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Anesthesia and Intensive Care

Study Between Lactate Clearance and Apache II Score as Predictor Prognosis of Septic Patients

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ABSTRACT

Background: Sepsis continues to be a major cause of death and high healthcare expenses around world. prevalence and fatality rate related to sepsis continue to rise. In management of sepsis, time is of the essence; recent studies have shown that early and intensive therapy is critical for lowering mortality. In 30–50% of cases, sepsis therapy begins in emergency department.

Aim of The Work: To detect efficacy of serial serum lactate and lactate clearance in comparison with APACHE Il as a prediction of fatality in septic patients within 28 days following initial resuscitation and within first 24 hours in intensive care unit.

Patients and Methods: This study was started from January to December 2021. It has been conducted on 53 adult patients (n = 53) who have been brought to Critical Care Unit with a diagnosis of sepsis as defined by current guidelines and who met inclusion criteria, but 3 patients excluded. One was developed gastrointestinal bleeding, 2nd patient was due to myocardial infraction, last one excluded due to data collection error, so we carried study on 50 patients (n=50).

Results: APACHE II shows a significant increase in non-survive group. Arterial lactate shows a highly significant increase in non-survive group, lactate clearance shows a significant decrease in non-survive group.

Conclusion: Serum lactate level and lactate clearance as an indicator of shock and resuscitation are more reliable predictors of mortality than APACHE II. if resuscitation decreased lactate clearance to normal levels in 12 to 24 hours, the patient has best chance of survival.

Keywords: *Lactat; Lacate clearance; APACHE II; Sepsis.*

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INTRODUCTION

Sepsis is an infection-induced syndrome comprising physiologic, pathologic, and metabolic problems. Sepsis, often known as septic shock, is a life-threatening organ malfunction induced from a dysregulated host response towards infection. [1]

. Sepsis has a very complicated nature. Because definite microbiological proof of a precipitating infection is rarely present, diagnosis frequently depends on clinician imaging. [2]

Sepsis continues to be a major cause of death and high healthcare expenses around the world. Time is the key in sepsis therapy; recent research has shown that early and intensive therapy is critical for reducing death. [3]

There are several methods for stratifying sepsis patients, including employing scoring systems, clinical judgement, or the Surviving Sepsis Campaign's sepsis categories. Stratification based on sepsis categories, on the other hand, is not as reliable as clinical assessment or an appropriate scoring system [4].

Several tools and scoring systems exist that predict sepsis-related mortality. These include age, serum lactate, predisposition, infection, APACHE-II, response, and organ dysfunction.

Anaerobic glycolysis produces lactate as a metabolic end-product. When pyruvate cannot access the mitochondria due to poor flow or cellular hypoxia, it is converted to lactate, and the arterial lactate level rises. Lactate is primarily metabolized and cleared by the kidneys and liver, and dysfunction in these organs has been linked to varying decreased clearance levels [5]. In recent years there has been recognition of the prognostic value of serum lactate measurement [6].

PATIENTS AND METHODS

Patients: Following clearance by the Medical Ethics Committee of the Al-Azhar Faculty of Medicine, written informed agreement has been taken from the patient or nearest of kin to include his or her data in this study. This study involved 50 adult patients (n = 50) who were hospitalized in the Critical Care

Medicine department with the diagnosis of sepsis between January and December 2021.

Inclusion Criteria: Age: 19- 92 years old, Sex: both and **Suspected sepsis source and the following three of four SIRS criteria:** Temp ≥ 38°C co or ≤ 36°C, HR ≥ 90 beats / min, RR ≥ 20 breaths / min or Paco2 ≤ 32 mmHg, WBC ≥ 12000 or ≤ 4000 cells per mm3 or 10% band cells and Hypotension that vasopressor therapy needed to elevate MAP >65 mmhg.

Exclusion Criteria: Pregnancy, acute pulmonary edema, status asthmaticus, acute coronary syndrome and Active Gastrointestinal Hemorrhage.

Methods

Study Design: The study was a prospective, observational study to investigate the predictive significance of serial serum lactate and lactate clearance in comparison with APACHE Il as a predictor of deaths in patients with sepsis.

Data Collection: Complete history taking from the patient or his relatives, Demographic data including age and sex and Previous past medical history (pre-existing disease).

Clinical scores: APACHE II Scores.

Clinical examination: Heart rate (beats / minute), Blood pressure (mmHg), Temperature (in degree centigrade), Respiratory rate (breath/ minute) and Urine output (mL/hour).

Investigations: Complete Blood Count, total and direct bilirubin, urea, serum creatinine and C-reactive protein, Complete sepsis workup to identify the source of sepsis. Chest x-ray and Echocardiography. Blood, sputum or tracheal aspirate, urine or any other site for microbiological cultures and Arterial Blood Gases (ABG) directly after admission including arterial lactate level (upon admission) and after 6,12 and 24 hours. The lactate clearance has been calculated using the equation ([initial lactate – lactate after 6 hours]/initial lactate) × 100. A positive score suggests a reduction in lactate levels.

Reference Values: *Lactate normal values (Arterial level <1.8 mmol/ I, Venous level <2.2 mmol/ I).

Follow up and measuring outcomes: All Patients were followed up till hospital discharge.

Treatment: All patients have been managed in accordance with the international sepsis guidelines. In addition, all patients are receiving empirical antibiotics that were adjusted according to culture results. Hemodynamic support was provided by fluid resuscitation and/or catecholamine infusion, if needed, to keep mean arterial pressure > 70 mmHg, and respiratory support was provided by oxygen administration or mechanical ventilation, if needed, to maintain SaO2 > 90% and pH > 7.25.

The patients were divided into two groups regarding the severity to Sepsis group included 31 patients. And Septic shock group included 19 patients. **And regarding the morality to** Survive group included 29 patients and non-survive included 21 patients.

Statistical analysis: Data was entered into the computer and evaluated by IBM SPSS Corp., which was released in 2013. IBM SPSS Statistics for Windows, Version 22.0, Armonk, NY: IBM Corp. Numbers and percentages have been employed to describe qualitative data. After assessing normality with the Kolmogrov-Smirnov test, quantitative data has been reported using the median (min and max) for non-parametric data and the mean and standard deviation for parametric data. The significance of the acquired findings has been determined at the (<0.05) level.

Qualitative data: When greater than 25% of cells in tables (> 2*2) have a count lower than 5, the Chi-Square test is employed to compare two or more groups, and the Monte Carlo test is performed to correct the Chi-Square test.

RESULTS

The present study is cross sectional study that is carried out on 50 adult patients of both sex with 31 case sepsis (62%) and 19 cases septic shock (38%) to assess validity of lactate clearance in sepsis (from January to December 2021)

stratification of critically ill-patients

	Total number =50	Sepsis		test of significance	Mortality		test of significance
		Septic shock n=19	Sepsis n=31		Survived n=29	Died n=21	
Age/years mean±SD	60.44±15.48	61.68±13.34	59.68±16.83	t=0.441 p=0.661	57.41±18.45	64.62±8.90	t=1.65 p=0.105
Sex		N(%)	N(%)				
Male	27	8(29.6%)	19(70.4%)	χ^2=1.75	16(59.3)	11(40.7)	χ^2=0.038
Female	23	11(47.8%)	12(52.2%)	p=0.186	13(56.5)	10(43.5)	p=0.845
ICU duration (days)		7.47±5.81 5.0(2.0-23.0)	8.74±4.63 8(2.0-20.0)	z=1.46 p=0.146	9.28±4.58 9(2.0-20.0)	6.86±5.51 5(2-23)	z=2.27 p=0.023*

Student t test χ2=Chi-Square test Parameters described as mean±SD, Median (Min-Max), Z:Mann Whitney U test

Table (1): Characteristics of the studied cases' demographics

Table (1) displays all of the enrolled patients' demographic data. This study had 27 male (54.0%) and 23 female (46.0%) participants. The difference in sex between the two groups was not statistically significant (p=0.845). All of the enrolled patients were 60.44 years old on average. The non-survivors had a statistically significant greater mean age (64.62) than the survivors (57.41) (p<0.074).

Possible cause of sepsis		Sepsis		test of significance	Mortality		test of significance
		Septic shock n=19(%)	Sepsis n=31(%)		Survived n=29	Died n=21	
DM	16	7(43.8)	9(56.2)	χ^2=0.330 p=0.566	8(50)	8(50)	χ^2=0.618 p=0.432
Hepatic	12	2(16.7)	10(83.3)	χ^2=3.05 p=0.081	9(75.0)	3(25.0)	χ^2=1.87 p=0.171
CVS	3	2(66.7)	1(33.3)	FET P=.549	1(33.3)	2(66.7)	FET P=0.565
CKD	9	5(55.6)	4(44.4)	χ^2=1.44 p=0.231	3(33.3)	6(66.7)	χ^2=2.74 p=0.098
IHD	2	1(50)	1(50)	FET P=1.0	1(50)	1(50)	FET P=1.0
CAF	5	2(40)	3(60)	FET P=1.0	2(40.0)	3(60.0)	FET P=0.638
COPD	1	0	1(100)	FET P=1.0	1(100)	0	FET P=1.0
Miscellaneous	2	0	2(100.0)	FET P=0.519	2(100)	0	FET P=0.503
Cellulitis	4	1(25.0)	3(75.0)	FET P=1.0	3(75.0)	1(25.0)	FET P=0.630
Pneumonia	18	8(44.4)	10(55.6)	χ^2=0.496 p=0.481	10(55.6)	8(44.4)	χ^2=0.069 p=0.793
UTI	8	3(37.5)	5(62.5)	χ^2=0.001 p=0.975	3(37.5)	5(82.5)	χ^2=1.64 p=0.20
Diabetic foot	1	0	1(100)	FET P=1.0	0	1(100)	FET P=0.420
Peritonitis	4	1(25.0)	3(75.0)	FET P=1.0	4(100)	0	FET P=0.129
Abdominal	4	2(50.0)	2(50.0)	FET P=1.0	2(50.0)	2(50.0)	FET P=1.0
Infected lines	3	1(33.3)	2(66.7)	FET P=1.0	2(66.7)	1(33.3)	FET P=1.0
Mix	7	2(28.6)	5(71.4)	χ^2=0.307 p=0.579	4(57.1)	3(42.9)	χ^2=0.002 p=0.960

HTN: Hypertension, DM: Diabetes Mellitus, CVS: Cerebrovascular stroke, IHD: Ischemic Heart Disease, Ch.AF: Chronic Atrial Fibrillation, COPD: Chronic Obstructive Pulmonary Disease, CKD: Chronic Kidney Disease. Miscellaneous: nephrolithiasis, neuromuscular diseases and rheumatic heart disease.

χ2: Chi square test FE: Fisher Exact p: p value for comparing between the studied groups

Table 2: Possible cause of sepsis among studied cases.

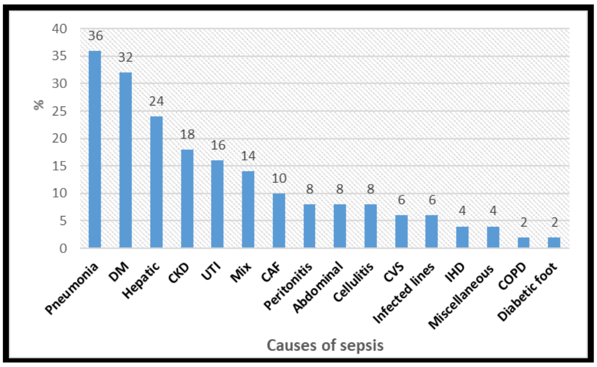

Fig. 1 : Possible cause of sepsis among studied cases

Table (2) and figure (1) illustrate that there is no statistically significant difference between cases with sepsis and septic shock as regarding causes of sepsis with the most frequent causes among studied cases is pneumonia (36%), Diabetes (32%), hepatic (24%), CKD (18%) and the least is detected for COPD &diabetic foot (2% each).Similarly ; no statistically significant relation between possible cases of sepsis and incidence of mortality among studied cases.

	Sepsis		test of significance	Mortality		test of significance
	Septic shock n=19	Sepsis n=31		Survived n=29	Died n=21	
Initial Lactate (mmol/l)	7.07±4.06 6.5(0.9-14.0)	5.09±3.0 4.4(1.6-12.0)	z=1.74 p=0.082	4.91±3.23 4(0.9-12.0)	7.14±3.61 6.5(2.2-14.0)	z=2.30 p=0.02*
Lactate after 6 hs (mmol/l)	9.37±5.96 8.1(0.6-22.0)	3.14±3.63 1.6(0.5-13.6)	z=3.54 p<0.001*	1.551±0.955 1.2(0.5-4.5)	10.97±4.40 9.9(5.75-22)	z=5.98 p<0.001*
Lactate clearance	-47.83±83.29 57.14(-207.69, 86.25)	37.19±59.93 63.75(-161.36, 86.67)	z=3.54 p<0.001*	62.67±18.86 66.67(15.79-86.67)	-74.92±62.14 -70(-207.669. 44.29)	z=5.89 p<0.001*

Parameters described as mean±SD, Median (Min-Max), Z:Mann Whitney U test, *statistically significant if p<0.05

Table 3: Comparison of mean Lactate concentration among studied cases

Table (3) shows that there is statistically significant lower median lactate after 6 hours among cases with sepsis than with septic shock (1.6 versus 8.1, respectively). Median lactate clearance was statistically significantly lower among group with septic shock than group with sepsis

.In prediction of immediate mortality					
	AUC	Pvalue	Cut of point	Sensitivity	Specificity
Initial Lactate (mmol/l)	0.6692 (0.546-0.838)	0.021*	4.70	71.4	58.6
Lactate after 6 hours (mmol/l)	1.0 (1.0-1.0)	<0.001*	5.125	100.0	100.0
Lactate clearance	0.801 (0.668-0.933)	<0.001*	47.15	84.5	67.7
APACHI-II scores	0.726 (0.578-0.874)	0.007*	19.5	81.0	44.8

AUC: Area Under Curve

Table 4: Validity of lacatate and lactate clearance in prediction of septic shock and mortality among studied cases

Table (4) shows that area under ROC curve is excellent (AUC >0.80) for lactate after 6 hours and lactate clearance in differentiating cases with septic shock and died cases. The highest sensitivity is detected for lactate after 6 hours in differentiating mortality (100%), lactate clearance in differentiating septic shock (95.2%), and in differentiating immediate mortality (84.5%). APACHI-II score have lower sensitivity and specificity in predicting mortality than lactate clearance and lactate after 6 hours.

DISCUSSION

Sepsis is life-threatening condition in which multi-organ failure occurs as a response to infection In the UK, it is over 37,000 patients die annually. This is more than people dying from lung cancer, breast and bowel cancer combined. [7]

In this study, 50 adult septic patients (as defined by the 2016 consensus criteria (Sepsis-3)) were enrolled, and their age, arterial lactate level, lactate clearance, and APACHE II were all documented. In this study, there were 31 patients with sepsis and 19 patients with septic shock among the 50 patients. According to the 7-days mortality (primary endpoint), 21 patients (42.0%) died (non-survivors' group) and 29 patients (58.0%) survived (survivors' group).

Pneumonia was the most common cause in septic patients.

Regarding baseline characteristics, patients were presented with a age ranged from 19-92 years and mean of age of 60.44±15.48 years. Men (54.0%) and women (46.0%) had comparable percentages.

In this study, non-survivors showed a statistically significant higher mean of age (64.6 years) and survivors was (57.41).

All disease intensity measures' AUCs (area under curves) were poor in older patients, ranging from 0.56 to 0.64, much lower than the good AUC range of 0.72 to 0.86 in younger patients. In elderly patients, the mortality in ED Sepsis (MEDS) showed the best AUC (0.64 (0.57–0.71)). [6]

In an observational multicenter study, 833 individuals admitted to the hospital with a suspected infection were divided into two groups based on their age: <70 and ≥70 years. In-hospital mortality in patients aged ≥70 was 9.2% (95% CI: 7.3 to 11.2), which was two times higher than the 4.6% (3.6-5.6) in patients aged <70. [8]

Non-survivors in this study had significantly greater arterial lactate (7.14 mmol/L) than survivors (4.91) (p <0.05), this might be indicating more severe tissue hypoperfusion or endogenous epinephrine stimulating beta-2 receptors. Excess pyruvate is converted into lactate. Arterial lactate level was a fair tool with AUC of 0.669 at a cut off value of ≥4.7 mmol/L (95% CI: 0.546 -0.838, p<0.021). It showed sensitivity and specificity of 71.4% and 58.6% respectively.

Arterial lactate after 6 hours shows AUC of 1.0 at a cut off value of ≥5.125 mmol/L (95% CI: 1.0 -1.0, p<0.001). It showed sensitivity and specificity of 100% and 100% respectively.

Lactate clearance was a good tool with AUC of 0.801 at a cut off value of 47.15 (95% CI: (0.668-0.933), p<0.001). It showed sensitivity and specificity of 84.5% and 67.7% respectively.

Sepsis patients admitted for more than a 40-month period were studied retrospectively in a cohort. A total of 338 patients have been separated into three groups depending on their initial serum lactate levels. Lactate concentrations were < 2 mmol/L in Group 1, 2–4 mmol/L in Group 2, and ≥ 4 mmol/L in Group 3. In-hospital mortality was the primary outcome. After controlling for underlying disease severity and organ dysfunction, an initial lactic acid concentration of 4 mmol/L was independently related to higher death.

Increasing lactate concentrations, on the other hand, were linked to greater disease severity and were inversely proportional to prognosis in the other two groups. [5]

According to Shetty and colleagues, specific serum lactate levels for bad results in individuals with suspected sepsis were investigated. There were a total of 12,349 adult ED visits, with 8310 (67.3%) receiving a serum lactate assay when they arrived. For every integer rise in serum lactate concentrations, the odds ratio of in-hospital mortality increased statistically significantly. The corresponding odds ratio for in-hospital mortality were 2.93 (95%CI: 2.08 to 4.13), 2.77 (95%CI: 2.34 to 3.29), 3.26 (95%CI: 2.80 to 3.80) and 4.01 (95%CI: 3.40 to 4.73), respectively (all p<0.0001). [6]

The APACHE scoring system takes into account a wide range of variables such as breathing, blood pressure, heart rate, consciousness, tissue perfusion, and major diseases. It is frequently used in the severity and prognosis assessment of many critical illnesses.

In this study Higher mean APACHE-II score is detected among died cases than survived with statistically significant APACHE II score show AUC of 0.726 at a cut off value of 19.5 mmol/L (95% CI: (0.578-0.874), p<0.007). It showed sensitivity and specificity of 81% and 44.8% respectively.

APACHE Il shows statistically significant P value (<0.001) between survivors and non survivors according APACHE ll. Receiver operator characteristic (ROC) for APACHE Il and lactate clearance. The best APACHE I l cutoff score for predicting ICU deaths was (227). For ICU deaths, this cutoff level had a sensitivity of 100% and a specificity of 88.24%. The optimal cutoff value for lactate clearance H 0-6 for predicting ICU deaths was (>6.67). This cutoff level had a sensitivity of 87.88% and a specificity of 100% for ICU deaths. The optimal cutoff value for lactate clearance H O12 for predicting ICU deaths was (>3.45). This cutoff level had a sensitivity of 87.88% and a specificity of 100% for ICU deaths. The optimal cutoff value for lactate clearance H O24 for predicting ICU deaths was (>-5.17). This cutoff level had a sensitivity of 100% and a specificity of 100% for ICU deaths. Blood lactate level and lactate clearance are both predictors of 28-day fatality in severe sepsis or septic shock, and they are equivalent to or better than the APACHE Il score. [9]

In this study lactate after 6 hours and lactate clearance in differentiating cases with septic shock and died cases. The highest sensitivity is detected for lactate after 6 hours in differentiating mortality (100%), lactate clearance in differentiating septic shock (95.2%), and in differentiating immediate mortality (84.5%).

As long as the blood lactate clearance rate is dynamically monitored, the diagnosis can be more correctly evaluated. Both blood lactate level and lactate clearance are predictors of 28-day fatality during serious sepsis or septic shock, and they are equivalent to or better than the APACHE Il score. Even after the golden hour, a protocol of lactate clearance-directed treatment must be explored in septic patients.

CONCLUSION

Serum lactate level and lactate clearance as an indicator of shock and resuscitation are more reliable predictors of mortality than APACHE II. When resuscitation attempts lead to lactate clearance to normal levels in 12 to 24 hours, the patient has the best chance of survival.

Conflict of interest : none

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