

Original Research Article

An analytical observational study on the prognostic implication of postoperative serial serum lactate level for complications and predicting length of intensive therapy unit stay after major abdominal surgery

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ABSTRACT

Background: Post-operative microcirculatory alteration causes hypoperfusion, tissue hypoxia and organ dysfunction, resulting in significant morbidity and mortality. Increase in serum lactate level in response to tissue hypoxia may serve as a cost effective tool to assess status of all organ dysfunction being sensitive but not organ specific and may help in early prognostication. Aim of this study was to investigate the association of blood lactate levels during the first 24 hours after surgery with postoperative morbidity and mortality, with length of ITU stay and to correlate the lactate values at various time points with different postoperative complications (POC).

Methods: 150 patients undergoing elective abdominal surgery were included. Blood lactate (mmol/lit) levels were measured immediately on admission to the Intensive Therapy Unit (ITU) and at 6, 12, and 24 hours of admission. The parameters of clinical outcome included were mortality, shock, Acute kidney injury (AKI), respiratory failure, wound dehiscence and length of ITU stay. Heart Rate, Mean Arterial Pressure, spo₂, Temperature and Urine output were also measured.

Results: There was statistically significant difference in the lactate levels measured at the above mentioned point of time (0, 6, 12 and 24h) in cases with death and without fatal outcome, with and without respiratory failure, with and without AKI, with and without shock and in cases with and without wound dehiscence ($p < 0.05$). There was a statistically significant difference in urine output, duration of ITU stay and duration of intubation ($p < 0.05$).

Conclusions: Increased serum lactate levels were significantly associated with postoperative complications, mortality and length of ITU stay in patients undergoing major elective abdominal surgery.

Keywords: Blood lactate, Post-operative period, ITU stay

INTRODUCTION

Microcirculatory alteration in patients undergoing major elective surgery is most obvious within the first 24 hour postoperatively, and its severity is significantly associated with morbidity and mortality, particularly in patients with

advanced age and poor physiological reserve. The etiology of postoperative complications is complex, but poor tissue perfusion and oxygenation caused by impaired microvascular flow, contributing to organ system dysfunction, remains a major cause.¹⁻⁵

An important adaptive mechanism to survive tissue hypoxia caused by hypoperfusion is increased production of lactate by anaerobic glycolysis.⁶ This increased serum lactate level (L Lactate form) is widely used as an indirect marker of tissue hypoxia. It is known that baseline lactate levels are independently correlated to mortality in surgical patients with sepsis or septic shock.^{7,8} Also, in patients after cardiac surgery, initial lactate levels at admission into the ITU and during ITU stay are related to postoperative complication.⁹ Furthermore, a cut off value of

1.46 mmol/L is described as the limit for the diagnosis of complications.¹⁰ Adequate resuscitation in patients with complications result in decrease in lactate levels, reflecting a reversal of tissue hypoxia and this decrease serves as an indicator of improved survival. An interventional study has suggested that interventions that attempt to keep serum lactate levels <1.7 mmol/l by adjusting intravenous fluid administration intraoperatively and up to 72 h postoperatively may be associated with reduced morbidity rates after major elective abdominal surgery.¹¹

Earlier studies have shown a strong correlation between the severity of microvascular alterations and blood lactate levels, and blood lactate clearance was shown to be significantly associated with improved microcirculatory flow.^{1,4,12} These results indicated that blood lactate can reliably reflect the adequacy of tissue perfusion and oxygenation.^{13,14} The purpose of this study was to observe the relationship between the dynamic changes in blood lactate concentration during the first 24 hour postoperatively and the postoperative complications in patients undergoing major elective abdominal surgery.

METHODS

After obtaining Institutional Ethical Committee clearance and informed consent, this analytical observational study was carried out in Intensive Therapy Unit in I.P.G.M.E. and R, S.S.K.M. Hospital on 150 patients of either sex, age between 20-60 years, undergoing major abdominal surgery during the period between February 2016 to October 2017.

The purpose of this study was to investigate the association of blood lactate levels during the first 24 h after surgery with postoperative morbidity and mortality, with length of ITU stay and to correlate the lactate values at various time points with different postoperative complications (POC).

Being an observational study, a formal sample size calculation was not done, however considering the time and logistic availability at a disposal, we proposed to recruit 150 number of subjects.

Patients with uncontrolled diabetes mellitus and hypertension, cardiovascular disease, documented hypersensitivity, history of alcohol or drug abuse, renal failure or use of nephrotoxic drugs before surgery and patients who develop drop in arterial oxygen saturation for

more than 15 minutes during operation were excluded from the study. Emergency or laparoscopic surgery or surgery less than 4 hours or where there is pre and intra operative severe lactic acidosis with use of Ringer lactate during surgery, were also not included.

Pre-operative data (age, sex, weight,) were collected from patients' medical files. Intraoperative data (blood loss and blood transfusion, vital signs, oxygen saturation, urine output) were collected from records noted during operation. Blood lactate (mmol/lit) levels were measured immediately on admission to the ITU and at 6, 12, and 24 hours of admission. Lactate levels were analysed by arterial blood gas analyser model no: cobas b221. Other parameters like heart rate, MAP, spo2, temperature, urine output were measured simultaneously.

The parameters of clinical outcome included were mortality, shock, acute kidney injury (AKI), respiratory failure, wound dehiscence and length of ITU stay along with length of ITU stay in intubated condition.

Data were summarised as 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. Association between blood lactate level and length of ITU stay were quantified through calculation of an appropriate correlation coefficient. Key result was expressed with 95% confidence intervals. Statistical version 6 (Tulsa, Oklahoma: StatSoft Inc., 2010) and MedCalc version 11.6 (Mariakerke, Belgium: MedCalc Software 2011) was used.

RESULTS

The demographic profile of patients is shown in the Table 1. The mean age is 49.41 years and there is male preponderance among the subjects.

Table 1: Demographic profile of patients.

Parameters	Values (mean±SD)
Age (in years)	49.41±7.47
Sex (m/f)	(86/64)

Out of 150 patients, 46 patients had shock (Table 2). There was statistically significant difference in the lactate level measured at the above-mentioned point of time in both the groups (p=0.000). There was a statistically significant difference in urine output, duration of ITU stay (including intubation) (p<0.05).

Out of 150 patients, 28 patients died (Table 3). Statistically significant difference in the lactate level measured at the above-mentioned point of time ($p=0.000$). There was a statistically significant difference in urine output, duration of ITU stay including intubation ($p<0.05$).

23 patients had respiratory failure (Table 4). Statistically significant difference in the lactate level measured at the above-mentioned point of time was found in both the groups ($p=0.000$). There was a statistically significant difference in urine output, duration of ITU stay including intubation ($p<0.05$).

Table 2: Descriptive statistics of cases with and without shock.

Parameters	Case without shock	Case with shock	P value (MannWhitney)
Number of patients	104	46	
Age (mean±SD) in years	49.15±7.86	49.98±6.58	0.685
Urine output (in ml) 6hrs	522.60±126.74	352.17±155.98	0.000
12 hrs	1249.52±770.84	785.87±377.516	0.000
24hrs	1982.21±354.85	1297.83±598.61	0.000
Lactate (in mmol/lit) 0hr	2.52±0.75	3.18±0.75	0.000
6hrs	2.14±0.70	3.05±1.06	0.000
12hrs	1.72±0.85	2.93±1.52	0.000
24hrs	1.27±1.21	2.87±2.12	0.000
Duration of surgery (in hours)	4.48±0.47	4.82±0.56	0.000
Duration of ITU stay (in days)	2.06±1.44	5.46±2.08	0.000
Duration of intubation (in days)	0.66±1.54	3.72±2.91	0.000

Table 3: Descriptive statistics of cases with and without death.

Parameters	Case without death	Case with death	P value (Mann-Whitney)
Number of patients	132	28	
Age (mean±SD)	49±7.47	51.18±7.37	0.094
Urine output (in ml) 6hrs	516.80±117.59	267.86±147.96	0.000
12 hrs	1225.00±712.56	594.64±384.26	0.000
24hrs	1945.90±336.09	1016.07±628.79	0.000
Lactate (in mmol/lit) 0hr	2.57±0.74	3.38±0.77	0.000
6hrs	2.08±0.55	3.89±0.77	0.000
12hrs	1.55±0.38	4.47±0.69	0.000
24hrs	0.97±0.28	5.20±0.81	0.000
Duration of surgery (in hours)	4.47±0.45	5.08±0.51	0.000
Duration of ITU stay (in day)	2.32±1.65	6.50±1.37	0.000
Duration of intubation (in days)	0.50±0.79	6.39±1.45	0.000

Table 4: Descriptive statistics of cases with and without respiratory failure.

Parameters	Case without respiratory failure	Case with respiratory failure	P value (Mann-Whitney)
Number of patients	127	23	
Age (mean±SD) in years	49.08±7.39	51.22±7.87	0.100
Urine output (in ml) 6hrs	506.69±133.54	269.57±123.16	0.000
12 hrs	1198.82±713.96	602.17±388.02	0.000
24hrs	1913.39±389.94	993.48±617.79	0.000
Lactate (in mmol/lit) 0hr	2.59±0.76	3.44±0.69	0.000
6hrs	2.14±0.64	3.97±0.73	0.000
12hrs	1.65±0.65	4.52±0.73	0.000
24hrs	1.15±0.95	5.11±0.87	0.000

Continued.

Parameters	Case without respiratory failure	Case with respiratory failure	P value (Mann-Whitney)
Duration of surgery (in hours)	4.50±0.49	5.03±0.46	0.000
Duration of ITU stay (in day)	2.48±1.85	6.52±1.16	0.000
Duration of intubation (in days)	0.73±1.44	6.39±1.27	0.000

Table 5: Descriptive statistics of cases with and without AKI.

Parameters	Case without AKI	Case with AKI	P value (Mann-Whitney)
Number of patients	135	15	
Age (mean±SD) in years	49.26±7.23	50.73±9.23	0.234
Urine output (in ml)	501.11±131.79	193.33±70.37	0.000
6hrs	1187.78±698.92	383.33±141.00	0.000
12 hrs			
24hrs	1901.48±395.31	610.00±202.84	0.000
Lactate (in mmol/lit) 0hr	2.64±0.75	3.49±0.90	0.000
6hrs	2.25±0.75	3.97±0.89	0.000
12hrs	1.82±0.93	4.57±0.66	0.000
24hrs	1.38±1.32	5.19±0.66	0.000
Duration of surgery (in hours)	4.53±0.49	5.06±0.49	0.000
Duration of ITU stay (in day)	2.66±1.92	7.07±1.22	0.000
Duration of intubation (in days)	1.01±1.79	6.87±1.45	0.000

Table 6: Descriptive statistics of cases with and without wound dehiscence.

Parameters	Case without wound dehiscence	Case with wound dehiscence	P value (Mann-Whitney)
Number of patients	93	57	
Age (mean±SD) in years	49.13±7.88	49.86±6.81	0.605
Urine output (in ml)	529.03±119.63	374.56±164.51	0.000
6hrs	1187.63±250.61	976.32±1094.75	0.000
12 hrs			
24hrs	2017.74±255.45	1371.93±644.89	0.000
Lactate (in mmol/lit) 0hr	2.49±0.73	3.10±0.79	0.000
6hrs	2.03±0.54	3.05±1.07	0.000
12hrs	1.53±0.37	3.01±1.55	0.000
24hrs	0.97±0.32	3.05±2.20	0.000
Duration of surgery (in hours)	4.40±0.39	4.88±0.57	0.000
Duration of ITU stay (in day)	1.89±1.34	5.07±2.08	0.000
Duration of intubation (in days)	0.35±1.01	3.63±2.83	0.000

Table 7: Correlation of serum lactate level with duration of ITU stay.

Lactate at 0,6,12,24 hours	Spearman's coefficient of rank correlation (rho)	Significance level	95% confidence interval for rho
Lactate 0	0.559	P<0.0001	0.438 to 0.660
Lactate 6	0.633	P<0.0001	0.526 to 0.720
Lactate 12	0.606	P<0.0001	0.494 to 0.699
Lactate 24	0.573	P<0.0001	0.455 to 0.672

Out of 150 patients, 15 patients had AKI (Table 5). Statistically significant difference in the lactate level measured at the above-mentioned point of time was found

in both the groups (p=0.000). There was a statistically significant difference in urine output, duration of ITU stay including intubation (p<0.05).

Out of 150, 57 patients had wound dehiscence (Table 6). Statistically significant difference in the lactate level measured at the above-mentioned point of time was found in both the groups ($p < 0.000$). There was a statistically significant difference in urine output, duration of ITU stay including intubation ($p < 0.05$).

Good (but not strong) correlation is observed between lactate levels at 0 h, 6 h, 12 h and 24 h of ITU stay with total length of ITU stay (Table 7). The highest value of Spearman's Rho is for 6 h.

DISCUSSION

Elevated blood lactate levels, commonly resulting from acute tissue hypoperfusion and anaerobic metabolism, have been shown to be a surrogate for oxygen debt or oxygen deficit accumulated over time.^{6,13-16} Lactate clearance indicates the success of resuscitation in improving tissue perfusion and repayment of the oxygen debt.¹⁶ Some authors have suggested that lactate clearance time is powerful predictor of outcome.^{8,17} 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.¹⁸

In the present study it was found that higher lactate levels after major abdominal surgery were associated with an increased risk of morbidity, mortality and increased length of ITU stay. Out of 150 patients, 28 patients had fatal outcome and in them there was consistently significant increased lactate level ($p < 0.000$). Highest predictability correlation was observed between lactate level (more than 1.85 mmol/l) at 24 hours and death.

Shimazaki et al studied postoperative arterial blood lactate level as a mortality marker in patients with colorectal perforation, and found that the postoperative lactate level was significantly higher in the mortality group than in the survivor group ($p < 0.001$).¹⁹

In the present study, good (but not strong) positive correlation was observed between lactate levels at different study point with total length of ITU stay. The highest value of Spearman's Rho is for 6 hours (3.11 mmol/l). It was also observed that increase in post operative lactate levels were significantly correlated with the duration of intubation, duration of ventilation, length of ITU stay and urine output.

In study conducted by Mak et al about outcomes of post-cardiac surgery patients with persistent hyperlactatemia in the ICU, it was found that hyperlactatemic 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.²⁰

A good correlation was found between serum lactate level and different complications. At 12 hrs the serum lactate

level was more than 2.16 mmol/l, which was the best predictor of shock in patients admitted to ITU with sensitivity 56.52% and specificity 90.38%.

In the present study, it was found that among 150 patients, 46 had shock, 104 did not have shock. In them there was statistically significant difference in the lactate level measured at the above-mentioned time ($p < 0.000$). At 12 hours serum lactate level more than 2.16 mmol/l had highest predictive value of shock.

Hyperlactatemia associated shock was previously demonstrated by another study.¹⁶ It was found that hypoperfusion by the presence of a $ScvO_2 < 70\%$, 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 this study, 15 patients developed AKI with statistically significant difference in urine output and serum lactate level measured at the above-mentioned time in both the groups. ($p < 0.000$). Serum lactate levels were higher in patients with AKI.

Caixia et al conducted a retrospective study about the relation between postoperative hyperlactatemia and acute kidney injury and found that AKI occurred in 45.1% patients, of which 8.6% needed CRRT. Hyperlactatemia at 6 hours postoperatively 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, a lactate level of 7.0 mmol/l identified patients needing CRRT.²¹

Respiratory failure was noted in 23 patients with significant higher lactate level in them.

In another study by Nanda et al it was found that Patients receiving mechanical ventilation had higher lactate compared to controls. Positive (statistically significant) correlations were observed between lactate and pCO_2 ($p < 0.05$) among the patients.²² In this study 57 patients developed wound dehiscence with statistically significant difference in lactate level at 0, 6, 12, 24 hrs in both the groups ($p < 0.05$).

Nicolas et al studied early hyperlactatemia as a predictor of pancreatic fistula and found that post operative serum lactate concentration at 6 hrs were significantly higher in the POPF (post-operative pancreatic fistula) group. According to the author, hyperlactatemia might reflect

global or regional hypoperfusion, which might be responsible for an impaired healing of the anastomosis.²³

The main limitation was absence of a control group. The details of pressor agents were not recorded, which could affect the lactate concentration. Technologically advanced measurements for estimating tissue perfusion, such as

SvO₂/ScvO₂ were not done. Surgery type which may affect the outcome were not mentioned.

CONCLUSION

This study shows that increase serum lactate levels were significantly associated with postoperative complications, mortality and length of ITU stay in patients undergoing major elective abdominal surgery. 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.

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