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Original Article

Close Correlations Between Serum Lactate and Blood Glucose Fluctuations in Children Undergoing Open-Heart Surgery: A Prospective Observational Study

Zahra Faritous[1], MD; Mohsen Ziyaeifard[1], MD; Ali Sadeghi[1], MD; Nahid Aghdaii[1], MD; Fatemehshima Hadipourzadeh[1*], MD; Hooman Bakhshandeh[2], MD; Amir Motamednejad[2], MS

ABSTRACT

Background: Changes and increases in blood glucose and lactate during and after cardiac surgery in the intensive care unit (ICU) can be associated with complications. Recognizing these changes during and after surgery can be significant.

Methods: The present prospective observational case-series study assessed 163 children aged between 1 and 170 months undergoing open-heart surgery on cardiopulmonary bypass (CPB) over a 3-month period. Blood glucose and lactate were assessed using arterial blood samples before surgery, during surgery (at 15 and 45 minutes on CPB, after warm-up, and after sternum closure), and at 1, 6, 12, 24, and 48 hours after admission to the ICU.

Results: In the first hour following ICU admission, a significant number of patients needed inotropes. Also at this time point, the percentage of patients with lactate levels >2.5 mmol/L was higher than that at the other time points. Further, most changes in blood glucose and lactate occurred in the first 6 hours following ICU admission. A significant relationship existed between changes in blood sugar and serum lactate in the first 6 hours post-ICU admission ($P<0.001$).

Conclusions: The results demonstrated a significant relationship between changes in blood glucose and serum lactate in the first 6 hours following ICU admission. ***(Iranian Heart Journal 2023; 24(1): 45-53)***

KEYWORDS: Blood glucose, Lactate, Congenital heart disease, Cardiac surgical procedures

[1] Cardiac Anesthesia Department, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran.
[2] Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran.

***Corresponding Author:** Fatemehshima Hadipourzadeh, MD; Cardiac Anesthesia Department, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran.
Email: shimahadipoorzadeh@gmail.com **Tel:** +982123923740

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Blood glucose levels are a significant factor for the body's normal metabolism, with hyperglycemia being a regular event in critically ill children after congenital cardiac surgery. Some recent studies have noted an association between hyperglycemia and increased postoperative morbidity and mortality in these patients. Hyperglycemia with critical illness is due to multiple factors, including endogenous stress hormones, inflammatory mediators, oxidative stress, and treatment measures, such as medication (eg, glucose and drug administration). Children undergoing cardiopulmonary bypass (CPB) cardiac surgery often receive corticosteroids to control inflammatory responses, although their clinical effect has not been established. [1] Mean blood glucose levels >126 mg/dL are defined as hyperglycemia, and blood levels >200 mg/dL are defined as severe hyperglycemia**.** Lactate is used as a marker for oxygen delivery defects in anaerobic metabolism at the cellular level. An increase in lactate concentration is associated with impaired cellular function due to the deposition of high-energy phosphate compounds. Lactate is produced by erythrocytes, perivenous hepatocytes, musculoskeletal myocytes, and skin and is increased by the liver and kidneys. Elevated blood lactate levels can occur due to increased lactate production or decreased lactate clearance, or both. [2] In patients undergoing CPB cardiac surgery, systemic hypoperfusion, hemodilution, and tissue hypoxia increase blood lactate levels. Moreover, cytokine responses to CPB and various metabolic conditions for stabilizing hemodynamics (eg, β2-agonists) and diabetes increase lactate levels. [3] High lactate levels following open-heart surgery can often be associated with increased postoperative mortality and morbidity rates. [4] Elevated lactate levels are a risk factor for lengthened stays in the intensive care unit (ICU) and increased severity of postoperative side effects. [5] Therefore, monitoring serum glucose and lactate levels before, during, and after surgery in patients undergoing congenital cardiac surgery can be a valuable indicator to determine the patient's condition and reduce their mortality.

METHODS

The current prospective observational case-series study was commenced after it had received approval from the Ethics Committee of Rajaie Cardiovascular Medical and Research Center. This investigation evaluated 162 children aged between 1 and 170 months undergoing open-heart surgery on CPB over a 3-month period. Only patients aged between 1 and 170 months undergoing cardiac surgery on CPB were included. The exclusion criteria were composed of renal problems and the need for dialysis and the need for postoperative extracorporeal membrane oxygenation. The patients were evaluated based on lactate levels below or above 2.5 mmol/L and blood glucose levels below or above 126 mg/dL. [6] After anesthesia induction and intubation, an arterial line was taken for the patients, and a sample of arterial blood was taken to measure blood glucose, pH, partial pressure of carbon dioxide, partial pressure of oxygen, bicarbonate, base excess, hemoglobin, and lactate. (If the blood sugar level was <75 mg/dL, all the children were given 0.5 mL/kg of 50% dextrose). If necessary, some patients received an epinephrine infusion at warm-up, 15 and 45 minutes on CPB, after warm-up, after sternum closure, and 1, 6, 12, 24, and 48 hours after ICU admission. An arterial line sample was sent to the laboratory to measure the mentioned parameters. Additionally, arrhythmias in the operating room and the ICU, intubation lasting more than 2 days, re-intubation, infection, renal problems, and neurological complications were evaluated with respect to lactate and blood sugar levels.

Statistical Analysis

The SPSS software, version 16.0, for Windows (SPSS, Chicago, IL, USA) was used for the statistical analyses. Definitive statistics were expressed as the mean ± the standard deviation (SD). Independent samples *t*, Mann–Whitney *U*, and χ^2 or Fisher exact tests were employed to determine the significance of the difference in average values between groups. A *P* value ≤0.05 was considered statistically significant.

RESULTS

Over a 3-month period, 163 pediatric patients undergoing cardiac surgery on CPB were evaluated. The patients' demographic characteristics are listed in Table 1.

Table 1: Demographic information (N=163)

Variable	
Age, y	24 (11 - 60)
Sex	
male	100 (61.3%)
female	63 (38.7%)
Weight (kg)	11 (8.3 - 15)
Previous diseases	
Cyanotic	59 (36.2%)
Other disease	104 (63.8%)
Procedural time	
CPB time (min)	85 (53.5 - 120)
Aortic Clamp time (min)	60 (26 - 92)
Opration time (min)	300 (240 - 360)

Arterial blood gas information before, during, and after CPB and in the ICU is listed in Table 2.

As shown in Table 3, 90.8% of patients need to receive milrinone in the first hour of admission to the ICU, also 65% of patients need epinephrine and 8% need norepinephrine in the first hour of admission to the ICU, 23.3% in this group have a lactate content above 2.5 mmol/L. And in this study was shown, in the first hour of admission to the ICU, more patients need to receive inotropes. Also the percentage of patients with lactate above 2.5mmol/L is higher than other hours of this study.

Table 2: Median (interquartile range) of blood gas and biochemistry indices during surgery and ICU stay

	Pre CPB	CPB 15 min	CPB 45 min	Warm-up	Sternotomy Closure	ICU 1 h	ICU 6 h	ICU 12 h	ICU 24 h	ICU 48 h
MAP, mm Hg	68 (57 - 80)	60 (52.25 - 65)	60 (53.75 - 64)	60 (58 - 67)	68 (61 - 73.3)	62.5 (60 - 70)	65 (60 - 73.3)	65 (60 - 68.3)	66 (58 - 75)	66 (61 - 75)
pH	7.37 (7.32 - 7.4)	7.32 (7.28 - 7.37)	7.36 (7.28 - 7.41)	7.35 (7.3 - 7.4)	7.33 (7.29 - 7.37)	7.4 (7.34 - 7.44)	7.39 (7.35 - 7.42)	7.405 (7.38 - 7.43)	7.42 (7.4 - 7.45)	7.44 (7.4 - 7.46)
Partial pressure of oxygen, mm Hg	253 (91 - 370)	345 (263 - 412)	333 (277 - 375)	238 (178 - 311)	180.5 (101 - 314)	245 (116 - 339)	189.5 (134 - 229)	172.5 (103 - 202.75)	125 (89 - 188)	92 (56.25 - 129)
Partial pressure of carbon dioxide, mm Hg	38 (33 - 43)	39 (36 - 45)	37 (32.5 - 42)	38 (35 - 43)	41 (33 - 46)	34 (28.5 - 42)	36 (32 - 42)	39 (35 - 42.75)	40 (36 - 42)	40 (35 - 45)
Bicarbonate	22 (21 - 23)	21 (19 - 23)	21 (19 - 23)	21 (20 - 23)	22 (20 - 23)	21 (19 - 23)	22 (20 - 24)	24 (21 - 26)	26 (24 - 27.25)	27 (24 - 30)
Base excess	-3 (-4 - -1)	-4 (-6 - -2)	-3 (-5 - -2)	-3 (-5 - -1)	-4 (-6 - -2)	-3 (-5 - -1)	-2 (-3 - 0)	0 (-2.75 - 2)	2 (0 - 3.25)	3 (1 - 5)
Temperature, ℃	37 (36.5 - 37)	32 (32 - 33.75)	30 (30 - 34)	35 (34 - 36)	37 (36.5 - 37)	36.5 (36 - 36.5)	36.5 (36 - 36.5)	36.25 (36 - 36.5)	36.25 (36 - 36.5)	36 (36 - 36)
Hemoglobin, g/dL	11.85 (10.9 - 13.3)	8.5 (7.7 - 9.45)	8.7 (7.95 - 9.6)	9 (8.55 - 10.2)	10.35 (9.25 - 11.5)	10.6 (9.5 - 11.7)	12.1 (11.2 - 12.925)	12.1 (11.5 - 13.3)	12.5 (11.2 - 13.025)	12.4 (11.55 - 13)
Blood glucose, mg/dL	77.5 (65 - 89.25)	110 (89 - 133.75)	124 (105 - 156)	138 (115 - 159)	117.5 (93 - 142)	135 (106 - 193.5)	170 (100 - 195.25)	125 (116 - 185)	109 (91 - 133)	111 (84 - 138)
Serum lactate, mg/dL	0.6 (0.5 - 0.8)	1.5 (0.9 - 2.4)	1.5 (1.2 - 2.4)	1.7 (1.1 - 2.5)	1.5 (1 - 2)	1.5 (1 - 2.6)	2.4 (1.2 - 3.9)	1.2 (1 - 1.8)	0.9 (0.6 - 1.3)	0.8 (0.6 - 1.3)

CPB, Cardiopulmonary bypass; ICU, Intensive care unit

Table 3: Prevalence of drug usage and high lactate during surgery

	Pre CPB	CPB 15 min	CPB 45 min	Warm-up	Sternotomy Closure	ICU 1 h	ICU 6 h	ICU 12 h	ICU 24 h	ICU 48 h
Vasopressors										
Milrinone				102 (62.6%)	112 (68.7%)	148 (90.8%)	140 (85.9%)	132 (81%)	127 (77.9%)	70 (42.9%)
Epinephrine				3 (1.8%)	97 (59.5%)	106 (65%)	94 (57.7%)	87 (53.4%)	72 (44.2%)	36 (22.1%)
Norepinephrine				(0%)	3 (1.8%)	13 (8%)	17 (10.4%)	12 (7.4%)	12 (7.4%)	11 (6.7%)
Serum lactate, mg/dL										
>2.5	0	28 (17.2%)	15 (9.2%)	29 (17.8%)	13 (8%)	38 (23.3%)	25 (15.3%)	15 (9.2%)	4 (2.5%)	8 (4.9%)

CPB, Cardiopulmonary bypass; ICU, Intensive care unit

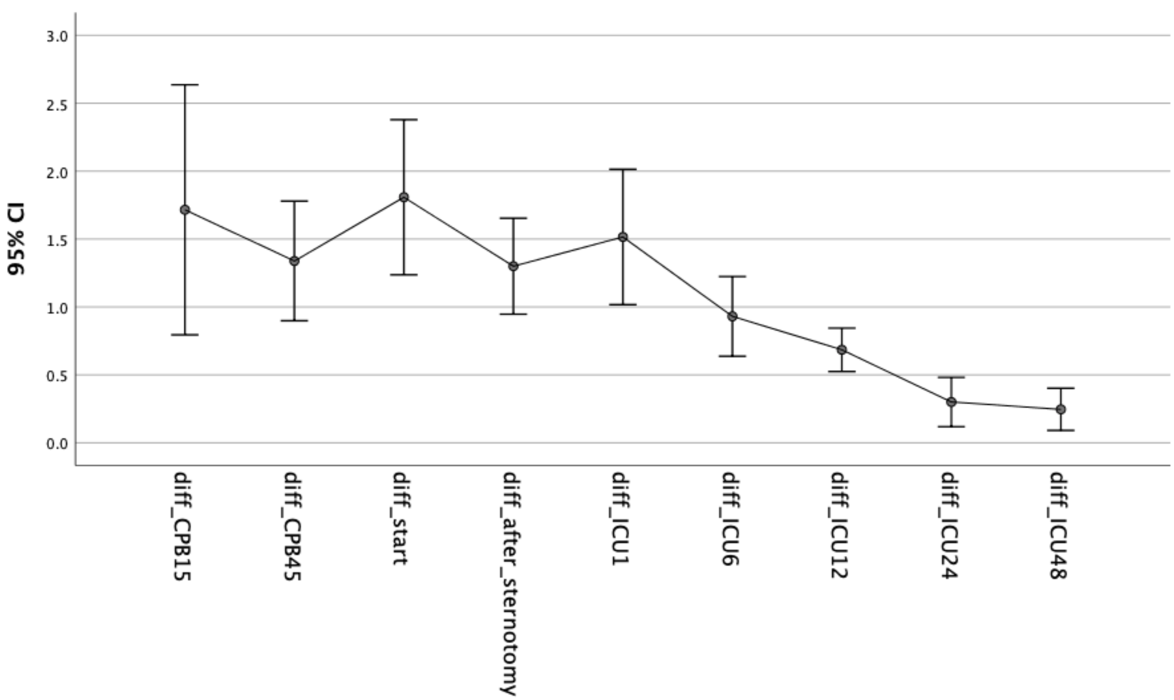

Figure 1: The image depicts changes in the study population's serum lactate during the study considering the baseline.

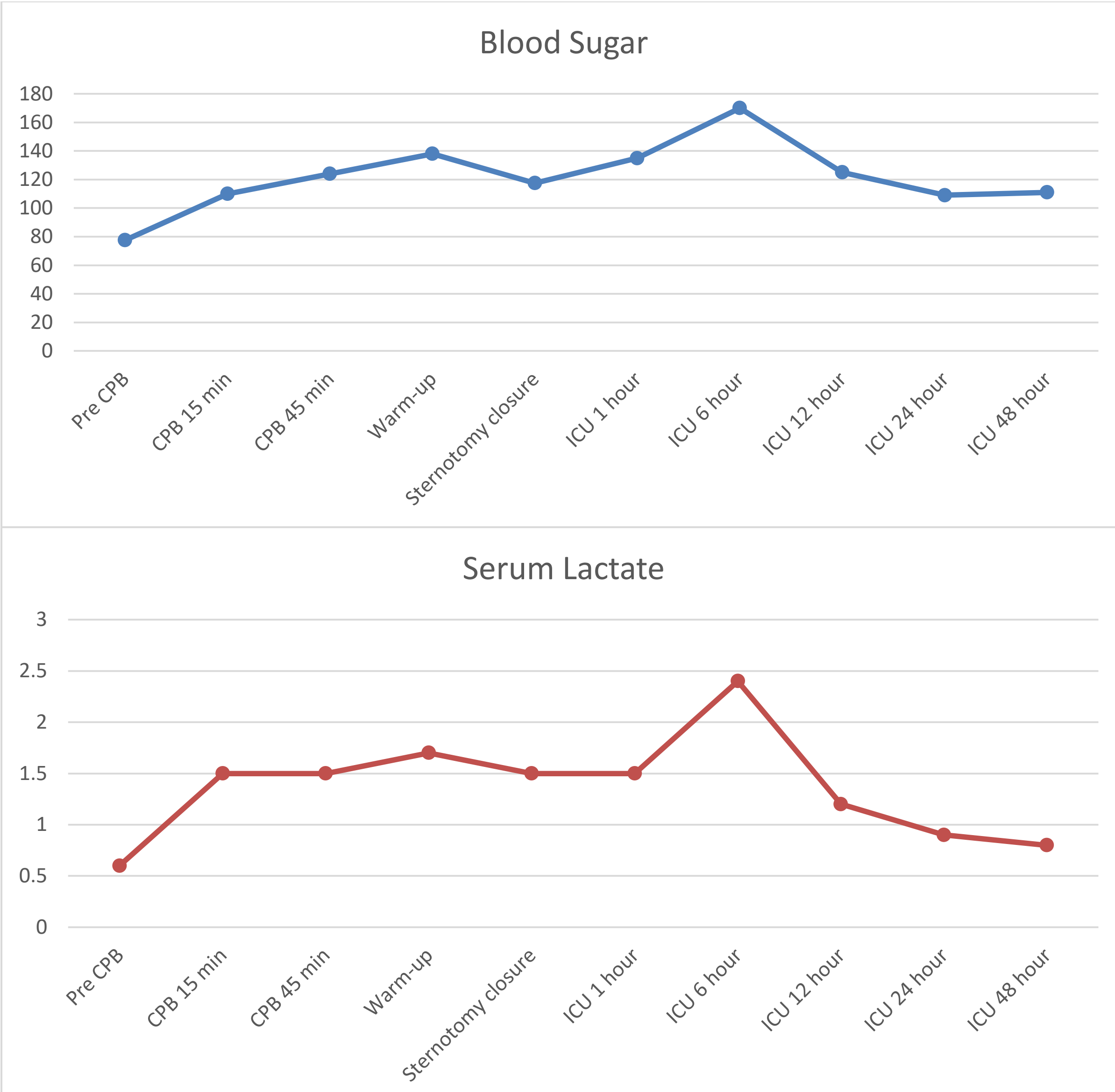

Figure 2: The image illustrates changes in the median of a) glucose and b) lactate concentrations during the study.

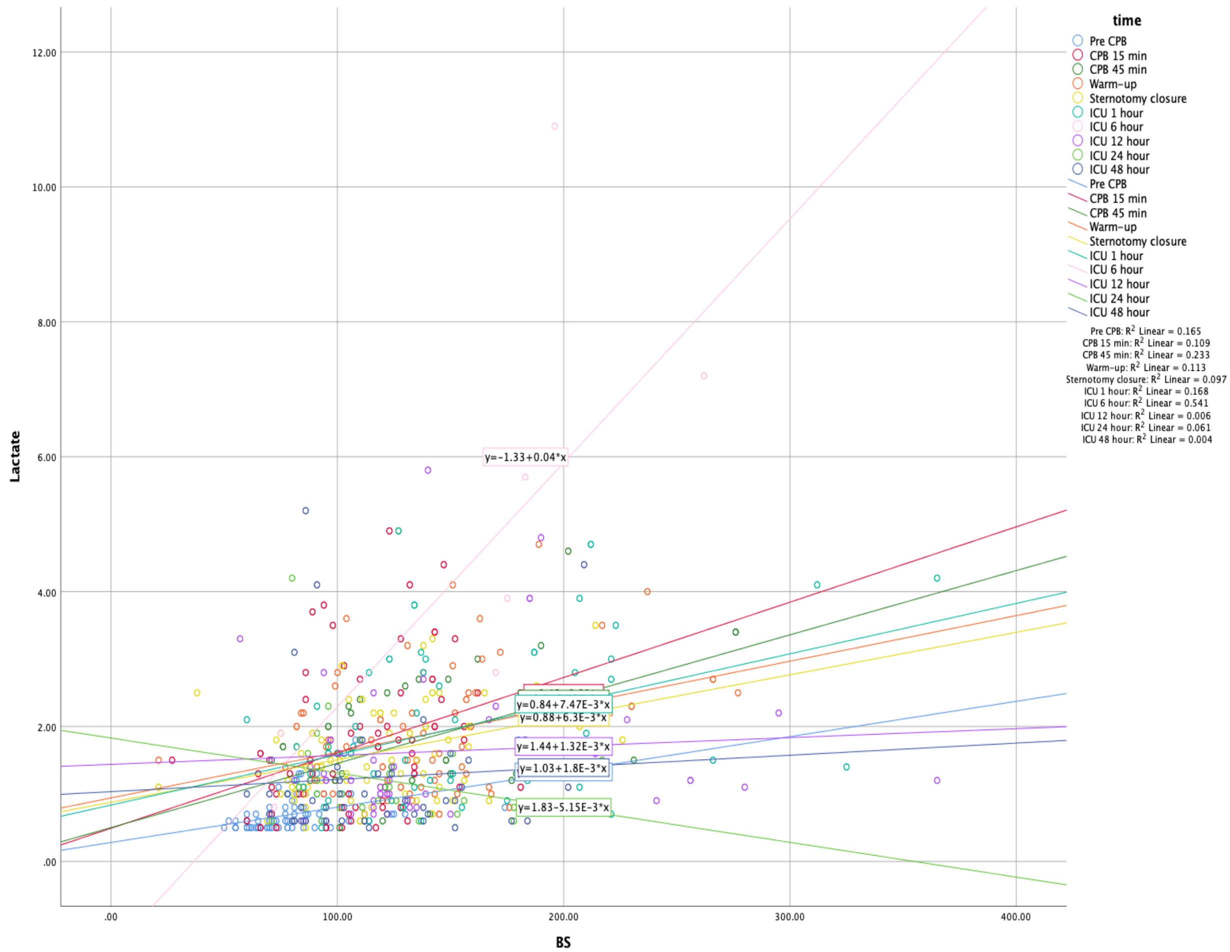

Figure 3: The image demonstrates the correlations between serum lactate and glucose (BS) at different time points during the study. The repeated measure correlation coefficient of the relationships between BS and lactate was 0.42 (*P*<0.001).

Figure 1 shows the changes in lactate relative to the baseline. These changes were considerable when the patients began to warm up on CPB compared with the other time points in the study. However, the changes exhibited a declining trend 48 hours after ICU admission.

Figure 2 presents the median changes in blood glucose and lactate concentrations during the study. According to these curves, most changes in blood glucose and lactate occurred in the first 6 hours after ICU admission. The 2 curves are compatible with each other, and Figure 3 demonstrates that these changes were significant (*P*<0.001).

DISCUSSION

According to our results, in the first hour of ICU admission, more patients needed inotropes, and the percentage of patients with lactate levels >2.5 mmol/L was higher than that at the other time points in the study. Moreover, most changes in blood glucose and lactate occurred in the first 6 hours after ICU admission. We also found a significant relationship between changes in blood sugar and serum lactate in the first 6 hours after admission to the ICU.

A previous prospective cohort study concluded that hyperglycemia was common in the early postoperative course after cardiac surgery on CPB for congenital heart diseases and return to normal within 48 hours. In addition, that study reported changes in lactate relative to the baseline: the changes were noticeable when the patients started to warm up on CPB, with the changes exhibiting a declining trend 48 hours after ICU admission. [7] These findings chime in with ours.

Another study assessed 379 pediatric patients after cardiac surgery and measured blood glucose levels on days 1, 2, 3, and 7 after surgery. A mean blood glucose level >126 mg/dL was considered hyperglycemia, and a level >200 mg/dL was considered severe hyperglycemia. The purpose of these measurements was to investigate major complications and mortality. In that study, hyperglycemia was common (86%), and no associations were found between hyperglycemia and major complications and mortality; nonetheless, patients with severe hyperglycemia had a higher mortality rate. [8]

A prior investigation demonstrated that hyperglycemia (glucose >126 mg/dL) during the first 72 postoperative hours was associated with a longer hospital stay. [9] According to another study, hyperglycemia was common after cardiac surgery in patients with congenital heart diseases and was not associated with short-term morbidity and mortality. [10]

In a retrospective study, 236 patients with congenital cardiac surgery were evaluated. The patients were divided into 2 groups: lactate levels <4.5 mmol/L and lactate levels >4.5 mmol/L. The patients with lactate levels >4.5 mmol/L were at a higher risk of mortality and morbidity and complications following cardiac surgery. [2]

Hazan et al [11] explained that high lactate levels within the first 12 hours post-cardiac surgery were associated with CPB duration, cross-clamp duration, RACHS-1 subgroups, and inotropic scores. Maarslet et al [12] reported that younger age, lower weight, high RACHS-1 scores, longer CPB duration, and inotropic administration were risk factors for higher lactate levels. They also concluded that elevated lactate levels (>4.5 mmol/L) increased the risk of dialysis and mortality.

A prior investigation reported that a timely measurement of lactate in high-risk patients could reduce postoperative mortality. [13] Oğuz et al [14] studied the relationship between hyperlactatemia and mortality and risk factors in children undergoing cardiac surgery and found that 27.3% of the patients had lactate levels exceeding the normal range. They also reported a significant relationship between lactate levels and mortality in their study population. Additionally, their results showed that body surface area, age, cardiac output syndrome, and oxygen delivery during and following cardiac surgery were factors affecting mortality.

Cardiac output syndrome, urinary incontinence, and decreased blood flow are factors associated with high lactate levels and metabolic acidosis. [15] Modified ultrafiltration following pediatric cardiac surgery improves the hemodynamic status of these patients and significantly lessens the need for inotropes in the first 48 hours after surgery. [16]

CONCLUSIONS

Based on the results of the present study, most changes in blood glucose and lactate occurred in the first 6 hours after ICU admission. Further, significant relationships existed between changes in blood glucose and serum lactate concentrations in the first 6 hours after admission to the ICU. The first 6 hours following ICU admission constitute a vital period in controlling blood glucose and lactate concentrations. Accordingly, controlling blood glucose and lactate in this period can prevent side effects caused by excessive concentrations of blood glucose and serum lactate. We suggest that future studies evaluate the side effects of high lactate and blood glucose concentrations in the first 6 hours after ICU admission.

Conflict of Interest: There are no conflicts of interest.

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Informed Consent: Informed consent was obtained from each eligible patient preoperatively.

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