they also showed elevated serum lactate strongly associated with mortality irrespective of elective or emergent nature of surgery. Elevated serum lactate is

Table 3: Length of hospital stay and mortality

Days	n	%
Length of hospital stay among study patients		
≤7 days	24	30.8
8–14 days	38	48.7
>15 days	16	20.5
Total	78	
Mean±SD (range)=12.1±6.81 (3–32 days)		
ICU mortality of study patients		
Yes	14	15.1
No	79	84.9
Total	93	
In-hospital mortality of study patients		
Yes	15	16.1
No	78	83.9
Total	93	

ICU: Intensive care unit, SD: Standard deviation, Data described as mean and standard deviation. *Statistically significant ($P<0.05$)

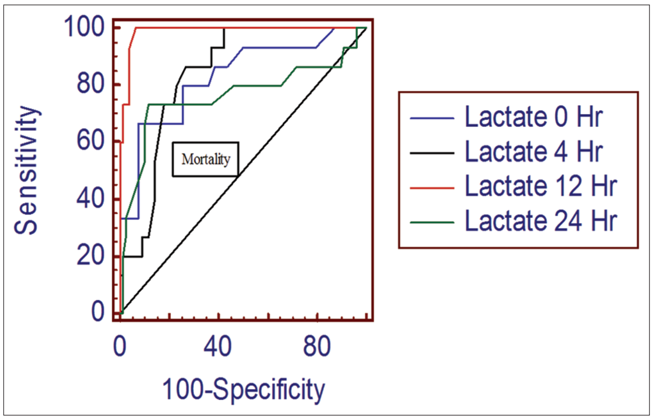

Figure 1: Receiver operating characteristic curve of serum lactate levels. Area under curve for lactate at 12 h is the highest to predict mortality (0.987, 95% Confidence interval: 0.938–0.998)

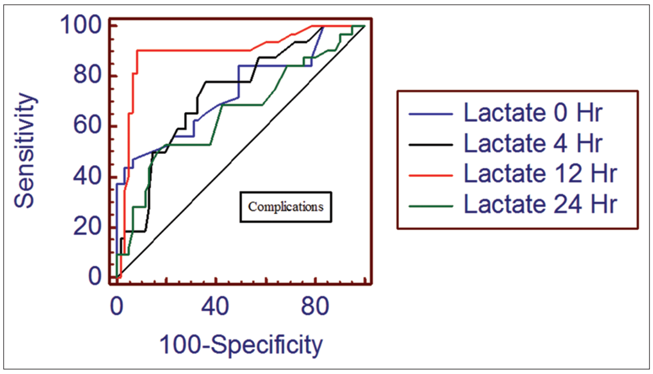

Figure 2: Receiver operating characteristic curve of serum lactate levels. Area under the curve for lactate at 12 h is the highest to predict the length of hospital stay (0.895, 95% Confidence interval (CI): 0.814–0.949)

independently associated with in-hospital mortality in post-operative gastrointestinal surgeries and is not less significant in the context of elective surgery.[3,10] Creagh–Brown BC et al.,[11] showed a linear relationship between lactate levels and risk of in-hospital mortality without differences between elective and emergency surgeries.[3,10] Only one patient died in post-operative ward while rest of the 14 patients died in the ICU. This can be attributed to the fact that all the patients shifted to ICU in post-operative period were critically ill compared to patients shifted to post-operative ward who were relatively stable. Chi–Min Park also observed that patients transferred to the ICU in post-operative period had higher mortality as these patients were already high risk and transferred to the ICU because of life-threatening complications in post-operative period.[12]

Mean length of hospital stay was 12.1±6.81 (3–32 days). Patients with mean lactate <2 mmol/L had an average hospital stay of 8.6 days and patients with lactate >2 mmol/L had a mean hospital stay >11 days which was statistically significant ($P<0.05$)

In our study, elevated serum lactate was associated with a longer length of hospital stay, with a $P<0.05$, which is consistent with other studies. AUC for lactate at 12 h was the highest to predict the length of hospital stay (AUC 0.895, 95% CI: 0.814–0.949). Soliman and Vincent[13] studied the association between lactate elevation and hospital length of stay and noticed that patients with elevated lactate who survived to discharge had a longer length of hospital stay, 4 (1–74) days than patients with normal lactate levels who had 2.3 (1–33) days of hospital stay. Although the total length of hospital stay varied in different studies, which could be attributed to the nature of surgeries, different numbers of patients enrolled, and turnover of patients.

Limitations of the study

It was a time-bound, observational study, and number of patients in our study were less as compared to other related studies. This study was done at a tertiary health-care facility and catering to referrals from other facilities, this could have led to time delay in managing these patients. Furthermore, there is a chance of patients not receiving standardized treatment. We only included emergency surgical patients which could be a limiting factor as well as add to the uniqueness of the study. The role of lactate in predicting outcomes in other non-abdominal surgeries needs to be explored in our subset of the population.

CONCLUSION

Serum lactate was independently associated with increased in-hospital mortality in emergency abdominal surgical procedures. Elevated serum lactate at 12 h had the highest accuracy in predicting outcome. Elevated serum lactate was associated with a longer length of hospital stay with lactate at 12 h having the highest predictive value. It can be used to risk stratify patients and is useful in determining patient's predisposition factors and the level of care needed.

ACKNOWLEDGMENT

None.

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Authors' Contributions:
SR- Implemented study protocol, data collection, prepared draft of the manuscript; **AWM-** Manuscript preparation, submission of an article; **SS-** Concept, design, intellectual content; **SAG-** Data analysis, editing**; MAS-** Editing, literature search; **FA-** Statistical analysis; **AMS-** Design; **AHM-** Statistics.

Work attributed to:
Sher i Kashmir Institute of Medical Sciences Soura Srinagar, J and K, India.

Orcid ID:
Safura Riaz - https://orcid.org/0009-0004-2196-4092
Abdul Waheed Mir - https://orcid.org/0000-0003-4467-507X
Suhail Sidiq - https://orcid.org/0000-0003-3544-0148
Showkat Ahmed Gurcoo - https://orcid.org/0000-0001-7873-3552
Mohammad Akbar Shah - https://orcid.org/0000-0003-0172-8282
Falak Ara - https://orcid.org/0009-0007-7124-006X
Akif Mutahar Shah - https://orcid.org/0009-0006-5792-7589
Altaf Hussain Mir - https://orcid.org/0009-0003-8684-1854

Source of Support: Nil, **Conflicts of Interest:** None declared.