RESEARCH ARTICLE

SERUM LACTATE LEVELS IN PROGNOSTICATION OF PATIENTS IN SEPSIS OR SEPTIC SHOCK

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ABSTRACT

Introduction: India has recorded a death rate of 7.3 / 1000 individuals in the year 2016. From the multicentric study done on 5,478 ITU admissions, mortality was 59% of which 25% of patient in SIRS with organ dysfunction of which 52.77% were due to sepsis. With such high prevalence, it becomes important to point our focus on early and aggressive measures to reverse sepsis. In a country like India, decision on type and extent of intervention is greatly affected by the financial aspect. Hence, it is important to prognosticate the patient early in order to make treatment decisions. Lactate is one such parameter which denotes sepsis, so we would like to study if serial lactate levels could help prognosticate.
Aims and Objective: 1. To measure the lactate levels at the time of presentation and 24 hrs and determine the better predictor of mortality. 2. To compare lactate clearance between survivors and non-survivors.
Methodology: It was a prospective observational study. 40 subjects who were in sepsis or septic shock were included in the study and lactate levels were measured at 0hrs and 24 hrs and the lactate clearance was also calculated.
Results: Initial lactate levels correlated best to mortality (p-0.003) whereas serial lactate and lactate clearance did not show any positive predictive value. An initial lactate levels of 1.45 could be taken as a cut off for predicting poor mortality and it showed 75% sensitivity and 65% specificity.
Discussion: When compared to other studies, certain studies showed near equal correlation of both initial lactate as well as lactate clearance to mortality whereas some other studies showed more correlation between lactate clearance and mortality. Though all our patients received standard care offered to a patient in sepsis but the degree of intervention varied from person to person due to a major concern of financial constraints by relatives.
Conclusion: Since initial lactate levels showed good predictability in mortality prediction , it could be used as a parameter to assess prognosis at the initial phase of presentation and thereby determine the extent of intervention to be implemented at the golden hours.

INTRODUCTION

India has recorded a death rate of 7.3 / 1000 individuals in the year 2016. From the multicentric study done on 5,478 ITU admissions, mortality was 59% of which 25% of patient in SIRS with organ dysfunction of which 52.77% were due to sepsis. The incidence of severe sepsis was 16.45% of all ICU admissions (Todi *et al*., 2010). With such high prevalence, it becomes important to point our focus on early and aggressive measures to reverse sepsis. In a country like India, decision on type and extent of intervention is greatly affected by the financial aspect. Hence, it is important to prognosticate the patient early in order to make treatment decisions. Various parameters can help point to sepsis like C-reactive protein, pro-

calcitonin but it is important to derive a quantitative parameter which could help prognosticate the patient early. One such parameter is the blood lactate levels. Recently, blood lactate levels have gained such importance as it has been proved that Lactate >4mmol/L could be definitive of sepsis. (Singer *et al*., 2016) Elevated blood lactate levels are frequently seen in critically ill patients. It is considered as an indirect marker of tissue hypoxia found elevated as a result of anaerobic metabolism. The persistence of tissue hypoxia lead to multisystem organ failure and death. Studies have shown increased blood lactate levels as well as persistently elevated blood lactate levels as a predictor of poor outcome. Hence, we did this study to determine the better prognostic parameter where initial lactate levels and lactate clearance was compared.

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Aims and Objectives

1. To measure the lactate levels at the time of presentation and 24 hrs and determine the better predictor of mortality.
2. To compare lactate clearance between survivors and non-survivors.

MATERIALS AND METHODS

Source of Data: Patients presenting to Father Muller Medical College in sepsis or septic shock over a period of six months.

Study Design: It was a observational prospective study

Methodology:

Sample size: $\quad = \quad$ $$\dfrac{Z\alpha^2 p\,(1\text{-}p)}{e^2}$$

Study was done on patients who had presented in sepsis or septic shock. Initially resuscitation was attempted through administration of crystalloids. If hypotension persisted, patients were started on Noradrenaline and dose was titrated till hypotension is controlled. The serum lactate levels were measured on admission to the ICU and at 24 hrs. Patients were followed till discharge or till death whichever occurs earlier. They were grouped as survivors and non-survivors. The lactate clearance was calculated. The baseline value and lactate clearance was compared among survivors and non-survivors
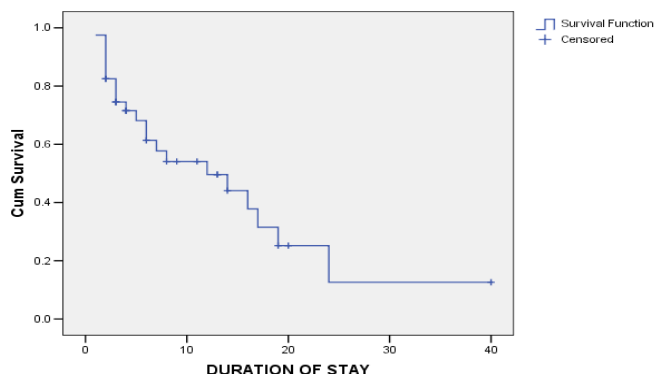
Inclusion criteria

1. Patients in sepsis or septic shock
2. >18 yrs age

Exclusion criteria

1. Chronic renal failure requiring dialysis
2. Decompensated liver disease

Survival Function

RESULTS

In our study 40 subjects were included of which 60% were male (n=22) and 40% were females (n=15). 55% of the subjects died (n=22) and 45% survived. The mean age of the study population was 58.80 ± 18.04. The mean age of survivors was 61± 20.132 and non survivors was 56.68± 16.32.
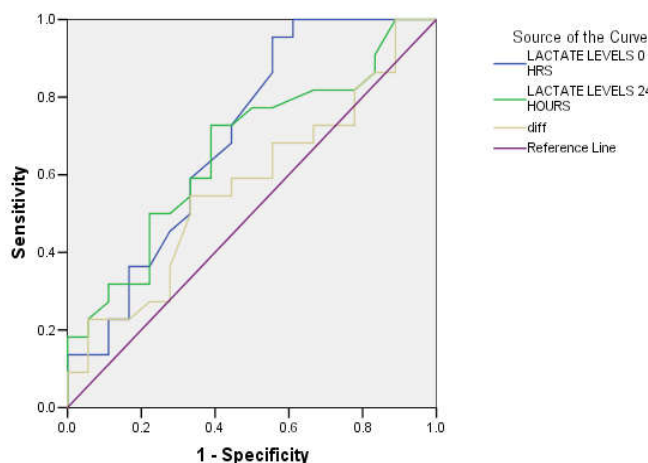
There was no significant relation between age and mortality (p-0.334) There was no significant relation between duration of stay and mortality but survivors was found to have longer duration of stay than non-survivors (9.89 ±9.45)

When the lactate levels were compared, there was significant correlation between initial lactate levels and mortality (p-0.033) but no significant correlation between lactate clearance and mortality.

	DEATH	N	Mean	Std. Deviation	Minimum	Maximum	Median(IQR)	Mannwhitney test Z value	p
LACTATE LEVELS 0 HRS	0	18	2.111	2.0886	.6	7.4	1.4(0.7-2.475	2.14	.033 sig
	1	22	3.559	3.5949	1.1	15.0	2.05(1.4-3.82		
LACTATE LEVELS 24 HOURS	0	18	2.617	2.2827	.3	8.6	1.75(1.15-3.6	1.77	.077 NS
	1	22	4.714	4.1380	.8	15.0	3.3(1.775-6.6		
diff	0	18	.506	.9213	-1.0	2.7	0.6(-0.225-1.	.74	.462 NS
	1	22	1.155	2.3818	-.8	10.9	0.85(-0.225-1		

The mean initial lactate levels was 3.55± 3.59 in non-survivors where as it was 2.111±2.08 in survivors. 7 out of 40 subjects (17%) had lactate levels >4mmol/L. and 71% of these subjects had in-hospital mortality. By the receiver operating curve, lactate levels measured at 0 hrs was found to be most specific with an AUC-0.698.

ROC Curve

Diagonal segments are produced by ties.

Area Under the Curve

Test Result Variable(s)	Area	Std. Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
LACTATE LEVELS 0 HRS	.698	.086	.033	.529	.868
LACTATE LEVELS 24 HOURS	.664	.087	.077	.495	.834
diff	.571	.092	.447	.391	.750

An initial lactate level of 1.45 was concluded to be 72% sensitive and 65% specific.

DISCUSSION

Sepsis is a syndrome which is determined by pathogen factors as well as host factors (sex, race, age, comorbidities), the characteristics of which change from time to time. The difference between infection and sepsis is that sepsis sets in when there is dysregulated host response. It has been recently recognized that sepsis causes early activation of both pro and anti-inflammatory mediators. It causes major alterations in the metabolic, hormonal, autonomic, neuronal, cardiovascular and

coagulation pathways. Hence any explained organ dysfunction must raise a suspicion of underlying infection. In the Third International Consensus, sepsis was finally defined as " *life threatening organ dysfunction caused by dysregulated host response to infection*". Organ failure was found to be predicted if the SOFA score (Sequential Organ Failure Assessment) increases by >2. Patient was said to be in septic shock when the circulatory failure was profound. Clinically it was distinguished *"if there was persistent hypotension requiring vasopressors to maintain a MAP (Mean Arterial Pressure) >65mmHg and if serum lactate levels were >2mmol/L despite adequate fluid resuscitation"*. Though serum lactate levels would not be easily available in third world countries, the inclusion of lactate levels as a criteria would help establish abnormalities at a cellular level. Henceforth,Septic shock has been defined as *" a subset of sepsis in which underlying circulatory and cellular metabolism abnormalities are profound enough to substantially increase mortality"*.

Glucose as well as lactate is used as energy sources depending on the type of cell. Lactate is used as energy source either in cells that lack mitochondria or by cells which may contain mitochondria but use lactate based on circumstances or by tissues which perform gluconegenesis where glucose is resynthesized from lactate by utilizing glucose. The two main energy producing processes are the Glycolysis pathway and the Oxidative phosphorylation process. Glycolysis pathway can proceed much faster in circumstances where excess energy production is required under stress and this will lead to conversion of the end product "pyruvate" to lactate. Thus lactate levels increase. In the presence of oxygen, provided that the OxyPhos can keep up with the glycolysis, the lactate will get utilized hence making acidosis less likely. In case of low oxygen levels, it will lead to sharp rise in lactate. Lactate levels may rise secondary to increased production or decreased clearance. Increased lactate production maybe seen secondary to hypoxia. It may also be seen secondary to accelerated glucose metabolism or following administration of epinephrine or when phosphofructokinase is stimulated. It has also been found to increase when Na-K ATP ase is increased as it requires a large amount of ATP which can occur on exposure to catecholamine. A decreased clearance of lactate is seen in the presence of liver dysfunction, following cardiac surgery and in case of sepsis due to depletion of the rate limiting enzyme, pyruvate dehydrogenase. (Cherloff *et al.*, 2015) Studies in the US as well as Netherlands has shown that rather than the initial lactate levels, it was the lactate clearance that was a better predictor of poor prognosis.

Studies (Marty *et al.*, 2013; Bakker *et al.*, 1996; van den Nouland *et al.*, 2017) were done when lactate levels were measures serially and it was found that value at 24 hrs was more specific (AUC-0.773) than the lactate levels measured in the initial hours. Lactate clearance (i.e difference in lactate levels between the initial and 24 hour value) also carried an equally important significance (AUC-0.791), this was in contrary to the results in our study where initial lactate levels

correlated best to poor outcome. This could be attributed to the situation where patient's with higher lactate levels would be in sepsis and aggressive intervention in such patients may not be supported by the next of kin in view of the financial constraints. Some other studies have shown near equal significance of initial lactate levels and lactate clearance in predicting mortality. (Regnier *et al.*, 2012) When lactate levels were categorized according to etiology it was found to be more predictive in cardiac and Gastrointestinal conditions followed by infective etiology and trauma. Mortality was also found to be higher in individuals with higher lactate values (23.9% when >4mmol/L and 7.8% when 2-3mmol/L) this was similar to the results in our study where 71% mortality was recorded in subjects with lactate >4mmol/L. Limitations of the study was a small sample size and not all patients admitted have received the same degree of aggressive intervention due to financial constraints from near relatives which could have been the reason serially measurement of lactate was not a good parameter.

Conclusion

Lactate levels measured initially is a reliable parameter which could help prognosticate the patient and thereby help treatment decisions.

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