

Serum Lactate Levels as a Prognostic Predictor of Septic Shock in Emergency Department Patients with Systemic Inflammatory Response Syndrome (SIRS) at Songklanagarind Hospital

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Objective: To determine whether serum venous lactate is associated with an increased risk of septic shock and risk of death in emergency department patients with systemic inflammatory response syndrome (SIRS).

Material and Method: This was a prospective observational study at the Songklanagarind Hospital Emergency Department. Between April 1 and October 31, 2009, 131 consecutive patients met the enrollment criteria of age older than 18 years and fulfilled the SIRS criteria. Serum venous lactate was obtained in all enrolled patients. The main outcome measurements were development of septic shock, death within 24 hours, and in-hospital mortality at 3- and 28-day of presentation.

Results: Of the 131 patients enrolled, 50 (38.1%) developed septic shock. A lactate level greater than 36 mg/dL was associated with death (odds ratio [OR] = 4.29, 95% confidence interval [CI] = 1.19-15.55) to predict 28-day hospitalization mortality. It was also statistically significant to the progression to septic shock ($p = 0.013$) with 50.0% sensitivity and 73.2% specificity (OR = 2.73, 95% CI = 1.22-6.13).

Conclusion: For patients presenting to the emergency department with clinical symptoms of SIRS, a single serum venous lactate level measurement of greater than 36 mg/dL provides valuable prognostic predictor information concerning the high-risk group likely to progress to septic shock, more serious disease severity, and death.

Keywords: Septic shock, Serum lactate level, Systemic inflammatory response syndrome

J Med Assoc Thai 2016; 99 (8): 913-8

Full text. e-Journal: <http://www.jmatonline.com>

Severe sepsis and septic shock are common and lethal life-threatening conditions that emergency physicians routinely confront. The mortality rate approaches 50% and the keys to decreasing it are early detection and treatment⁽¹⁾. According to the recent Early Goal-directed Therapy and Surviving Sepsis Campaign Guidelines, serum lactate is one of the risk stratification tools to detect cardiovascular insufficiency, global tissue hypoxia, and increased metabolic demands resulting from sepsis before a change in the blood pressure^(2,3). There is much research to verify the use of various biomarkers to predict the progression to a worsened clinical outcome of systemic inflammatory response syndrome (SIRS) patients who visit the emergency department with a variety of conditions^(4,5). Several previous studies showed that the measured

serum lactate is a predictor of mortality in emergency department patients with infection and concluded that the mortality rates increased as lactate increased^(4,5). Some studies showed that elevated lactate levels were significantly associated with the subsequent development of septic shock^(6,7).

The present study aimed to determine the clinical utility of serum lactate level as a prognostic predictor of septic shock and in-hospital mortality in emergency department patients with SIRS.

Material and Method

This was a prospective observational study of 131 patients between August 1 and December 31, 2009. Enrolled patients were 18 years or older and fulfilled the SIRS criteria. Peripheral venous lactate levels were drawn and lactate levels were measured by enzymatic methods. The data consisted of demography, initial vital signs, and vital signs when septic shock occurred, laboratory results, venous lactate levels, bacterial culture results, results of treatment, and death.

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The SIRS criteria included body temperature hotter than 38°C (100.4°F) or lower than 36°C (96.8°F), pulse rate greater than 90/minute, respiratory rate greater than 20/minute (or PaCO₂ less than 32 mmHg), and WBC greater than 12,000/mm³ or less than 4,000/mm³, or band form greater than 10%⁽⁸⁾.

The following terms and conditions were defined as follows:

Sepsis defines as the clinical syndrome defined by the presence of both infection and a systemic inflammatory response.

Severe sepsis refers to sepsis complicated by organ dysfunction.

Septic shock refers to a state of acute circulatory failure characterized by persistent arterial hypotension unexplained by other causes.

The statistical analysis was conducted using Stata version 7.0 software. Continuous variables were analyzed and reported as mean, standard deviation, median, and range while discrete variables were reported as percentage. We determined the specificity and the sensitivity of lactate levels upon progression to septic shock in patients who presented with SIRS, sepsis, and severe sepsis. Chi-square and Fisher's exact tests were used to compare between two groups of data. The Kruskal-Wallis H test was used to identify a median value of lactate levels and disease severity. An association between lactate levels and the mortality rates were also reported at 24 hours, three days, and 28 days. A *p*-value <0.05 was considered statistically significant.

Results

Demographic data

One hundred thirty one patients were enrolled in the present study, 59 (45%) men and 72 (55%) women. One hundred four (79%) patients had underlying diseases. The three main underlying diseases were hypertension (24.4%), diabetes mellitus type II (22.1%), and cancer (19%). The SIRS scores in the present study were 2, 3, and 4 in 31 (23.7%), 50 (38.2%), and 50 (38.2%) patients, respectively. There were significant variables between septic shock group and non-shock group such as hemodynamic variables include lactate levels, bandemia, positive hemoculture, antibiotic prescription, hospital length of stay, and disposition status (Table 1).

Lactate levels and disease prognostication

Fifty patients (38.1%) developed septic shock. The serum lactate levels did not correlate with disease

severity (*p* = 0.075) (Fig. 1). The present study showed that an increased SIRS score did not correlate with the median value of serum lactate levels (*p* = 0.170) and the progression of septic shock did not correlate with SIRS scores (*p* = 0.657) (Fig. 2).

All patients who died within 24 hours and at day 3 of admission had higher lactate levels than the patients who died at day 28 (Fig. 3). Death within 24 hours and in-hospital mortality at day 3 and 28 of presentation increased as lactate levels increased (Fig. 4).

The serum lactate levels greater than 36 mg/dL had statistical significance with the progression to septic shock (*p* = 0.013) with 50.0% sensitivity and 73.2% specificity. At levels greater than 36 mg/dL the odds ratio (OR) was 2.73 to predict progression to septic shock (95% CI = 1.22-6.13) (Table 2). At lactate levels between 22.6 and 35.9 mg/dL there was statistical significance with 28-day in-hospital mortality. All lactate levels greater than 36 mg/dL had statistical significance with death. At levels greater than 36 the OR was 4.29 to predict 28-day in-hospital mortality (Table 3).

Discussion

Several studies showed the usefulness of risk stratification tools in patients presenting with SIRS

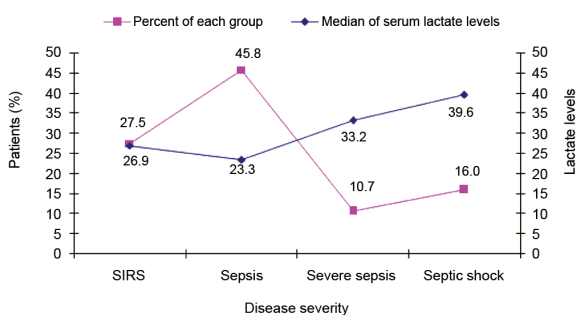


Fig. 1 Association between serum lactate levels and disease severity (n = 131).

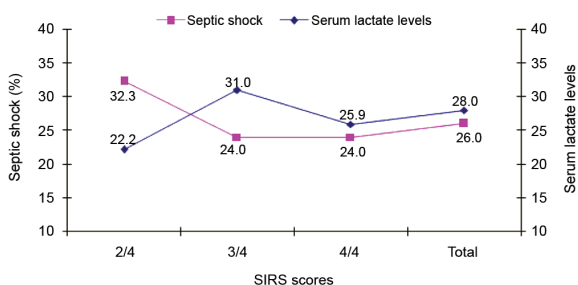


Fig. 2 Association between SIRS scores with septic shock and serum lactate levels.

Table 1. Demographic and baseline characteristics of patients

Characteristic	Septic shock group n = 34	Non-shock group n = 97	Total	p-value
Age (year), mean ± SD	57.4±19.6	53.5±20.3	54.5±20.1	0.334
Sex, n (%)				
Male	16 (47.1)	43 (44.3)	59 (45.0)	0.783
Female	18 (52.9)	54 (55.7)	75 (55.0)	
Underlying disease, n (%)				
Present	31 (91.2)	73 (75.3)	104 (79.4)	0.048
Absent	3 (8.8)	24 (24.7)	27 (20.6)	
Hemodynamic variables, mean ± SD				
Systolic blood pressure (mmHg)	105.8±28.3	135.7±23.4	127.9±27.9	<0.001
Diastolic blood pressure (mmHg)	62.5±18.0	81.5±16.2	76.5±18.6	<0.001
Arterial pH, median (IQR)	7.4 (7.3-7.5)	7.4 (7.4-7.5)	7.4 (7.4-7.5)	0.036
HCO ₃ (mmol/L), median (IQR)	18.9 (15.4-22.0)	22.8 (20.7-24.9)	21.4 (18.5-24.2)	0.009
Venous lactate level (mg/dL), median (IQR)	37.6 (19.7-73.9)	25.6 (17.4-37.8)	28.0 (18-41.6)	0.007
Laboratory test, median (IQR)				
WBC (cell/uL)	11,375 (5,995-15,940)	13,670 (8,765-17,510)	12,810 (8,200-17,120)	0.135
Bandemia (%)	8 (3-15)	2 (1-6)	4 (1-8)	0.006
Positive hemoculture, n (%)	11 (32.4)	12 (12.4)	23 (17.6)	0.008
Causes of SIRS, n (%)				
<i>Escherichia coli</i> septicemia	6 (17.6)	2 (2.1)	8 (6.1)	0.001
Antibiotics, n (%)				
Prescribed	29 (85.3)	62 (63.9)	91 (69.5)	0.020
Un-prescribed	5 (14.7)	35 (36.1)	40 (30.5)	
Time variables, median (IQR)				
Time to antibiotic (minutes)	120 (100-167)	180 (115-262)	157 (103-232)	0.016
Emergency Department length of stay (hours)	245 (165-337)	250 (175-360)	250 (170-355)	0.856
Hospital length of stay (days)	13 (7-23)	3 (1-8)	6 (1-13)	<0.001
Disposition status, n (%)				
Admit	25 (73.5)	48 (49.5)	73 (55.7)	0.015
Refer	9 (26.5)	24 (24.7)	33 (25.2)	0.842
Discharge	0 (0.0)	25 (25.8)	25 (19.1)	0.001

WBC = white blood cell; SIRS = systemic inflammatory response syndrome
Data are expressed as mean ± SD, median (IQR), or n (%)

Table 2. Serum lactate and septic shock

Lactate (mg/dl) (n)	Sensitivity (%)	Specificity (%)	Septic shock (n = 34)	Non-shock (n = 97)	p-value	Odds ratio (95% CI)
<18 (32)	20.6	74.2	7	25	0.545	0.75 (0.29-1.93)
18-22.5 (20)	11.8	83.5	4	16	0.509	0.68 (0.21-2.18)
22.6-35.9 (36)	17.6	69.1	6	30	0.136	0.48 (0.18-1.28)
≥36 (43)	50.0	73.2	17	26	0.013	2.73 (1.22-6.13)

Table 3. Serum lactate and mortality

Lactate levels (mg/dL) (n)	24-hour in-hospital mortality		3-day in-hospital mortality		28-day in-hospital mortality	
	p-value	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)	p-value	Odds ratio (95% CI)
<18 (32)	0.418	-	0.202	-	0.878	1.12 (0.27-4.71)
18-22.5 (20)	0.545	-	0.385	-	0.645	0.60 (0.07-5.32)
22.6-35.9 (36)	0.380	-	0.095	-	0.039	0.14 (0.02-1.16)
≥36 (43)	0.041	-	0	-	0.020	4.29 (1.19-15.55)

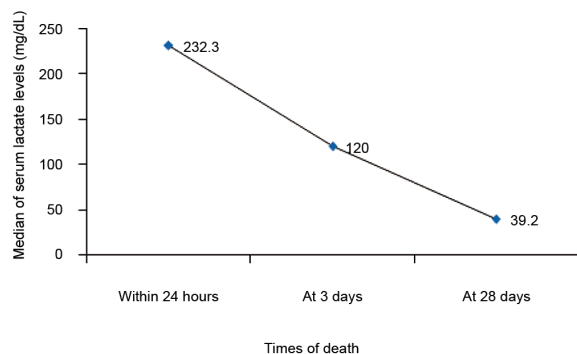


Fig. 3 Lactate levels at various times of death.

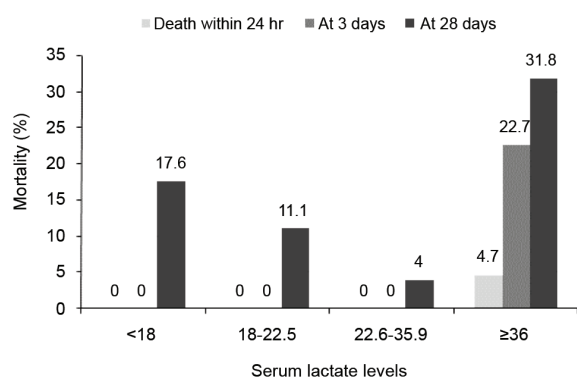


Fig. 4 Lactate as a predictor of mortality.

and infection. Rangel-Fausto et al⁽⁹⁾ found that 4% of patients diagnosed as SIRS will progress to septic shock and the median interval from SIRS to sepsis was inversely correlated with the number of SIRS criteria. Mato et al⁽⁷⁾ concluded from his study that about 8% of patient with SIRS will develop septic shock and that lactate levels greater than 18 mg/dL were associated with septic shock. However, in the present study we found that 16% of SIRS progress to septic shock. Markedly elevated serum lactate levels refer to severe global tissue hypoxia, multiple organ failure and lead to early death (Fig. 3, 4). Shapiro et al⁽⁴⁾ found that the 28-day and 3-day mortality rates of the patients who had initial lactate levels more than 36 mg/dL were about 28% and 22%, respectively, which is similar to the present study (Fig. 4). Therefore, serum lactate levels can serve as a prognostic predictor in SIRS. The SIRS patients who had serum lactate levels greater than 36 mg/dL had a 2-fold chance of developing septic shock. The serum lactate levels were beneficial in predicting mortality in septic shock as shown in previous studies and in our study. However, there are several limitations of our study. During the time of the

present study, serum lactate measurement was not a routine laboratory test and it was not available 24 hours a day. We measured only single lactate levels and the lactate levels were not compared with other physiologic scores such as Acute Physiology and Chronic Health Evaluation (APACHE) II, Multiple Organ Dysfunction Syndrome (MODS) or Sepsis-Related Organ Failure Assessment scores (SOFA scores). Moreover, finding the cut points of lactate levels using a receiver operating characteristics curve (ROC) and performing a subgroup analysis between the shock group and non-shock group may provide valuable data.

Conclusion

A serum lactate level greater than 36 mg/dL is a prognostic predictor for septic shock and in-hospital mortality. For inpatients presenting at the emergency department with clinical symptoms of SIRS, a single measurement of the serum venous lactate level provides valuable prognostic predictor information concerning the high-risk group likely to progress to septic shock, more serious disease severity, and death. It clearly demonstrates that the lactate level may be helpful in identifying the high-risk patient population the emergency department. Moreover, using the lactate level as an additional tool simultaneously with other clinical predictors should be considered.

What is already known on this topic?

Several studies showed the usefulness of risk stratification tools in patients presenting with sepsis and septic shock.

What this study adds?

The study present the more earlier parameter detecting sepsis in the patient who presented with systemic inflammatory response syndromes in the emergency department with a lactate level of greater than 36 mg/dL.

Compliance with Ethical Requirements

The Institutional Ethics Committee Board approved the present study.

Author contributions

Dadeh A performed the literature search, study design, data collection, data analysis, data interpretation, and writing. Wuthisuthimethawee P did the study design and critical revision.

Acknowledgements

The authors thank Kingkarn Waiyanak for article searching and retrieval, Glenn K Shingledecker for his help in editing the manuscript, and the Faculty of Medicine, Prince of Songkla University for funding this research.

Potential conflicts of interest

None.

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การใช้ระดับแลคเตทในเลือดเพื่อพยากรณ์การเกิดภาวะช็อกจากการติดเชื้อในผู้ป่วยที่มีการอักเสบทั้งระบบ ที่ห้องฉุกเฉิน
โรงพยาบาลสงขลานครินทร์

อาอัยชะห์ ดาเด๊ะ, ประสิทธิ์ วุฒิสุทธิเมธาวิ

วัตถุประสงค์: เพื่อศึกษาความสัมพันธ์ ระหว่างระดับแลคเตทในกระแสเลือดกับการพยากรณ์ความเสี่ยงต่อการเกิด septic shock และอัตราการตายในผู้ป่วยที่มาห้องฉุกเฉินด้วยภาวะ systemic inflammatory response syndrome (SIRS)

วัสดุและวิธีการ: เป็นการศึกษาเปรียบเทียบโดยการสังเกตการณ์ไปข้างหน้า ที่ห้องฉุกเฉิน โรงพยาบาลสงขลานครินทร์ โดยเก็บข้อมูลระหว่าง วันที่ 1 เมษายน พ.ศ. 2552 ถึง 31 ตุลาคม พ.ศ. 2552 ศึกษาในผู้ป่วยอายุ 18 ปีขึ้นไป ที่เข้าเกณฑ์การศึกษาจำนวน 131 ราย ที่มีอาการอักเสบทั้งระบบ

ผลการศึกษา: ข้อมูลจากผู้ป่วยทั้งหมด 131 ราย ผู้ป่วย 50 ราย (ร้อยละ 38.1) เกิด septic shock ระดับแลคเตทที่มากกว่าหรือเท่ากับ 36 มิลลิกรัมต่อเดซิลิตร มีความสัมพันธ์ทางสถิติอย่างมีนัยสำคัญกับอัตราการตายที่ระยะเวลาต่างๆ มีค่า odds ratio เท่ากับ 4.29 (95% CI 1.19-15.55) ต่ออัตราการตายที่ 28 วัน อีกทั้งยังมีความสัมพันธ์กับการเกิด septic shock อย่างมีนัยสำคัญทางสถิติอีกด้วย ($p = 0.013$) โดยมีค่าความไวและความจำเพาะต่อการเกิด septic shock เท่ากับร้อยละ 50.0 และร้อยละ 73.2 ตามลำดับ โดยมีค่า odds ratio เท่ากับ 2.73 (95% CI 1.22-6.13)

สรุป: การใช้ระดับแลคเตทในเลือดค่าที่เจาะครั้งแรกที่ห้องฉุกเฉินที่ค่าระดับมากกว่า 36 มิลลิกรัมต่อเดซิลิตร มาใช้พยากรณ์โรคในผู้ป่วยที่มาที่ห้องฉุกเฉินด้วยกลุ่มอาการของ SIRS นั้นถือว่ามีประโยชน์ สามารถใช้เป็นข้อมูลการพยากรณ์โรคอย่างหนึ่ง ในการคัดแยกผู้ป่วยที่มีความเสี่ยงที่จะเกิด septic shock มีความรุนแรงของโรคมากขึ้น และมีโอกาสที่จะเสียชีวิตได้
