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Original Research Article

An Observational Study on Prognostic Implication of Post-Operative Blood Lactate Level for Complications and Predicting Length of ICU Stay after Major Abdominal Surgery

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Abstract

Background: In this study, we wanted to evaluate the association of blood lactate levels during the first 24 hours after surgery with post-operative morbidity and mortality, correlate the lactate values at various time points with different post-operative complications (POC), observe the correlation between lactate levels and length of intensive care unit (ICU) stay, detect any abnormal lactate level and treat this to improve tissue perfusion.

Materials and Methods: This was a hospital based observational study conducted among 60 patients who were posted for major abdominal surgery under general anaesthesia in the Department of Anaesthesiology and Critical Care of S.C.B. Medical College & Hospital, Cuttack, over a period of 12 months from September 2020 to August 2021 after obtaining clearance from Institutional Ethics Committee and written informed consent from the study participants.

Results: There was statistically significant difference with regard to lactate level, urine output, duration of surgery, duration of ICU stays and duration of intubation measured at the point of time (0, 6, 12 and 24) in cases with shock as compared to cases without shock ($p < 0.05$), in cases with death as compared to cases without fatal outcome ($p < 0.05$), in cases with acute kidney injury (AKI) as compared to cases without AKI ($p < 0.05$), in patients who required extended respiratory support as compared to cases who did not require extended respiratory support ($p < 0.05$), and in cases with wound dehiscence as compared to cases without wound dehiscence ($p < 0.05$).

Conclusion: Increased serum lactate levels were significantly associated with post-operative complications, mortality and length of ICU stay in patients undergoing major abdominal surgery. Serial lactate measurements in early post-operative period were able to discriminate between patients with and without post-operative complications. This result warrants a “golden hour and silver day” perspective of early resuscitation in this patient. Further studies are needed to establish a lactate-directed treatment protocol within 12 - 24 hours of surgery.

Keywords: Prognostic Implication, Post-Operative Blood Lactate Level, Complications, Length of ICU Stay, Major Abdominal Surgery

Introduction

Two types of blood lactate are being used in clinical practice, L-lactate and D-lactate. L-lactate is the lactate form that is most commonly measured by clinicians as a marker for hypo perfusion and hypoxemia. D-lactate on the other hand, is a product of bacterial fermentation, and its use is described more frequently in studies on diagnosing acute mesenterial ischemia. [1,2,3] It is known that baseline lactate levels are independently correlated to mortality in surgical patients with sepsis or septic shock. [4,5] Also, in patients after cardiac surgery, initial lactate levels at admission into the intensive therapy unit (ICU) and during ICU stay are related to post-operative complications. [6] Furthermore, a cut off value of 1.46 m mol/L is described as the limit for the diagnosis of complications. [7] When adequate resuscitation is applied in patients with complications, this can result in a decrease of lactate levels, which reflects a reversal of tissue hypoxia. This decrease in lactate levels is an indicator of improved survival. Both the duration and area under the curve of increased lactate concentrations are related to morbidity and mortality. [8] Despite considerable advances in surgical techniques and perioperative care, significant morbidity and mortality still remains after major abdominal surgery, particularly in patients with advanced age and poor physiological reserve. [9] The aetiology of post-operative complications is complex, but poor tissue perfusion and oxygenation caused by impaired micro vascular flow, which can contribute to organ system dysfunction remains a major cause. [10-14] Clinical and hemodynamic parameters, such as blood pressure, urine output, and central venous pressure are unreliable or late signs of inadequate tissue perfusion and, hence, have limited value in risk-stratifying patients and guiding timely therapy. [15] An important adaptive mechanism to survive tissue hypoxia caused by hypo perfusion is increased production of lactate by anaerobic glycolysis. [16] The subsequent elevation of blood lactate is easy to measure. Earlier studies have shown a strong correlation between the severity of micro vascular alterations and blood lactate levels. Blood lactate clearance was shown to be significantly associated with improved microcirculatory flow. [17] These results indicated that blood lactate can reliably reflect the adequacy of tissue perfusion and oxygenation. [18] Many studies have confirmed that increased blood lactate levels at admission were independently associated with morbidity and mortality in critically ill patients, irrespective of arterial hypotension and that, over time, early changes in these levels can predict patient outcomes. [18-24] The initial lactate level and lactate clearance time (time to the normalization of blood lactate) may be useful in predicting outcomes after major abdominal surgery. Furthermore, one interventional study has suggested that interventions that attempt to keep serum lactate levels < 1.7 mmol/L by adjusting intravenous fluid administration intra-operatively and up to 72 hours post-operatively may be associated with reduced morbidity rates after major elective abdominal surgery. [25] In addition, microcirculatory alteration in patients undergoing major elective surgery is most obvious within the first 24 hours post-operatively, and its severity is significantly associated with outcomes. However, the association between changes in blood lactate concentration during the first 24 post-operative hours and post-operative morbidity after major abdominal surgery has not yet been investigated. The purpose of this study was to observe the relationship between dynamic changes in blood lactate concentration during the first 24 hours post-operatively and the post-operative complications in patients undergoing major elective abdominal surgery.

Aims and Objectives

1. To observe the correlation between lactate levels and length of ICU stay.
2. To detect any abnormal lactate level and to treat this to improve tissue perfusion and improved patient outcome.

Materials and Methods

This was a hospital based observational study conducted among 60 patients who were posted for major abdominal surgery under general anaesthesia in the Department of Anaesthesiology and Critical Care of S.C.B. Medical College & Hospital, Cuttack, over a period of 12 months from September 2020 to August 2021 after obtaining clearance from Institutional Ethics Committee and written informed consent from the study participants.

Inclusion Criteria

- Patients giving consent for surgery.
- Either sex.
- Age between 20 - 60 years.
- Undergoing major abdominal surgery.
- Anticipated duration of surgery more than 2 hours.

Exclusion Criteria

- Patient’s refusal.
- Emergency surgery patients with uncontrolled diabetes mellitus, hypertension and pre-existing renal disease.
- With cardiovascular disease.
- Documented hypersensitivity, egg allergy, soy allergy
- History of alcohol or drug abuse.
- Duration of surgery less than 2 hours.
- Laparoscopic surgery.
- Pre and intra-operative severe lactic acidosis and who were given Ringer lactate in operation theatre.
- Renal failure or use of nephrotoxic drugs before surgery.
- Patient who develops drop in arterial oxygen saturation for more than 15 minutes during operation.

Statistical Analysis

Data were summarised as a mean and standard deviation for numerical variables that were normally distributed as median and inter quartile range when skewed and as counts and percentages for categorical variables. Predictive ability of blood lactate level at a particular time point towards selected post-operative complications were quantified in terms of standard diagnostic indices (sensitivity, specificity, positive predictive value, negative predictive value) using pre specified cut offs. An attempt was made to identify the best predictive cut off towards selected complications by receiver operating characteristics (ROC) curve analysis. Association between blood lactate level and length of intensive care unit stay were quantified through calculation of an appropriate correlation co-efficient. Key results were expressed with 95 % confidence intervals.

Results

Out of 60 patients who were included in the study, age was comparable between two groups

Table 1: Descriptive Statistics of Cases with Shock and without Shock

Age Group	Male n (%) n = 37	Female n (%) n = 23
20 - 30	2 (40)	3 (60)
31 - 40	3 (60)	2 (40)
41 - 50	10 (45.5)	12 (54.5)
51 - 60	22 (78.6)	6 (21.4)
Mean Age = 48.52 ± 9.48		

Demographic Distribution	**Parameter**	**Cases with Shock (Mean ± SD)**	**Cases without Shock (Mean ± SD)**	**P value (Mann-Whitney)**
	Number of Patients	16	44	
	Age	50.31 ± 9.21	47.86 ± 9.59	0.306
Urine Output (in ml)	In 6 hr	325.0 ± 188.85	540.91 ± 116.27	< 0.001
	In 12 hr	784.38 ± 480.87	1363.64 ± 1135.85	0.002
	In 24 hr	1318.75 ± 691.34	1995.45 ± 342.32	0.001
Lactate (in mmol/lt)	In 0 hr	3.20 ± 1.09	2.27 ± 0.93	0.002
	In 6 hr	3.02 ± 1.44	1.88 ± 0.74	0.002
	In 12 hr	2.94 ± 1.75	1.43 ± 0.67	0.007
	In 24 hr	3.24 ± 2.35	0.99 ± 0.77	0.002
	Duration of surgery	4.94 ± 0.72	4.47 ± 0.52	0.013
	Duration of ICU stay	5.75 ± 2.17	1.84 ± 1.11	< 0.001
	Duration of intubation	4.56 ± 3.26	0.39 ± 1.01	< 0.001

Table 2: Descriptive Statistics of Cases with Death and without Death

Parameter	Cases with Death (Mean ± SD)	Cases without Death (Mean ± SD)	P value (Mann-Whitney)
Number of Patients	10	50	
Age	49.10 ± 10.63	48.40 ± 9.35	0.705
Urine Output (In ml)			
In 6 hr	215.00 ± 122.58	537.00 ± 116.41	< 0.001
In 12 hr	505.00 ± 307.72	1350.00 ± 1069.80	< 0.001
In 24 hr	950.00 ± 572.51	1988.00 ± 339.65	< 0.001
Lactate (in mmol/lt)			
In 0 hr	3.67 ± 1.07	2.28 ± 0.90	< 0.001
In 6 hr	3.96 ± 1.21	1.83 ± 0.62	< 0.001
In 12 hr	4.37 ± 1.07	1.32 ± 0.33	< 0.001
In 24 hr	5.12 ± 1.30	0.89 ± 0.25	< 0.001
Duration of surgery	5.07 ± 0.64	4.50 ± 0.56	0.006
Duration of ICU stay	7.0 ± 1.7	2.06 ± 1.23	< 0.001
Duration of intubation	7.0 ± 1.7	0.40 ± 0.63	< 0.001

Table 3: Descriptive Statistics of Cases with AKI and without AKI

Parameter	Cases with AKI (Mean ± SD)	Cases without AKI (M ± SD)	P Value (Mann-Whitney)
Number of Patients	6	54	
Age (In yrs.)	46.67 ± 13.15	48.72 ± 9.12	0.782
Urine Output (In ml)			
In 6 hr	175.0 ± 98.74	517.59 ± 136.03	< 0.001
In 12 hr	375.0 ± 189.07	1301.85 ± 1046.69	< 0.001
In 24 hr	641.67 ± 233.27	1945.37 ± 391.69	< 0.001
Lactate (in mmol/lt)			
In 0 hr	3.70 ± 1.35	2.38 ± 0.94	0.017
In 6 hr	4.05 ± 1.35	1.98 ± 0.84	< 0.001
In 12 hr	4.59 ± 0.95	1.52 ± 0.84	< 0.001
In 24 hr	5.24 ± 1.02	1.19 ± 1.17	< 0.001
Duration of surgery	4.99 ± 0.68	4.56 ± 0.59	0.120
Duration of ICU stay	7.50 ± 1.64	2.37 ± 1.67	< 0.001
Duration of intubation	7.50 ± 1.64	0.83 ± 1.71	< 0.001

Table 4: Descriptive Statistics of Cases Requiring Extended Respiratory Support and not Requiring Extended Respiratory Support

Parameter	Cases Requiring Extended Respiratory Support (Mean ± SD)	Cases not Requiring Extended Respiratory Support (Mean ± SD)	P Value
Number of Patients	7	53	
Age (in years.)	49.71 ± 12.88	48.36 ± 9.09	0.442
Urine output (in ml)			
In 6 hr	242.0 ± 130.47	515.09 ± 145.63	< 0.001
In 12 hr	557.14 ± 345.72	1295.28 ± 1063.34	< 0.001
In 24 hr	1028.57 ± 629.05	1918.87 ± 445.19	0.002
Lactate (in mmol/lt)			
In 0 hr	4.00 ± 0.78	2.32 ± 0.93	< 0.001
In 6 hr	4.22 ± 1.19	1.92 ± 0.74	< 0.001
In 12 hr	4.53 ± 1.25	1.47 ± 0.70	< 0.001
In 24 hr	4.97 ± 1.56	1.15 ± 1.09	< 0.001
Duration of surgery	5.03 ± 0.60	4.54 ± 0.59	0.025
Duration of ICU stay	6.71 ± 1.60	2.38 ± 1.82	< 0.001
Duration of intubation	6.71 ± 1.60	0.81 ± 1.85	< 0.001

Table 5: Descriptive Statistics of Cases with Wound Dehiscence and without Wound Dehiscence

Parameter	Cases with Wound Dehiscence (Mean ± SD)	Cases without Wound Dehiscence (Mean ± SD)	P value (Mann-Whitney)
Number of Patients	22	38	
Age (in yrs.)	48.95 ± 9.03	48.26 ± 9.84	0.788
Urine Output (in ml)			
In 6 hr	381.82 ± 190.57	542.11 ± 121.10	0.002
In 12 hr	1229.55 ± 1690.07	1197.37 ± 279.22	0.050
In 24 hr	1445.45 ± 698.28	2028.95 ± 264.99	0.001
Lactate (in mmol/lt)			
In 0 hr	3.06 ± 1.08	2.20 ± 0.91	0.001
In 6 hr	2.79 ± 1.40	1.83 ± 0.65	0.005
In 12 hr	2.66 ± 1.74	1.35 ± 0.37	0.011
In 24 hr	2.75 ± 2.35	0.92 ± 0.35	0.010
Duration of surgery	4.96 ± 0.67	4.39 ± 0.46	< 0.001
Duration of ITU stay	4.59 ± 2.42	1.89 ± 1.46	< 0.001
Duration of intubation	3.27 ± 3.29	0.47 ± 1.39	< 0.001

There was statistically significant difference with regard to lactate level, urine output, duration of surgery, duration of ICU stays and duration of intubation measured at the point of time (0, 6, 12 and 24) in cases with shock as compared to cases without shock ($p < 0.05$), in cases with death as compared to cases without fatal outcome ($p < 0.05$), in cases with acute kidney injury (AKI) as compared to cases without AKI ($p < 0.05$), in patients who required extended respiratory support as compared to cases who did not require extended respiratory support ($p < 0.05$), and in cases with wound dehiscence as compared to cases without wound dehiscence ($p < 0.05$).

Discussion

Elevated blood lactate levels commonly result from acute tissue hypo perfusion and anaerobic metabolism and have been shown to be a surrogate for oxygen debt or oxygen deficit accumulated over time. [26,27] Lactate clearance (normalization of primarily elevated lactate levels) indicates the success of resuscitation in improving tissue perfusion and repayment of the oxygen debt. Some authors have suggested that lactate clearance time is a powerful predictor of outcome. It has also been shown that relative hyperlactatemia within the normal reference range (2 mmol/L) is an independent risk factor for increased hospital mortality in critically ill patients.21

Highest predictability correlation was observed between lactate level at 24 hours and at death. At 24 hours, serum lactate level was more than 1.83 mmol/L. Jiro Shimazaki et al. [28] studied post-operative arterial blood lactate level as a mortality marker in patients with colorectal perforation and found that the post-operative lactate level was significantly higher in the mortality group than in the survivor group ($p < 0.001$). In another study, [29] the post-operative lactate concentration was assessed to predict the outcome of infants aged 6 weeks or less after intra-cardiac surgery and it was found that the non-survivors had higher lactate concentrations compared with survivors on admission to the paediatric intensive care unit and non survivors took longer time to return for lactate concentration to normal level (2 mmol/l) than intact survivors. The authors found that lactate concentrations of less than 7 mmol/L on admission or less than 8 mmol/L at day 1 predicted survival with 82 % sensitivity and 83 % specificity respectively (P < .001).

Though plasma lactate concentrations were associated with adverse outcome, the predictive values were lower when compared with that of non-survival. In the present study, there was statistically significant difference in the lactate level in the cases with and without fatal outcome (p-0.000). Various previous studies have also demonstrated the correlation between post-operative serum lactate level and length of ICU stay. In study conducted by Nicole T. J. J. Mak et al. [30] about outcomes of post-cardiac surgery patients with persistent hyperlactatemia in the intensive care unit, the study parameters were length of ICU stay, time on mechanical ventilation and hospital mortality. With respect to these measures, it was found that hyper lactatemic patients had poorer outcomes, having a longer ICU stay (p < 0.0001), greater time on mechanical ventilation (p < 0.0001), and higher hospital mortality (p < 0.0001) as compared to patients with normal lactate level. In contrast Soliman HM, Vincent [31, 32] studied the prognostic value of admission serum lactate concentrations in intensive care unit patients and found that there was no overall difference in length of ICU stay (LOS) between survivors and non survivors though non-survivors had higher lactate level.

Li et al. studied [33] initial serum lactate level as predictor of morbidity after major abdominal surgery and found out that the median initial lactate level of the patients with post-operative complications was significantly higher than that of the patients without complication. Multivariate analysis showed that lactate level and simplified acute physiology score II (SAPSII) were significantly predictive of post-operative morbidity. The optimal value of lactate to discriminate between patients who did or did not develop post-operative complications was associated with the highest sum of sensitivity and specificity. The lactate level more than 2.7 mmol/L was associated with post-operative complications. After adjustment for SAPII, the higher lactate level (> 2.7 mmol/L) remained strongly associated with morbidity. In the present study, it was found that among the study subjects (n = 60), 16 patients had shock.

Hyperlactatemia associated shock was previously demonstrated by another study. It was found that hypo perfusion by the presence of a ScvO2 < 70 %, together with hyperlactatemia exhibited severe circulatory dysfunction with higher vasopressor requirements, and a trend to longer mechanical ventilation days, ICU stay, and more rescue therapies. In another study, by Bakker J et al. [34] it was observed that oxygen delivery (Do2), oxygen uptake (Vo2) and serum lactate level could be related to outcome of critically ill patients. They measured cardiac output, oxygen-derived variables, and blood lactate levels in 48 patients with documentation of septic shock. There were 27 survivors and 21 non-survivors from the shock episode. For all 174 observations, there was a significant linear relationship between Vo2 and Do2 (p < 0.001). There were no significant differences in Do2 between survivors and non-survivors at the onset of septic shock or in the final phase of septic shock.

Caixia R, et al. [35] conducted a retrospective study about the relation between post-operative hyperlactatemia and acute kidney injury and found that AKI occurred in 45.1 % patients, of which 8.6 % needed continuous renal replacement therapy (CRRT). Hyperlactatemia at 6 hours post-operatively was correlated with development of AKI. A threshold of 5.05 mmol/L at 6 hours after surgery was independently associated with the risk of AKI. Additionally, lactate level of 7.0 mmol/L identified patients needing CRRT. Similarly, Zhang Z et al. [36] studied normalized lactate load is associated with development of acute kidney injury in patients who underwent cardiopulmonary bypass (CPB) surgery, and it was found that serum lactate level was significantly higher in AKI as compared with non-AKI group and serum lactate level was independently associated with post-operative AKI after CPB.

In a previous study, by Matthew G Wiggans et al. [37] it was found that the patients with renal dysfunction and fatal outcome had significantly higher lactate concentration (more than 6 mmol/L) than patients without complications. The study revealed that 27.5 % patients were with an initial lactate concentration greater than 6 mmol/L (positive predictive value PPV = 0.28, *P* = < 0.001) when compared to the 2.2 % patients with an initial lactate concentration less than 2 mmol/L who developed renal dysfunction. Requirement of extended respiratory support was noted in 7 patients with significantly higher lactate level in this study. There were statistically significant differences in serum lactate level and duration of intubation at specified time points between the two groups ($p < 0.05$). In a previous study, done by Leyla A [38] et al. it was found that patients with hyperlactatemia context exhibited more severe circulatory dysfunction with higher vasopressor requirements, and a trend to longer mechanical ventilation days, ICU stay, and more rescue therapies. In another study, [39] it was found that patients receiving mechanical ventilation had higher lactate compared to controls. Positive correlations were observed between lactate and pCO_2 ($p < 0.05$) among the patients. These correlations were statistically significant ($p < 0.05$). Wound dehiscence was another outcome of this study and 22 patients developed wound dehiscence. There was statistically significant difference in lactate level at 0, 6, 12, 24 hours in both the groups ($p < 0.05$) Nicolas De S et al. [40] studied early hyperlactatemia as a predictor of pancreatic fistula after surgery was demonstrated in a study and found that post-operative serum lactate concentration at 6 hours was significantly higher in the POPF (post-operative pancreatic fistula) group. According to the author, hyperlactatemia might reflect global or regional hypo perfusion which might be responsible for an impaired healing of the anastomosis. [41]

Conclusion

The increased serum lactate levels were significantly associated with post-operative complications, mortality and length of ICU stay in patients undergoing major abdominal surgery. Serial lactate measurements in early post-operative period were able to discriminate between patients with and without post-operative complications. This result warrants a “golden hour and silver day” perspective of early resuscitation in patients. Further studies are needed to establish a lactate-directed treatment protocol within 12 - 24 hours of surgery.

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