



Original Article

Study on Significant Correlation of Postoperative Hyperlactatemia with Poor Prognosis in Cardiac Surgery Patients

Junaid Mahmood Alam^{1,*}, Amna Hussain¹, Humaira Howrah Ali¹, Sarah Sughra Asghar², Syed Riaz Mahmood³

¹Department of Biochemistry, Lab services and Chemical Pathology, Liaquat National Hospital and Medical College, Karachi-74800, Pakistan.

²Department of Anatomy, Sir Syed Medical College for Girls, Karachi. Pakistan.

³Department of Pathology, Govt Lyari General Hospital, Karachi. Pakistan.

ARTICLE INFO

A B S T R A C T

Received: 16 Jun 2016
Accepted: 29 Jun 2016

Conditions such as lactic acidosis or hyperlactatemia are suggested as potential marker of inadequate oxygen perfusion, mostly in cardiac surgeries or critical care surgery patients. It was also reported that patients with hyperlactatemia exhibited mortality and elevated levels are associated with longer Intensive Care Units (ICUs) stay. Present study described the post-operative hyperlactatemia in cardiac surgery patients and its correlation with poor prognosis. This observational retrospective study was conducted for the period Dec 2010 to Dec 2015 and demographic data of all patients undergone cardiac surgeries and admitted to ICUs were collected and documented through review of files, HIMS and LIS. Standard inclusion and exclusion criteria were followed and patients within age range >30 yrs and <65 years were included. Final count of patients were forty five (n = 45) and their samples were analyzed for pre-operative and post-operative lactate and other biochemical parameters such as uric acid, creatinine, albumin, magnesium, calcium, phosphorus, lactate dehydrogenase and sugar as per standard IFCC methods. Results showed that six hours postoperative assessment of biochemical parameters inclusive of lactate (21.4 ± 12.55 mg/dl) manifested alerted levels, depicting post-operative complications and development of co-morbid. Patients with higher lactate >20mg/dl had to stay longer in ICUs (14 days stay) as compared to those with normal range of lactate level (7 day stay). Two mortality was also noted in patients with strong lactic acidosis (>20 mg/dl) as compared to none in group with normal lactate levels. Conclusion can be drawn that post-operative hyperlactatemia and lactic acidosis in cardiac surgery patients is a significant marker to detect poor outcome and 6 hrs post-operative lactate level can predict length of stay in ICUs and prospect of developing adverse outcome and co-morbid.

Key Words: Hyperlactatemia, post-operative, cardiac surgery, COPD

1. INTRODUCTION

Etiology of hyperlactatemia and lactic acidosis is complex, from factors causing tissue hypoxia, pulmonary abnormalities, Ischemic shock, low levels of hemoglobin and generalized an-aerobic conditions¹⁻

Corresponding author *

Dr Junaid M Alam
Liaquat National Hospital and Medical College, Karachi-74800,
Pakistan.
E Mail: dr_jmalam@hotmail.com

⁵. In hypoxic state body continue to receive oxygen through an-aerobic glycolytic pathway, thus increasing production of lactate⁶. In healthy individuals, lactate overproduction is maintained through balance between production and clearance^{7,8}. Conditions such as lactic acidosis or hyperlactatemia are noted as potential marker of inadequate oxygen perfusion, mostly in cardiac surgeries or critical care surgery patients⁷. However, accelerated production of lactate doesn't always meant hypoxic conditions, as lactic acidosis can also occur in non-hypoxic conditions as well⁹.

Lactate is also known an acute critical care marker, used mostly as prognostic tool for patient's undergone cardiac or critical care surgeries to assess better or worsening outcome^{1,10-12}. It was reported that patients with hyperlactatemia or those with slow normalizing lactate levels exhibited mortality and non-normalization of elevated levels are associated with longer Intensive Care Units (ICUs) stay and 100% post-operative complication and mortality rate¹³.

Present study described the post-operative hyperlactatemia in cardiac surgery patients and its correlation with poor prognosis, increase in length of stay in ICUs and development of several physiological dysfunctions resulting in alterations in biochemical parameters.

2. MATERIAL AND METHODS

2.1 Patient's selection and Study Design: It's an observational retrospective study conducted at Departments of Biochemistry Laboratory services, Liaquat National Hospital, Karachi and Pathology, Govt Lyari General Hospital, Karachi, for the period Dec 2010 to Dec 2015. Demographic data of all patients undergone cardiac surgeries and admitted to ICUs were collected and documented through review of files, HIMS and LIS. Inclusion criteria is dependent on history of myocardial infarction, hypertension, congestive heart failure, vascular surgery COPD and

co-morbid such as diabetic and renal insufficiency and age >30 yrs and <65 years. Patients with indigenous multiple surgeries other than cardiac, <30 yrs and >65 yrs, missing history of co-morbid and patients on dialysis were excluded. Data of a total of 102 patients were reviewed, out of which only fifty (n = 50) were documented as per availability of all demographic data, pre and post-operative information, including biochemical parameters statistics. Final count of patients were forty five (n = 45), post-operatively as five were excluded from cardiac surgery procedures due to pre-operative complications.

2.2 Analytical methods: Blood samples were analyzed for lactate and other biochemical parameters such as uric acid, creatinine, albumin, magnesium, calcium, phosphorus, lactate dehydrogenase and sugar according to the methods described earlier¹⁴⁻¹⁶. Post-operative blood sample analyses were performed 4-6 hrs after surgery and after 24 hrs post-operatively. Normal ranges for biochemical parameters are; lactate 4.5-19.8 mg/d, urea < 50 mg/dl; creatinine 0.5-1.5 mg/dl; albumin 3.4-4.8 gm/dl; magnesium 1.70-2.55 mg/dl; calcium 8.6-10.2 mg/dl; phosphorus 2.5-4.5 mg/dl; sugar 80-160 mg/dl. Data is reported as mean \pm SD.

2.3 Statistical analysis: Biochemical parametric data of Pre, post-operative and during ICUs stay were compared and analyzed by SPSS ver 13.0. Results were considered significant when $P < 0.05$.

3. RESULTS

Results are summarized in Table 1 to 4. Pre-operative demographic and biochemical parameters including lactate level of cardiac surgery patients showed normal within the reference range values (Table 1). A total of 50 patients were selected for cardiac surgeries with average age of 46.45 ± 15.25 , 39 males and 11 females. However, five were removed from the list of surgery because of pre-operative complications. Thus post-operative final counts of patients were males 35 and

females 10 (Table 2). Six hours postoperative assessment of biochemical parameters inclusive of lactate, showed alerted levels, manifesting post-operative complications and development of co-morbid. All metabolic and organ function parameters showed higher or lower than normal levels with strong evidence of lactic acidosis (Table 2). Twenty four to forty eight hours post-operative assessment showed gradual normalization of lactic acidosis and metabolic biochemical parameters (Table 3). This confirms the correlation of declining lactic acidosis with normalization of body functions. It was also noted that patients with higher lactate >20mg/dl (Table 4) had to stay longer in ICUs (14 days stay) as compared to those with normal range of lactate level (7 day stay). Two mortality was also noted in patients with strong lactic acidosis (>20 mg/dl) as compared to none in group with normal lactate levels.

4. DISCUSSION

Present study described the role of lactic acidosis or hyperlactatemia, post-operatively, in cardiac surgery patients that resulted in lengthy stay in ICUs, alterations of body functions and metabolic parameters, and in some cases, mortality. Lactate levels were normally determined in ICU settings to monitor development of lactic acidosis, most importantly in cardiac surgery patients, post-operatively^{1,17,18}. Previous reported studies have mentioned correlation of post-operative elevated lactate levels with increased risk of mortality and poor outcome^{19,20}. Earlier studies emphasized association of post-operative mortality with intra and post hyperlactatemia^{4, 13, 21}. Previously reported data also suggested that elevation of post-operative lactate concentration in ICU was a significant indicator of poor outcome²²⁻²⁴. Similarly, the plethora of delayed hyperlactatemia as occurred mostly 4-24 hrs post-operatively in some cardiac surgeries results in onset of

co-morbid such as hyperglycemia, elevated catecholamine and altered biochemical parameters^{6,7}. In addition, elevated lactate level was reported to be associated with excess mortality²⁵. Our data also suggested similar correlation as two patients that had prolonged ICU stays and lactate greater than 20 mg/dl suffered mortality. Furthermore, those with normalized lactate levels, although did admitted in ICU, recovered early and showed no adverse outcome or mortality. Earlier studies suggested cardiopulmonary and cardiogenic reasons for lactic acidosis post-operatively^{1, 26}. Kidney dysfunction, as seen in our study as well, reported to be one of such co-morbid^{1, 26}. Other non-cardiogenic factor might include precipitation of systemic inflammation²⁷ that resulted in hyperlactatemia. It was also noted that continual and delayed hyperlactatemia also synergies hypo-perfusion resulting in lengthy ICU stay, persistent hyperlactatemia and alteration of blood creatinine levels¹.

Table 1: Pre-Operative demographic and biochemical characteristic of cardiac patients

Parameters	Data, Mean ± SD
Patients	n = 50
Age	46.45 ± 15.25
Gender	--
Males	39 (78.0%)
Females	11 (22.0%)
History of previous cardiac diseases	23
Lactate levels (pre-Operative) (mg/dl)	3.4 ± 1.0
Pre-Operative biochemical characteristics	
Urea (mg/dl)	15.0 ± 2.5
Creatinine (mg/dl)	0.80 ± 0.02
Albumin (g/dl)	3.95 ± 0.85
Magnesium (mg/dl)	2.15 ± 0.90
Calcium (mg/dl)	8.95 ± 2.50
Phosphorus (mg/dl)	3.5 ± 1.10
LDH (IU/L)	255.45 ± 20.55
Sugar (mg/dl)	108.10 ± 18.70

Results are expressed in mean ± SD

Table 2: Post-Operative (6 hrs) demographic and biochemical characteristic of cardiac patients

Parameters	Data, Mean ± SD
Patients	n = 45
Age	49.75 ± 16.30
Gender	--
Males	35 (70.0%)
Females	10 (20.0%)
History of previous cardiac diseases	21/45 (46.66%)
Lactate levels (Post-Operative) mg/dl	21.4 ± 12.55
Post-Operative biochemical characteristics	
Urea (mg/dl)	65.0 ± 10.60
Creatinine (mg/dl)	2.55 ± 1.25

Albumin (g/dl)	2.68 ± 0.85
Magnesium (mg/dl)	1.65 ± 0.75
Calcium (mg/dl)	7.4 ± 4.30
Phosphorus (mg/dl)	5.5 ± 2.35
LDH (IU/L)	454.70 ± 68.55
Sugar (mg/dl)	145.25 ± 57.30

Results are expressed in mean ± SD

N = 5 didn't recommended for cardiac procedures

Table 3: Post-Operative (24 hrs-48 hrs) demographic and biochemical characteristic of cardiac patients

Parameters	Data, Mean ± SD	
	24 hrs	48 hrs
Patients	n = 45	
Age	49.75 ± 16.30	
Gender	--	
Males	35 (70.0%)	
Females	10 (20.0%)	
History of previous cardiac diseases	21/45 (46.66%)	
Lactate levels (Post-Operative) mg/dl	16.55 ± 11.60	14.40 ± 9.45
Post-Operative biochemical characteristics		
Urea (mg/dl)	45.35 ± 11.45	35.45 ± 9.60
Creatinine (mg/dl)	2.00 ± 1.50	1.45 ± 0.85
Albumin (g/dl)	3.10 ± 1.15	3.44 ± 1.25
Magnesium (mg/dl)	2.01 ± 0.95	2.35 ± 0.75
Calcium (mg/dl)	8.10 ± 4.45	8.45 ± 3.40
Phosphorus (mg/dl)	4.20 ± 3.10	3.10 ± 2.15
LDH (IU/L)	385.45 ± 75.60	355.55 ± 65.35
Sugar (mg/dl)	110.25 ± 55.35	98.80 ± 34.60

Results are expressed in mean ± SD

N = 5 didn't recommended for cardiac procedures

Table 4: Post Operative length of stay in hyperlactatemic and normo-lactate patients

Parameters	Lactate > 20 mg/dl (hyperlactatemia) n = 16*	Lactate 10-18 mg/dl (normo-lactate) n = 29**	P < 0.05
Length of stay	14 days	7 days	0.01
Admission in ICU	n = 14 (87.50%)*	n = 11 (37.93%)**	0.02
Duration in ICU	8.10 ± 2.15 days	4.50 ± 1.45 days	0.001
Mortality (ICU admitted)	n = 2 (14.28%)*	None**	--
Morbidity (ICU admitted)	n = 12 (85.71%)*	n = 3 (27.27%)**	0.001

Results are expressed in mean ± SD

5. CONCLUSION

Preset study described hyperlactatemia, 6 hrs post-operatively in cardiac surgery patients and its resultant adverse outcomes and lengthy ICU stay. It was observed that after 24-48 hrs, normo-lactatemia did occur in patients with normalization of metabolic and biochemical parameters. However in some cardiac surgery patients, that exhibited hyperlactatemia (>20 mg/dl), ICUs stay extended upto 14 days, with sever co-morbid and few mortalities. Moreover, normo-

lactatemia patients stayed less in ICUs, recovered better, and manifested less co-morbidity. Thus it is concluded that post-operative hyper-lactatemia and lactic acidosis in cardiac surgery patients is a significant marker to detect poor outcome and 6 hrs post-operative lactate level can predict length of stay in ICUs and prospect of developing adverse outcome and co-morbid.

6. REFERENCES

1. Mak NTJJ, Sameena I, de Varennes B, Khwaja K. Outcomes of post-cardiac surgery patients with persistent hyper-lactatemia in the intensive care unit: a matched cohort study. *J Cardiothoracic surgery* 2016; 11: 33-39
2. Boldt J, Piper S, Murray P, Lehmann A. Case 2-1999 severe lactic acidosis after cardiac surgery. Signs of Perfusion defects?. *J Cardiothorac Vasc Anesth*, 1999; 13 (2): 220-224.
3. Okorie ON, Dellinger P. Lactate biomarker and potential therapeutic target. *Crit Care Clin.*, 2011; 27 (2): 299-326.
4. Mustafa I. Effects of cardio-pulmonary bypass on lactate metabolism. *Intensive Care Med.*, 2003; 29 (8): 1279-1285.
5. Luft FC. Lactic acidosis updates for critical care clinicians. *J Am Soc Nephrol.*, 2001; 12 (1): 1515-1519
6. O'Connor E, Fraser JF. The interpretation of peri-operative lactate abnormalities in patients undergoing cardiac surgery. *Anaesth Intensive Care.* 2012; 40 (4): 598-603.
7. Jabbari A, Banihashem N, Alijanpour E, Vafaey HR, Aleraza 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
8. Khosravani H, Shahpoori R, Stelfox HT, Kirkpatrick AW, Laupland KB. Occurrence and

- adverse effect on outcome of hyperlactatemia in the critically ill. *Crit Care* 2009; 13: R90
9. Maillet JM, Le Besnerais P, Cantoni M, Nataf P, Ruffenach A, Lessana A, Brodaty D. Frequency, risk factors, and outcome of hyperlactatemia after cardiac surgery. *Chest* 2003; 123: 1361-1366.
 10. Kogan A. The impact of hyperlactatemia on post-operative outcome after adult cardiac surgery. *J Anesth* 2012; 26 (2): 174-178.
 11. Zanate B, Kubik M, Reichenspurner H. Lactate level as prognostic factor of mortality in patients after cardiac surgery. *Thorac Cardiovasc Surg* 2010; 58: 43-49
 12. Mirmohammad-sadeghi M, Etesampour A, Gharipour M, Saeidi M, Kiani A, Shamsolkotabi H, Torknezhad Mr, Farahmand N. Relationship between serum lactate levels and morbidity outcomes in cardiovascular patients after CABG. *J Surg Pak Int.* 2008; 13 (2): 88-91.
 13. McNelis J, Marini CP, Jurkiewicz A, Szomstein S, Simms HH, Ritter G, Nathan IM. Prolonged lactate clearance is associated with increased mortality in the surgical intensive care unit. *Am J Surg* 2001; 182 (5): 481-485.
 14. Alam JM, Zia ul Islam, Sherwani SK, Asghar SS, Mahmood SR, Sultana I, Ansari MA. Determination of Hyperlactatemia and Acidosis in Adult Patients with Cardiac Diseases and Dysfunctions. *FUUAST J. BIOL.*, 2012; 2(2): 49-54
 15. Junaid M Alam, S.K.Sherwani, Amna Hussain, S.Matinuddin, R.Kausar, Aijaz Ahmed and M.A.Ansari Comparative assessment of analytical performance of conventional chemistry analyzer and modular Cobas 6000 system using routine chemistry parameters. *Middle-East Journal of Scientific Research* 2014 21(8): 1283-1287.
 16. Sheikh matinuiddin, Junaid Mahmood Alam, Mahwish Amin, Howarh Ali, Shiek Khalid Mahmood. Precision standardization of lactate assay on Cobas 6000 c501 and comparative analysis with corresponding lactate dehydrogenase concentrations. *IJSET-international Journal of innovative Science, Engineering & Technology: Vol 2 (10): 36-38*
 17. Hajjar LA, Almeida JP, Fukushima JT, Rhodes A, Vincet JL, Osawa EA, Galas FRBG. High lactate levels are predictors of major complications after cardiac surgery. *Surgery* 2013; 146 (2): 455-460
 18. Attana P, Lazzeri C, Picariello C, Dini CS, Gensini GF, Valente S. Lactate and lactate clearance in acute cardiac care patients. *Eur Heart J Acute Cardiovasc Care*, 2012; 1 (2): 115-121.
 19. Joudi M, Fathi M, Soltani G, Izanloo A. Factors affecting on serum lactate after cardiac surgery. *Anesth Pain Med.*, 2014; 4 (4): e181514
 20. Perfacto SM, Casas LSR, Balderas JJ, Azcueta MB. Lactate level as an early prognostic marker of major adverse events in Pediatric open heart surgery. *Phil Heart Center J* 2012; 16 (2): 27-34.
 21. Toraman F. Lactic acidosis after cardiac surgery is associated with adverse outcome. *Heart Surg Forum* 2004; 7 (2): 155-159.
 22. Ranucci M. Anaerobic metabolism during cardiopulmonary bypass: predictive value of carbon dioxide derived parameters. *Ann Thorac Surg.*, 2006; 811 (6): 2189-2195
 23. Ranucci M. Hyperlactatemia during cardiopulmonary bypass: determinants and impact on post-operative outcomes. *Crit Care.*, 2006; 10: R167.
 24. Marty P. 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; 3: 3

25. Duke T, Butt W, South M, Karl T. Early markers of adverse events in children after cardiac operations. *J Thorac Cardiovasc Surg.*, 1997; 114: 1042-1052
26. Meregalli A. Occult hypoperfusion is associated with increased mortality in hemodynamically stable, high-risk, surgical patients. *Crit Care* 2004; 8 (2): 60-65
27. Ryan T, Balding J, Mc Govern EM, Hinchion J, Livingstone W, Chughtai Z, Smith OP. Lactic acidosis after cardiac surgery is associated with polymorphism in tumor necrosis factor and interleukin 10 genes. *Ann Thorac Surg.*, 2002; 73: 1905-1909

Conflict of Interest: None

Source of Funding: Nil