ORIGINAL ARTICLE

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The Effect of Lactate and Lactate Clearance on Mortality in Sepsis Patients Admitted to the Emergency Department

Acil Servise Başvuran Sepsis Hastalarında Laktat ve Laktat Klirensinin Mortaliteye Etkisi

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ABSTRACT

Objective: *Early prognosis of sepsis, which affects millions of people all over the world every year and, can have a mortality of more than 25%, is very important especially for emergency rooms where patients spend their most critical golden hours. Lactate and lactate clearance are also potential marker candidates that can be used to predict mortality, which has now started to take place in sepsis guidelines. The aim of this study is to investigate the power of lactate and lactate clearance to predict mortality in sepsis.*

Material and Method: *All patients over the age of 18 with a diagnosis of severe sepsis and septic shock who presented to the emergency department during a one-year period were included in this prospective observational cohort study. The lactate clearance was calculated by taking the blood gase samples of the patients at the time of admission and six hours later, and evaluated in terms of predicting mortality along with other parameters.*

Results: *The decrease in lactate values at the sixth hour of 90 patients included in the study was found to be statistically significant (p=0.001). A positive and significant correlation was found between the lactate values of the patients at admission and mortality (p=0.046). A negative significant correlation was found between lactate clearance of the patients and mortality (p=0.001).*

Conclusion: *In patients with sepsis, lactate level is important in determining prognosis. Regardless of arrival lactate level, the rise of lactate reduction rate at the sixth hour indicates a good prognosis. In addition, it was determined that the sixth hour lactate level also had an effect on predicting mortality. When all these results are taken into consideration, it can be said that the lactate level and lactate clearance are useful predictors of prognosis in sepsis patients admitted to the emergency department. However, they are not sufficient on their own to determine the prognosis and should be used together with other markers and clinical evaluation.*

ÖZET

Amaç: *Her yıl tüm dünyada milyonlarca insanı etkileyen ve mortalitesi %25'ten fazla olabilen sepsisin erken dönemde prognoz tayini özellikle hastaların en kritik altın saatlerini geçirdikleri acil servisler için çok önemlidir. Laktat ve laktat klirensi de artık sepsis kılavuzlarında yerini almaya başlamış mortalite öngörmede kullanılabilecek potansiyel belirteç adaylarındandırlar. Bu çalışmanın amacı laktat ve laktat klirensinin sepsiste mortaliteyi öngörme gücünün araştırılmasıdır.*

Gereç ve Yöntem: *Bu prospektif gözlemsel kohort çalışmasına bir yıllık dönemde acil servise başvuran 18 yaş üzeri tüm ağır sepsis ve septik şok tanılı hastalar dâhil edilmiştir. Hastaların başvuru sırasında ve altı saat sonra kan gazı alınarak laktat klirensi hesaplanmış ve diğer parametreler ile birlikte mortaliteyi öngörme açısından değerlendirilmiştir.*

Bulgular: *Çalışmaya alınan 90 hastanın altıncı saatteki laktat değerlerindeki düşme istatistiksel olarak anlamlı bulunmuştur (p=0.001). Hastaların başvurudaki laktat değerleri ile mortalite arasında pozitif yönde anlamlı ilişki saptanmıştır (p=0.046). Hastaların laktat klirensleri ile mortalite arasında negatif yönde anlamlı ilişki saptanmıştır (p=0.001).*

Sonuç: *Sepsis hastalarında geliş laktat değerinin mortalite ve prognozu belirlemede önemi vardır. Geliş laktat değerinden bağımsız olarak altıncı saatte laktatın düşme oranının yüksekliği iyi prognozu gösterir. Ayrıca altıncı saat laktat değerinin de mortaliteyi öngörmede etkisi olduğu belirlenmiştir. Tüm bu sonuçlar göze alındığında geliş laktat değerinin ve laktat klirensinin acil servise gelen sepsis hastalarında prognozu göstermede yararlı belirteçler olduğu söylenebilir. Ancak prognozu belirlemede tek başlarına yeterli değildirler, diğer belirteçler ve klinik değerlendirme ile beraber kullanılmalıdırlar.*

Keywords:
Emergency room
Lactate
Lactate clearance
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Anahtar Kelimeler:
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INTRODUCTION

Sepsis is a syndrome characterized by the development of life-threatening organ failure as a result of an uncontrolled inflammatory response to infection (1). More than 1/4 of millions of patients diagnosed with sepsis in the world die every year, and initiation of appropriate treatment in sepsis management is very effective in preventing mortality, so it is of great importance that emergency physicians recognize sepsis accurately and in a timely manner (2). Scoring systems are used to predict mortality in emergency and intensive care units. "Mortality in Emergency Department Sepsis" (MEDS), "Sequential Organ Failure

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Assessment" (SOFA) score is most commonly used scores in the emergency department, and the "Predisposition, Infection, Response and Organ Dysfunction" (PIRO) score has been developed for the intensive care unit (ICU). However, discussions about the usefulness of these scores continue and conflicting results have been reported in different studies (3-10). For years, data and results of patients with sepsis have been collected from many countries to create guidelines within the scope of the "Surviving Sepsis Campaign" (SSC). "Sepsis Severity Score" (SSS) was defined by Osborn et al. in 2014 to predict the prognosis of sepsis, by using the data of this

Table 1: Characteristics and Mortality

		n	%	Mortality		p
				No n=54 (60%)	Yes n=36 (40%)	
Age (years)	Min-Max (Median)	19-97 (62.5)		19-90 (61.5)	26-97 (68)	[a]0.113
	Mean±Sd	61.33±16.55		59.07±16.39	64.2±16.44	
	< 65 years	47	52.2%	31 (66.0%)	16 (34.0%)	
	≥ 65 years	43	47.8%	23 (53.5%)	20 (%46.5%)	
Blood Pressure	Hypotensive	28	31.1%	17 (60.7%)	11 (39.3%)	[b]0.844
	Normotensive	55	61.1%	32 (58.2%)	23 (41.8%)	
	Hypertensive	7	7.8%	5 (71.4%)	2 (28.6%)	
Systolic Blood Pressure	Min-Max (Median)	55-200 (102.5)		40-100 (70)	40-100 (70)	[a]0.767
	Mean±Sd	110.41±28.72		68.52±17.53	67.78±17.87	
Diastolic Blood Pressure	Min-Max (Median)	40-100 (70)		60-180 (102.5)	55-200 (102.5)	[a]0.846
	Mean±Sd	68.22±17.57		111.15±27.13	109.31±31.31	
Body Temperature	Min-Max (Median)	34-40 (37)		35.6-40 (37.7)	34-39 (36)	[a]0.001*
	Mean±Sd	36.93±1.36		37.54±1.09	36.02±1.21	
	Hypothermia	15	16.7%	0 (0%)	15 (100%)	
	Normothermia	36	40.0%	19 (52.8%)	17 (47.2%)	
	Hyperthermia	39	43.3%	35 (89.7%)	4 (10.3%)	
Respiratory Rate	Min-Max (Median)	16-40 (25)		16-40 (24)	16-40 (27)	[a]0.951
	Mean±Sd	26.20±6.24		26.17±6.08	26.25±6.56	
	Normal	21	23.3%	11 (52.4%)	10 (47.6%)	
	High	69	76.7%	43 (62.3%)	26 (37.7%)	
Glascow Coma Scale	Min-Max (Median)	3-15 (15)		8-15 (15)	3-15 (13)	[c]0.002*
	Mean±Sd	13.02±2.99		13.83±2.18	11,81±3.62	
Comorbidity	No	4	4.4%	2 (50.0%)	2 (50.0%)	[b]1.000
	Yes	86	95,6%	52 (60.5%)	34 (39.5%)	
	0	4	4.4%			
	1	42	46.7%			
	≥ 2	44	48.9%			
Need for Ventilation	No	46	51.1%	46 (100%)	0 (0%)	[d]0.001*
	Yes	44	48.9%	8 (18.2%)	36 (81.8%)	
Treatment area	Emergency Room	26	28.9%	26 (100)	0 (0)	[d]0.001*
	Other Clinics	21	23.3%	21 (100)	0 (0)	
	Intensive Care Unit	43	47.8%	7 (16,3)	36 (83,7)	

*[a]Student t Test [b]Fisher'sExact Test [c]Mann Whitney U Test [d]Pearson Chi-square Test *p<0.01*

Table 2: Sepsis Sources

		Total (%)	Mortality	
			No (%)	Yes (%)
Diagnosis	Pneumosepsis	41 (45.6%)	23 (42.6%)	18 (50%)
	Urosepsis	17 (18.9%)	14 (25.9%)	3 (8.3%)
	Gastrointestinal infection	7 (7.8%)	4 (7.4%)	3 (8.3%)
	Decubitus ulcer infection	7 (7.8%)	3 (5.6%)	4 (11.1%)
	Diabetic foot infection	5 (5.6%)	1 (1.9%)	4 (11.1%)
	Catheter infection	5 (5.6%)	4 (7.4%)	1 (2.8%)
	Soft tissue infection	4 (4.4%)	3 (5.6%)	1 (2.8%)
	Central nervous system infection	3 (3.3%)	2 (3.7%)	1 (2.8%)

very large patient population (11). In the same study, both the definition and validation of this scoring were carried out. This scoring, which is found to be very successful in estimating mortality in patients with sepsis, has some limitations (3).

In addition, at the "The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis 3)" meeting held in 2016, "respiratory rate, systolic blood pressure and mental status change" was introduced in order to evaluate patients outside the intensive care unit and to identify patients at risk of death in terms of sepsis early. A new scoring system consisting of three parameters has been defined. This score is a modified version of the currently used SOFA and is named as quick SOFA (qSOFA) (1,12,13). However, this scoring system has also been discussed since its definition, and it is suggested that it may be insufficient in estimating mortality and its effectiveness should be supported by prospective studies.

The study of Rivers et al. revealed that one of the targets of hemodynamic therapy in early stage is to reduce lactate level, and that there is a strong relation between decreased lactate level reduced mortality in the early period (14). In general, lactate increases when tissue perfusion is impaired in all types of shock, and the degree of elevation is associated with mortality (15).

In this study, the power of predicting mortality of lactate level at the time of admission and the role of lactate clearance in predicting mortality after appropriate targeted therapy were investigated in patients diagnosed with sepsis admitted to the emergency department.

MATERIAL AND METHOD

All patients with a diagnosis of severe sepsis and septic shock, aged >18 years, who applied to a university hospital emergency medicine outpatient clinic between 2016 and 2017, were included in this prospective observational cohort study after obtaining their or their first-degree relatives' consent. The study was carried out in accordance with the ethics committee approval of the faculty, dated 13/03/2017 and numbered 31887016-604.01.02-98644.

For the diagnosis of sepsis, standard sepsis criteria determined in the Sepsis Survival Campaign 2016 guideline were used. Sepsis treatment was carried out in line with the same guideline, taking into account the clinical picture of the patient.

Data Collection

Demographic characteristics, hospitalization diagnoses, comorbidities, systolic and diastolic blood pressure values, respiratory rate, fever, laboratory values, glaskow coma scores were recorded under the heading of vital signs within the first 24 hours of the diagnosis of sepsis and septic shock. The lactate values in arterial blood gas taken at the first admission to the emergency department (H0) and the lactate values taken at the sixth hour (H6) after appropriate treatment were recorded. Lactate clearance was calculated and recorded according to the appropriate formula.

Lactate Clearance = [(Initiative lactate – Follow-up lactate)/ l Initiative lactate] x 100%]

The focus of infection was recorded as lung, urinary system, catheter, soft tissue, diabetic foot, decubitus ulcer, central nervous system and gastrointestinal system.

The antibiotic treatments received by the patients, the need for ventilation, the service they were followed, their discharge status and thirty-day mortality status were determined and recorded.

RESULTS

Most of the 90 sepsis patients included in the study were over 65 years of age. While 60.0% (n=54) of the cases could be treated, 40.0% (n=36) died. When the relationship between mortality and descriptive data was investigated, a statistically significant negative correlation was found between Glascow Coma Score (GCS) and mortality ($p=0.002$; $p<0.01$). A statistically significant negative correlation was also found between the degree of

Table 3: Antibiotic Therapy

Antibiotic	n	%
Piperacillin-Tazobactam	24	26.7%
Meropenem + Vancomycin	16	17.8%
Piperacillin-Tazobactam +Clarithromycin	13	14.4%
Seftriakson	13	14.4%
Meropenem + Teicoplanin	6	6.7%
Piperacillin-Tazobactam + Teicoplanin	4	4.4%
Ertapenem	4	4.4%
Meropenem	3	3.3%
Teicoplanin	2	2.2%
Meropenem + Vancomisin + Acyclovir	2	2.2%
Meropenem + Vancomisin + Antituberculosis	2	2.2%
Ampicillin-Sulbactam	1	1.1%

Table 4: Laboratory Results and Mortality

				Mortality		p
		n	%	No (n=54) n (%)	Yes (n=36) n (%)	
Hemoglobin	Min-Max (Median)	5.6-15.8(9.5)		6-15.8(9.6)	5.6-13.9(9.5)	[a]0.890
	Mean±Sd	9.87±2.06		9.84±2.09	9.90±2.05	
	Normal	54	60.0%	32 (59.3)	22(40.7)	
	Low	36	40.0%	22 (61.1)	14(38.9)	
WBC	Min-Max (Median)	400-84.000(13950)		600-84.000(13750)	400-73900(15150)	[b]0.234
	Mean±Sd	15.888±14.157		15029.63±14685.77	17177.78±13426.27	
	Low	13	14.4%	10(76.9)	3(23.1)	
	Normal	19	21.1%	10(52.6)	9(47.4)	
	High	58	64.4%	34(58.6)	24(41.4)	
Platelet	Min-Max (Median)	14-562(211)		49-562(212)	14-507(210)	[b]0.526
	Mean±Sd	235.72±135.45		243.25±134.22	224.42±138.40	
	Low	26	28.9%	15(57.7)	11(42.3)	
	Normal	47	52.2%	29(61.7)	18(38.3)	
	High	17	18.9%	10(58.8)	7 (41.2)	
Neutrophil count	Min-Max (Median)	0.10-66(8.8)x10 9/L		0.1-66(6.6)	0.1-61.6(11.3)	[b]0.002**
	Mean±Sd	10.39±10.38 x10 9/L		8.38±9.45	13.40±11.10	
Neutrophil (%)	Min-Max (Median)	21-98.2(80)		23-95(73.5)	21-98.2(87)	[b]0.005**
	Mean±Sd	74.83±19.37		70.60±19.66	81.19±17.32	
Neutrophil count	Low	11	12.2%	9 (81.8)	2(18.2)	[b]0.002**
	Normal	20	22.2%	16 (80.0)	4(20.0)	
	High	59	65.6%	29(49.2)	30(50.8)	
CRP	Min-Max (Median)	1-500(164)		10-500(137)	1-471(175)	[b]0.556
	Mean±Sd	181.48±123.19		175.54±123.17	190.39±124.42	
	Normal	1	1.1%	0(0)	1(100)	
	High	89	98.9%	54(60.7)	35(39.3)	
AST	Min-Max (Median)	5-898(28)		5-898(21.5)	11-633(35)	[b]0.001**
	Mean±Sd	63.65±127.52		48.32±128.92	86.64±123.61	
	Normal	64	71.1%	45(70.3)	19(29.7)	
	High	26	28.9%	9(34.6)	17(65.4)	
ALT	Min-Max (Median)	2.2-443(19)		2.2-443(18.5)	6.5-410(19.5)	[b]0.052
	Mean±Sd	40.64±71.81		35.38±71.45	48.53±72.63	
	Normal	68	75.6%	43(63.2)	25(36.8)	
	High	22	24.4%	11(50.0)	11(50.0)	
Total bilirubin	Min-Max (Median)	0.14-49(0.7)		0.14-12(0.5)	0.2-49(0.9)	[b]0.003**
	Mean±Sd	2.34±6.34		0.91±1.64	4.48±9.51	
	Normal	68	75.6%	45(66.2)	23(33.8)	
	High	22	24.4%	9(40.9)	13(59.1)	
Urea	Min-Max (Median)	11-455(71)		11-230(61)	15-455(98.5)	[b]0.015*
	Mean±Sd	91.33±81.77		69.19±47.11	124.56±108.41	
	Normal	34	37.8%	22(64.7)	12(35.3)	
	High	56	62.2%	32(57.1)	24(42.9)	
Creatinine	Min-Max (Median)	0.23-9.9 (1.2)		0.23-9.9(1)	0.4-9.1(1.5)	[b]0.063
	Mean±Sd	1.79±1.84		1.59±1.69	2.10±2.02	
	Normal	50	55.6%	34(68.0)	16(32.0)	
	High	40	44.4%	20(50.0)	20(50.0)	

*[a]Student t Test [b]Mann Whitney U Test *p<0.05 **p<0.01*

temperature and mortality (p=0.001; p<0.01). However, a statistically significant positive correlation was found between the need for ventilation, intensive care unit tranfers and mortality (p=0.001; p<0.01). Descriptive Characteristics and mortality analyses are in Table 1.

The most common infection source of the patients is the

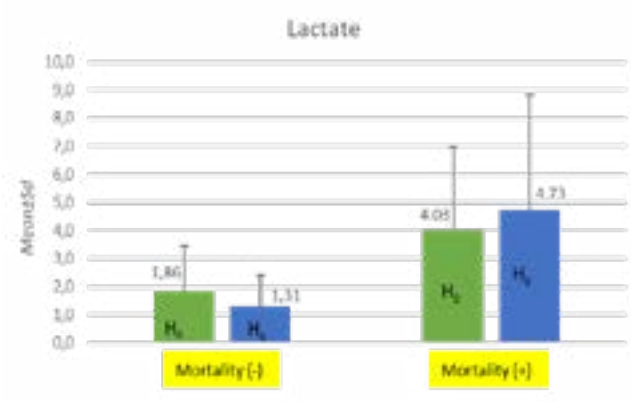

Figure 1: Lactate Levels According to the Presence of Mortality

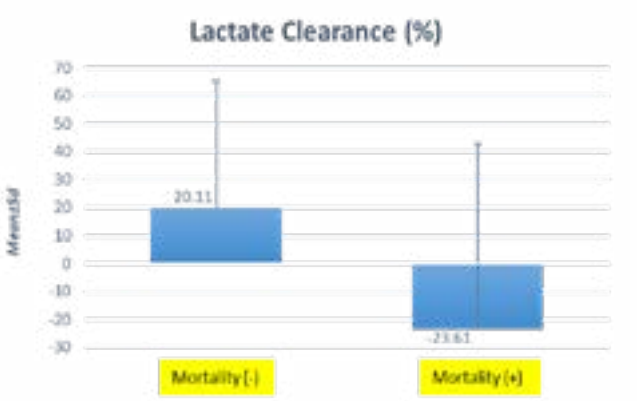

Figure 2: Lactate Clearance (%) Levels According to the Presence of Mortality

lungs followed by the urinary system. Less frequently, gastrointestinal tract, catheter, diabetic foot ulcers and decubitus ulcers are also seen to be the source (Table 2).

The most commonly used antibiotic in the treatment of sepsis is piperacillin-tazobactam combination. Detailed antibiotic therapy is available in Table 3.

The majority of patients have elevated CRP, leukocytosis and neutrophilia. When the relationship between laboratory findings and mortality is examined, neutrophil count ($p=0.002$; $p<0.01$), neutrophil percentage ($p=0.005$; $p<0.01$), AST ($p=0.001$; $p<0.01$), ALT ($p=0.052$; $p>0.05$) total bilirubin ($p=0.003$; $p<0.01$) 0.01), urea ($p=0.015$; $p<0.05$), and creatinine ($p=0.063$; $p>0.05$) levels were positively correlated with mortality. Other laboratory values and mortality rates are available in Table 2.

Lactate and Lactate Clearance

H0 lactate levels of all cases ranged from 0.4 to 13, with a mean of 2.73±2.46; The lactate level of 43.3% (n=39) was normal and of 56.7% (n=51) was high. H6 lactate measurements of the cases ranged from 0.4 to 18.7, with an average of 2.67±3.20.

The decrease in the H6 lactate levels of the cases compared to the H0 hour was statistically significant ($p=0.001$; $p<0.01$). Accordingly, lactate level of 2.2% (n=2) of the cases remained normal, while 63.3% (n=57) decreased and 34.4% (n=31) increased.

According to the presence of mortality, a statistically significant positive correlation was found between the H0 lactate levels of the cases ($p=0.046$; $p<0.05$); H0 lactate levels of the cases with mortality were significantly higher than those without mortality. A statistically significant positive correlation was found between the H6 lactate levels of the cases according to the presence of mortality ($p=0.001$; $p<0.01$); H6 hour lactate levels of cases with mortality were significantly higher than those without mortality (Table 5).

The decrease in the H6 lactate levels of the cases without mortality was statistically significant ($p=0.001$; $p<0.01$). The change in the H6 lactate levels of the cases with mortality was not statistically significant ($p=0.289$; $p>0.05$).

The change in the H6 lactate levels of the cases showed a statistically significant difference according to the presence of mortality ($p=0.001$; $p<0.01$). While a decrease was observed in lactate levels in patients without mortality, an increase was observed in patients with mortality (Table 5, Figure 1).

The lactate clearance (%) of the cases ranged from -200 to 80, with a mean of 2.62±58.39 and a median of 15. Accordingly, 40.0% (n=36) of the cases' lactate were low and 60.0% (n=54) were high.

A statistically significant negative correlation was found between the lactate clearance (%) of the cases according to the presence of mortality ($p=0.001$; $p<0.01$); lactate clearance (%) of cases with mortality were significantly lower than those without mortality (Table 5, Figure 2).

DISCUSSION

Among the parameters that are thought to affect mortality in sepsis patients, lactate level is preferred because it is fast, practical, inexpensive, does not require invasive intervention, and is available in all emergency services (14). In recent years, lactate and lactate clearance have gained importance in the follow-up of sepsis patients and in determining the weight, since it has been reported to have prognostic value in studies conducted abroad (15). In the light of these studies, lowering the lactate value is among the treatment goals in the latest guideline (1,12,13). In a study conducted by Marty et al. in 2013, 91 intensive care patients were examined and lactate clearance was calculated by taking H0 H6 H12 H24 lactate values by being followed for 24 hours (16). Based on 28-day mortality, it has been shown that treatment with a 20% clearance target has a strong effect on reducing mortality. In our study, lactate clearance was calculated using H0 and H6 lactate values, and it was found that patients with a clearance above 10% had a lower 30-day mortality compared to other patients.

Again, in a study conducted between 2006 and 2008 in which 348 intensive care patients with a lactate level >3 mEg/L were included, the effect of normalizing the lactate level on tissue oxygenation was investigated. The patients were divided into two groups as the lactate group (171 patients) and the control group (177 patients), and the treatment protocol determined for that group was applied to both patient groups for 8 hours. While it was aimed to reduce the lactate level by 20% within 2 hours in the lactate group, the central venous oxygen saturation (ScvO2) target value of 70% was used in the control group. When the 28-day mortality rates of both patient groups were compared, it was found that the mortality rate was lower

Table 5: Lactate, Lactate Clearence (%) and Mortality

		Total (n=90)	Mortality		p
			No (n=54)	Yes (n=36)	
H0 Lactate	Min-Max (Median)	0.4-13 (1.9)	0.4-10.6 (1.4)	0.8-13 (2.9)	0.001**
	Mean±Sd	2.73±2.46	1.86±1.58	4.03±2.96	
	Normal	39 (43.3%)	32 (82.1%)	7 (17.9%)	
	High	51 (56.7%)	22 (43.1%)	29 (56.9%)	
H6 Lactate	Min-Max (Median)	0.4-18.7 (1.4)	0.4-5.8 (0.9)	0.7-18.7 (3.6)	0.001**
	Mean±Sd	2.67±3.20	1.31±1.11	4.73±4.11	
H0 - H6 change	Min-Max (Median)	-4.8-12.7 (-0.3)	-4.8-3.1 (-0.4)	-4.8-12.7 (0.3)	0.006**
	Mean±Sd	-0.06±2.26	-0.56±1.2	0.7±3.14	
	Normal	2 (2.2%)	2 (100%)	0 (0%)	
	Decreased	57 (63.3%)	43 (75.4%)	14 (24.6%)	
	Increased	31 (34.4%)	9 (29.0%)	22 (71.0%)	
Lactate clearance (%)	Min-Max (Median)	-200 – +80 (15)	-123 – +75 (33)	-200 – +80 (-17)	[a]0.001**
	Mean±Sd	2.62±58.39	20.11±45.07	-23.61±66.43	
	Low	36 (40.0)	12 (33.3)	24 (66.7)	
	High	54 (60.0)	42 (77.8)	12 (22.2)	

[a]Mann Whitney U Test *$p<0.05$ **$p<0.01$

in the lactate-reducing targetted group (17). In the light of all these studies, the recommendation to normalize the lactate level has taken its place in the 2012 guideline. In our study, the upper limit of lactate was accepted as 1.2, and patients with an admission lactate below this value were also included in the study. In our study, the effect of lowering the lactate level with treatment on mortality was investigated, and in accordance with this study, patients with lactate clearance below 10% had a higher mortality.

In the study conducted by Levraut et al. in 2003, the pronogstic value of lactate clearance was investigated in 56 intensive care unit patients with a lactate level <3mmol (18). Control arterial blood gas was taken 45 minutes after sepsis patients whose admission lactate was not high, and lactate clearance was calculated, and it was found that patients with low admission lactate were associated with poor outcome, independent of their admission lactate values. In our study, H0 lactate value was found to be effective on mortality. This may be because patients with normal and high lactate levels were included in the study. Again, H6 lactate value was found to be associated with mortality in our study. The absolute value of the control lactate value is effective on mortality, and at this point, our study is compatible with this study. The H0 value was found to be ineffective in this study, and at this point, our study is inconsistent with this study.

In a study conducted by Mikkelsen et al. in the emergency department in May 2009, the effect of elevated serum lactate on mortality independent of organ failure and shock was investigated in 830 severe sepsis patients (19). The patients were divided into low <2mmol, moderate (2-3.9) and high >4 lactate groups, and the presence of shock, hypotension, severity of the disease, age, gender, and organ failure were recorded. Mortality was found to be high in patients with moderate and high lactate, independent of other factors. In our study, it was determined that the presence of comorbidity had no effect on mortality. However, it was observed that the presence of kidney and liver dysfunction increased mortality. In addition, lactate values were not grouped, and values of 1.2 and above were considered high. Therefore, it can be said that our results are partially compatible with this study. However, the fact that we did not evaluate lactate elevation independently of other factors may be a shortcoming of our study.

In the study conducted by Nguyen et al. in August 2004, it was seen that patients with high lactate clearance compared to H0 and H6 values in 111 patients with sepsis who were taken from the emergency room before the intensive care unit and taken to the intensive care unit during follow-up showed less mortality compared to those with low lactate clearance (20). These results are consistent with our study. However, in our study, patients whose H6 lactate control was performed outside the emergency department were excluded from the study. As a result of insufficient number of intensive care beds in the hospital, patients in need of intensive care are mostly referred to intensive care units in an external center. As a result, patients who were referred before 6 hours were not included in the study, as there would be problems in the H6 follow-up of the patients.

In our study, the mean age was 61.33, 52% of patients were under 65 years old, 47.8% of them were over 65 years of age. In the study of Nguyen et al., the average age is higher, and this may be due to the fact that our hospital is a university hospital where young immunological hematological patients with a large number of sub-branch departments are followed.

In the study conducted by Philippe Marty et al. in sepsis patients in 2013, mortality was found to be 45%, in the study of Levraut et al. 38%, and similarly 40% in our study (16,18).

In the study of Mikkelsen et al. on sepsis, the mean lactate value was found to be 2.9, and it was similarly found to be

2.7 in our study (19).

When we look at the relationship between thrombocytopenia and sepsis, it was reported in a short review published in 2016 that thrombocytopenia is a common source of morbidity and increases mortality in sepsis patients (21). In our study, platelet count was found to be ineffective on mortality. This result may be due to the smaller number of patients with thrombocytopenia in our study and the fact that the majority of thrombocytopenia was not caused by sepsis.

Rhiong zahi et al. investigated the effect of total bilirubin elevation on mortality and the risk of 60-day ARDS and mortality in 1006 sepsis patients in the USA (22). Bilirubin was found to be higher in the patient group with mortality, and it was determined that each 1mg/dl increase in total bilirubin increased the mortality rate by 7%. In our study, according to the presence of mortality, the total bilirubin measurements of the cases were higher than those without mortality ($p=0.003, p<0.01$).

In a retrospective, multicenter study conducted in Germany in 2007 and including 3877 sepsis patients in the intensive care unit, the rate of acute renal failure was found to be 41.4% in sepsis patients (23). In our study, this rate was found to be 62%. This may be because patients with chronic renal failure were not excluded from our study. Again in this study, patients with high urea and creatinine levels were found to have higher mortality than those without. The results of our study are compatible with this study.

In our study, it was determined that there were significant differences in terms of glaskow coma scale, respiratory rate, fever, neutrophil count, urea, creatinine, ventilation need, follow-up of the patient in the intensive care unit, AST, total bilirubin, and mortality in sepsis patients. However, it was observed that blood pressure, age, comorbidities, hemoglobin, platelet count, CRP, ALT values had no effect on mortality.

In a prospective multicenter randomized controlled study conducted by Clemmer et al. in 1992, a 9% hypothermia rate was observed (24). In our study, this rate was 16.7% (n=15). While mortality in hypothermic patients was 70% in this study, it was 100% in our study. In our study, a significant relationship was found between body temperature and mortality in sespsis. Mortality was higher in hypothermic patients compared to normothermic and hyperthermic patients. This may be due to the fact that the low immune system response of these patients affected the fever response and the host response to sepsis was weak for the same reason. Our study is compatible with these studies in terms of hypothermia-mortality relationship.

The retrospective study of Haas at al. showed that decreased lactate clearence and high lactate levels (>10 mmol/L) have strong relation with high mortality rates in critically ill patient (25). A retrospective study wich compares lactate level and lactate clearance with 1060 septic shock patients demonstrate that both are convenient goals for treatment howewer 6th hour lactate level is better for predicting prognosis and mortality (26). So using lactate clearence as a objective for guiding early sepsis therapy could improve mortality rates in adult (27). According to a recent meta-analyse to use lactat clearence based therapy in early sepsis (6th hour) is more beneficial in terms of reducing mortality, ventilation need, in hospital time and APACHE-II scores in ICU than ScvO2 based therapy (28). Despite all this, the lactate mechanism is actually very complex, its clearence may not jus due to an over production or poor metabolisation so simply reducing the lactate level may not be a logical goal (29).

As a result of this study, it was found that the lactate value at admission and the decrease in lactate level after six hours were effective on mortality, and the absolute lactate value at the sixth hour was effective on determining mortality. Therefore, taking into account the lactate value in arterial blood sample taken at the time of admission to the emergency department, it may be appropriate to apply lactate-reducing treatment in the follow-up. However, the rate of clearance, not the absolute value of the control lactate value, is more effective on mortality. At the other hand, it may be more appropriate to use all markers together instead of a single marker in determining the prognosis in sepsis patients. Lactate clearance can be an important prognostic marker when combined with other factors.

As a conclusion, the high rate of lactate level decrease at the sixth hour indicates a good prognosis in sepsis patients, regardless of the lactate value. When all these results are taken into consideration, it can be said that the lactate value and lactate clearance are useful markers in predicting prognosis in sepsis patients admitted to the emergency department. However, they are not sufficient on their own to determine the prognosis and should be used together with other markers and clinical evaluation.

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