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Original Article

Hypothermia and Blood Lactate During Cardiopulmonary Bypass in Pediatric Patients

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ABSTRACT

Background: Hypothermic perfusion is widely used in pediatric cardiac surgery units. The present study evaluated the effects of hypothermia severity on the serum levels of lactate during cardiopulmonary bypass (CPB) in the surgical repair of congenital heart defects in children.

Methods: A total of 185 pediatric patients candidated for the elective surgical repair of congenital heart diseases were recruited. The patients' arterial serum lactate, central venous pressure, diuresis, glucose level, and arterial blood gases were measured and recorded at 4 time points: before CPB, in the cooling stage, in the warming stage, and after CPB and upon admission to the intensive care unit (ICU).

Results: The mean age of the patients was 28.1 ± 19.6 months. The lactate level was significantly increased more quickly in the patients with hypothermia less than 30 °C than in those with hypothermia of 30 °C or greater ($P < 0.001$). These 2 groups were significantly different in terms of the duration of CPB ($P < 0.001$), the duration of cross-clamping ($P < 0.001$), and the volume of the blood filtered ($P < 0.001$). No statistically significant difference in the volume of the red blood cell transfused was observed between the 2 groups ($P = 0.12$).

Conclusions: Deep hypothermia is associated with higher blood lactate levels, which may be associated with poor outcomes during and after CPB. It is recommended that normothermia or mild hypothermia be used during CPB in pediatrics. When the use of deep hypothermia is inevitable, patients should be strictly monitored and screened for adverse outcomes associated with hyperlactatemia. ***(Iranian Heart Journal 2020; 21(3): 96-108)***

KEYWORDS: Cardiac surgery, Congenital defects, Lactate, Hypothermia, Cardiopulmonary bypass

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Congenital heart diseases are amongst the most prevalent birth defects. [1-4] In severe cases of the disease, timely interventions are required to prevent further anomalies and death. [1,2] Treatment usually includes the surgical correction of the anomaly, which is done on cardiopulmonary bypass (CPB). During CPB, a heart-lung machine is used that encompasses a blood pump and an oxygenator. Mostly, CPB involves the administration of a cardioplegic solution and the cessation of the cardiac and pulmonary blood flow. The cardiac tissue, in such situations, undergoes ischemia, which causes enhanced oxidative stress, anaerobic metabolism, and adenosine triphosphate (ATP) depletion. After the re-establishment of the blood flow, reperfusion injury happens; it is characterized by enhanced circulatory inflammatory cytokines and lactate levels. [4-11]

Induced hypothermia is used during CPB to protect the brain and the myocardial tissue, as well as other low-flow regions, against ischemia. Although induced hypothermia in pediatric cardiac surgery is applied to reduce cellular metabolism and limit tissue damage, it has some adverse effects on patients. [7,12] Kruse et al [13] (2011) reported that after inducing hypothermia during CPB, their patients often required prolonged postoperative mechanical ventilation and inotropic support. Additionally, deep hypothermia prolonged the duration of the patients' cooling and warming in CPB.

In low- and medium-risk pediatric cardiac surgeries, lactate is a risk marker of inadequate blood circulation in the organs and is associated with poor surgical outcomes. [14] It is also allied to increased mortality in patients undergoing cardiac surgery. [15] While increased blood lactate is correlated with poor postoperative outcomes, mainly due to an imbalance between oxygen supply and demand during CPB or after cardiac surgery, most studies have focused on the conditions and outcomes after hyperlactatemia. Only a few investigations have examined the causes and risk factors of hyperlactatemia. The relationship between factors such as the severity of hypothermia and the circulatory lactate level has yet to be fully elucidated. Tissue undergoes ischemia as a result of possible low-flow periods in deep hypothermia; nonetheless, it might be preferred to mild or normothermia in some centers.

The present study was conducted to evaluate the effects of hypothermia severity on serum lactate levels during CPB in the surgical repair of congenital heart defects in children.

METHODS

Setting and the Study Design

This prospective observational causal-comparative study was conducted on a population consisting of pediatric candidates for the elective surgical repair of congenital heart defects admitted to Rajaie Cardiovascular Medical and Research Center and Children's Medical Center in Tehran, Iran. This research was approved by the Ethics Committee of Rajaie Cardiovascular Medical and Research Center (registration code: RHC.AC.IR.REC.1395.27). Prior to patient recruitment, the study objective was explained to each patient's parents or legal custodians and verbal consent was obtained for the use of the patients' data. Four surgeons in each hospital permitted the inclusion of their patients in the present study. All the surgeons induced hypothermia based on surgical complexities.

Exclusion and Inclusion Criteria

A total of 185 eligible pediatric candidates for the surgical repair of congenital heart defects were included in the study. The patients were included if they met the following criteria: age of 3 months to 6

years, being a candidate for elective open-heart surgery with CPB, the American Society of Anesthesiologists (ASA) class 2 to 3, gestational age over 37 weeks (not preterm), not having infectious diseases, and not having liver or kidney failure. Patients were excluded from the study if they met 1 or more of the following criteria: receiving lactate solutions such as Ringer's lactate solution, receiving preoperative inotropes, lactate levels more than 3 mmol/L before CPB, duration between the end of anesthesia and the start of CPB of more than 30 minutes (to reduce possible environmentally-induced hypothermia during prepping and draping), ambient temperature of less than 24 °C before the start of CPB, pre-CPB nasopharyngeal temperature of less than 35 °C, a hematocrit level of lower than 24 mg/dL before CPB, cardiopulmonary resuscitation before CPB, defibrillation before CPB, blood pressure of less than 40 mm Hg during CPB, a hematocrit level of lower than 20% during CPB, receiving inotropes during CPB, CPB durations longer than 180 minutes, hypothermia less than 22 °C, low cardiac output at the end of CPB (defined as cardiac index < 2.4 L/min/m^2 with evidence of organ dysfunction), [16] peritoneal dialysis after CPB, and requiring extracorporeal membrane oxygenation (ECMO) (Fig. 1). Three patients were excluded because they had CPB durations of longer than 180 minutes.

Outcome Measures and Data Registration

Data were collected by recording the patients' serum arterial lactate, blood glucose, central venous pressure, arterial blood gases, and diuresis at 4 time different points: before CPB, in the cooling stage (at 30 °C), in the warming stage (at 32 °C), and after CPB (10 minutes after protamine injection) and upon admission to the intensive care unit (ICU) (along with the continuous monitoring of blood pressure; heart rhythm; heart rate; arterial blood oxygen saturation; blood, rectal, and nasopharyngeal temperature; ambient temperature; and the amount of inotropes needed). The aorta de-clamping time was mostly at around 32 °C. The demographic data were recorded in forms, and monitoring charts were prepared.

The amounts of arterial blood gases and the levels of serum lactate in the patients were measured in both centers by arterial blood sampling with arterial catheters using an ABG device (Gem Premier 3000, Instrumentation Laboratory, MA, USA) and by blood sampling from the arterial catheter.

Surgical Procedure

It was explained to every single perfusionist in both hospitals that blood flow should be kept in about 100% of the amount calculated for each patient during the warming of the patient. Sorin Dideco 901 (Lilliput 1) and 902 (Lilliput 2), with total prime volumes of the oxygenator and the circuit of up to 350 and 500 cc in sequence, were used. Blood flow during CPB was calculated by multiplying the body surface area by the cardiac index. At a normal temperature range (> 35 °C), the bypass flow rate was kept at 2.4 to 3.5 L/min/m^2 in normothermia and at temperatures of 32, 30, 28, 26, and 24°C, and the bypass flow rate was maintained at 2.4, 2.2, 2, 1.8, and 1.6 L/min/m^2, respectively. [17] Both calculated and effective blood flows, either in cooling or rewarming, were charted in percentage terms in the pump chart. Effective blood flow was written as a percentage of the calculated one. During surgery, the patient's blood pressure was kept at 40 to 60 mm Hg. [17] During warming, the flow was increased, if required, to elevate blood pressure. Any low-flow limitation was defined based on

any decrease in brain oximetry 15% below the baseline level. The patients' blood, nasopharyngeal, and rectal temperatures were monitored continuously during CPB with 3 electronic thermometers. Additionally, the ambient temperature was recorded with a non-electronic thermometer. A heater-cooler device was used to warm and cool the patients at a 6 °C to 8 °C temperature gradient between the blood and the water inside the device. A temperature gradient of 2 °C was maintained between the patients' blood and their nasopharynx and rectum. At the end of CPB, inotropes, consisting of adrenalin (0.1 µg/kg/min) and dopamine (0.15 µg/kg/min) in both groups were infused, as needed. The patients were transferred to the ICU as soon as possible. Monitoring was continued until discharge from the ICU or until 36 hours after admission, and the changes in the lactate levels were recorded. The duration of CPB and cross-clamp was recorded.

Statistical Analysis

The data were analyzed using the SPSS software, version 20 (IBM, New York, US). The data for the continuous variables were presented as the mean ± the standard deviation (SD) if they followed a normal distribution. In the case of violations from a normal distribution, the data were presented as the median (the interquartile range [IQR]). The categorical data were presented as relative frequencies and frequency percentages. A mixed analysis of variance (ANOVA) was used for the analysis of the changes in the measurements of the continuous variables over time if required. To control the post-intervention measures of the variables for the differences in pre-intervention measures, we set these values as covariates in mixed ANOVA models. The Mann–Whitney *U* test was utilized for the comparison of the continuous variables between the groups if data distribution violated the normal distribution assumption. The χ^2 test was used for the comparison of the frequency of the categorical variables between the 2 groups. To adjust for the potential confounding effects of background and other related variables on the main outcome measures, we employed multiple regression analysis for the prediction of lactate levels from the baseline lactate measurements, cross-clamp time, CPB duration, and body temperature. The levels of significance and power of the analysis were set to 0.05 and 0.8, respectively.

RESULTS

A total of 185 patients were included in the current study. Ninety patients 90 received moderate hypothermia (temperature ≥ 30 °C) and 95 underwent deep hypothermia (temperature < 30 °C). The mean age of the subjects was 24 (8–36) months in the group with deep hypothermia and 24 (12–48) months in the group with moderate hypothermia (P = 0.026). No significant difference was observed between the subjects in terms of the demographic variables except for height, which was significantly higher in the group with moderate hypothermia (P = 0.025) (Table 1). In both groups, the highest number of patients was related to ventricular septal defects: in 49.4% (44/89) of the patients in the moderate hypothermia group and in 53.8% (50/93) of the patients in the deep hypothermia group. Further details on the distribution of the anomalies in the groups are summarized in Table 2.

The present study evaluated the effects of hypothermia severity on the serum levels of lactate during CPB in the surgical repair of congenital heart defects in children. The highest levels of lactate were observed in the warming stage during CPB (mean = 3.19 ± 2.4 mmol/L) in the deep hypothermia group and in the warming stage after CPB (2.09 ± 0.8 mmol/L) in the moderate hypothermia group (Table 3). The mixed ANOVA model

adjusted for measuring blood lactate levels showed that although there were some differences in lactate levels in the pre-CPB stage between the 2 groups ($P < 0.001$), the lactate elevation curves were significantly different between them. This elevation was notably high in the deep hypothermia group compared with the moderate hypothermia group from the time of cooling until the ICU entry ($P < 0.001$) (Table 3 & Fig. 2). The difference in the lactate level reached 1 mmol/L when the 2 groups hit their maximum lactate level. The Lactime (time during which blood lactate was > 2.0 mmol/L) recorded was over 18 hours for the patients in the deep hypothermia group and less than 18 hours in the moderate hypothermia group. [18] Upon admission to the ICU, the mean recorded lactate level was 2.8 mmol/L for the deep hypothermia group and 1.9 mmol/L for the moderate hypothermia group (Table 3).

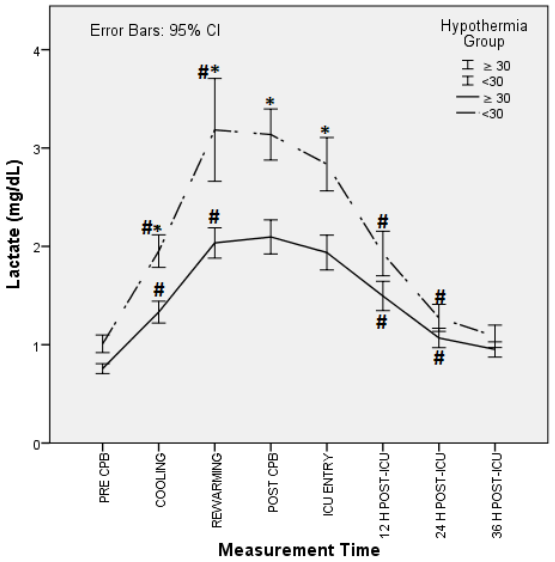

Figure 2: Serum lactate levels in the patients undergoing moderate hypothermia (body temperature ≥ 30 °C) or deep hypothermia (body temperature < 30 °C) during cardiopulmonary bypass surgery for the correction of congenital heart diseases.
$P < 0.01$ compared with the previous measurement in the same group and $P < 0.01$ compared with the measurement in the other group at the same time

Table 1: Comparisons of the demographic variables of age, sex, height, and weight between the 2 groups: hypothermia < 30 °C and hypothermia ≥ 30 °C
Data are presented as the median (the interquartile range) for the continuous data and as frequencies and frequency percentages for the categorical data. Comparisons were made using the Mann–Whitney *U* test for the continuous variables and the χ2 test for the categorical variables.

Group	< 30 °C	≥ 30 °C	*P* value
Age (y)	24 (8-36)	24 (12-48)	0.026
Sex (male %)	42/93 (45.16%)	50/89 (56.18%)	0.09
Weight (kg)	10 (6.45-12)	10 (8.15-14)	0.084
Height (cm)	84 (75.5-102)	87 (75.5-102.5)	0.025

Table 2: Relative frequencies and frequency percentages of the distribution of the patients based on their diagnosis by group
Between-group comparisons were made using the χ2 test.

Group	≥ 30 °C	< 30 °C	Pearson χ2
Tetralogy of Fallot (ToF)	19/89 (21.3%)	19/93 (20.4%)	χ(2) = 0.375 *P* = 0.829
VSD and mix[1]	44/89 (49.4%)	50/93 (53.8%)	
Other types[2]	26/89 (29.2%)	24/93 (25.8%)	

[1] VSD+PH, Ventricular septal defect+ pulmonary hypertension; DORV, Double-outlet right ventricle; SV, Single ventricle; VSD+COA, Ventricular septal defect+ coarctation of the aorta; TRUNCUS-DILV, Double-inlet left ventricle
[2] PAPVC, Partial anomalous pulmonary venous connection; TA, Tricuspid atresia; WEB–PA, Pulmonary atresia; ccTGA, Congenitally corrected transposition of the great arteries; ALCAPA, Anomalous left coronary artery from the pulmonary artery; PS, Pulmonary stenosis: ASD, Atrial septal defect; HRHS, Hypoplastic right heart syndrome; AS, Aortic stenosis; CORTATRIUM-DTGA, Transposition of the great arteries; LVOTO, Left ventricular outflow tract obstruction

Table 3: Comparisons of the changes in the patients' serum lactate (mmol/L) between the 2 groups at different time points

Time/ Group	≥ 30 °C	< 30 °C	*P* value
Before CPB	0.75 ± 0.2	1.01 ± 0.4	< 0.001
Cooling stage	1.3 ± 0.5	1.9 ± 0.7	< 0.001
Warming stage	2.0 ± 0.7	3.19 ± 2.4	0.002
After CPB	2.09 ± 0.8	3.15 ± 1.2	< 0.001
ICU entry	1.9 ± 0.8	2.8 ± 1.2	0.001
12 h post-ICU	1.4 ± 0.7	1.9 ± 1.1	0.19
24 h post-ICU	1.1 ± 0.5	1.2 ± 0.6	0.4
36 h post-ICU	0.9 ± 0.4	1.08 ± 0.5	0.9
***P* value**	<0.001	<0.001	

CPB, Cardiopulmonary bypass; ICU, Intensive care unit

Table 4: Comparisons of the changes in the patients' blood glucose (mg/dL) between the 2 groups at different time points

Time/ Group	≥ 30 °C	< 30 °C	*P* value
Before CPB	84 ± 22	107 ± 36	<0.001
Cooling stage	128 ± 33	160 ± 44	
Warming stage	166 ± 39	201 ± 58	
After CPB	170 ± 42	210 ± 58	
ICU entry	148 ± 49	202 ± 60	
12 h post-ICU	147 ± 53	176 ± 62	0.08
24 h post-ICU	120 ± 45	148 ± 41	< 0.001
36 h post-ICU	117 ± 30	134 ± 29	0.001
***P* value**	<0.001	<0.001	

CPB, Cardiopulmonary bypass; ICU, Intensive care unit

Table 5: Comparisons of the changes in the patients' central venous pressure (cmH_2o) between the 2 groups at different time points

Time/ Group	≥ 30 °C	< 30 °C	*P* value
Before CPB	8.1 ± 2.7	7.3 ± 2.9	0.048
After CPB	11.9 ± 3.4	9.7 ± 3.2	< 0.001
ICU entry	13.7 ± 4.0	8.8 ± 3.2	< 0.001
12 h post-ICU	14.2 ± 3.5	12.4 ± 6.8	0.038
24 h post-ICU	14.6 ± 3.7	12.4 ± 3.3	< 0.001
36 h post-ICU	14.6 ± 3.5	11.9 ± 2.8	< 0.001
***P* value**	<0.001	<0.001	

CPB, Cardiopulmonary bypass; ICU, Intensive care unit

Table 6: Comparisons of the changes in the patients' diuresis corrected for patients' weight (mL/kg) between the 2 groups at different time points

Time/ Group	≥ 30 °C	< 30 °C	*P* value
Before CPB	7.31 ± 5.66	11.66 ± 10.44	0.001
Cooling stage	9.8 ± 7.65	14.24 ± 7.28	0.003
Warming stage	10.93 ± 8.03	13.96 ± 8.8	0.102
After CPB	12.79 ± 8.02	20.26 ± 16.26	0.001
ICU entry	5.68 ± 5.52	7.24 ± 5.23	0.119
12 h post-ICU	42.43 ± 13.91	55.07 ± 21.65	>0.001
24 h post-ICU	41.88± 13.14	46.53 ± 21.04	0.501
36 h post-ICU	42.72 ± 10.92	52.37 ± 21.89	0.003
***P* value**	<0.001	<0.001	

CPB, Cardiopulmonary bypass; ICU, Intensive care unit

Table 7: Comparisons of the changes in the duration of CPB, the duration of cross-clamp, and the amount of blood filtered and transfused between the 2 groups at different time points

Variables/ Group	< 30 °C	≥30 °C	*P* value
CPB duration (min)	115 ± 53.1	81.7 ± 28.9	< 0.001
Cross-clamp duration (min)	76.3 ± 43.2	50.2 ± 24.8	
Blood filtered (mL)	703.7 ± 430	331.5 ± 266.8	
Blood transfused (mL)	450 (350-500)	400 (300-500)	0.122

CPB, Cardiopulmonary bypass

Table 8: Analysis of blood gases during the study
Partial pressure of carbon dioxide (pCO_2) and partial pressure of oxygen (pO_2) were measured in all the patients during surgery and presented as the mean ± standard deviation (SD) of pO_2 and pCO_2 in Torr units.
< 30 body temperature below 30 ºC (also deep hypothermia) and ≥ 30 body temperature equal to or above 30 ºC (moderate hypothermia) during induced hypothermia

Group	< 30 °C	≥ 30 °C	*P* value
pO_2 before cross-clamp	278.7 ± 65.3	261.5 ± 60.7	0.068
pO_2 in the cooling stage	294.4 ± 47.6	286.3 ± 51.8	0.287
pO_2 in the rewarming stage	275.0 ± 53.3	269.8 ± 49.2	0.5
pO_2 post pump	220.1 ± 45.9	213.9 ± 46.1	0.371
pO_2 before cross clamp	32.7 ± 5.01	32.2 ± 5.07	0.467
pO_2 in the cooling stage	31.7 ± 4.2	31.2 ± 4.1	0.366
pO_2 in the rewarming stage	33.48 ± 4.1	33.8 ± 4.8	0.4
pO_2 post pump	36.7 ± 3.7	35.8 ± 3.6	0.147
***P* value**	<0.001	<0.001	

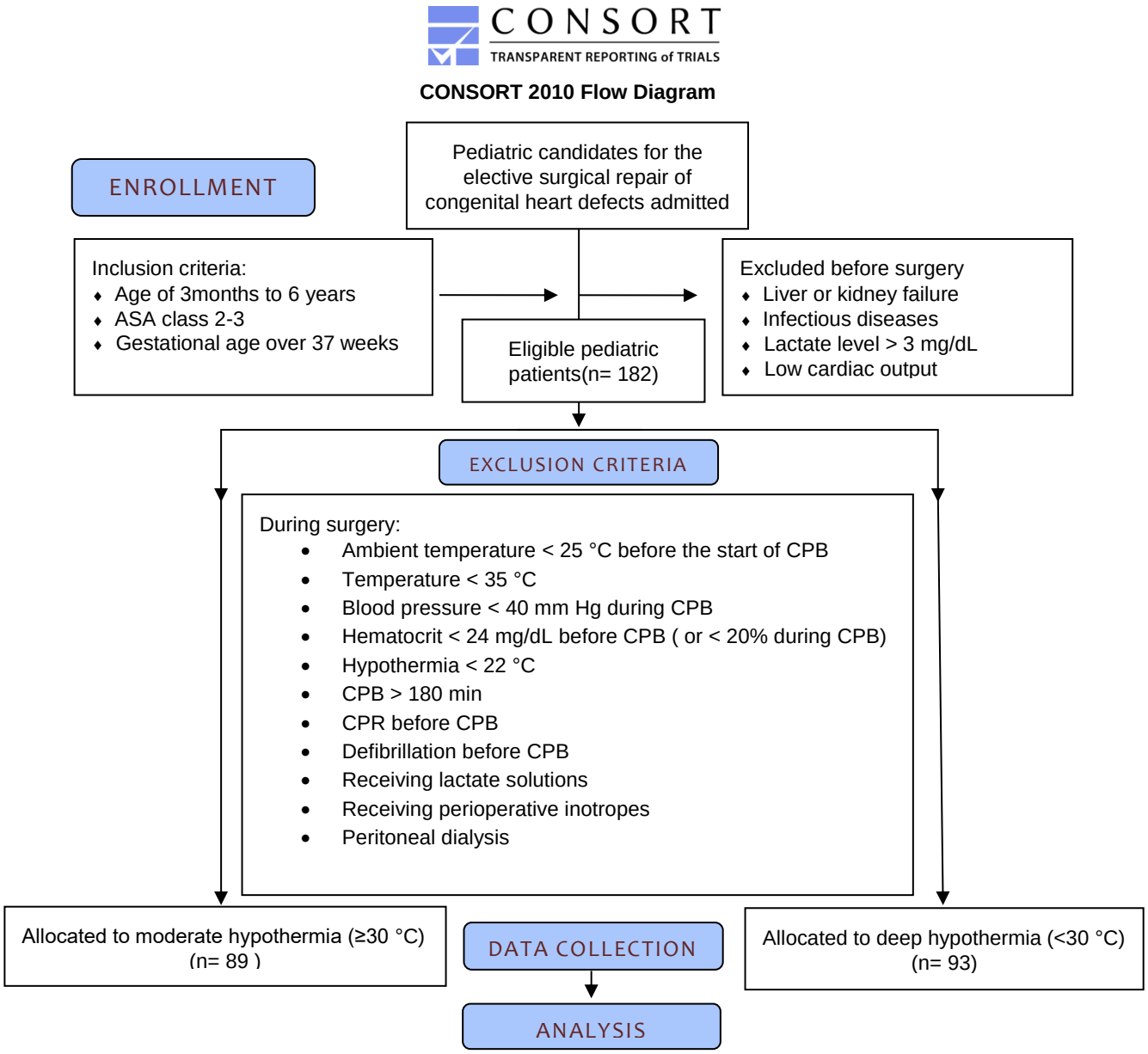

Figure 1: CONSORT flow diagram of the study

ASA, American Society of Anesthesiologists; CPB, Cardiopulmonary bypass; CPR, Cardiopulmonary resuscitation

Higher blood glucose levels were observed in the deep hypothermia group and higher central venous pressure in the moderate hypothermia group (Table 4 & Table 5). Diuresis was higher in the deep hypothermia group (Table 6). The duration of CPB, the duration of cross-clamp, and the amount of blood filtered and transfusion were also higher in the deep hypothermia group (Table 7). The blood gas analysis did not find any significant variations in the partial pressure of carbon dioxide (pCO_2) and the partial pressure of oxygen (pO_2) between the 2 groups (Table 8). Effective pump flow

(presented as the ratio of the actual pump flow to the calculated flow ×100) in the deep hypothermia group (85.74% ± 8.22) and the moderate hypothermia group (86.61% ± 7.61) was similar ($P = 0.461$).

A multiple regression analysis was run to predict serum lactate levels in the rewarming stage among the pre-CPB lactate level, the pump time, the effective pump flow to the calculated flow percentage, the clinical center of the patient recruitment, the cross-clamp time, and the body temperature. The final model was developed using the backward-stepwise best subset method. Rewarming lactate levels were distinguishable only by pre-CPB lactates and induced temperatures, F regression df, residual df (4, 173) of 6.943, a P value of less than 0.005, and R^2 of 0.138. Only 2 variables of pre-CPB lactate ($\beta = 1.129$ and $P = 0.005$) and temperature ($\beta = -0.124$, $P = 0.003$) added statistically significantly to the prediction. The pump time and the cross-clamp time did not show correlations with the lactate level.

DISCUSSION

In the current study, the serum levels of lactate in pediatric patients undergoing CPB were measured. The patients were divided based on induced hypothermia into 2 groups of deep and moderate hypothermia. The patients in the deep hypothermia group had a higher mean level of blood lactate from cooling to ICU discharge. Both groups experienced elevations in the serum lactate level during bypass, which lasted until the ICU entry and finally approximated the baseline (pre-CPB) level or gradually improved until the time of discharge. We ran a multiple regression analysis to diagnose the effects of confounding factors. It demonstrated that among the factors that were suspected to have an effect on blood lactate levels (eg, the pre-CPB blood lactate level, the pump time, the cross-clamp duration, and induced hypothermia), only 2 factors of induced hypothermia and pre-CPB lactate levels contributed to the changes in serum lactate levels in the period between the cooling stage and ICU entry. Pre-CPB blood lactates were directly correlated with serum lactates measured subsequently during CPB. This correlation was negative unless body temperature was considered. Elevated lactate is one of the known risk factors for postoperative adverse outcomes in CPB operations. The intraoperative evaluation of arterial lactate can indicate high-risk postoperative conditions even in low-risk procedures. [6] In a study by Kanazawa et al [19] (2015), the results demonstrated that higher lactate levels in patients were closely correlated with the length of ICU stay and a higher incidence rate of postoperative adverse effects. The subjects, in their study, varied widely in age, and since basal metabolism varied in different age groups, this wide age range was considered a limitation and reduced the reliability of the research findings.

The multivariable analysis performed in this study demonstrated no significant relationships between lactate levels and weight ($P = 0.084$); however, height in the moderate hypothermia group was significantly higher ($P = 0.025$). The amount of urination was higher than normal in both groups, which along with a normal central venous pressure had a significant role in lowering lactate levels within 36 hours after ICU admission, such that the lactate levels were reduced to 1.08 mmol/L in the deep hypothermia group despite a greater negative slope; in the moderate hypothermia group, the lactate levels were reduced to 0.9 mmol/L (Table 3 & Figure 2). A large body of evidence emphasizes the role of lactate clearance. Jansen et al [15] examined the

efficacy of lactate monitoring and interventions in reducing lactate levels with a view to improving patient outcomes in patients admitted to the ICU with lactate levels greater than or equal to 3 mmol/L. In the lactate group, a treatment aimed at a 20% or higher amount of reduction in lactate was performed in the patients at the ICU every 2 hours for the first 8 hours of the ICU stay. They also received more fluids and vasodilators. The patients in this group demonstrated less organ failure postoperatively, their inotropes were discontinued earlier, and they were separated from the mechanical ventilator and discharged from the ICU sooner as well. They also had a lower rate of hospital mortality ($P = 0.006$).

In a systemic study, Zhang et al [20] introduced lactate clearance as a protective factor in patients and explained that it predicted postoperative complications and had a clinical diagnostic application.

Renal blood circulation mostly reflects whole-body circulation; therefore, it is expected that in a near-normal circulation, patients have better lactate clearance. [21] No negative correlations were recorded in the patients between lactate levels and diuresis during CPB.

Blood glucose is an important clinical outcome predictor [22] in ICU patients, including after cardiac surgery. Hyperglycemia increases the amount of substrates for lactate formation (pyruvate from glucose). [23] The trend of changes in the glucose level was similar in both groups, but glucose elevated higher in the deep hypothermia group and was 40 mg/dL higher than that in the moderate hypothermia group at its maximum. It also took longer to decrease in this group. In line with the increase and decrease in lactate, glucose levels also fluctuated in the patients (Table 4).

Blackwood et al [24] found that red blood cell transfusion in patients younger than 6 weeks undergoing stage 1 of the Norwood procedure was not associated with poor physical and mental development or increased early death after surgery (even up to 2 years).

The increased oxygen transport capacity of blood and improved tissue oxygenation are the known advantages of blood transfusion during pediatric CPB, which is directly related to lactate levels. [25] Despite the complications of blood transfusion in children such as the increased risk of infection and death (in spite of using low-leukocyte blood), this procedure is sometimes essential; the problem is the lack of a minimum hemoglobin level to serve as a transfusion trigger for all children needing cardiac surgery. [26] In this study, we observed no significant difference between the 2 groups in terms of the volume of red blood cells transfused ($P = 0.12$).

In the present study, the conventional form of hemofiltration was performed in the rewarming period in both groups. Sometimes hemofiltration was used to remove extra fluids. The amount of blood filtered differed significantly between the 2 groups in this study and was associated with changes in the lactate level ($P < 0.001$) (Table 7).

Durandy et al [27] (2008) examined children weighing less than 10 kg with a normal body temperature and concluded that cardiac surgery with long cross-clamping periods (> 90 min) was safe in normothermic children. They reported no pulmonary complications resulting from poor pulmonary protection as a result of surgery in their subjects. Moreover, the authors reported that automatic respiration returned in the 31 of the 38 normothermic surgery patients with cross-clamping periods above 90 minutes before 4 days (the defined limit for prolonged mechanical ventilation in the study), and the prolonged ventilation in the remaining 7 patients was attributed to infections or surgical reasons.

Naka and Bellomo [28] reported that hemofiltration could cause mild metabolic

acidosis due to plasma bicarbonate secretion caused by the excretion of anions as a result of this therapy and also argued that lactic acidosis did not clear with more hemofiltration.

This finding urges that surgeons consider reducing postoperative complications in accordance with their patients' depth of hypothermia and not limit their performance to surgical outcomes. According to previous research, the excessive elevation of lactate levels as a result of deeper hypothermia and the design of CPB machines is associated with some postoperative complications. [19,29]

We also found that a greater increase in lactate levels in the warming stage and after CPB increased our patients' need for the inotrope epinephrine for separation from the CPB machine.

Although our study provides evidence that deep hypothermia is associated with higher blood lactate levels in patients specifically in the rewarming stage, the lack of randomization limits the generalizability of the study results. We recommend that future randomized clinical trials be undertaken in various settings to consolidate the findings of the current study.

CONCLUSIONS

Deep hypothermia is associated with higher blood lactate levels, which may worsen patients' health during and after CPB. It is recommended that normothermia or mild hypothermia be used during CPB in pediatrics. When the use of deep hypothermia is inevitable, patients should be strictly monitored for hyperlactatemia because of the possible adverse outcomes associated with it.

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