J Nepal Health Res Counc 2025 Oct-Dec; 23 (69):638-645

Blood Lactate Clearance as a Predictor of Mortality in Children Undergoing Cardiac Surgery with Cardiopulmonary Bypass

Smriti Mahaju Bajracharaya,[1] Ushna Shrestha,[1] Ashish Govinda Amatya[1]

[1]Shahid Gangalal National Heart Centre, Bansbari, Kathmandu, Nepal.

ABSTRACT

Background: Pediatric cardiac surgery is still a high-risk procedure, with mortality being a significant concern. Lactate clearance has been demonstrated to enhance outcomes in critically ill adult populations; however, data regarding its significance in the context of pediatric cardiac surgery has been limited, particularly in resource-limited settings like Nepal. The aim of this study was to evaluate lactate clearance as a predictor of mortality in children undergoing cardiac surgery with cardiopulmonary bypass (CPB).

Methods: This was a prospective observational cohort study conducted at Shahid Gangalal National Heart Center (SGNHC) involving 129 pediatric patients (≤14 years) undergoing elective cardiac surgery for congenital heart disease. Lactate levels were measured at several time points: T0 (post-induction), T1 (ICU admission), and T6, T12, T18, and T24 hours postoperatively. Patients were classified into two groups based on their lactate clearance rates: high (≥10%) and low (<10%). The primary outcome was in-hospital mortality; secondary outcomes included duration of mechanical ventilation, inotropic support, and ICU stay.

Results: Non-survivors (n=20) had significantly lower lactate clearance at all time points compared to survivors (n=109) ($p<0.001$). High lactate clearance was associated with reduced mortality (1.9% vs. 22%, $p=0.03$), shorter mechanical ventilation (11.29±4.73 vs. 14.56±6.73 hours, $p<0.001$), and shorter ICU stay (48.85±7.26 vs. 66.64±25.46 hours, $p=0.004$).

Conclusions: Lactate clearance is a significant prognostic marker of mortality in pediatric patients undergoing elective cardiac surgery for congenital heart defects. The ongoing monitoring of lactate clearance may facilitate the early identification of high-risk patients in the early postoperative period and guide interventions that could potentially improve postoperative outcomes.

Keywords: Blood lactate clearance; cardiopulmonary bypass; mortality, Nepal; pediatric cardiac surgery.

INTRODUCTION

Pediatric cardiac surgery is still a high-risk procedure, with mortality being a significant concern despite the progress made in both surgical techniques and perioperative management. Lactate has been recognized as a good diagnostic, therapeutic, and prognostic marker of global tissue hypoxia.[1] Lactate is easily available cost-effective and routinely done in cardiac surgery.

Although several studies have evaluated lactate clearance after cardiac surgery [2-5], most have been retrospective and conducted in selected adult or pediatric populations, consistently demonstrating that impaired lactate clearance is associated with increased mortality and postoperative morbidity, In pediatric populations, particularly those undergoing cardiac surgery with cardiopulmonary bypass (CPB), there is a lack of comprehensive studies addressing lactate clearance as a marker for postoperative mortality. There is limited prospective evidence in our national or regional databases evaluating lactate clearance as an outcome predictor after cardiac surgery in pediatric population.[2] As pediatric congenital cardiac diseases are highly prevalent in our region[6], it is important to understand the role of lactate clearance in predicting outcomes in early identification and intervention This

Correspondence: Dr Smriti Mahaju Bajracharya, Department of cardiac Anesthesia Shahid Gangalal National Heart Centre, Bansbari, Kathmandu, Nepal. Email: smriti.mahaju@gmail.com, Phone: +9779840096156.

study aimed to evaluate lactate clearance as an early prognostic marker of mortality in children undergoing cardiac surgery with cardiopulmonary bypass.

METHODS

This was a prospective observational study conducted at the Shahid Gangalal National Heart Center (SGNHC), Kathmandu, Nepal.The study took place over a period of 1 year from March 2022 to feburary 2023 in pediatric patients 14 years of age or younger undergoing elective cardiac surgery with cardiopulmonary bypass (CPB) for congenital heart disease. Ethical approval was obtained from the Institutional Review Committee of SGNHC (Ref No: SGNHC/IRC No: 8-2022) prior to enrollement of patients for the study. Informed written consent was obtained from the patients parents or legal guardians meeting the inclusion criteria on pre-operative visit before enrollment in the study of all participating children. Exclusion criteria comprised patients with pre-existing congestive heart failure, renal dysfunction (serum creatinine >2 mg/dL), hepatic dysfunction (AST >40 U/L or ALT >40 U/L), coagulopathy, systemic infections, or those requiring reoperation

Based on a previous study [2], the mortality rate was estimated at 1.9% for the high lactate clearance group and 22% for the low clearance group. With a significance level of 5% and power of 80%, the required sample size was calculated to be 129, accounting for a 20% dropout rate. Consecutive sampling was used.

Anesthesia management and operative technique was done as per the standard institutional protocol and was left to the discretion of the attending team. The standard American Society of Anesthesiologists monitoring was used in all children along with invasive arterial pressure monitoring, central venous pressure monitoring, and transesophageal echocardiography as approprite. All surgeries were performed by the pediatric surgical team. Induction was performed with ketamine (1–2 mg/kg), fentanyl (2–5 µg/kg), and vecuronium bromide. Anesthesia was maintained with oxygen–air–isoflurane (0.5–2%), fentanyl, midazolam, and vecuronium. CPB was conducted on all children using a membrane oxygenator (Sorin, Lilliput 1,2), occlusive roller pumps(stockert SS), and mild hypothermia (32-34°C). The CPB circuit was primed with 20-25 mL/kg of plasmalyte solution, 1 mL/kg of sodium bicarbonate 8.4% (w/v), 1 g/kg of mannitol 20% (w/v), and 100 U/kg of heparin. Human albumin 20% 5gm/kg, Packed red blood cells were added on CPB, and conventional ultrafiltration was performed during the CPB to maintain a hematocrit value of 30%. Myocardial protection was achieved using a crystalloid CPG(Del-nido CPG) in a dose of 30 mL/kg. CPB flows were maintained between 2.4-2.8 lit/min/m^2. Modified ultrafiltration (MUF) were done in children below 15kgs for 10 minutes. Patients was shifted to ICU after the procedure under mechanical ventilation. Patients were then weaned from mechanical ventilation at the discretion of the ICU team.

Preoperative data included demographic data, hemoglobin, oxygen saturation, and baseline lactate level (T0). Intraoperative data included CPB time, aortic cross-clamp time, and inotrope use. Lactate levels were measured at T0 after induction of anesthesia and prior to surgical incision, and were considered a preoperative reference value, T1: Upon ICU admission,T6: 6 hours after ICU admission,T12: 12 hours after ICU admission, T18: 18 hours after ICU admission and T24: 24 hours after ICU admission using a commercial blood gas analyzer (ABL 835 Flex, Radiometer, Copenhagen). Lactate measurements were performed at ICU admission and at 6-hour intervals up to 24 hours to capture early postoperative metabolic trends. These time points reflect routine ICU monitoring practices and allow assessment of early lactate clearance during the period of greatest hemodynamic instability following cardiopulmonary bypass. Lactate clearance was calculated using the formula: Lactate Clearance (%) = ([Initial lactate – Subsequent lactate] / Initial lactate) × 100 Clearance was calculated for intervals T1–T6, T1–T12, T1–T18, and T1–T24.[2] This calculation was applied for serial time intervals (T1–T6, T1–T12, T1–T18, and T1–T24) to assess the dynamic change in lactate over the first postoperative/critical period. The use of this relative change formula is consistent with prior clinical studies in critical care and cardiac surgery settings investigating lactate kinetics and outcomes.

The primary outcome was in-hospital mortality. Secondary outcomes included duration of mechanical ventilation, duration of inotropic support, and length of ICU stay

Data were analyzed using SPSS version 27 (IBM Corp., Chicago, IL, USA).

Patients were primarily compared between two groups: survivors and non-survivors. Continuous variables were assessed for normality using the Shapiro–Wilk test. Normally distributed continuous variables are expressed as mean ± standard deviation and compared using the independent Student's t-test. Non-normally distributed continuous variables were analyzed using the Mann-

Whitney U test.

Categorical variables, including sex and mortality, are expressed as frequencies and percentages and were compared using the Chi-square test .

Univariate analyses were performed to evaluate the association of lactate clearance at different time intervals (T1-T6, T1-T12, T1-T18, and T1-T24) with mortality and postoperative outcomes, using appropriate tests. A p-value < 0.05 was considered statistically significant. Lactate clearance groups (high vs low clearance) were compared separately using the same statistical approach. A p-value < 0.05 was considered statistically significant.

RESULTS

A total of 129 pediatric patients who underwent cardiac surgery were included in the study, with 109 survivors and 20 non-survivors resulting in-hospital mortality rate of 15.5%. The mean age of survivors was significantly higher than non-survivors (5.50 ± 4.33 years vs. 2.78 ± 3.77 years, p=0.010). Non-survivors were significantly younger, shorter, and had lower body weight than survivors. Preoperatively, non-survivors also had higher hemoglobin levels (16.0±3.8 vs. 13.7±2.8 g/dL, p=0.002) and markedly lower arterial oxygen saturation (70.8±13.4% vs. 89.0±13.1%, p<0.001) compared to survivors (Table 1). Intraoperatively, non-survivors experienced significantly longer cardiopulmonary bypass (177.6±44.1 vs. 112.9±54.1 min, p<0.001) and aortic cross-clamp times (110.1±48.8 vs. 74.2±38.2 min, p=0.005) (Table 1). Postoperatively, they required prolonged mechanical ventilation, inotropic support, and ICU stay (Table 1).

Table 1. Demographic and Peri-Opeartive characteristics of survivors and non-survivors.

Variable	All Patients (n=129)	Survivors (n=109)	Non-survivors (n=20)	p-value
Age (years)	5.12 ± 4.14	5.50 ± 4.33	2.78 ± 3.77	0.010
Sex (Male/Female)	58/71	58/51	14/6	0.165
Height (cm)	94.67 ± 31.98	102.48 ± 31.13	75.85 ± 22.89	<0.001
Weight (kg)	15.58 ± 19.59	19.34 ± 19.43	8.16 ± 4.63	<0.001
Preoperative Hb (g/dL)	14.42 ± 3.12	13.73 ± 2.84	16.01 ± 3.83	0.002
Preoperative Sao2(%)	82.12 ± 16.22	89.03 ± 13.14	70.75 ± 13.44	<0.001
CPB (min)	129.77 ± 64.22	112.89 ± 54.12	177.60 ± 44.14	<0.001
ACX (min)	81.17 ± 43.52	74.23 ± 38.21	110.15 ± 48.75	0.005
Duration of IS (hours)	28.96 ± 19.03	24.19 ± 13.28	30.78 ± 18.49	<0.001
Duration of MV (hours)	26.61 ± 13.98	24.19 ± 13.28	30.78 ± 18.49	<0.001
Duration of ICU Stay (hours)	60.57 ± 25.91	48.85 ± 7.26	66.64 ± 25.46	0.004

**Values are expressed as mean±SD for continuous variables and number (percentage) for categorical variables.. P<0.05 is considered significant; Hb, Hemoglobin; Sao2, Oxygen saturation; CPB,Cardiopulmonary Bypass Time;ACX, Aortic Cross-clamp Time; IS,Inotropic Support; MV,Mechanical Ventilation; ICU,Intensive Care Unit*

Table 2. Comparison of serial lactate levels between survivors and non-survivors at multiple time intervals.

Variable	Survivors (n=109)	Non-survivors (n=20)	p-value
Preoperative Lactate (T0, mmol/L)	3.43± 21.7	1.86± 1.67	0.52
Initial Lactate (T1, mmol/L)	2.15 ± 1.35	3.71 ± 2.97	<0.001
Lactate at 6 h (T6, mmol/L)	2.74 ± 1.62	5.95 ± 3.58	<0.001
Lactate at 12 h (T12, mmol/L)	2.19 ± 1.18	5.61 ± 3.37	<0.001
Lactate at 18 h (T18, mmol/L)	1.92 ± 1.05	6.49 ± 4.19	<0.001
Lactate at 24 h (T24, mmol/L)	1.63 ± 1.18	5.50 ± 4.25	<0.001

****Values are expressed as mean±SD or number (%). P<0.05 is considered significant***

Serial measurements of lactate levels was done as shown in Table 2. Preoperative lactate did not differ significantly between survivors and non-survivors (p=0.52). However, immediately after CPB and at 6, 12, 18, and 24 h postoperatively, non-survivors consistently maintained significantly higher lactate concentrations than survivors (all p<0.001) (Table 2).

Table 3. Lactate clearance rate at different time points between survivors and non-survivors during the first 24 hours post-surgery.

Variable	Survivors (n=109)	Non-survivors (n=20)	p-value
Lactate Clearance (T1-T6, %)	-36.05 ± 70.24	-101.62 ± 148.46	0.002
Lactate Clearance (T1-T12, %)	-12.84 ± 60.07	-105.57 ± 157.22	<0.001
Lactate Clearance (T1-T18, %)	-2.27 ± 59.57	-141.36 ± 174.99	<0.001
Lactate Clearance (T1-T24, %)	13.33 ± 57.69	-135.52 ± 246.38	<0.001

Values are expressed as mean±SD or number (%). P<0.05 is considered significant

Survivors exhibited markedly greater blood lactate clearance in the first 24 hours after cardiopulmonary bypass than non-survivors. By 24 h, the mean lactate clearance in survivors was +13.3% (±57.7) versus -135.5% (±246.4) in non-survivors (p<0.001). In fact, at each interval (T1-T6, T1-T12, T1-T18, and T1-T24), survivors had significantly higher lactate clearance (all p≤0.002) than non-survivors (Table 3).

Table 4. Univariate comparison of perioperative variables between high and low lactate clearance groups.

Variable	High Lactate Clearance (n=43)	Low Lactate Clearance (n=12)	p-value
Age (years)	3.08 ± 1.39	2.62 ± 0.96	0.06
Sex (Male/Female)	70/38	27/14	0.89
Height (cm)	87.53 ± 5.35	88.80 ± 5.53	0.20
Weight (kg)	9.72 ± 3.12	9.41 ± 2.61	0.57
Preop Hb (g/dL)	20.24 ± 2.03	19.82 ± 1.71	0.09
Preop SaO2 (%)	74.82 ± 6.62	76.12 ± 7.35	0.32
CPB (min)	89.01 ± 9.03	93.63 ± 8.05	0.09
ACX (min)	62.68 ± 4.07	64.05 ± 5.11	0.12
Duration of IS (hours)	24.19 ± 13.28	30.78 ± 18.49	<0.001
Duration of MV (hours)	11.29 ± 4.73	14.56 ± 6.73	<0.001
Duration of ICU Stay (hours)	48.85 ± 7.26	66.64 ± 25.46	0.004
Mortality (%)	2 (1.9%)	9 (22%)	0.03
Preop Lactate (T0, mmol/L)	1.65 ± 0.51	1.59 ± 0.40	0.48
Initial Lactate (T1, mmol/L)	4.65 ± 1.07	4.78 ± 0.93	0.47
Lactate at 6 h (T6, mmol/L)	3.40 ± 1.01	4.57 ± 0.82	0.001
Lactate at 12 h (T12, mmol/L)	3.11 ± 1.01	4.37 ± 0.92	0.001
Lactate at 18 h (T18, mmol/L)	2.89 ± 0.98	4.27 ± 1.08	0.001
Lactate at 24 h (T24, mmol/L)	2.40 ± 1.02	4.25 ± 1.34	0.001

Values are expressed as mean±SD for continuous variables and number (percentage) for categorical variables. P<0.05 is considered significant; Pre-op,Preoperative;Hb,Hemoglobin; Sao2, Oxygen saturation; CPB,Cardiopulmonary Bypass Time;ACX, Aortic Cross-clamp Time; IS,Inotropic Support; MV,Mechanical Ventilation; ICU,Intensive Care Unit

High lactate clearance was defined as lactate clearance ≥10% at 24 hours (T1-T24), and low lactate clearance as lactate clearance <10%. Further comparison between high lactate clearance (≥and low lactate clearance groups,

independent of survival status, revealed that the high-clearance group had significantly better clinical outcomes, including reduced need for inotropic support, shorter duration of mechanical ventilation, and decreased ICU stay. Mortality was significantly higher in the low-clearance group (22% vs. 1.9%) (Table 4).

DISCUSSION

In our study, we found that the serial lactate clearance is important predictor of postoperative mortality and the patients with higher lactate clearance (≥10%) had improved survival with significantly lower mortality rates (1.9% vs. 22%, p = 0.03). Our study has shown that lactate clearance can be applied to our pediatric post-cardiac surgical patients for assessing outcomes and ensures the delivery of timely optimal treatment. There is paucity of studies regading this in our specific context. However, lactate clearance has been widely used in several studies evaluating its outcome including mortality especially in adults and our study adds to this growing body of evidence supporting its usefulness in predicting in-hospital mortality.[7-9]

Our study found an overall in-hospital mortality rate of 15.5%. Similarly in our cohort of patients, non-survivors showed worsening clearance rates (−135.52% in non-survivors vs. +13.33% in survivors at T1–T24) compared to survivors in postoperative period reflecting body's ablility to eliminate ananerobic byproducts and maintain tissue oxygenation. Lactate which is a by-product of anaerobic metabolism either due to inadequate oxygen delivery or utilization has already been recognized as a marker of tissue hypoxia.[1] However, several studies have demonstrated that lactate clearance, rather than single absolute lactate values, is a more reliable predictor of mortality and morbidity.[2-5] While the role of lactate clearance has been well-described in adult cardiac surgery, there is limited research on its significance in pediatric populations. Prior studies have established the prognostic value of lactate clearance in adult patients, and our findings extend these insights to pediatric patients undergoing congenital cardiac procedures. Unlike earlier studies that primarily focused on absolute lactate levels, our research highlights the utility of serial lactate measurements for more accurate postoperative risk assessment.

Furthermore, our study demonstrated that non-survivors presented with significantly lower clearance rates compared to survivors.Specifically we observed moartality rate of 1.9% in high clearance group compared to 22% in low clearance group. A study review by Nguyen et al.[10] demonstrated that every 10% increase in lactate clearance reduced mortality risk by 11% in sepsis. Similarly, the use of lactate clearance in prognosis has been demonstrated in various acute care settings, including sepsis, trauma, and cardiac surgery. Several studies by Lopez-Delgado et al.,[4] and Marty et al.[10] recognized impaired clearance as the strongest predictor of mortality in cardiac surgery patients and in critically ill patients. Murtuza et al.[9] have shown the importance of lactate clearance in predicting outcomes particularly in pediatric cardiac surgery patients.

In addition to mortality, our study found that patients with delayed lactate clearance required longer mechanical ventilation(30.78 ± 18.49 vs. 24.19 ± 13.28 hours, p < 0.001) and had extended ICU stays (66.64 ± 25.46 vs. 48.85 ± 7.26 hours, p = 0.004) in early postoperative period. This is consistent with numerous studies which have indicated delayed lactate clearance may reflect underlying issues such as impaired tissue perfusion, respiratory failure, or hemodynamic instability, all of which contribute to the need for prolonged ventilation and ICU monitoring.[11-13] Interestingly, these findings suggests that with the early identification of patients with poor lactate clearance, timely interventions such as optimization of oxygen delivery, ventilation support, and inotropic therapy, can be done which could potentially improve outcomes.[13-17]

Our study identified several preoperative and intraoperative risk factors that are associated with delayed lactate clearance. Patients with delayed lactate clearance were significantly younger (2.78 ± 3.77 vs. 5.50 ± 4.33 years, p = 0.010), had lower preoperative oxygen saturation (70.75 ± 13.44% vs. 89.03 ± 13.14%, p < 0.001), and higher preoperative hemoglobin levels. Intraoperatively, longer cardiopulmonary bypass (CPB) and aortic cross-clamp (ACX) durations were also associated with delayed lactate clearance, suggesting greater exposure to circulatory interruption and ischemic stress during surgery. Delayed lactate clearance reflects impaired lactate metabolism and persistent tissue hypoxia, which may be particularly pronounced in younger pediatric patients due to immature hepatic and renal lactate handling and limited metabolic reserve.[18] Lower preoperative oxygen saturation, commonly seen in cyanotic congenital heart disease, predisposes patients to chronic hypoxemia and reduced oxygen delivery, thereby amplifying postoperative lactate production. Elevated preoperative hemoglobin in this context likely represents a compensatory response to chronic hypoxia rather than improved oxygen-carrying capacity, which may explain its association with delayed

lactate normalization.[19]

Prolonged CPB and ACX times increase the duration of non-physiological circulation, systemic inflammatory response, and regional hypoperfusion, all of which impair lactate clearance. Similar associations have been reported by Cheung et al.[20] and Basaran et al.[21] in pediatric cardiac surgical populations. In contrast, adult cardiac surgery studies often identify comorbidities such as diabetes, renal dysfunction, and low cardiac output as stronger predictors of impaired lactate clearance, highlighting important population-specific differences related to age, disease etiology, and physiological reserve.

Several potentially important risk factors were not evaluated in this study, including elevated preoperative serum creatinine, specific inotropic agents, and perioperative glucose levels, despite prior evidence demonstrating that acute kidney injury, reduced preoperative ejection fraction, hyperglycemia, prolonged cardiopulmonary bypass and aortic cross-clamp times, blood transfusion requirements, and inotropic support are independently associated with hyperlactatemia during cardiac.[22-23]

Polonen et al. [24] found that normalizing lactate concentrations in postsurgical cardiac patients decreased morbidity and length of hospital stay in their cohort of 400 patients . Several studies have demonstrated that different parameters like lactate, central venous oxygen saturation are strong predictors of major adverse events following on-pump cardiac surgery and even in pediatric cardiac surgery. [25] Multiple studies have shown elevated lactate levels associated with increased postoperative complications—including cerebral complications [26] bleeding [27], and low cardiac output syndrome [28] , increased need for postoperative intra-aortic balloon pump (IABP) usage. [29]

Noteworthyly, serial lactate measurements can provide information into metabolic recovery, facilitationg early identification of high-risk patients. These findings emphasize the importance of early interventions on optimizing perioperative management to improve lactate clearance through judicious and tailored use of ionotropes, shorter CPB and ACX times ,fluid management or glycemic management ultimately to improve patient outcome. This approach aligns with the lactate-guided therapy approach proposed by Jansen et al.[30] which has been shown to reduce mortality in critically ill patients.

Our study has several limitations. Firstly, this study was a single-center, and findings may not be generalizable to other institutions with different patient populations and perioperative management protocols. Secondly , we had relatively small cohort of 129 patients may have limited our ability to identify more subtle differences in lactate clearance trends. Thirdly, we did not assess long-term outcomes, which would be valuable in understanding the long-term impact of lactate clearance on survival and quality of life post-surgery. Finally, our study included all congenital heart defects . A more focused approach examining a specific diagnosis could have strengthened our findings. Future research should focus on establishing national heart surgery database to allow for the comprehensive assessment of outcomes in our settings.

CONCLUSIONS

In conclusion, lactate clearance is a valuable predictor of mortality and adverse outcomes in pediatric patients undergoing elective cardiac surgery for congenital heart defects. Our findings support the findings of serial lactate measurements in the early postoperative period, enables early identification of high-risk patients in perioperative management for pediatric cardiac surgery to guide clinical decisions and improve patient outcomes. Future multicenter studies are necessary to validate these findings and explore therapeutic strategies to enhance lactate clearance in critically ill children.

ACKNOWLEDGEMENTS

Miss Lalita Shakya(perfusionist) Department Of Cardiac Anesthesia and Critical care; Cardiac Surgery ; Nursing Department. Language and structural assistance during manuscript preparation was supported by OpenAI. The authors take full responsibility for the content.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Mizock BA, Falk JL. Lactic acidosis in critical illness. Crit Care Med. 1992 Jan;20(1):80-93. doi: 10.1097/00003246-199201000-00020. PMID: 1309494.

2. Ladha S, Kapoor PM, Singh SP, Kiran U, Chowdhury UK. The role of blood lactate clearance as a

predictor of mortality in children undergoing surgery for tetralogy of Fallot. Ann Card Anaesth. 2016 Apr-Jun;19(2):217-24. doi: 10.4103/0971-9784.179589. PMID: 27052060; PMCID: PMC4900343.

3. Haanschoten MC, Kreeftenberg HG, Arthur Bouwman R, van Straten AH, Buhre WF, et al. Use of Postoperative Peak Arterial Lactate Level to Predict Outcome After Cardiac Surgery. J Cardiothorac Vasc Anesth. 2017 Feb;31(1):45-53. doi: 10.1053/j.jvca.2016.04.017. Epub 2016 Apr 22. PMID: 27542901.

4. Lopez-Delgado JC, Esteve F, Javierre C, Torrado H, Rodriguez-Castro D, et al. Evaluation of Serial Arterial Lactate Levels as a Predictor of Hospital and Long-Term Mortality in Patients After Cardiac Surgery. J Cardiothorac Vasc Anesth. 2015 Dec;29(6):1441-53. doi: 10.1053/j.jvca.2015.04.024. Epub 2015 Apr 29. PMID: 26321121.

5. Zhang Z, Xu X. Lactate clearance is a useful biomarker for the prediction of all-cause mortality in critically ill patients: a systematic review and meta-analysis*. Crit Care Med. 2014 Sep;42(9):2118-25. doi: 10.1097/CCM.0000000000000405. PMID: 24797375.

6. Bahadur KC, Sharma D, Shrestha MP, Gurung S, Rajbhandari S, et al. Prevalence of rheumatic and congenital heart disease in schoolchildren of Kathmandu valley in Nepal. Indian Heart J. 2003 Nov-Dec;55(6):615-8. PMID: 14989511.

7. Minton J, Sidebotham DA. Hyperlactatemia and Cardiac Surgery. J Extra Corpor Technol. 2017 Mar;49(1):7-15. PMID: 28298660; PMCID: PMC5347225.

8. Régnier MA, Raux M, Le Manach Y, Asencio Y, Gaillard J, Devilliers C, et al. Prognostic significance of blood lactate and lactate clearance in trauma patients. Anesthesiology. 2012 Dec;117(6):1276-88. doi: 10.1097/ALN.0b013e318273349d. PMID: 23168430.

9. Murtuza B, Wall D, Reinhardt Z, Stickley J, Stumper O, et al. The importance of blood lactate clearance as a predictor of early mortality following the modified Norwood procedure. Eur J Cardiothorac Surg. 2011 Nov;40(5):1207-14. doi: 10.1016/j.ejcts.2011.01.081. Epub 2011 Mar 29. PMID: 21450476.

10. Marty P, Roquilly A, Vallée F, Luzi A, Ferré F, Fourcade O, et al. Lactate clearance for death prediction in severe sepsis or septic shock patients during the first 24 hours in Intensive Care Unit: an observational study. Ann Intensive Care. 2013 Feb 12;3(1):3. doi: 10.1186/2110-5820-3-3. PMID: 23398782; PMCID: PMC3614435.

11. Lindsay AJ, Xu M, Sessler DI, Blackstone EH, Bashour CA. Lactate clearance time and concentration linked to morbidity and death in cardiac surgical patients. Ann Thorac Surg. 2013 Feb;95(2):486-92. doi: 10.1016/j.athoracsur.2012.07.020. Epub 2012 Sep 7. PMID: 22959571.

12. Lopez-Delgado JC, Esteve F, Javierre C, Torrado H, Rodriguez-Castro D, et al. Evaluation of Serial Arterial Lactate Levels as a Predictor of Hospital and Long-Term Mortality in Patients After Cardiac Surgery. J Cardiothorac Vasc Anesth. 2015 Dec;29(6):1441-53. doi: 10.1053/j.jvca.2015.04.024. Epub 2015 Apr 29. PMID: 26321121.

13. Corral-Velez V, Lopez-Delgado JC, Rojas-Lora M, Betancur-Zambrano N, Lopez-Suñe N,et al. Serial arterial lactate levels as a predictor of short- and long-term mortality in patients after cardiac surgery. Intensive Care Med Exp. 2015 Oct 1;3(Suppl 1):A104. doi: 10.1186/2197-425X-3-S1-A104. PMCID: PMC4796211.

14. Nazir M, Wani W, Dar SA, Mir IH, Charoo BA, et al. Lactate clearance prognosticates outcome in pediatric septic shock during first 24h of intensive care unit admission. J Intensive Care Soc. 2019 Nov;20(4):290-298. doi: 10.1177/1751143719855202. Epub 2019 Jun 12. PMID: 31695733; PMCID: PMC6820231.

15. Jaiswal P, Dewan P, Gomber S, Banerjee BD, Kotru M, et al. Early lactate measurements for predicting in-hospital mortality in paediatric sepsis. J Paediatr Child Health. 2020 Oct;56(10):1570-1576. doi: 10.1111/jpc.15028. Epub 2020 Aug 29. PMID: 32861227.

16. Merkle-Storms J, Djordjevic I, Weber C, Avgeridou S, Krasivskyi I,et al. Impact of Lactate Clearance on Early Outcomes in Pediatric ECMO Patients. Medicina (Kaunas). 2021 Mar 18;57(3):284. doi: 10.3390/medicina57030284. PMID: 33803807; PMCID: PMC8003148.

17. Stephens EH, Epting CL, Backer CL, Wald EL. Hyperlactatemia: An Update on Postoperative Lactate. World J Pediatr Congenit Heart Surg. 2020 May;11(3):316-324. doi: 10.1177/2150135120903977. PMID: 32294015.

18. Desplanque L, Hamaide-Defrocourt F, Berkia I, Tourneur T, Albinni S, Bojan M. Lactate clearance in infants undergoing surgery for congenital heart disease. Artif Organs. 2019 Jan;43(1):54-59. doi: 10.1111/aor.13402. Epub 2019 Jan 1. PMID: 30512202.

19. Zabala LM, Guzzetta NA. Cyanotic congenital heart disease (CCHD): focus on hypoxemia, secondary erythrocytosis, and coagulation alterations. Paediatr Anaesth. 2015 Oct;25(10):981-9. doi: 10.1111/pan.12705. Epub 2015 Jul 17. PMID: 26184479.

20. Cheung PY, Chui N, Joffe AR, Rebeyka IM, Robertson CM; Western Canadian Complex Pediatric Therapies Project, Follow-up Group. Postoperative lactate concentrations predict the outcome of infants aged 6 weeks or less after intracardiac surgery: a cohort follow-up to 18 months. J Thorac Cardiovasc Surg. 2005 Sep;130(3):837-43. doi: 10.1016/j.jtcvs.2005.04.029. PMID: 16153937.

21. Basaran M, Sever K, Kafali E, Ugurlucan M, Sayin OA, Tansel T, Alpagut U, Dayioglu E, Onursal E. Serum lactate level has prognostic significance after pediatric cardiac surgery. J Cardiothorac Vasc Anesth. 2006 Feb;20(1):43-7. doi: 10.1053/j.jvca.2004.10.010. Epub 2005 Dec 1. PMID: 16458212.

22. Govender P, Tosh W, Burt C, Falter F. Evaluation of Increase in Intraoperative Lactate Level as a Predictor of Outcome in Adults After Cardiac Surgery. J Cardiothorac Vasc Anesth. 2020 Apr;34(4):877-884. doi: 10.1053/j.jvca.2019.10.039. Epub 2019 Nov 1. PMID: 31787432.

23. Hajjar LA, Almeida JP, Fukushima JT, Rhodes A, Vincent JL, Osawa EA, Galas FR. High lactate levels are predictors of major complications after cardiac surgery. J Thorac Cardiovasc Surg. 2013 Aug;146(2):455-60. doi: 10.1016/j.jtcvs.2013.02.003. Epub 2013 Mar 15. PMID: 23507124.

24. Pölönen P, Ruokonen E, Hippeläinen M, Pöyhönen M, Takala J. A prospective, randomized study of goal-oriented hemodynamic therapy in cardiac surgical patients. Anesth Analg. 2000 May;90(5):1052-9. doi: 10.1097/00000539-200005000-00010. PMID: 10781452.

25. Laine GA, Hu BY, Wang S, Thomas Solis R, Reul GJ Jr. Isolated high lactate or low central venous oxygen saturation after cardiac surgery and association with outcome. J Cardiothorac Vasc Anesth. 2013 Dec;27(6):1271-6. doi: 10.1053/j.jvca.2013.02.031. Epub 2013 Sep 5. PMID: 24011873.

26. Zhang Z, Ni H. Normalized lactate load is associated with development of acute kidney injury in patients who underwent cardiopulmonary bypass surgery. PLoS One. 2015 Mar 30;10(3):e0120466. doi: 10.1371/journal.pone.0120466. PMID: 25822369; PMCID: PMC4378943.

27. Gaudino M, Angiolillo DJ, Di Franco A, Capodanno D, Bakaeen F, et al. Stroke After Coronary Artery Bypass Grafting and Percutaneous Coronary Intervention: Incidence, Pathogenesis, and Outcomes. J Am Heart Assoc. 2019 Jul 2;8(13):e013032. doi: 10.1161/JAHA.119.013032. Epub 2019 Jun 27. PMID: 31242821; PMCID: PMC6662343.

28. Ranucci M, Baryshnikova E, Simeone F, Ranucci M, Scolletta S. Moderate-degree acidosis is an independent determinant of postoperative bleeding in cardiac surgery. Minerva Anestesiol. 2015 Aug;81(8):885-93. Epub 2015 May 26. PMID: 26006154.

29. Rao V, Ivanov J, Weisel RD, Cohen G, Borger MA, Mickle DA. Lactate release during reperfusion predicts low cardiac output syndrome after coronary bypass surgery. Ann Thorac Surg. 2001 Jun;71(6):1925-30. doi: 10.1016/s0003-4975(01)02634-0. PMID: 11426770.

30. Jansen TC, van Bommel J, Schoonderbeek FJ, Sleeswijk Visser SJ, van der Klooster JM, et al; LACTATE study group. Early lactate-guided therapy in intensive care unit patients: a multicenter, open-label, randomized controlled trial. Am J Respir Crit Care Med. 2010 Sep 15;182(6):752-61. doi: 10.1164/rccm.200912-1918OC. Epub 2010 May 12. PMID: 20463176.