

ROLE OF SERUM LACTATE AS A PREDICTOR OF MORTALITY IN BURNS PATIENTS >15% TBSA

Royce Varghese¹, Abdul Siyad A K², Haridas T V³

¹⁻³Department of General Surgery, Government Medical College Thrissur, Kerala, India.

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Corresponding Author:
Dr. Abdul Siyad A K,
Email: abdulsiyadak@gmail.com

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Abstract

Background: India is a highly populated country in the world which has an estimated annual burn incidence of 6-7 million. 70 % of burn victims are in most productive age group 15-40 yrs and belong to poor socioeconomic status. Serum lactate levels are commonly elevated in acutely ill patients, in which tissue hypoperfusion is probably the most common cause of elevation. Correlation between elevated lactate levels and the clinical outcomes has been well accepted in hemorrhagic and septic shock. According to National Programme for Prevention, Management and Rehabilitation of Burn Injuries (NPPMRBI) under MOH&FW all burns above 15% in adults are considered major burns and need hospitalization and fluid resuscitation. This study attempts to assess the role of initial serum lactate value in predicting the mortality in burns patient with TBSA > 15 %. **Materials and Methods:** A prospective observational study was done in year 2021-2022 64 patients admitted with burns TBSA >15% , in department of general surgery , Govt. Medical College Thrissur were included in the study. History , examination was done. Serum lactate was measured within the first day of admission and patients were divided in two groups, one with serum lactate more than 2 mmol/l and other group with less than or equal to 2 mmol/l and was observed for the treatment days to assess whom survived. **Results:** Out of 64 patients evaluated, 38 patients had serum lactate value > 2 mmol/l , of the 38 patients 34 patients succumbed, which is about 89.5% of participants. 26 patients had serum lactate value less than or equal to 2mmol/l of which 25 patients survived, which is about 96.2% of participants. Age of participants ranged from 15-88 years with mean of participants age was 46.5years (19.9%). Out of the patients participated 54.7% were females. Majority of patients belonged to 15-45 TBSA of burns, coming around 50% of those involved in the study. 20.3 % belonged to the range of 45-75 TBSA and 29.7% participants belonging to 75-100 TBSA. Based on the type of burns , full thickness burns was present in 45.3 % participants and inhalational burns in 53.3 %. Fischers exact test was done to check association between serum lactate level and outcome. Logistic regression analysis was done to measure the association between the same in terms of risk ratio. Multilevel logistic regression analysis was done to estimate risk ratio of death based on percentage of burns. 75-100% burns predicted death perfectly hence was not analysed in the model. 45 – 75% burns had a risk ratio of 4.1 [95% CI 1.9 – 8.9] with p-value < .001 suggested significant association between death and serum lactate level > 2mmol/l. Logistic regression analysis revealed a risk ratio 23.3 [95% CI 3.4 – 159.4] of death for serum lactate level > 2mmol/l compared to lactate level less than or equal to 2mmol/l with p-value .001 Among patients with serum lactate value below or equal to 2mmol/l , 96.2% survived with only 3.8% succumbed to death. Whereas those patients with value more than 2mmol/l, 89.5% succumbed to death with only 10.5% survived. **Conclusion:** There has been significant association between serum lactate value and mortality in burns patients. Those patients with high serum lactate value had worse outcome. Serum lactate levels clearly predict life or death following serious burns, which helps care giver to take aggressive measures or therapeutic options to reduce the mortality.

INTRODUCTION

A serious burn causes a fast reduction in intravascular volume. Burn shock is initially hypovolemic, with hemodynamic alterations such as decreased plasma volume, cardiac output, urine output, and increased systemic vascular resistance, resulting in reduced peripheral blood flow.

Resuscitation of trauma and surgical critical care patients has traditionally been guided by a combination of basic laboratory results, invasive monitoring, and clinical findings, but the best guide to the resuscitation endpoint is still up for debate. The ideal resuscitation marker would evaluate tissue hypoxia resolution and be predictive of patient death and prognosis. Abnormal plasma lactate and delayed lactate clearance are thought to be precise markers of cellular hypoxia and stress, though this is not universally recognised. Lactate has been demonstrated to be a strong predictor of outcome in severe burns. Jenget colleagues discovered that the initial lactate level might be used to distinguish survivors from non-survivors.

Kamolz et al⁷⁷ reported similar results using a threshold level of 2 mmol/L for first lactate in a prospective analysis. They also discovered that quick lactate clearance was linked to lower mortality rates. Furthermore, because sepsis with multisystem organ failure is a major cause of morbidity and mortality in burn patients, lactate values should be obtained and considered while dealing with burn patients, even though lactate's usefulness as a resuscitation end point is debatable.

Smoke inhalation victims are especially vulnerable to high lactate levels due to the possibility of inhaling cyanide or carbon monoxide. In hemorrhagic and septic shock, the link between lactate and clinical prognosis is well established. The goal of this study is to see if plasma lactate may be used to predict burn patients' mortality and, as a result, their outcome.

MATERIALS AND METHODS

Study Setting Department of General Surgery, Govt. Medical College, Thrissur.

- Study design Prospective observational study
- Study population: Patients admitted following burns in Govt. Medical College, Thrissur.

Inclusion Criteria

- Patients admitted for treatment following >15% burns in Govt. Medical College, Thrissur.

Exclusion Criteria

- Patients who are not willing to participate in the study
- Patients suffering from malignancy, liver disease
- Patients suffering from metabolic derangements like DKA/ mitochondrial disease.

Sample size calculation

Sample size

$$n = (Z\alpha + Z\beta)^2 \times 2pq/d^2$$

$$P = P1 + P2/2 = 0.53, q = 1 - p$$

P1=32% Percentage of people died with lactate value < 2mmol/l

P2=73% percentage of people died with lactate value > 2mmol/l

Z α = 1.96, for 5% level of significance

Z β = 0.84 for 80% power

d = P1 - P2

n = 23

There are 4 variables taken into consideration. Hence 10 samples per variable will be taken. 4 variables are {age, TBSA, inhalational burns, full thickness burns} 4 × 10 = 40, minimum required sample size

Finally, the sample size has been calculated and fixed to be 60, for better study outcome

4. n = 60

Study tools Serum lactate value for burns patients admitted

Study period One year from date of Ethical committee clearance.

Methodology

Serum lactate of all burns patients with burns above TBSA 15% will be sent within the first day of admission to the Clinical Biochemistry department, Govt. Medical College Thrissur. Based on serum lactate value patients will be classified into 2 groups. Group A with value more 2mmol/l & Group B with value less than or equal to 2mmol/l. Patients will be observed for the following days till discharge and the mortality will be assessed compared to the serum lactate value. All expenditure of the study will be taken by the investigator and laboratory test will be conducted at Clinical Biochemistry department at Govt. Medical College Thrissur. All results will be entered into an excel sheet and will be tabulated and analyzed.

Statistical Analysis

The data of study subjects and the outcome will be statistically analyzed using the latest version of SPSS software. Mean, median, mode and standard deviation of the data will be calculated which will be helpful in standardizing and comparing the results of the study. Logistic regression methods will be used to ascertain the mortality associated with Serum Lactate levels. 'p' value less than 0.05 will be considered significant.

RESULTS

Data were entered in Microsoft Excel Software and analysed using R software version 4.0.1. Age was summarized as mean and standard deviation or median and IQR depending on distribution. Categorical variables like sex, comorbidities, type of burns and outcome were summarized as frequencies and proportions. Percentage of burns and serum lactate levels are also categorized and summarized as frequencies and proportions. Fisher's exact test was done to check association between serum lactate level and outcome. Logistic regression

analysis was done to measure the association with between the same in terms of risk ratio.

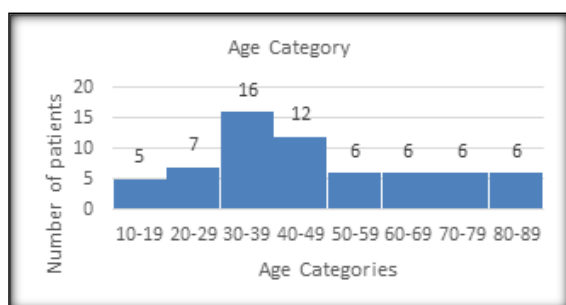


Figure 1: Age distribution of study participants (N = 64)

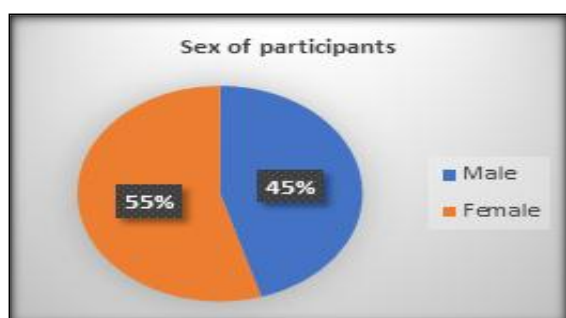


Figure 2: Sex distribution of study participants (N = 64)

- The age of the participants ranged from 15 to 88 years.
- The mean (SD) of the participants age was 46.5(19.9) years.
- Out of the 64 patients, 35 (54.7%) were females

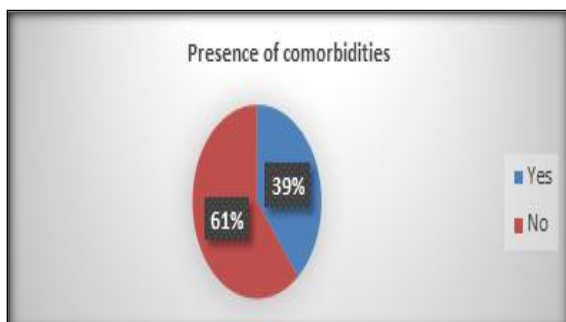


Figure 3 Distribution of study participants based on comorbidities (N = 64)

Out of the 64 patients, 39 (60.9%) had no comorbidities

Table 1: Distribution of study participants based on percentage of burns (TBSA) (N = 64)

Percentage of burns(TBSA)	n (%)
15-45	32 (50.0)
45-75	13 (20.3)
75-100	19 (29.7)

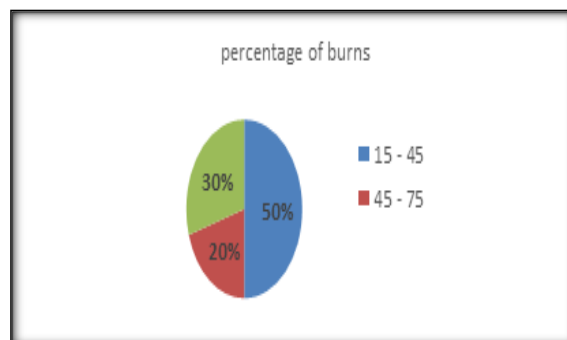


Figure 4: Distribution of participants based on percentage of burns(TBSA) (N = 64)

Table 2 Type of burns (N=64)

	Yes	No	Total
Full thickness	29 (45.3)	35 (54.7)	64 (100)
Inhalational	34 (53.3)	30 (46.9)	64 (100)

Table 3: Distribution of study participants based on serum lactate(N = 64)

Serum lactate	n (%)
≤ 2 mmol/l	26 (40.6)
>2 mmol/l	38 (59.4)

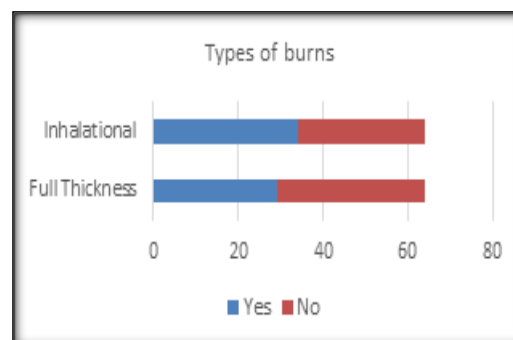


Figure 5 Type of burns (N = 64)

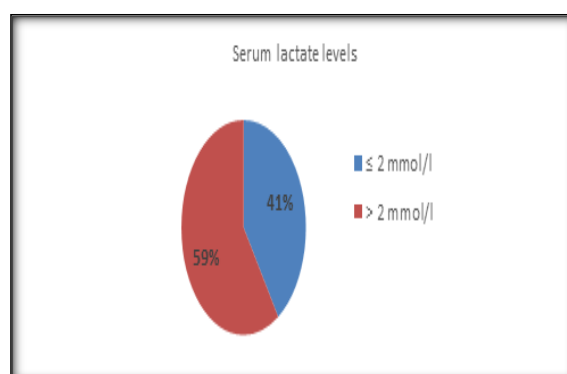


Figure 6: Distribution of participants based on serum lactate levels (N = 64)

Table 4: Distribution of study participants based on outcome (N = 64)

Outcome	n (%)
Survived	29 (45.3)
Dead	35(54.7)

Table 5: Serum lactate level with death

Serum lactate	Death	Survived	Total
>2 mmol/l	34 (89.5)	4 (10.5)	38 (100)
≤2 mmol/l	1 (3.8)	25 (96.2)	26 (100)

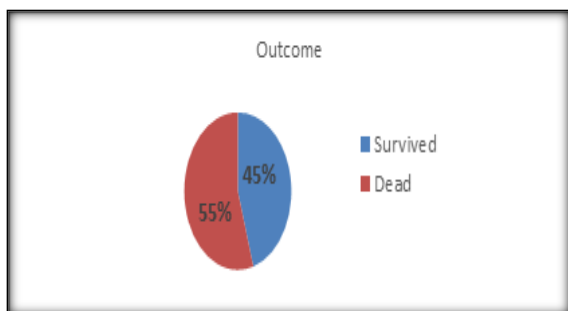


Figure 7 Distribution of participants based on outcome (N = 64)

Among patients with serum lactate value below or equal to 2mmol/l, 96.2% survived with only 3.8% succumbed to death. Whereas those patients with value more than 2mmol/l, 89.5% succumbed to death with only 10.5% survived.

Fisher's exact p-value < .001 suggested significant association between death and serum lactate level > 2mmol/l. Logistic regression analysis revealed an risk ratio 23.3 [95% CI 3.4 – 159.4] of death for serum lactate level > 2mmol/l compared to lactate level ≤ 2mmol/l with p-value .001.

Table 1: Death rate and percentage of burns among participants (N = 64)

Percentage of burns	Death	Total	Fatality rate	Risk ratio	p-value
15-45	6	32	18.8	Baseline	-
45-75	10	13	76.9	4.1 [95% CI 1.9 – 8.9]	<.001
75-100	19	19	100.0	-	-

Multilevel logistic regression analysis was done to estimate risk ratio of death based on percentage of burns. 75-100% burns predicted death perfectly hence was not analysed in the model. 45 – 75% burns had a risk ratio of 4.1 [95% CI 1.9 – 8.9] with p-value <.001.

DISCUSSION

Lactate levels are commonly evaluated in acutely ill patients. Most commonly used in evaluating shock, lactate can be elevated for many reasons. Tissue hypoperfusion is the most common cause of elevation. Lactate levels in clinical practice are used as a surrogate for illness severity and to gauge response to therapeutic interventions. The use of lactate as a clinical prognostic tool was first suggested in 1964 by Broder and Weil when they observed that a lactate excess of >4 mmol/l was associated with poor outcomes in patients with shock. Lactate is produced by most tissues in the body, mainly by muscle and is rapidly cleared by liver with small amount by kidneys.

Under anaerobic conditions lactate is produced in large amount and is the end product of glycolysis and feeds into the Krebs cycle as a substrate for gluconeogenesis. Lactate elevation is multifactorial, disease specific and patient specific and is caused by increased production, decreased clearance or a combination of both. Etiology is best studied in shock states and many factors like hypoperfusion, mitochondrial dysfunction, liver dysfunction, hypermetabolic states contributes to its elevation.

In severe burns, lactate has been found to be a strong predictor of outcome. Jeng et al, through studies showed that the initial lactate level was a useful parameter to separate survivors from non survivors Another prospective study by Kamolz et al. found similar results with a cut off level for initial lactate of 2mmol/l. Since sepsis with multiorgan failure is a major cause of morbidity and mortality in burns, lactate values should be obtained and taken into consideration when dealing burns patients.

Smoke inhalation victims are at particular risk of elevated lactate due to potential inhalation of

cyanide and carbon monoxide. A burn injury destroys the cutaneous barrier protecting the patient from a hostile environment and produces profound changes in almost all other organs. The deleterious effect of burn injury on the organ system are proportional to the extend of burns. In addition to the gross changes seen at local site of burns, there are marked circulatory changes in the form of increased capillary permeability. This capillary permeability is not confined to burn site alone but involves the whole body. This is seen maximum in first 12 hours and then slowly phases out but still remains high up to 24-36 hours.

This increased capillary permeability creates a situation of hypovolemic shock which is seen in the form of

- Tachycardia
- Dehydration
- Hypothermia
- Hypotension
- Oliguria

Initially body tries to compensate this by generalize vasoconstriction and constriction of splanchnic circulation to maintain cardiac output. But this compensatory mechanism fails if no correction of fluid loss is made and cardiac output is not maintained, will lead to a state of hypovolemic shock, condition in which lactate value will be seen elevated.

All persons with burns should be hydrated well to maintain adequate perfusion with a minimal urine output of .5ml/kg/hr. Ringer lactate is the fluid of choice to replace for the loss. Fluid loss is maximum in first 8 hours, therefore half the calculated amount of fluid by Parkland formula is infused in first 8 hours and the rest in next 16 hours. After 24 hours resuscitation fluid is nearly half of first 24 hours. Before stopping resuscitative measures the patient should start taking sufficient amount of fluids orally.

The study was conducted to assess whether the serum lactate can be used to predict mortality in burns patients so that based on initial serum lactate value. Based on review by Kruse et al on the measurement of lactate concluded that peripheral venous lactate levels are highly correlated with arterial blood lactate levels, thus establishing that either methods can be used. In the study conducted by Kamolz et al, in assessing whether lactate can be used as a predictor of mortality and morbidity in burns, patients were classified based on initial serum lactate value $<2\text{mmol/l}$ and $>2\text{mmol/l}$. Patients with value $>2\text{mmol/l}$ were again divided in two groups based on their lactate clearance. Patients who attained lactate value below 2mmol/l within 24 hours had a mortality of 32% and who were not able to clear within 1 day had a mortality of 73%. Linear discriminant analysis was highly significant. Lactate burns severity index was calculated in the study and with a cut off, it was able to calculate the mortality with a 100% specificity. In a study done by Jeng et al, serum lactate in predicting mortality after major burns. Serum lactate and base deficit was measured at time of admission and then every 2 hour for the duration of resuscitation during the initial 48 hours of admission. Initial statistical analysis with cox regression model was used to determine the relationship between survival, resuscitation parameters and demographics. Then a logistic regression was used to determine if any of these variables were quickly predictive of risk of death.

Cox regression model two variables were predictive serum lactate and age. Furthermore by logistic regression revealed that the initial lactate value was separately predictive of mortality. As per data obtained from different studies, we conducted the study in the burns patients admitted with burns of TBSA more than 15 percent. Prospective observational study was done on patients with their consent. Serum lactate was sent within the first day of admission to divide the patients into two categories one with lactate value more than 2mmol/l and those with value 2 or less than 2mmol/l . 4 variables like age, TBSA, inhalational burns, full thickness burns were taken into consideration. 64 patients were evaluated in this study. The patients participated in the study were observed during their admission days to assess the mortality based on their serum lactate value. Data that was obtained was analysed using R software version 4.0.1.

Age of participants ranged from 15-88 years with mean of participants age was 46.5 years (19.9%) Out of the patients participated 54.7% were females. Majority of patients belonged to 15-45 TBSA of burns, coming around 50% of those involved in the study. 20.3% belonged to the range of 45-75 TBSA and 29.7% participants belonging to 75-100 TBSA. Based on the type of burns, full thickness burns was present in 45.3% participants and inhalational burns in 53.3%. Around 38 patients had serum lactate value more than 2mmol/l and 26 patients had 2 or less than 2mmol/l . Of these patients 89.5% of

participants having serum lactate value more than 2mmol/l succumbed to death while 96.2% of participants having 2 or less than 2mmol/l survived. All these data was analysed. Fisher's exact test was done to check association between serum lactate level and outcome. Logistic regression analysis was done to measure the association between the same in terms of risk ratio.

Fisher's exact p-value $<.001$ suggested significant association between death and serum lactate level $>2\text{mmol/l}$. Logistic regression analysis revealed an risk ratio 23.3 [95% CI 3.4 – 159.4] of death for serum lactate level $>2\text{mmol/l}$ compared to lactate level $\leq 2\text{mmol/l}$ with p-value .001. Multilevel logistic regression analysis was done to estimate risk ratio of death based on percentage of burns. 75-100% burns predicted death perfectly hence was not analysed in the model. 45 – 75% burns had a risk ratio of 4.1 [95% CI 1.9 – 8.9] with p-value $<.001$.

Data analysis has shown significant association between the serum lactate value and the mortality, which has been confirmed using Fisher's.

CONCLUSION

Lactate levels are elevated in many conditions in which tissue hypoperfusion is a major contributing factor. In major burns lactate has been found to be a strong predictor of outcome. Burns patients with initial serum lactate value more than 2mmol/l have poor outcome as compared to those with value less than or equal to 2mmol/l . This study has clearly shown significant association between the serum lactate value and the mortality which has been confirmed using Fisher's test and Logistic regression analysis. This helps the caregiver to take aggressive measures or therapeutic options to reduce the mortality in burns patients.

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Conflict of interest none declared

Ethical approval the study was approved by the Institutional Ethics Committee.

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