Original Research Article

Predictive value of lactate clearance for in-hospital mortality in cardiogenic shock following ST elevation myocardial infarction (STEMI)

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Abstract

Introduction: Hyperlactatemia indicates widespread inadequate tissue perfusion and oxygenation. In patients with critical and severe illnesses, the prolonged presence of lactic acidosis correlates with overall oxygen debt, multi organ dysfunction and mortality.

Objective: To determine predictive value of lactate clearance for in-hospital mortality in cardiogenic shock following STEMI and to correlate lactate clearance with TIMI and GRACE risk scores.

Materials and methods: Fifty patients of ≥18 years of age (Mean age 55.76 ± 11.22 years, 78% Males) in cardiogenic shock following STEMI were observed between January 2018 to December 2019. Venous blood lactate was done at admission and twelve hours after admission. Lactate clearance (LC) was correlated with in-hospital mortality and with clinical risk scores.

Results: Out of fifty patients 17 (34%) died during hospital stay. In-hospital mortality was 89.47% in patients with LC ≤10% against no mortality in patients with LC >10% (P= 0.000). LC ≤10% predicted in-hospital mortality with sensitivity of 100%, specificity of 93.93%, PPV of 89.5 and NPV of 100%.

Conclusion: Lactate clearance at first twelve hours of admission is a very sensitive and specific test to predict mortality in patients with cardiogenic shock due to STEMI.

Key words

Glycolysis, Hyperlactatemia, Lactic acidosis, Lactate clearance, Cardiogenic shock, ST elevation MI.

Introduction

Lactate is produced during glycolysis under both aerobic and anaerobic conditions. Normal daily production of lactate is up to 20 mmol/kg. Lactate from cells is transported back to the liver. In liver lactate is converted into pyruvate by the Cori cycle, using the enzyme lactate dehydrogenase. Pyruvate is the designated substrate of gluconeogenesis and is converted to glucose 6 phosphate. Thus lactate is the largest source of gluconeogenesis in both kidney and liver [1].

Glycolysis is a process by which glucose is converted to two pyruvate molecules, and a hydrogen ion, in the cytoplasm. In aerobic metabolism, pyruvate is transported to mitochondria and is oxidized into acetyl CoA which then enters citric acid cycle to produce energy. Ultimately 36 molecules of ATP are generated for every molecule of glucose. Hypoxia impairs metabolism of pyruvate which is then oxidized to its alternate metabolite, lactate. Elevated circulating lactate concentration thus indicates widespread inadequate tissue perfusion and oxygenation [1, 2].

A blood lactate level above the normal value of 2 mol /litre (mM/L)) is defined as hyperlactatemia. A blood lactate concentration >5 mM/L associated with metabolic acidemia (blood pH < 7.35) is defined as lactic acidosis [2]. In patients with critical illneses the presence of either has major prognostic significance. Overall, the level of lactic acidosis and it's persistence in critically ill patients correlates with overall oxygen debt, potential organ dysfunction, increased mortality and poor prognosis [3, 4, 5].

Lactate clearance is defined as lactate at ED presentation minus lactate at specified time interval, divided by lactate at ED presentation, then multiplied by 100. Serial blood lactate measurements are used to calculate lactate clearance and it has shown to be predictive for in-hospital mortality in critically ill patients [3, 6] Previously some studies have evaluated the utility of blood lactate in predicting either the development of cardiogenic shock following STEMI [7]. Hyperactatemia, especially if sustained can predict in hospital mortality in STEMI with circulatory failure [8, 9] as well as 30 day mortality [10] But there are very few studies on lactate clearance in ST-elevation myocardial infarction with circulatory failure. Hence we conducted this study at our centre to evaluate the utility of the same in patients with STEMI and cardiogenic shock.

TIMI risk score is a convenient bed side scoring system using clinical variables like age, presence of diabetes, Hypertension, angina, systolic blood pressure, heart rate at admission, Killip's class, weight, presence of anterior wall infarction or LBBB. It is useful to assess mortality risk in STEMI [11]. GRACE score is a scoring system used to predict in hospital mortality in acute coronary syndromes. It uses eight parameters, namely, age, heart rate, SBP, serum creatinine at admission, Killip's class, cardiac arrest at admission, positive troponin T, and ST segment deviation. A score less than 60 at admission has a mortality of less than 0.2%. If the score is 250 or more, the mortality is more than 50% [12]. We correlated lactate clearance with both these scores in patients in cardiogenic shock.

Materials and methods

Study design: Prospective observational study.
Place of study: Osmania General Hospital, Hyderabad.
Study duration: Two years (January 2018 to December 2019).

Patient selection

Inclusion criteria: All patients ≥ 18 years of age in cardiogenic shock, defined by systolic blood pressure less than 90 mmHg lasting more than 30 minutes or vasopressors required to achieve a systolic pressure more than 90 mmHg following ST elevation myocardial infarction, admitted in Osmania General Hospital, Hyderabad from January 2018 to December 2019.

Exclusion criteria:

- Age less than 18 years.
- Death/LAMA within 12 hours of admission.
- Do not resuscitate orders.
- Inborn errors of metabolism.
- Trauma patients
- Patients having other systemic disease.
- Refusal for the consent.

Institutional Ethics committee approval was obtained for study protocol. Written consent was taken from all the study participants. Demography, history and clinical examination of all cases of STEMI in cardiogenic shock was noted. All preliminary investigations for detecting myocardial infarction and organ failure including those needed to assess TIMI and GRACE risk scores (e. g. ECG, Cardiac enzymes, Creatinine etc.) were done at admission. Blood gas analysis (ABG) including lactate was done with 'Radiometer Copenhagen ABL 555' blood gas analyzer at admission and twelve hours after admission. All patients were managed with IV inotropic support, diuretics where indicated, IV fluid aliquots and dobutamine in case of inferior wall infarctions.

Temporary pacemaker implantation was done where indicated. Intraaortic balloon pulsation support was not available during the study at our institute. Lactate clearance was defined as lactate at ED presentation minus lactate at twelve hours, divided by lactate at ED presentation, then multiplied by 100. TIMI and GRACE risk scores were calculated with online calculators. Final diagnosis and outcome (in-hospital mortality) was recorded.

Statistical analysis

We stratified patients into two groups depending upon lactate clearance:

Lactate clearance group (LC >10%)

Delayed or Non-clearance group (LC ≤10%)

We compared the two groups with each other and correlated lactate clearance with in-hospital mortality. We also calculated TIMI and GRACE risk score at admission for prediction of expected mortality and correlated the same with lactate clearance. Quantitative data values were presented as mean ± SD. Survivors and non-survivors were compared using the Mann-Whitney test for continuous values and with Fisher's exact test for categorical variables. Pair wise comparison was done by Wilcoxon's signed-rank test. Chi-square test was used for continuous variables. A p value of <0.05 was taken as statistically significant. Sensitivity, specificity, positive predictive value and negative predictive value of lactate clearance were calculated. The statistical package used was Microsoft SPSS version 21.0.

Results

Out of 50 patients, eighty percent were above 45 years of age while twenty percent presented at earlier age of ≤ 45 years. Mean age was 55.76 ± 11.22 years. Eleven (22 %) were females and 39 (78 %) males with a male to female ratio of 3.54:1. A total of 33 (66%) patients survived and 17 (34%) died during hospital stay. Mortality was slightly higher in females but statistically insignificant (P=0.560). Mortality rate increased with age, being highest (72.2%) in patients above 60 years of age suggesting age as one of the strongest predictors.

Mean lactate levels were inversely related with survival. Mean lactate levels at presentation and at 12 hours after admission were significantly different in survived (P = 0.000) and dead (P=0.003) patients. Lactate clearance was significantly high in survived patients (P= 0.000). AUROC for lactate clearance in relation with mortality at 12 hours of admission was 0.989 (P= 0.000). Lactate clearance at first

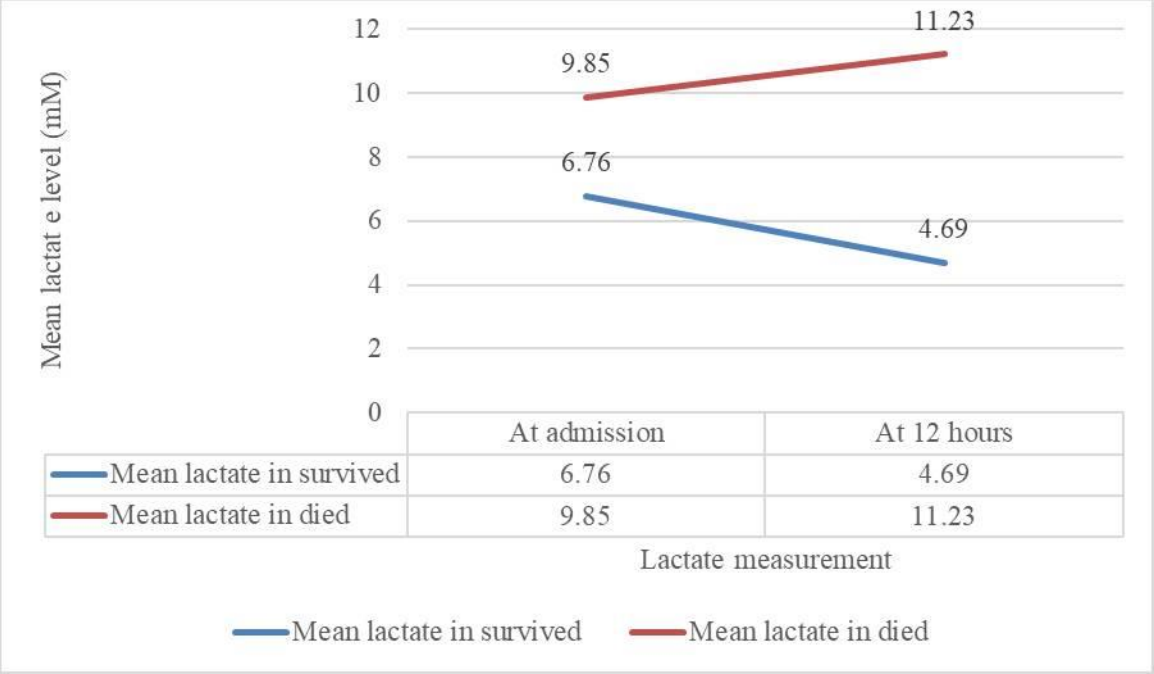
twelve hours of admission is a very sensitive (Sensitivity = 100%) and specific (Specificity = 93.93%) test with positive predictive value of 89.5% and negative predictive value of 100% to predict mortality in patients with cardiogenic shock due to STEMI.

Almost all patients belonged to high risk category according to both TIMI and GRACE risk scores. There was inverse relationship between risk scores and lactate clearance. There was significant correlation of lactate clearance with GRACE score (*P* = 0.004) in survived patients but was insignificant correlation with TIMI score (*P*= 0.279). Insignificant correlation of lactate clearance with both scores was seen in dead patients (**Table – 1, 2** and **Figure – 1, 2**).

Table - 1: Territory of infarction and percentage of patients.

Diagnosis	Number of patients	Percent	Cumulative percent
AWMI	23	46.0	46.0
ALWMI	20	40.0	86.0
ILWMI	2	4.0	90.0
IPWMI	1	2.0	92.0
IWMI	1	2.0	94.0
IPWMI+RV	2	4.0	98.0
IWMI+RVM	1	2.0	100.0
Total	50	100.0	

Figure - 1: Mean lactate levels in died vs. survived.



Discussion

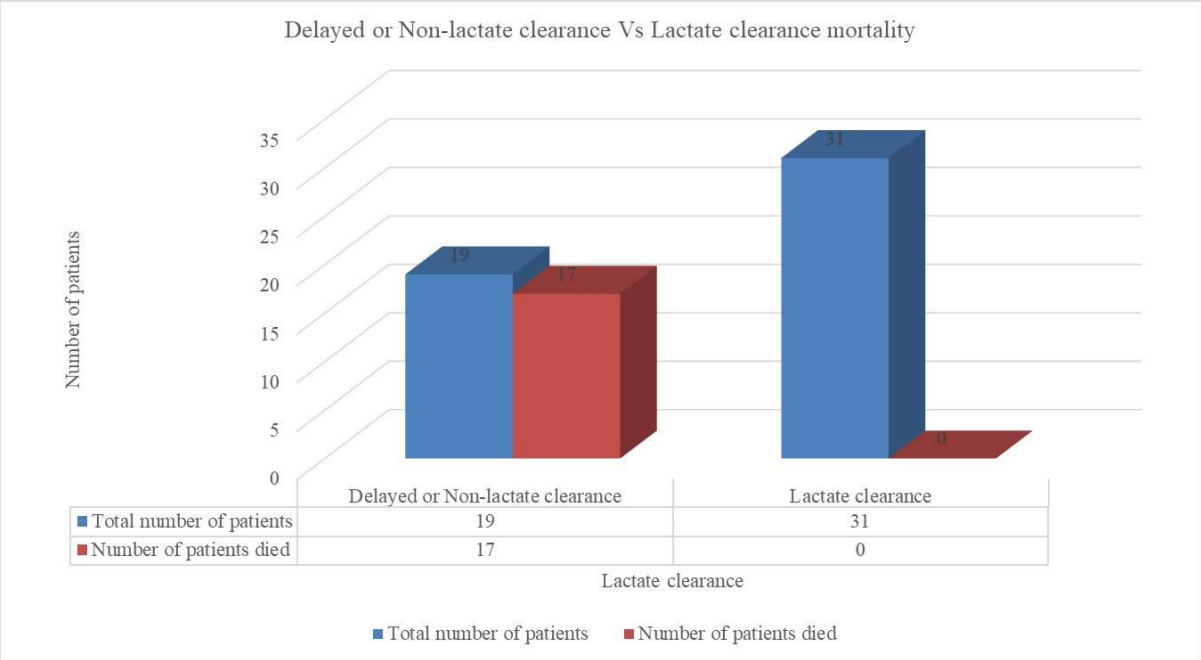
This study was performed with the aim to determine predictive value of lactate clearance at twelve hours after admission for in-hospital mortality in cardiogenic shock following ST elevation myocardial infarction.

In 2000, Suistomaa, et al. studied 98 unspecified ICU admitted patients with arterial lactate every 2 hour for 24 hours and showed that persistent hyperlactatemia (> 6 hours) was associated with lower survival rates than transient hyperlactatemia (36.8% vs. 0%, p =0.008) [13].

Similarly, in our study lower survival was noted in subjects with persistent hyperlactatemia at the end of 12 hours. (89.5% vs. 0%, p =0.000).

Nguyen, et al. suggested the value of monitoring for a lactate clearance of 10% or more during the early resuscitation of subjects with severe sepsis showing evidence of hypoperfusion [14]. In subjects with lactate clearance of less than 10% there was 41% higher mortality than those with clearance of more than 10% (60% vs. 19% mortality, respectively) during the early resuscitative period. In our study there was 89.5% mortality in patients who failed to reach lactate clearance of 10% against zero percent whose lactate clearance was ≥10%.

Figure - 2: Delayed or non-lactate clearance vs lactate clearance mortality.



Kliegel, et al. evaluated patients who were cardiac arrest survivors at least for 48 hours [15]. In these patients sustained hyperlactatemia (>2.0 mM after 48 hours) was predictive for mortality with a specificity of 86%. It was also associated with neurological sequelae. Similarly, sustained hyperlactatemia >2 Milimole (mM) at 12 hours is predictive for mortality with specificity of 93.93% in our study.

Attana P, et al. in 2012 studied 51 patients with cardiogenic shock following STEMI. At 12 hours after admission, survivors had better lactate clearance (P = 0.013) and patients with 12 hour lactate clearance <10% showed a significantly lower survival rate [16]. Similarly, in our study survivors had higher mean lactate clearance. (p = 0.000). A lactate clearance < 10% correlated with higher mortality at the end of 12 hours (P = 0.000).

In our study, secondary outcome was to establish correlation of TIMI and GRACE scores with lactate clearance. There was significant correlation of lactate clearance with GRACE score (p= 0.004) in survived patients but was insignificant with TIMI score (p = 0.279). Insignificant correlation of lactate clearance with both scores in died patients.

Similar to most of the studies discussed above, in our study a lactate clearance ≤10% at 12 hours is having high prediction for in-hospital mortality. Hence, lactate clearance is a very sensitive screening test for prediction of mortality. It can also guide the efforts to hemodynamically stabilize the patient.

Table - 2: Mean lactate levels at admission and at 12 hours, and lactate clearance in both survived and dead patients.

Parameters	**Number: N (%)**	***P* value**
Number of patients	50	-
Gender: Male Female	39 (78%) 11 (22%)	0.000
Mortality: Survived Died	33 (66%) 17 (34%)	0.000
Mean lactate in survived : At admission At 12 hours	 6.764 ± 1.395 4.697 ± 1.520	0.000
Mean lactate in died : At admission At 12 hours	 9.853 ± 2.357 11.235 ± 2.781	0.003
Mean LC : Survived Died	 31.456 ± 13.848 -14.649 ± 15.611	0.000
LC >10% (N=31): Survived Died	 31 (100%) 0 (0%)	0.000
LC≤10% (N=19): Survived Died	 2 (10.52%) 17 (89.47%)	0.000
Predictive value of LC at 10% cutoff: Sensitivity Specificity PPV NPV	 100% 93.93% 89.5% 100%	-

Limitations

We considered only critically ill patients, so we couldn't predict role of lactate clearance in non-critically ill patients. We have considered a sampling interval of 12 hours which is too long for early prediction of mortality in critical subjects. The study included diabetics receiving metformin though metformin was stopped once patients were admitted. The cut-off value of lactate clearance that we used needs to be validated by larger studies with better sample size. Relationship of lactate clearance with TIMI or GRACE risk score could not be established well, probably due to small sample size.

Conclusion

Lactate clearance at first twelve hours of admission is a very sensitive (sensitivity = 100%) and specific (specificity = 93.93%) test with positive predictive value of 89.5% and negative predictive value of 100% to predict mortality in patients with cardiogenic shock due to STEMI.

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