# ROLE OF BLOOD LACTATE LEVELS IN PREDICTING MORBIDITY AND MORTALITY OUTCOMES FOLLOWING CARDIAC SURGERIES

*Ananda Bhat[1], Perumala Ramanna Balajibabu[2], Chilukoori Raghu[3]*

*[1]Associate Professor, Department of Anaesthesiology, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bengaluru, Karnataka.*
*[2]Associate Professor, Department of Anaesthesiology, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bengaluru, Karnataka.*
*[3]Postgraduate Student in D.M. Cardiac Anaesthesia, Sri Jayadeva Institute of Cardiovascular Sciences and Research, Bengaluru, Karnataka.*

**ABSTRACT**

**BACKGROUND**

Blood lactate is a product of anaerobic metabolism. Tissue hypoxia because of hypo perfusion or impaired oxygen extraction causes rise in blood lactate levels. An elevated blood lactate level has been postulated as a marker for adverse outcomes and increased mortality risk in patients undergoing cardiac surgery under cardiopulmonary bypass (CPB). This study was carried out to evaluate the association between blood lactate levels and mortality following cardiac surgery.

**METHODS**

This retrospective record-based cross-sectional study was carried out among 503 patients who underwent cardiac surgery under CPB. Apart from baseline lactate value, serum lactate was measured every thirty minutes during CPB (CPBL1, CPBL2, CPBL3 and so on) and during post-operative period (POL1, POL2, POL3 and so on). Duration of the CPB, lowest temperature attained during the CPB, duration of mechanical ventilation, IABP usage, maximum number of inotropes and vasopressors used and mortality in the peri-operative period were noted.

**RESULTS**

The incidence of mortality in this study was 2.2%. Blood Lactate levels were high in the third measurement during CPB (CPBL3) and for all the post-operative measurements among those who did not survive. There was a significant association between lactate levels and intra operative lowest temperatures ($p<0.05$).

**CONCLUSIONS**

Lactate levels during CPB and post-operative period can be used as a predictor of increased mortality and morbidity. Prolonged bypass and deeper levels of hypothermia is associated with increased lactate levels.

**KEYWORDS**

Cardiopulmonary Bypass, Hyperlactatemia, Hypothermia, Metabolic Acidosis

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## BACKGROUND

Cardiac surgeries are considered to be one of the major and complicated surgeries involving general anaesthesia. According to the Society of Thoracic Surgeons, the 30 days mortality for coronary artery bypass surgeries was said to be 2.3% and for isolated valve surgeries the same was 3.4%.[1] Cardiac surgeries involve increased risk of both in- hospital mortality and also post-surgical morbidity and mortality. There are several factors that determine the outcome of the cardiac surgery including patient characteristics, timing of surgery, and post-operative length of stay in hospital, Intensive care unit (ICU) stay and likelihood of in-hospital mortality.

Although several extraneous factors are associated with predicting the morbidity and mortality outcomes following cardiac surgery, there are certain issues concerning intra operative period that are likely to determine the outcomes of cardiac surgeries. Central or mixed venous oxygen saturation monitoring has very important role in the hemodynamic management of patients undergoing major surgical procedures. The other important factor is blood lactate level. Blood lactate levels are also linked to the duration of stay in the intensive care unit for the adult patients. Low values of central venous oxygen saturation during the intra-operative period are interpreted as an inadequate oxygen delivery ($DO_2$) and/or increased consumption of oxygen ($VO_2$). This condition results in increased oxygen extraction ratio in order to satisfy the peripheral oxygen needs without the need for anaerobic

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*Corresponding Author:*
*Dr. Balajibabu P. R.,*
*Department of Anaesthesiology,*
*Sri Jayadeva Institute of Cardiovascular Sciences and Research,*
*Bengaluru- 560069, Karnataka.*
*E-mail: drbalajibabupr@gmail.com*
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metabolism. If the fall in the $DO_2$ is below the critical value (260 ml/min/$m^2$), there is progressive increase of lactate which is a marker of anaerobic energy production.[2] Hyperlactatemia is a result of several mechanisms. Type A hyperlactatemia is defined as impaired tissue oxygenation resulting in increased anaerobic metabolism and excessive production of pyruvate. Pyruvate is marker of global tissue hypoxia and circulatory shock etc. While Type A hyperlactatemia is due to the lack of oxygen at the tissue level, Type B hyperlactatemia occurs as a result of the inability of the peripheral tissues to use the available oxygen. The lactate concentrations depend on the balance between the production and its elimination in the liver. Therefore, hyperlactatemia coupled with low central venous oxygen saturation has been postulated as one of the major indicators of tissue hypoxia and increased risk of anaerobic metabolism. The onset of anaerobic metabolism sets during the intra operative period and this directly influences the prognostic outcomes following the surgeries. Several studies have established the role of hyperlactatemia in determining the morbidity and mortality outcomes following cardiac surgeries. However, there is still a dark area surrounding the causes and risk factors which are associated with hyperlactatemia. It is essential to evaluate the factors in the peri-operative period which could predispose to the occurrence of hyperlactatemia. Thorough understanding of this will help in early detection of hyperlactatemia and prevent the mortality associated with it which will indirectly increase the survival outcomes following cardiovascular surgeries.

This study was carried out to evaluate the role of blood lactate levels in predicting the morbidity and mortality associated with cardiovascular surgeries among adult population.

## METHODS

### Study Setting and Study Participants

This retrospective record based cross sectional study was carried out in the Department of Anaesthesia of our tertiary teaching institution. A total of 503 patients who underwent cardiac surgery under cardiopulmonary bypass were included in the study. Mortality was documented based on follow up of the patients till discharge.

### Selection Criteria

At least three values of lactate during the CPB period and three values during the post-operative were required to be included in the study. Patients whose baseline lactate levels exceeded 2.0 mmol or patients undergoing emergency surgery where excluded from the study.

### Ethical Approval

Approval was obtained from the Institutional Ethics Committee prior to the commencement of the study.

### Data Collection Tools

Anaesthetic protocol was standardized for all the patients who underwent cardiac surgery. Patients were premeditated with Inj. Fentanyl 3 mcg/kg, Inj. Midazolam 0.03 mg/kg, IV. Induction was done with Inj. Propofol sleep dose up to 1.5 mg/kg, Inj. Vecuronium 0.15 mg/kg. Maintenance of anaesthesia was provided with 50% oxygen in air + Isoflurane 0.6 to 1%. Inj. Fentanyl 2 mcg/kg and Inj. Vecuronium 0.1 mg/kg added to pump and during re-warming. Blood lactate was measured prior to induction, 10 minutes after institution of CPB, and every 30 minutes till end of CPB(CPBL1, CPBL2, CPBL3 and so on)and after weaning from CPB, repeated if required. After 1 hour of shifting to recovery, then after 6 hours & every 6 hours for two days (POL1, POL2, POL3 and so on). Additional measurements were done when required. Maximum of five blood lactate levels were noted during CPB period and three values were noted during the post-operative period. If there were more number of values the higher values were taken. Other information recorded included duration of CPB, lowest temperature attained during CPB, duration of mechanical ventilation, IABP usage and maximum number of inotropes/ vasopressors used. Particulars related to mortality were also noted.

### Data Analysis

Data was entered and analysed using SPSS version 20 software. Percentages were used to document the mortality and morbidity rates. Independent sample t test was used to analyse the association between mortality and lactate levels. A p value $<0.05$ was considered statistically significant.

## RESULTS

This study was carried out among 502 patients who underwent cardiac surgery under cardiopulmonary bypass. Majority of the participants were males (62.4%) and the mean age of the participants was 35.45±20.63 years. The incidence of mortality in this study was 2.2% (table 1). Serum lactate levels measured after ninety minutes of initiation of the CPB (CPBL3) was significantly ($p<0.005$) higher among the non survivors. Throughout the post-operative period, the lactate levels remained high among non survivors ($p<0.001$). The serum lactate levels were persistently higher at all times of measurement in the post-operative group among non survivors compared to those who survived (Table 2). Our study observed a strong association between the intra- operative serum lactate levels and the duration of CPB. With an increase in the duration of CPB, CPBL3 was significantly higher ($p<0.05$). There was a strong association between the post- operative serum lactate levels and the duration of CPB. In the post-operative period, the lactate levels were higher in the patients with longer CPB ($p<0.001$) (Table 3). Our study observed a significant difference in the serum lactate levels intra operatively with a decrease in the temperature. Hypothermia was associated with an increased risk of elevated lactate levels measured throughout the CPB ($p<0.05$) (Table 4). In this study, we observed statistically significant ($p<0.001$) association between number of post-operative inotropes/vasopressors, and post-operative lactate levels (Table 5). The usage of IABP did not show any correlation to blood lactate levels during CPB or post-operative period.

Similarly, the duration of mechanical ventilation did not correlate with the any blood lactate level measurements.

| Sl. No. | Mortality | Frequency (n=502) | Percentage (%) |
|---|---|---|---|
| 1. | Present | 11 | 2.2 |
| 2. | Absent | 491 | 97.8 |

***Table 1. Incidence of Mortality in Patients Studied***

| Sl. No. | Characteristic | Mortality | | p Value |
|---|---|---|---|---|
| | | No | Yes | |
| **1.** | **Intra operative period** | | | |
| | CPB Lactate 3 | 2.65±1.26 | 4.04±0.55 | 0.004** |
| **2.** | **Post-operative period** | | | |
| | PO Lactate 1 | 2.40±1.24 | 6.72±3.90 | <0.001** |
| | PO Lactate 2 | 2.02±1.21 | 5.59±2.87 | <0.001** |
| | PO Lactate 3 | 1.48±0.81 | 6.15±2.28 | <0.001** |

***Table 2. Relationship of Serum Lactate with Mortality in Intra-Operative and Post-Operative Period***

| Sl. No. | Characteristic | CPB time | | | | p Value |
|---|---|---|---|---|---|---|
| | | Up to 50 | 51-100 | 101-150 | >150 | |
| 1. | **CPB Serum Lactate Levels** | | | | | |
| | CPB Lactate 3 | 2.23±1.68 | 2.49±1.04 | 2.69±1.07 | 3.19±1.70 | 0.046* |
| 2. | **Post-operative Serum Lactate Levels** | | | | | |
| | PO Lactate 1 | 1.99±0.88 | 2.47±1.34 | 2.69±1.52 | 3.37±2.57 | <0.001** |
| | POP Lactate 2 | 1.71±0.84 | 2.01±1.19 | 2.42±1.66 | 2.66±1.99 | <0.001** |
| | PO Lactate 3 | 1.33±0.65 | 1.51±0.85 | 1.80±1.44 | 2.13±1.87 | <0.001** |

***Table 3. Relationship between CPB Time and Intra/Post-Operative Lactate Levels***

| Sl. No. | Charac-teristic | CPB Temperature | | | | | p Value |
|---|---|---|---|---|---|---|---|
| | | 22-28 | 28-30 | 30-32 | 32-34 | 34-38 | |
| 1. | CPB Lactate 1 | 2.54±0.87 | 2.28±1.11 | 2.34±1.17 | 2.07±0.91 | 2.17±0.89 | 0.032* |
| 2. | CPB Lactate 2 | 3.08±1.46 | 2.57±1.68 | 2.76±1.32 | 1.19±0.91 | 2.15±0.69 | <0.001** |
| 3. | CPB Lactate 3 | 2.97±1.22 | 2.71±1.26 | 3.20±1.36 | 2.15±1.05 | 2.33±1.33 | 0.003** |

***Table 4. Relationship of CPB Serum Lactate According to CPB Temperature***

| Sl. No. | Charact-eristic | Number of Supports | | | | | p Value |
|---|---|---|---|---|---|---|---|
| | | Nil | 1 Support | 2 Supports | 3 Supports | 4 Supports | |
| 1. | **Post-Operative Serum Lactate Level** | | | | | | |
| | PO Lactate 1 | 2.12±1.12 | 2.38±1.22 | 2.62±1.63 | 4.13±1.86 | 5.82±5.62 | <0.001** |
| | PO Lactate 2 | 1.83±0.95 | 2.04±1.25 | 2.18±1.53 | 2.72±1.17 | 4.80±3.71 | <0.001** |
| | PO Lactate 3 | 1.36±0.49 | 1.51±0.84 | 1.67±1.32 | 2.42±2.50 | 4.96±2.94 | <0.001** |

***Table 5. Relationship of Post-Operative Serum Lactate according to Number of Supports***

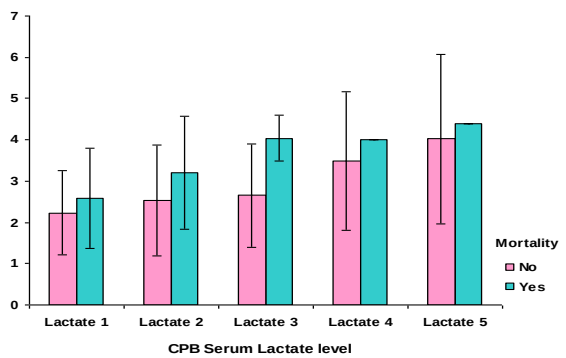


***Figure 1. Comparison of CPB Serum Lactate Levels Among Survivors and Non-Survivors***

## DISCUSSION

Our study demonstrated a significant correlation between the post-operative lactate values and the incidence of mortality. Lactate values, at all of the post-operative periods were higher in the patients who died. This was statistically significant (P<0.001). We also evaluated the association between the duration of CPB and lactate levels.It was observed that the blood lactate levels rose after an hour on cardiopulmonary bypass. When the post-operative lactate values were compared with the duration of CPB all post-operative lactates were higher in those with prolonged CPB. The observations of our study were similar to several studies published. In a study done by Naik et al, he observed that there was a gradual increase in the lactate levels during the intra operative periods and it continued to remain high during the post-operative period in the ICU for up to six hours initially. The study also observed that patients with high levels of lactate had significantly longer duration of CPB which was similar to our study.[3] A study done by Munoz et al showed that there was an increase in median lactate levels from the baseline to the cooling and cooling versus re-warming period with significant difference in each of these values. There was also a statistically significant difference in the intra operative and post-operative values of lactate levels during the immediate post-operative periods. Similar to our study this study also reported that patients who did not survive the surgery had higher median lactate levels at all-time points especially during the post-operative period which is similar to our findings.[4]

A study done by Inoue S et al explored the difference in the patterns of response towards CPB procedures with respect to normal and high lactate level groups. The study observed that lactate concentration was higher in patients with longer duration of CPB, hypotension during initiation of CPB. The lactate levels in the hyperlactatemia group was elevated within one hour following surgery and remain elevated for 6 hours after surgery and this was found to be statistically significant, similar to our study.[5] A study done by Bennett J.M et al explored the mortality patterns for patients who underwent type A aortic dissection surgeries. The study observed the mortality rate of 17% which was higher than our finding. However, the study also demonstrated an increase in the serum lactate levels among patients who died following surgery during 1 year follow up period.[6]

The mortality following cardio- vascular surgeries is determined by the oxygen delivery at the peripheral level. One of the important biomarkers which determine the prognosis of cardio-vascular surgery is lactate. Serial measurement of lactate significantly helps in identifying the need for intervention during intra operative and post-operative periods in order to prevent death. Several studies have demonstrated that intra operative lactate increases in patients within 1 hour of initiation CPB in patients who did not survive the procedure. Studies have also shown that very high lactate levels (>10 mmol/l) in the post-operative period is associated with high adverse (>40% mortality) outcomes. It has been demonstrated that such high levels of lactate saturate the kidney and liver mechanisms to clear lactate. Cardiogenic shock, mesenteric ischemia and compartment syndromes were associated with such high lactate levels and this may ultimately result in multi organ failure.[7]

In our study, lactate levels among the patients who did not survive were significantly higher during the third ABG during CPB in the intra operative period. The third lactate

value (CPBL3) during the CPB and post-operative lactate values were higher for those who had prolonged duration of CPB. The post-operative lactate levels were significantly higher for the non survivors. Diabetic status and duration of ventilation did not show any correlation with the lactate levels. However, the CPB lactate levels were significantly higher in patients with deep hypothermic CPB. Inotropic supports had positive correlation with post-operative lactate levels but not with intra operative levels. Under anaerobic conditions, anaerobic glycolysis occurs when there is an imbalance in the oxygen delivery and tissue oxygen consumption resulting in lactate acidosis. Blood lactate levels are increased in clinical conditions involving circulatory shock, extra corporeal support and in paediatric population following complex congenital heart disease. Serial blood lactate determination may be necessary to detect the problems in the intra operative period. It also helps in assessing the response of patients in shock to therapy. There is a positive correlation between estimated intra operative oxygen deficit and post-operative lactate concentration observed in several studies.

Lactate can also be used to assess the degree of accumulated oxygen deficit and in titrating therapy to support post-operative physiologic compensation. Correction of high lactate levels can be done by providing tissue oxygenation by adjusting the flow rate (cardiac output), body temperature, gas flow and haemoglobin. Our study observed significant relationship between the temperature (hypothermia) levels and lactate levels. Studies have implicated splanchnic hypo perfusion resulting in production of endogenous vaso-active mediators and decreased arterial oxygen content during CPB which could elevate blood lactate levels. In addition, extreme haemodilution and excessive neuro hormonal activation are also implicated in lactic acidosis. During hypothermia, the impaired hepatic clearance of lactate during CPB may be related to decreased pyruvate metabolism. In the early post-operative period an hyper metabolic response characterized by increased oxygen consumption and carbon-dioxide production which may represent high risk period for decompensation.[8] A study done by Abraham B et al demonstrated that low CPB flow rate and mean blood pressure during CPB were essential risk factors for hyperlactatemia and mortality. He also observed that post-operative hyperglycaemia was linked to post-operative hyperlactatemia which was not observed in our study.[9]

## CONCLUSIONS

This study demonstrated a strong association between lactate levels and mortality of patients undergoing cardiac surgery under cardiopulmonary bypass. Among patients who died, lactate levels remained persistently high in the post-operative period during the ICU stay. Our study also demonstrated that patients with longer CPB times had higher post-operative lactate levels. This study has envisaged the need for serial monitoring lactate levels from the start of the surgery to the post-operative period in order to detect abnormalities in tissue perfusion and the responsiveness to therapy and provide considerable corrective measures in order to achieve better outcomes. Further studies to explore the role of CPB flow rate, haematocrit concentration and temperatures during the intra operative period are required in order to obtain an in-depth analysis of risk factors which could have triggered the increase in anaerobic metabolism and increased lactate levels.

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