COLLEGE OG HEALTH SCIENCE

SCHOOL OF MEDDICINE

DEPARTMENT OF SURGERY

ASSESSMENT OF THE EFFECT OF LACTATE ON PATIENT OUTCOMES AND ASSOCIATED FACTORS AMONG PATIENTS WHO UNDERWENT CARDIOPULMONARY BYPASS SURGERY AT CARDIAC CENTER ETHIOPIA, ADDIS ABABA, ETHIOPIA 2021.

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Full Title Of The Research	**Assessment of the effect of lactate on patient outcomes and associated factors among patients who underwent cardiopulmonary bypass surgery at Cardiac Center Ethiopia, Addis Ababa, Ethiopia 2021.**
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ABBREVIATIONS AND ACRONYMS

CI	Confidence Interval
CPB	Cardio pulmonary Bypass
ICU	Intensive Care Unit
OR	Odds Ratio
SPSS	Statistical Package for Social Science
TASH	Tikur Anbessa Specialized Hospital
US	United States
WHO	World Health Organization
CHF	Congestive Heart Failure
BSA	Body Surface Area
NYHA	New York Heart Association
IABP	Intra Aortic Balloon Pump
MI	Myocardial Infarction
ESRD	End-Stage Renal Disease
CABG	Coronary Artery Bypass Graft
SBP	Systolic Blood Pressure
DBP	Diastolic Blood Pressure
LOS	Length of stay

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ABSTRACT

Introduction: Hyperlactatemia and lactic acidosis are commonly encountered during and after cardiac surgery. Perioperative lactate production increases in the myocardium, skeletal muscle, lungs and in the splanchnic circulation during cardiopulmonary bypass. Hyperlactatemia is highly suggestive of tissue ischemia and is associated with a prolonged intensive care unit stay, a prolonged requirement for respiratory and cardiovascular support and increased postoperative mortality.

Objective: The objective of the study was to assess effect of lactate on patient outcomes and associated factors among patients who underwent cardiopulmonary bypass surgery at Cardiac Center Ethiopia, Addis Ababa, Ethiopia from December 2020 to February 2021.

Method: An institution-based retrospective cross-sectional study was done among all patients who underwent cardiopulmonary bypass surgery from December to January. Data was collected from patient chart review. The collected data was entered into Epidata version 4.2 and export to SPSS 23 for analysis. Descriptive statistics for categorical and continuous variables was done. A chi-square test was done to show the presence of an association between the outcome variable and independent variables. A variables fitted on bivariate analysis was entered into multivariable analysis to show the strength of association and statically significant variable.

Result: The prevalence of hyperlactatemia in this study among patients who underwent cardiac surgery procedures at Cardiac Center Ethiopia was 37.5 %. Rise in lactate level prolongs ICU stay, Prolongs intubation duration and increase need of Inotropes support. Lactate level was measured on immediate postoperative day within 10 hours after the surgery and was defined as lactate level > 3 mmol/L in the first hour after surgery. Age > 50 years [AOR: 6.8 (95% CI 1.7-25), P=<0.008]. female gender [AOR: 1.8 (95% CI 1.1-3.8), P=0.048]. Variables statistically significant were declared at 95 % CI, p-value < 0.05.

Conclusion and Recommended: Early rise in lactate level in patients who underwent cardiopulmonary bypass surgery is a strong and robust predictor of morbidity and mortality. Different patient and operative factors involved in this pathophysiology. As a result, strict follow up management of those factors are recommended.

Keywords: Hyperlactatemia, Associated factors, Adverse outcomes

1. Introduction

1.1. Background

Hyperlactatemia and lactic acidosis are regularly experienced during and after heart medical and surgical procedures. Perioperative lactate creation increments in the myocardium, skeletal muscle, lungs, and, in the splanchnic dissemination during the cardiopulmonary procedures. Hyperlactatemia has a bimodal circulation in the perioperative period. An early expansion in lactate levels, emerging intra-operatively or not long after the emergency unit is recognizable and concerning finding for most clinicians. It is profoundly reminiscent of tissue ischemia and is related to a delayed emergency unit, a drawn-out prerequisite for respiratory and cardiovascular help, and expanded postoperative mortality (1).

During cardiovascular medical procedure patients giving late cresting blood lactate post-operatively are at expanded danger for helpless ICU result and mortality. Tenacious pinnacle level of lactate is a superior marker of forecast when contrasted and transitory pinnacle lactate in post-CPB patients. The tirelessness of hyperlactatemia is a more significant determinant of postoperative patient outcomes(2).Post-operative hyperlactatemia and lactic acidosis in cardiovascular medical procedure patients is a critical marker to identify undesired results in 6 hrs. post-operative lactate level can anticipate the length of stay in ICUs and the prospect of creating adverse results and morbidity(3).

The preoperative status of the patients, alongside the explicit sedative, procedural, and postoperative elements will result serious short-term long-term morbidity and mortality. Surrogate markers of tissue perfusion such as central venous oxygen saturation and blood lactate. Bigger differences in lactate level after CPB would be related to prolonged span of ICU remain and the occurrence of postoperative genuine undesired outcomes. Various studies uncovered that an intraoperative increment in lactate level is an inherent and explicit indicator of patients at high risk for morbidity and mortality after operations for congenital cardiac disease. lactate level during the cardiopulmonary bypass and the possible predictive value in identifying patients at high risk of morbidity and mortality after surgery for cardiac disease(4).

1.2. Statement of the problem

The persistence of hyperlactatemia is a more important determinant of postoperative outcome than the absolute value of the peak lactate concentration. Blood lactate concentration of 4.0 mmol/L or higher during CPB identifies a subgroup of patients with increased risk of postoperative morbidity and mortality. Postoperative hemodynamic instability occurred in 29.5% of patients with elevated levels of lactate during CPB contrasted with 10.9% of patients with lower lactate levels. Postoperative mortality was 11% higher when it is contrasted with patients who had peak blood lactate levels of less than 4.0 mmol/L during CPB.(5).

It distinct that post operative dismalness irregular in patients going through a cardiovascular procedure. More than 66% (70.2%) of patients had at least one major complication. With the most regularly happening intricacy was low cardiac output state (29.8%), trailed by renal dysfunction (25.4%), mechanical ventilation (15.7%), and atrial fibrillation (14.6%). Almost one-fourth (23.2%) of the patients remained in the ICU for > 2 days, and LOS in the emergency room was for > 7 days for particularly over 60% of the patients(6).

Postoperative mortality was higher among patients with lactate levels over 4 mmol/L on ICU admission (18.7% versus 6.2%) when contrasted and the individuals who have under 4mmol/L(7).

1.3. Significance of the study

There is no evidence that studies conducted in this title in our country Ethiopia since; advanced cardiac surgery had been introduced in recent years. This study will benefit the cardiac team in identifying the factors associated with lactate and its effect on patient's outcome following cardiac surgery under cardiopulmonary bypass.

The finding from the study will provide significant benefit in promoting prevention and early control mechanisms, conscious the policy makers and national programs about the need of diagnostic and treatment facilities and will play a fundamental role in reducing morbidity from hyperlactetmia.

Therefore, result of this study may contribute important evidence that can be used by the policy makers, program planners and educators to design appropriate strategy to address the problem.

Further, the result of the study can be used as a baseline data for future studies in the topic area.

2. Literature Review

In spite of the fact that hyperlactatemia after heart medical procedure is normal, hyperlactatemia after cardiac surgery is common, the implications of raised levels remain dubious. In various studies high lactate levels after cardiac surgery are predictors of major complications including mortality(8).The rate of postoperative bleakness including complications, prolonged ICU stay, and hospital stay is high among patients going through cardiac surgery under CPB. Despite its affectability, the lactate assessment stays a clinically worthwhile test that can make a clinician aware of discovering fundamental hypo-perfusion needing prompt treatment or an etiology not promptly clear on initial evaluation(9).

2.1. Effect of Elevated lactate among patients undergone cardiopulmonary bypass surgery

A retrospective study pointed out that 469 patients who underwent post-cardiovascular medical intervention were admitted to the ICU for more than 24 hours. Of these, 144 of these patients had arterial blood lactate ≥ 3.0 mmol / L. Of the deaths, 78.9% had hyperlactatemia. Patients whose lactate concentrations continued to rise> 30 h after surgery were more likely to die(10).Another study showed that the rate of patients with hyperlactatemia during CPB was 5.7%. while the global incidence of hyperlactatemia was 11.4%(11)

A retrospective observational study showed the morbidity rate of hyperlactatemia in patients with cardiopulmonary bypass. As shown, atrial fibrillation (19.9% vs 5.3%; P = 0.004), prolonged need for inotropes (34% vs 11.8%; P = 0.001), longer ICU stay (P = 0.013) and in hospital (P = 0.001) were found to be the result of an elevated level of lactate in the blood(12).

A two-way follow-up study conducted in Iran found that patients with a poor outcome had significantly higher lactate levels in ABG samples. The patient with a serum lactate level greater than 5 had a period of apnea after extubation and suffered neurological damage. Additionally, patients with serum lactate levels between 3 and 5 required an aortic balloon after surgery and were admitted to the ICU for 1 week. Laboratory results of a serum lactate level between 2 and 3 showed that the patient had arrhythmia(13).

Observational studies conducted in Pakistan showed that increased lactate levels led to longer stays in the intensive care unit and hospital and could be used as a marker of worse postoperative

outcomes in terms of morbidity. As a result, prolonging the stay in the intensive care unit entails high hospital costs and more complications.(14).

Postoperative mortality was higher in patients with hyperlactatemia (lactate value> 4) than in patients with peak blood lactate levels of less than 4.0 mmol / L during CPB (11.0% vs 1.4%; p <0.001, relative risk (3) 9.0). Postoperative hemodynamic instability occurred in 29.5% of patients with elevated lactate levels during CPB compared with 10.9% of patients with lower lactate levels. Overall, serious postoperative complications with higher and lower lactate levels occurred in 43.2% and 21.8% of patients in each group(15).

Hyperlactatemia has been found to be a strong predictor of postoperative morbidity and mortality. For example, the change in lactate levels during CPB increased with surgical complexity. Postoperative complications increased with increasing surgical complications.(16).

2.2. Factors Associated with elevated lactate and post-operative morbidity.

The outcome after any heart surgery is determined by the patient's pre-existing symptoms as well as intra-operative factors. These various factors contribute to the development of hyperlactatemia and to the outcome of undesirable postoperative outcomes for patients. Studies have shown that Intra-operative factors such as CPB duration are associated with the development of postoperative morbidity and mortality. Patients with hyperlactatemia had significantly higher rates of postoperative morbidity such as atrial fibrillation, longer need for inotropes, and longer stay in ICU (17).

Cross-clamping and cardiopulmonary bypass times and very positive fluid balance at the end of surgery are associated with a significant increase in the level of postoperative lactate, resulting in increased need for pump assistance. With intra-aortic balloon, the probability of intensive care> 24 h unit stay, increased need for red blood cell bleeding, hospital stay and increased mortality. In addition, clamping and CPB an increase in time and a very positive water balance at the end of the operation is associated with an initial increase in postoperative lactate levels, associated with an increased need for IABP support, length of stay in ICU, need for red blood transfusions, length of hospitalization, and mortality.(18).

Non-elective surgery, prolonged CPB, and intraoperative vasopressor use were independent risk factors for immediate hyperlactatemia after cardiac surgery and also showed that immediate hyperlactatemia had a higher ICU mortality rate than late hyperlactatemia(19).

Prospective observational study showed that preoperative serum creatinine value, the presence of active endocarditis, the cardiopulmonary bypass duration, the lowest oxygen delivery during cardiopulmonary bypass, and the peak blood glucose level were found to be independent associated factors for hyperlactatemia among patients undergoing cardiac surgery with cardiopulmonary bypass were admitted to this prospective observational study(11).

Cross sectional study done in Iran revealed that the number of received blood units, Ejection fraction before operation, having diabetes, pump duration, and average storage time of transfused blood significantly affected postoperative lactate level. As the study bared that decrease in EF and increase in serum lactate are both signs of reduced blood volume and inadequate oxygen delivery to tissues were associated with increase in serum lactate. (20). Similarly, another study showed that CPB time (Pearson correlation coefficient r = 0.024; P = 0.003) and aortic cross clamp time (r = 0.02, P = 0.007) had significant association with peak intraoperative blood lactate levels.

In general, elevated lactate level cause serious morbidity and reduce survival outcome. Atrial fibrillation, increased hospital stay, prolonged requirement of inotropes and complicated post op outcome were some of the outcomes related to hyperlactatemia. Preoperative serum creatinine value, the presence of active endocarditis, diabetes, aortic cross clamp time, CBP time, the cardiopulmonary bypass duration, the lowest oxygen delivery during cardiopulmonary bypass, and the peak blood glucose level were a associated factors for elevated lactate level.

2.3. Conceptual framework

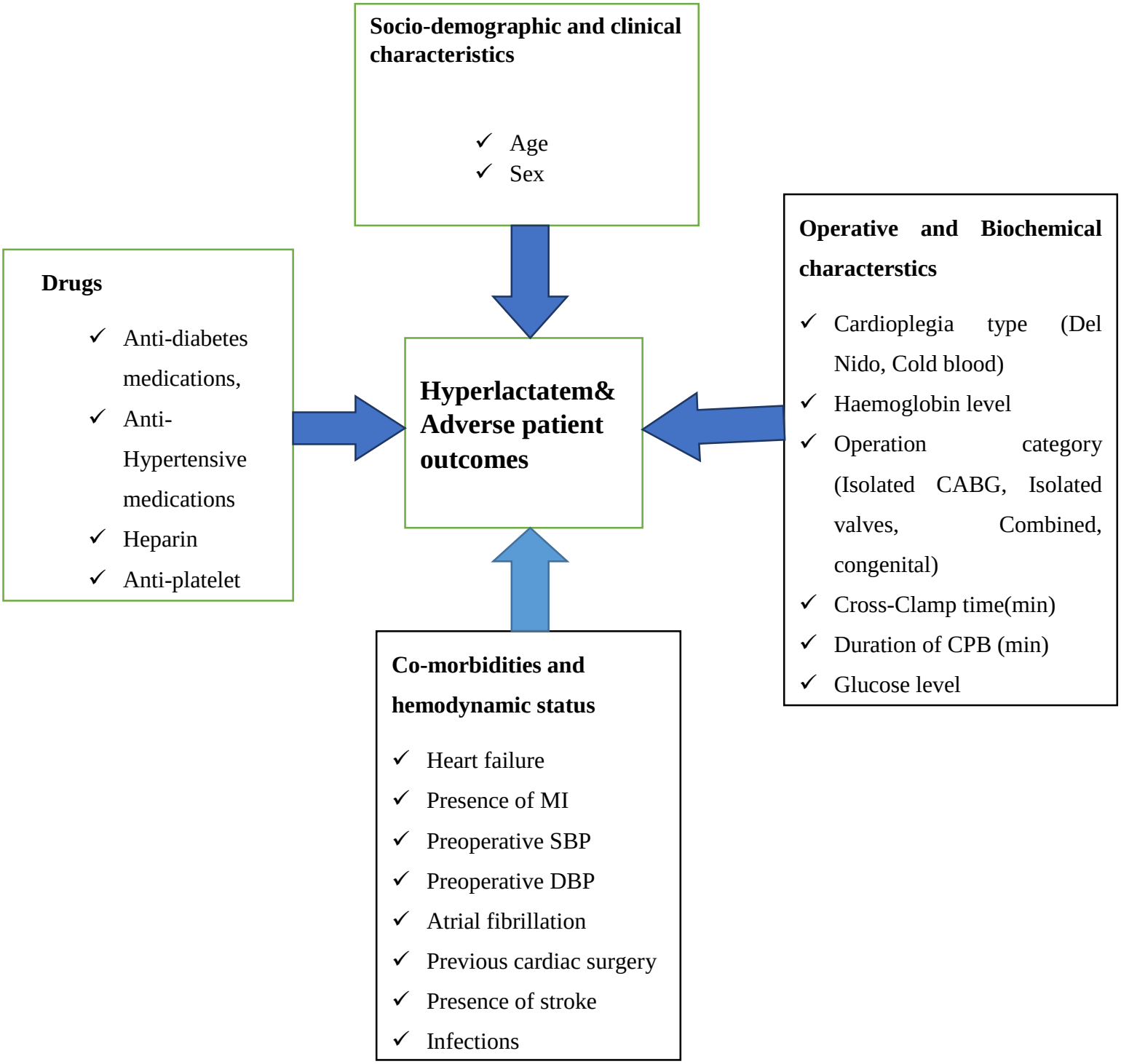

Figure 1: conceptual framework showing the relationship between factors associated with hyperlactatemia and adverse patient outcomes. (11),(15),(18),19).

3. Objectives

3.1 General objective

- To assess the effect of lactate level on patient outcomes and associated factors among patients who underwent cardiopulmonary bypass surgery at Cardiac Center Ethiopia Addis Ababa, Ethiopia, 2021.

3.2 Specific objectives

- To determine the magnitude of of Hyprlactatemia among patients who underwent cardiopulmonary bypass surgery at Cardiac Center Ethiopia, Addis Ababa, Ethiopia 2021.
- To identify adverse patient outcomes of Hyprlactatemia among patients who underwent cardiopulmonary bypass surgery at Cardiac Center Ethiopia, Addis Ababa, Ethiopia 2021.
- To identify factors associated with Hyperlactatemia in patients who underwent cardiopulmonary bypass surgery at Cardiac Center Ethiopia Addis Ababa, Ethiopia, 2021.

4. Methods and Materials

4.1. Study area and Period

This study was conducted in December 2020 to February 2021 at Cardiac Center Ethiopia; Cardiac Center Ethiopia is the first cardiac center in Ethiopia was inaugurated on February 12, 2009 GC. This non-profit Center specializes in heart disease and is especially committed to helping children with cardiac problems. The center performs all types of cardiac surgeries for rheumatic, valvular and congenial heart disease for infants, children, adolescents and adults by a qualified Ethiopian team, operating on various cardiac surgical interventions with 2 fully dedicated operation theaters, 10 ICU beds and 2 functional cath-lab machines.

4.2. Study design

Retrospective cross-sectional documentary review was employed.

4.3. Population

4.3.1 Source population

The source population of the study was all patients who underwent open heart surgery from February 2009 to October 2020.

4.3.2 Study Population

The study population was all patients underwent cardiac surgery under cardiopulmonary bypass from February 2009 to October 2020.

4.4. Eligibility criteria

4.4.1. Inclusion criteria

All selected registered and complete patients who underwent cardiopulmonary bypass surgery.

4.4.2. Exclusion criteria

Missed, patient charts were excluded from the study and incomplete charts were replaced by other charts.

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4.5. Sample Size determination

The sample size for the study was determined by using a single population formula by using a 95% confidence interval 50% population proportion and a 5% margin of error.

$n=Z\alpha/2^2 \times p\ (q)\ /d^2 = (1.96)^2 \times 0.5(0.5) / (0.05)^2 = 384$

Since the study population is less than 10,000, sample size reduction was used.

Nf = ni/1+ni/N

Where:-nf= final Sample Size

ni= initial Sample Size

N= total population

nf=384/1+384/1149

nf=384/1.3

nf=259.34

nf=296

After adding 10% non response rate the final sample size was 326.

4.6. Sampling Techniques

The required sample size was selected systematically every three interval by using the Medical Record Number (MRN) from Health Service Management and Information System (HMIS) of patients as a sampling frame.

4.7 Study Variables

4.7.1. Dependent variable

- Hyperlactatemia and post-operative adverse outcomes (Prolonged ICU stay, prolonged intubation & Inotrope support).

4.7.2. Independent Variables

Age, Sex, Co-morbidities (Diabetes, hypertension), Drugs (Anti-diabetes medications, Antihypertensive medications, Heparin, Anti-platelet), Preoperative SBP, Preoperative DBP, NYHA class HF, Presence of MI, Previous cardiac surgery, Presence of Stroke, Cardioplegia type (Del Nido, Cold blood), Haemoglobin level, Glucose level, Atrial fibrillation, Operation category (Isolated CABG, Isolated valves, Combined, Others), Intra operative variables (Cross Clamp time (min), Duration of CPB (min), PO2 level (mmhg)).

4.8. Data collection tools and procedures

Data collection tool (questionnaire) was used which was adapted from the previous studies. (11)(15),(18),19).The tools consisted of checklists that was prepared in English version and had five parts (Socio-demographic characteristics, clinical or biochemical characteristics, co-morbidities, drugs and intra-operative variables). The cardiac patient's chart was reviewed retrospectively by using the data collection checklist. The data collectors and supervisor were from the center. The data collection procedure was review of medical chart. Detailed review was done on the systematically selected patient charts.

4.9. Operational definitions

Outcome = patients with elevated lactate and one or more adverse outcomes like prolonged ICU stay, Prolonged intubation or need of inotrophic support.

Hyperlactatemia = blood lactate level measure >3mmol.

Prolonged ICU stay = patients who stayed admitted in ICU longer than 72 hour.

Prolonged Intubation = patients who stayed intubated longer that 24 hour.

4.10. Data Quality Assurance

To assure the quality of the data one-day training was given for 3 data collectors and 1 supervisor prior to data collection. The questionnaire was carefully designed and English version was used for data collection. Before actual data collection time, the questionnaire was checked for clarity and comprehensiveness. During data collection, the supervisor has monitored the data collection process by checking completeness of the data and take corrections on the site of data collection when any problem happened. The principal investigator has checked data for its completeness during data entry and the cleaning process.

4.11. Data processing and analysis

The data were collected from the medical records of patients who underwent cardiac surgery under CPB. Epi data version 4.2 was used for data entry and recoding, cleaning and analysis was done with SPSS version 23. Descriptive statistics such as frequencies, proportions, means, and Standard deviations were calculated. Adverse post-operative outcomes secondary to hyperlactatemia were assessed. The bivariate analysis was used to assess the relationship between each independent variable and lactate level. Variables that were considered as significantly associated at p value < 0.25 in the bivariate analysis were entered into the multivariable analysis logistic regression model. Finally, the variables which had significant association were identified on the basis of the odds ratio (OR), with 95% CI. The finding was expressed with 95% CIs and a significant variable was declared at p < 0.05 which was statistically significant.

4.12. Ethical Considerations

The study was conducted after getting ethical clearance from research and ethical committee of Addis Ababa University, College Health Science and School of Medicine. Permission was taken from the hospital. The information collected from the patient's medical chart was used only for the research purpose and kept confidential. In addition to this in order to maintain confidentiality, study subjects were not identified by name.

4.13. Dissemination and Utilization of results

The result of this study was submitted for and presented to Addis Ababa University, College Health Science, School of medicine and Department of surgery. The final result of this study will be given for the hospital and the center where the study was conducted, other concerned governmental and non-governmental organizations. Moreover, the findings of the study will be disseminated through publication by international journals.

5. Results

5.1. Socio demographic and clinical characteristics

From the total of 1149 patients who underwent cardiopulmonary bypass surgery at Cardiac Center Ethiopia 326 samples were systematically selected. From this, 297 was compete charts, 23 was incomplete and replaced by other charts. Finally 320 complete patient charts were reviewed for this study. This gives the response rate (the completeness rate of 98.1%).Their mean age was [23.5 ± 14.8] years and 188 were females (58.8%). (Table1).

Table 3: Socio demographic and Co-morbidity characteristics of patients who underwent cardiopulmonary bypass surgery at Cardiac Center Ethiopia, Addis Abeba, Ethiopia, February 2021**.**

Characteristics	N=320	Freq.	Percent
Lactate	≤3 mmol/l	200	62.5
	>3mmol/l	120	37.5
Sex	Male	132	41.2
	Female	188	58.8
Age in years	≤10 yrs	47	14.7
	11-20yrs	128	40
	21-30yrs	74	23.1
	31-40yrs	37	11.6
	41-50yrs	34	10.6
Diabetes	Yes	3	0.9
	No	217	99.1
Hypertension	Yes	5	1.6
	No	315	98.4
Heart failure	Yes	24	7.5
	No	296	92.5
Myocardial infarction	Yes	1	0.3
	No	319	99.7
Previous cardiac surgery	Yes	2	0.6
	No	318	99.4
Atrial fibrillation	Yes	46	14.4
	No	274	85.6
ICU stays	≤72	175	54.7
	>72	145	45.3
Intubation duration	≤24	120	37.5
	>24	200	62.5
Inotropes	Yes	195	60.9
	No	125	39.1

During open heart surgical procedures hemodynamic fluctuation and un-stabilities are common. Monitoring those hemodynamic measuring parameters in the entire procedure is the crucial component of the procedure as well as predictors of patient outcomes and prognosis. In this study the data of hemodynamic status of the study subjects shown as follows. Above half of the study subjects used the Del-Nido cardioplegia 189 (53.4%) and 180 (56.2%) patients Glucose level was 126-200.

Table 4: Operative and hemodynamic status of patients who underwent Cardiopulmonary bypass surgery at Cardiac Center Ethiopia, Addis Abeba, Ethiopia, February 2021**.**

Variables	Characteristics	Freq.	Percent
Cardioplegia type	Del-Nido	189	53.4
	Cold blood	131	46.6
Hemoglobin level	≤11.5 g/dl	62	19.4
	>11.5 g/dl	258	81.6
Systolic Blood pressure	≤ 90 mmHg	50	15.6
	90mmHg	270	84.4
Diastolic blood pressure	≤60 mmHg	140	43.8
	>60 mmHg	180	56.2
Glucose level	<126 g/dl	108	33.8
	126-200 g/dl	180	56.2
	>200g/dl	32	10
CBP time	≤180 min	276	86.2
	>180min	44	13.8
PO2 level	<150	47	14.7
	≥150	273	85.3

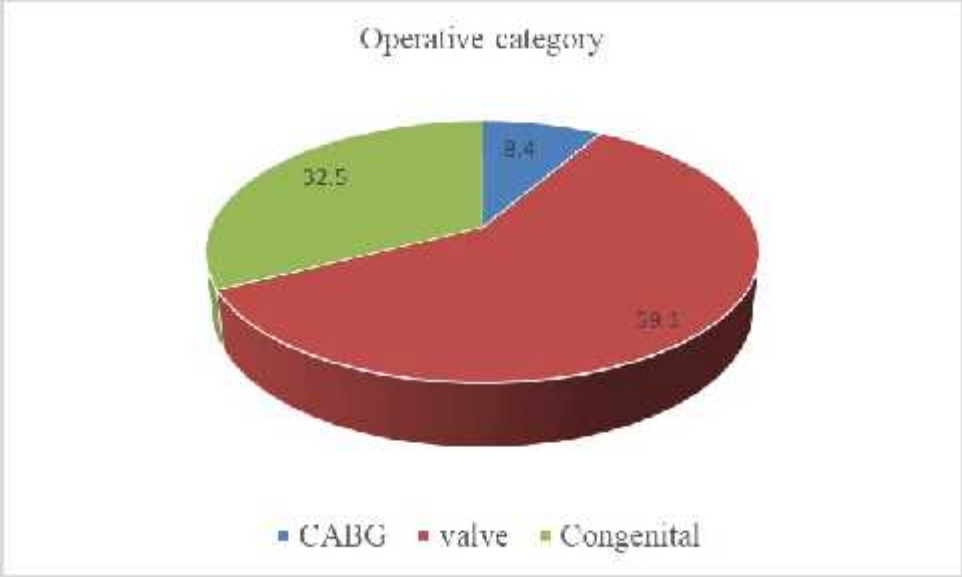

Figure 2: Showing operative categories of patients who underwent cardiopulmonary bypass surgery at Cardiac Center Ethiopia, Addis Ababa, Ethiopia, February 2021.

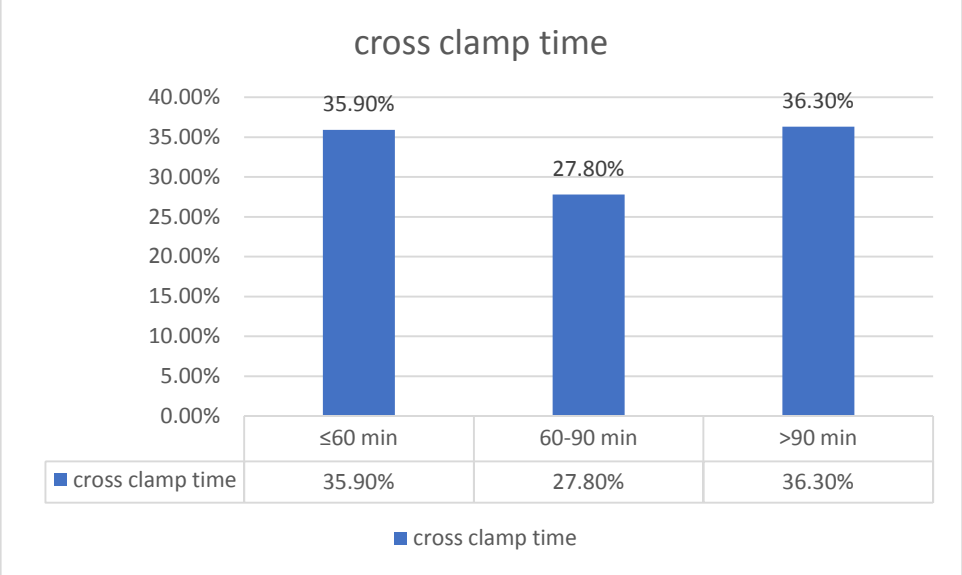

Figure 3: Represents the cross-clamp time of patients who underwent cardiopulmonary bypass surgery at Cardiac Center Ethiopia, Addis Abeba, Ethiopia, February 2021.

5.2. Adverse outcomes of Hyperlactatemia patients who underwent cardiopulmonary bypass surgery.

The outcome after any heart surgery is determined by the patient's pre-existing symptoms as well as intraoperative factors. These various factors contribute to the development of hyperlactatemia and to the outcome of undesirable postoperative outcomes for patients. In this study hyperlactatemia adversely affects patient outcomes and prognosis. ICU stay adversely affected by rise in lactate level. Patients with elevated lactate stay in ICU longer durations when compared with those with low lactate level [(74 % vs 47%), P=0.000]. In addition, patients with elevated lactate level also needs more ionotropic drug use when compared with their counter parts [(66.6 vs 57.7), P=0.000). Likewise, lactatemia increases the duration of intubation than those who had normal lactate level [(85 vs 47), P=0.000). (Table 3)

Table 5 Adverse outcomes Associated with hyperlactatemia patients who underwent cardiopulmonary bypass surgery at Cardiac Center Ethiopia, Addis Ababa, Ethiopia, February 2021.

Adverse outcomes	Classifications	Lactate level		Chi-square correlation	Comparisons
		≤3mmol/l	>3mmol/l		
ICU stays	≤ 72hrs	106	39		74 % vs 47 %
	>72 hrs.	94	81	0.000	
Prolonged intubation	≤24 hrs.	196	4		85% vs 47%
	>24 hrs.	86	34	0.000	
Ionotropic drug use	Yes	115	80	0.000	66.6% vs 57.5%
	No	85	40		

Prevalence of Hyperlactatemia

The prevalence of hyperlactatemia was assessed in this study. The result in this study is showed a higher prevalence of 37.5% (95 CI 27.1- 48.9.1).

5.3. Associated factors of hyperlactatemia among patients underwent cardiopulmonary bypass surgery

A logistic regression model was used to evaluate independent predictor's hyperlactatemia. First, a bi-variable logistic regression model was done to screen potential candidate variables for multi-variable logistic regression. Variables those had a *P* value of < 0.25 were included in a multivariable logistic regression model. After conducting bivariate analysis variables like Age, sex, systolic BP, diastolic BP, glucose level, Hemoglobin level, Heparin, Atrial fibrillation, anti-platelet drugs and operative category entered to multi-variable analysis for further analysis.

Variables having a statistically significant association in multivariable logistic regression were with hyperlactatemia were older age and female gender.

The odds of hyperlactatemia among patients underwent cardiopulmonary bypass surgery patients age > 50 years were 6.8 times higher compared with those ≤ 50years of age [AOR: 6.8 (95% CI 1.7-25), P=<0.008]. Similarly, the odds of developing hyperlactatemia among female patients underwent cardiopulmonary bypass surgery is 1.8 times higher when compared with their counterpart's [AOR: 1.9 (95% CI 1.1-3.8), P=0.048]. (Table 3).

Table 6 Bi-variable and multi-variable logistics regression of factors associated with hyperlactatemia at Cardiac Center Ethiopia, Addis Ababa, Ethiopia, February 2021.

Variables	Characteristics	Hyperlactatemia		COR 95% CI	AOR 95 % CI
		Yes	No		
Diastolic BP	≤60 mmHg	58	82	1.4(1.1-2.4)	1.8(1.2-3.9)
	>60	62	118	1	1
Systolic BP	<90	22	28	1.1(0.5-2.4)	1(0.4-2.5)
	≥90	98	172	1	1
Sex	Male	60	72	1	1
	Female	60	128	2.2(1.2-4)	1.8(1.1-3.8) *
Age	≤10	14	33	1	1
	11-20	55	73	2.6(1.1-7.9)	2.6(0.8-8.4)
	21-30	20	54	1(0.5-3.6)	1.1(0.3-4.8)
	41-50	13	24	3(1.2-10)	3.8(0.9-12.5)
	>50	18	16	5.1(3.0-15)	6.8(1.7-25) *
Atrial fibrillation	Yes	14	32	0.6(0.2-1.5)	0.6(0.2-1.4)
	No	106	168	1	1
Heparin	Yes	17	20	1.7(0.8-3.8)	2(0.8-5.2)
	No	103	180	1	1
Anti-platelet	Yes	3	1	1.7(0.6-5.6)	2.1(0.5-7.4)
	No	117	199	1	1
Glucose level	≤125	41	67	1	1
	126-200	61	119	0.8(0.4-1.8)	0.6(0.3-1.3)
	>200	18	14	1.2(0.6-3.2)	1.2(0.4-3.5)
Hemoglobin level	<11.5 g/dl	22	40	1(0.6-2)	1.8(0.7-4.3)
	≥11.5	96	160	1	1
Operative category	CABG	10	17	0.9(0.4-2.)	0.4(0.1-1.3)
	Valves	70	119	1.1(0.4-3.2)	0.5(0.2-1.5)
	Congenital	40	64	1	1

Note:

******* *Statistically significant with P-value ≤0.05,*

AOR: adjusted odds ratio, BP: blood pressure, CABG: coronary artery bypass graft, COR: crude odds ratio.

6. Discussion

In most open-heart surgeries hyperlactatemia can arise from different factors. It can be secondary to hypoxic state or non-hypoxic. Several studies showed that post-operative hyperlactatemia resulted worsen patient outcomes and longer hospital stay.

Various factors contribute to the development of hyperlactatemia and undesirable post operative outcomes for patients. In this study hyperlactatemia adversely affects patient outcomes. ICU stay adversely affected by elevated lactate level. Patients with elevated lactate stay in ICU longer durations when compared with those with low lactate level [(74 % vs 47%), P=0.000]. This is supported by different studies longer ICU stay (P = 0.013) was found to be the result of an elevated level of lactate in the blood(12)(18).

In addition, patients with elevated lactate level also needs more ionotropic drug use when compared with their counter parts [(66.6% vs 57.5%), P=0.000). this is in line with other studies (34% vs 11.8%; P = 0.001). Some surgeries require the patient to be on the ventilator for a short time after surgery as part of the plan. But patients with hyperlactatemia may need prolonged respiratory support with ventilator. In this study patients with hyperlactatemia has longer duration of intubation than their counter parts. Hyperlactatemia increases the duration of intubation than those who had normal lactate level [(85% vs 47%), P=0.000)(12)(17)(18).

The prevalence of hyperlactatemia varies according to the timing of lactate measurement. In this study was 37.5 % relatively high which is not in line with when compared studies conducted in Egypt which is 26 %(21). This variation may be due to the difference in setting and timing of lactate measurement.

Difference in lactate level among male and female after open heart surgery is uncertain but, different studies showed there is gender difference in morbidity and mortality after patients underwent open heart surgeries. In this study females have 1.8 higher chance developing hyperlactatemia when compared with their counter parts. This is supported by studies conducted in Peking Union Medical College China(24).

Risks of hyperlactatemia and prolonged hospital stay in older adults are common. In this study patients above 50 years of age had a higher chance of developing higher lactate level when

compared with those who are less than 50 years of age. Due to metabolic changes as age increases the risk of increase in lactate also increases. This is in line with study done in US America(25)

7. Strength and Limitation of the study

This study has some limitations. This is an observational single-center retrospective study which makes it susceptible to inherent selection and information biases. In addition, important variables like infections, some co-morbidities were not registered.

The strength of the study is Important adverse outcomes of hyperlactatemia were assessed. I have attempted to use rigorous statistical regression analysis to control for confounders; however, I admit that adverse outcomes and regression analysis accounts only for known confounders that are included in the multivariable model and does not account for unknown or unmeasured confounders.

8. Conclusion and Recommendations

Early rise in lactate level in patients who underwent cardiopulmonary bypass surgery is a strong and robust predictor of morbidity and undesired patient outcomes. Different patient and operative factors involved in this pathophysiology. As a result, the following recommendations are forwarded.

- ✓ **For clinicians**: - better to follow and strictly manage risk factors of hyperlactatemia as well as designing preventive and management protocols is recommended.
- ✓ **For Policy makers**: - better to design effective management and preventive policies and strategies
- ✓ **For researchers:** - it is better if it is studied by adding additional variables and prospective follow up to better identify cause and effect relationships**.**

References

1. O'connor E, Fraser J. The interpretation of perioperative lactate abnormalities in patients undergoing cardiac surgery. Anaesthesia and intensive care. 2012;40(4):598-603.
2. Mak NT, Iqbal S, de Varennes B, Khwaja K. Outcomes of post-cardiac surgery patients with persistent hyperlactatemia in the intensive care unit: a matched cohort study. Journal of Cardiothoracic Surgery. 2016;11(1):33.
3. Alam JM, Hussain A, Ali HH, Asghar SS, Riaz S. Study on Significant Correlation of Postoperative Hyperlactatemia with Poor Prognosis in Cardiac Surgery Patients. International Journal of Pharma Research and Health Sciences. 2016;4(5):1225-8.
4. Munoz R, Laussen PC, Palacio G, Zienko L, Piercey G, Wessel DL. Changes in whole blood lactate levels during cardiopulmonary bypass for surgery for congenital cardiac disease: an early indicator of morbidity and mortality. The Journal of thoracic and cardiovascular surgery. 2000;119(1):155-62.
5. Demers P, Elkouri S, Martineau R, Couturier A, Cartier R. Outcome with high blood lactate levels during cardiopulmonary bypass in adult cardiac operation. The Annals of thoracic surgery. 2000;70(6):2082-6.
6. Patra C, Gatti PC, Panigrahi A. Morbidity After cardiac surgery under cardiopulmonary bypass and associated factors: A retrospective observational study. Indian heart journal. 2019;71(4):350-5.
7. Noval-Padillo J, Serra-Gomez C, Gomez-Sosa L, Hinojosa-Perez R, Huici-Moreno M, Adsuar A, et al., editors. Changes of lactate levels during cardiopulmonary bypass in patients undergoing cardiac transplantation: possible early marker of morbidity and mortality. Transplantation proceedings; 2011: Elsevier.
8. Hajjar LA, Almeida JP, Fukushima JT, Rhodes A, Vincent J-L, Osawa EA, et al. High lactate levels are predictors of major complications after cardiac surgery. The Journal of Thoracic and Cardiovascular Surgery. 2013;146(2):455-60.
9. Andersen LW, Mackenhauer J, Roberts JC, Berg KM, Cocchi MN, Donnino MW, editors. Etiology and therapeutic approach to elevated lactate levels. Mayo Clinic Proceedings; 2013: Elsevier.
10. Mak NTJJ, Iqbal S, Varennes Bd, Khwaja aK. Outcomes of post-cardiac surgery patients with persistent hyperlactatemia in the intensive care unit: a matched cohort study. Journal of Cardiothoracic Surgery

2016:11:33.
11. Ranucci M, Toffol BD, Isgrò G, Romitti F, Conti D, Vicentin M. Hyperlactatemia during cardiopulmonary bypass: determinants and impact on postoperative outcome. Critical Care 2006;10:R167
12. Naik R, George G, Karuppiah S, Philip MA. Hyperlactatemia in patients undergoing adult cardiac surgery under cardiopulmonary bypass: Causative factors and its effect on surgical outcome Ann Card Anaesth 2016:19:668-75.
13. Jabbari A, Banihashem N, Alijanpour E, Vafaey HR, Alereza H, Rabiee SM. Serum lactate as a prognostic factor in coronary artery bypass graft operation by on pump method. Caspian J Intern Med 2013;4(2):662-666.

14. M M-S, A E, M G, M S, A K, H S, et al. RELATIONSHIP BETWEEN SERUM LACTATE LEVELS AND MORBIDITY OUTCOMES IN CARDIOVASCULAR PATIENTS AFTER CABG. Journal of Surgery Pakistan (International) 2008;13 (2)
15. Demers P, Elkouri Sp, Martineau R, Couturier A, Cartier R. Outcome With High Blood Lactate Levels During

Cardiopulmonary Bypass in Adult Cardiac

Operation

Ann Thorac Surg DEMERS ET AL 2083. 2000:70:2082–6.
16. Ricardo Munoz M, Peter C. Laussen M, Guillermo Palacio M, Lynne Zienko B, Gary Piercey B, David L. Wessel M. CHANGES IN WHOLE BLOOD LACTATE LEVELS DURING CARDIOPULMONARY BYPASS FOR SURGERY FOR CONGENITAL CARDIAC DISEASE: AN EARLY INDICATOR OF MORBIDITY AND MORTALITY. The Journal of Thoracic and Cardiovascular Surgery

2000.
17. Naik R, George G, Karuppiah S, Philip MA. Hyperlactatemia in patients undergoing adult cardiac surgery under cardiopulmonary bypass: Causative factors and its effect on surgical outcome. Ann Card Anaesth. 2016;19(4):668-75.
18. Toraman F, Evrenkaya S, Yuce M, Aksoy N, Karabulut H, Bozkulak Y, et al. Lactic Acidosis after Cardiac Surgery Is Associated with Adverse Outcome

The Heart Surgery Forum #2004-1002. 2004;7 (2), 2004 [Epub March 2004].
19. JM M, P LB, M C. Frequency, risk factors, and outcome of hyperlactatemia after cardiac surgery. Chest

123:1361-6. 2003.
20. Joudi M, Fathi M, Soltani G, Izanloo A. Factors Affecting on Serum Lactate After Cardiac Surgery. Anesth Pain Med 2014;4(4): e18514.
21. Algarni KD. The effect of hyperlactatemia timing on the outcomes after cardiac surgery. The Cardiothoracic Surgeon. 2020;28(1):18.
22. Yılmaz Ş, Yurtseven N, Tuygun AK, Yavuz Y, Canik S. Hyperlactatemia after coronary artery bypass surgery: risk factors and effect on mortality. Turk Gogus Kalp Dama. 2011;19:30-5.
23. Maillet J-M, Le Besnerais P, Cantoni M, Nataf P, Ruffenach A, Lessana A, et al. Frequency, risk factors, and outcome of hyperlactatemia after cardiac surgery. Chest. 2003;123(5):1361-6.
24. Fu SP, Zheng Z, Yuan X, Zhang SJ, Gao HW, Li Y, et al. Impact of off-pump techniques on sex differences in early and late outcomes after isolated coronary artery bypass grafts. Ann Thorac Surg. 2009;87(4):1090-6.
25. Madhavan MV, Gersh BJ, Alexander KP, Granger CB, Stone GW. Coronary Artery Disease in Patients ≥80 Years of Age. Journal of the American College of Cardiology. 2018;71(18):2015-40.

Annex

Annex I. **Questionnaire** (checklist)

Lactate level	Pre-operative	Intra-operative	Post-operative	
1. Demographics and Clinical profile				
Age				
Sex		Male		
		Female		
BSA in m^2				
Duration of intubation in days				
ICU stay in days				
2.Co-morbidities		Diabetes	Yes	
			No	
		Hypertension	Yes	
			No	
		Heart failure	Yes	
			No	

		Presence of MI	Yes	
			No	
		Previous cardiac surgery	Yes	
			No	
		Presence of stroke	Yes	
			No	
		Atrial fibrillation	Yes	
			No	
		Others		
3.Drugs	Anti-diabetes medications		Yes	
			No	
	Anti-Hypertensive medications		Yes	
			No	
	Inotropic drugs		Yes	
			No	
	Heparin		Yes	
			No	
	Anti-platelet		Yes	
			No	
	Others			
Hemodynamic status				
SBP (mmHg)	Pre-op	Intra-op	Post-op	

DBP (mmHg)	Pre-op	Intra-op	Post-op
Hemoglobin level	Pre-op		Post-op
4.Operation category	Isolated CABG		
	Isolated valves		
	Combined		
	Others		
Intraoperative variables	Cross-clamp time(min)		
	Duration of CPB (min)		
Cardioplegia type	Del-Nido	Cold Blood	
PO2 level			
Glucose level mg/dl			
Infections	Pneumonia		
	Endocarditis		
	Others		
Patient status at last.	Recovered		
	Died		