

## Association between clinical parameters and risk of sepsis

Nahatai Jongprasitkul\*

Watchara Petchratchatanon\* Chatchasa Charanyananda\*

**Jongprasitkul N, Petchratchatanon W, Charanyananda C. Association between clinical parameters and risk of sepsis. Chula Med J 2018 Jan – Feb; 62(1): 27 - 38**

**Background** : *Sepsis is a severe life-threatening condition and has a great diversity in symptoms that causes a rapid response of inflammation; as a result, it might damage the internal organs throughout the body. Nowadays, there is insufficient medical instrument and reliable treatment strategies that provide a promising diagnosis which can indicate the right sepsis condition. The aim of this research is to improve the clinical judgment, which might lead to earlier aggressive therapeutic interventions.*

**Objectives** : *To study the association and risk factors between emergency department patients with sepsis.*

**Methods** : *In all, 400 retrospective medical data records among emergency department patients were retrieved from a variety of sources (retrospective chart reviews). The samples were divided into culture positive and culture negative results of sepsis. After that the data were analyzed statistically to determine the relationship and risk factors in sepsis patients.*

**Results** : *This study showed that sepsis was associated with male gender, diabetes mellitus, chronic kidney diseases, alcohol dependence, low hemoglobin level (less than 10 g/dL), albumin (less than 3.5 g/dL), lactate (more than 2.1 mmol/L), systolic blood pressure (less than 90 mmHg), respectively. It was also found that the risk factors were corresponding to diabetes mellitus ( $P = 0.033$ ), chronic kidney disease ( $P = 0.008$ ), low hemoglobin level (less than 10 g/dL) ( $P = 0.001$ ), albumin (less than 3.5 g/dL) ( $P = 0.043$ ), systolic blood pressure (less than 90 mmHg) ( $P = 0.001$ ).*

**Conclusions** : *Sepsis is a common condition which is often seen in emergency department. It is severely harmful and needs to be treated urgently. We found that the systolic blood pressure less than 90 mmHg was associated with the highest risk. Hopefully, this research could be an alternative to supplement the diagnosis and treatment of patients with sepsis in the future.*

**Keywords** : *Sepsis, association, risk factors, emergency department, Somdech Phra Pinklao Hospital.*

Correspondence to: Jongprasitkul N. Department of Emergency Medicine, Somdech Phra Pinklao Hospital. Naval Medical Department, Bangkok 10600, Thailand.

Received for publication. July 26, 2017.

ณัททัย จงประสิทธิ์กุล, วิชระ เพ็ชรรัชตานนท์, ชัชชา จรรย์ยานนท์. ความสัมพันธ์  
ระหว่างคุณลักษณะของผู้ป่วยห้องฉุกเฉิน และการตรวจพบภาวะติดเชื้อในกระแสเลือด.  
จุฬาลงกรณ์เวชสาร 2561 ม.ค. - ก.พ.; 62(1): 27- 38

- เหตุผลของการทำวิจัย** : ภาวะติดเชื้อในกระแสเลือดเป็นกลุ่มอาการที่มีความรุนแรง และมีความหลากหลาย โดยลักษณะ คือ การอักเสบของระบบในร่างกายอย่างรวดเร็ว และนำไปสู่อันตรายต่ออวัยวะต่าง ๆ เนื่องจากในปัจจุบันยังไม่มีเครื่องมือ หรือการวินิจฉัยใดยืนยัน การวินิจฉัยว่าผู้ป่วยรายใดมีภาวะติดเชื้อในกระแสเลือด เป้าหมายของการวิจัยนี้เพื่อช่วยในการตัดสินใจ และเพื่อนำไปสู่การรักษาที่รวดเร็วยิ่งขึ้น
- วัตถุประสงค์** : ศึกษาความสัมพันธ์และปัจจัยเสี่ยงระหว่างลักษณะของผู้ป่วยห้องฉุกเฉิน และการตรวจพบภาวะติดเชื้อในกระแสเลือดของผู้ป่วยที่มารับบริการที่ห้องฉุกเฉิน โรงพยาบาลสมเด็จพระปิ่นเกล้า
- วิธีการทำวิจัย** : เก็บข้อมูลย้อนหลังจากแฟ้มประวัติผู้ป่วยที่เป็นเอกสารและอิเล็กทรอนิกส์ จำนวน 400 ตัวอย่าง โดยแบ่งกลุ่มตัวอย่างเป็นผลเพาะเชื้อในกระแสเลือดเป็นบวกและลบ จึงนำมาวิเคราะห์ข้อมูลทางสถิติ เพื่อหาความสัมพันธ์และปัจจัยเสี่ยงกับภาวะติดเชื้อในกระแสเลือด
- ผลการศึกษา** : พบความสัมพันธ์กับภาวะติดเชื้อในกระแสเลือด คือ เพศชาย โรคเบาหวาน โรคไตเรื้อรัง ภาวะติดเชื้อรา ระดับฮีโมโกลบินในเลือด  $< 10$  กรัมต่อเดซิลิตร ระดับแอลบูมินในเลือด  $< 3.5$  กรัมต่อเดซิลิตร สารแลคเตท  $\leq 2.1$  ความดันเลือดช่วงหัวใจบีบตัว  $< 90$  มิลลิเมตรปรอท และพบว่าปัจจัยเสี่ยงที่เกี่ยวข้องกับภาวะติดเชื้อในกระแสเลือด คือ โรคเบาหวาน ( $P = 0.033$ ) โรคไตเรื้อรัง ( $P = 0.008$ ) ระดับฮีโมโกลบินในโลหิต  $< 10$  กรัมต่อเดซิลิตร ( $P = 0.001$ ) ระดับแอลบูมินในเลือด  $< 3.5$  กรัมต่อเดซิลิตร ( $P = 0.043$ ) ความดันเลือดช่วงหัวใจบีบตัว  $< 90$  มิลลิเมตรปรอท ( $P = 0.001$ )
- สรุป** : ภาวะติดเชื้อในกระแสเลือดเป็นภาวะที่พบได้บ่อยในห้องฉุกเฉิน เป็นภาวะที่อันตรายและต้องได้รับการรักษาอย่างรวดเร็ว โดยพบว่าความดันเลือดช่วงหัวใจบีบตัว  $< 90$  มิลลิเมตรปรอท เป็นปัจจัยเสี่ยงที่สูงที่สุด และหวังว่างานวิจัยนี้จะเป็นส่วนหนึ่งในการช่วยวินิจฉัยและรักษาผู้ป่วยติดเชื้อในกระแสเลือดได้
- คำสำคัญ** : ภาวะติดเชื้อในกระแสเลือด, ความสัมพันธ์, ปัจจัยเสี่ยง, ห้องฉุกเฉิน, โรงพยาบาลสมเด็จพระปิ่นเกล้า.

Sepsis is a severe life-threatening condition and has a number of diversities of manifestation that cause rapid immune responses of inflammation; as a result, it may damage the internal organs throughout the entire body. Nowadays, there are insufficient clinical instruments and reliable treatment strategies to provide a promising diagnosis that can indicate the right sepsis condition. This research is aimed to improve the decision-making which might lead to a better and faster treatment. The most common cause of sepsis is infections, i.e., bacterial, viral, fungi and protozoa in origin. During the early stage of sepsis, the immune response is triggered throughout the system as well as the rises of heart rate and body temperature. Subsequently, the oxygen transports to other tissues are impaired. Ultimately, it progresses rapidly to septic shock leading to multiple organ failure and death. Sepsis condition comprises of many systems involvement, difficult to be diagnosed in the early stage.<sup>(1)</sup> Patients with sepsis have varieties of signs and symptoms. In this case, the statistical data showed that in every 100,000 patients, 300 to 1,000 had sepsis a year.<sup>(2)</sup> Sepsis condition is aggressive and has high hospital mortality rate up to 20% and particularly in septic shock which is increasing in death rate to more than 50% despite the patients were admitted on time.<sup>(3)</sup> In addition, the mortality rate is noticeably higher than other severe conditions such as acute myocardial infarction and stroke.<sup>(4)</sup> Every year sepsis has drawn many attentions and on the watch list of several nations including the United States of America, European Union, Australia and Thailand.<sup>(5)</sup> Thailand, in particular, sepsis has become more common than previously expected and more important in the National Health Services. Many researchers

and medical associations have been investigating and providing medical efforts to find new ways to recognize the condition more quickly and effectively.<sup>(6)</sup>

Originally, the definition of sepsis was based on Surviving Sepsis Campaign in 2012.<sup>(7)</sup> The definition was revised by The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) in 2016 and Surviving Sepsis Campaign in 2016.<sup>(8, 9)</sup> Currently, medical technologies have been advanced than previously ones and increased the survival rate of patients as well as raising higher cost of treatment. In each emergency room (ER) in the hospital, it is crucial to treat this condition.<sup>(10)</sup> The treatment and diagnosis given should be performed quickly and efficiently. Thus, the association and risk factors must be determined in order to manage the condition.

## Methods

There were 7,054 patients admitted to ER who diagnosed with sepsis from August 1<sup>st</sup> 2015 to August 1<sup>st</sup> 2016 at Somdech Phra Pinklao Hospital. Six hundred and forty-six patients were culture-positive sepsis, and 6,408 patients were culture-negative sepsis. On the basis of retrospective study should gather all the case to analyze. However, Human resource was insufficient in this study, thus we calculated the sample size by using graph from Chase G.<sup>(11)</sup> with alpha ( $\alpha$ ) = 0.05 ( $K = 1.00$ ), Beta ( $\beta$ ) = 0.20,  $P = 0.59$ <sup>(12)</sup>, and magnitude  $C = 3$ . The ordinate 89 is read which mean the sample size from each group should be at least 89 (in total 178) to yield the statistical significance at 0.05 ( $P < 0.05$ ). As a result, 400 patients were enrolled in this study.

Four hundred medical data records during those periods were retrieved from hospital sources,

the medical chart review and electronic medical records (EMR). The documents were collected based on population criteria, which were divided into 2 groups: culture-positive sepsis and culture-negative sepsis, and randomly selected in this study by, collected every 4 of the overall sample to each group (maximum 200) that we anticipated to eliminate the selection bias.

Statistical indicators were tracked and recorded in data archives and spreadsheet program. After the indicators were completely collected, the data was analyzed in order to determine the association and risk factors between several values corresponding to sepsis.

### Definition

In this study, sepsis is life-threatening organ dysfunction due to deregulated host responses to infection. Organ dysfunction is defined as an increase of 2 points or more in the Sequential Organ Failure Assessment (SOFA) scores or qSOFA. Septic shock is defined as sepsis and presence of hypotension requiring vasopressors to maintain *mean arterial pressure* (MAP) greater than or equal to 65 mm Hg, and lactate greater than or equal to 2 mmol/L despite sufficient fluid administration is provided, according to the Third International Consensus Definitions for sepsis and septic shock (Sepsis-3) in 2016 and Surviving Sepsis Campaign 2016.<sup>(8, 9)</sup>

### Statistical analysis

A comparative study of patients at the Department of Emergency Medicine with sepsis was analyzed, descriptive statistic was used to explain the results accordingly, i.e., frequency distribution,

percentage, mean and standard deviation. Qualitative analysis was to test the statistical relationship via *Chi-square* test. In quantitative analysis, we used multiple regression analysis with enter regression model to identify the risk factors with statistical significance that was less than 0.05. A statistical analysis software was applied to analyze all data.

### Results

A total of four hundred patients with sepsis, there were 207 males (51.8%) and 193 females (48.3%). The majority of them were Thai (n = 377, 94.3%), followed by Burmese (n = 14, 3.5%), Chinese (n = 7, 1.8%) and Laotians (n = 2, 0.5%), respectively. The mean age ( $\pm$  standard deviation) was  $62.0 \pm 18.4$  years. The most common comorbidities found were diabetes mellitus (n = 251, 62.8%); followed by chronic kidney diseases (n = 155, 38.8%); and, coronary artery diseases (n = 107, 26.8%). Besides, 63 patients were staying in elder homecare services (15.8 %); and 43 patients had long-term vascular access (10.8 %).

In univariate analysis, factors associated with sepsis condition have 5 aspects, namely: 1) individual characteristic; 2) clinical characteristics; 3) comorbidities; 4) clinical laboratory characteristic; and 5) organ dysfunctions. (Table 1)

The individual characteristic of the patient with sepsis was significantly associated ( $P < 0.05$ ), which was male gender; whereas the clinical characteristic of the patient with sepsis showed no association with sepsis. In the comorbidities characteristics, sepsis was associated with comorbidities ( $P < 0.05$ ), namely: diabetes mellitus, chronic kidney disease and alcohol dependence. Clinical laboratory characteristic

associated with sepsis ( $P < 0.05$ ) were, namely: serum hemoglobin  $< 10$  g/dL, and serum albumin  $< 3.5$  g/dL. Regarding the relationship of organ dysfunctions and sepsis showed significant association ( $P < 0.05$ ) with lactate  $> 2.1$  mmol/L, and systolic blood pressure  $< 90$  mmHg.

Risk factors for development of sepsis were determined by multiple regression analysis between

(individual characteristic, clinical characteristic, comorbidities, clinical laboratory characteristic, organ dysfunctions) and sepsis. As a result, the associated risk factors were diabetes mellitus, chronic kidney disease, serum hemoglobin  $< 10$  g/dL, serum albumin  $< 3.5$  g/dL and systolic blood pressure  $< 90$  mmHg, as shown in Table 2.

**Table 1.** A comparison of patient characteristics of culture positive and culture negative with sepsis.

	Blood culture						P
	Positive		Negative		Total		
	Count	(%)	Count	(%)	Count	(%)	
<b>Sex</b>							
Male	105	(52.5)	102	(51.0)	207	(51.8)	0.034
Female	95	(47.5)	98	(49.0)	193	(48.3)	0.399
<b>Race</b>							
Thai	190	(95.0)	187	(93.5)	377	(94.3)	0.273
Burmese	6	(3.0)	8	(4.0)	14	(3.5)	
Laos	1	(0.5)	1	(0.5)	2	(0.5)	
Chinese	3	(0.2)	4	(2.0)	7	(1.8)	
<b>Clinical characteristic</b>							
Nursing home status	32	(16.0)	31	(15.7)	63	(15.8)	0.959
Presence of long-term vascular access	20	(10.0)	23	(11.5)	43	(10.8)	0.580
<b>Triage diastolic blood pressure (mmHg)</b>							
$< 50$	29	(14.5)	24	(12.0)	53	(13.3)	0.510
$\geq 50$	171	(85.5)	176	(88.0)	347	(86.8)	0.123
<b>Respiratory rate (per minute)</b>							
$< 22$	32	(16.0)	28	(14.0)	60	(15.0)	0.328
$\geq 22$	168	(84.0)	172	(86.0)	340	(85.0)	
<b>Comorbidities</b>							
Diabetes mellitus	117	(58.5)	134	(67.0)	251	(62.8)	0.044
Coronary artery disease	48	(24.0)	59	(29.5)	107	(26.8)	0.223
Congestive heart failure	49	(24.5)	54	(27.0)	103	(25.8)	0.490
Cirrhosis	21	(10.5)	29	(14.5)	50	(12.5)	0.199
Chronic kidney disease	73	(36.5)	82	(41.0)	155	(38.8)	0.019
Chronic obstructive pulmonary disease/asthma	40	(20.0)	47	(23.5)	87	(21.8)	0.340
Alcohol dependence	23	(11.5)	32	(16.0)	55	(13.8)	0.013
Cancer	37	(18.5)	47	(23.5)	84	(21.0)	0.183

**Table 1.** (Cont.) A comparison of patient characteristics of culture positive and culture negative with sepsis.

	Blood culture						P
	Positive		Negative		Total		
	Count	(%)	Count	(%)	Count	(%)	
Clinical laboratory characteristic							
Serum bicarbonate (mmol/L)							
< 20	123	(61.5)	102	(51.0)	225	(56.3)	0.879
≥ 20	77	(38.5)	98	(49.0)	175	(43.8)	
Serum hemoglobin (g/dL)							
< 10	142	(71.0)	135	(67.5)	277	(69.3)	0.012
≥ 10	58	(29.0)	65	(32.5)	123	(30.8)	0.374
Serum albumin (g/dL)							
< 3.5	137	(89.5)	127	(85.2)	264	(87.4)	0.047
≥ 3.5	16	(10.5)	22	(14.8)	38	(12.6)	0.613
Serum sodium (mmol/L)							
≤ 145	45	(22.5)	68	(34.0)	113	(28.3)	0.254
> 145	155	(77.5)	132	(66.0)	287	(71.8)	
Serum glucose (mg/dL)							
< 60 or > 300	54	(27.0)	33	(16.5)	87	(21.8)	0.503
60 - 300	146	(73.0)	167	(83.5)	313	(78.3)	
Organ dysfunctions							
Creatinine (mg/dL)							
Increase < 0.5	188	(94.0)	184	(94.4)	372	(94.2)	0.879
Increase > 0.5	12	(6.0)	11	(5.6)	23	(5.8)	
INR							
≤ 1.5	72	(64.3)	94	(71.8)	166	(68.3)	0.212
> 1.5	40	(35.7)	37	(28.2)	77	(31.7)	
Activated partial prothrombin time (aPTT) (s)							
≤ 60	99	(88.4)	110	(84.0)	209	(86.0)	0.367
> 60	13	(11.6)	21	(16.0)	34	(14.0)	
Platelet count (uL)							
≤ 100,000	41	(20.5)	32	(16.0)	73	(18.3)	0.274
> 100,000	159	(79.5)	168	(84.0)	327	(81.8)	
Total bilirubin (mg/dL)							
≤ 4.0	121	(88.3)	119	(86.2)	240	(87.3)	0.603
> 4.0	16	(11.7)	19	(13.8)	35	(12.7)	
Lactate (mmol/L)							
≤ 2.1	27	(29.4)	23	(27.4)	50	(28.4)	0.456
> 2.1	65	(70.7)	61	(72.6)	126	(71.6)	0.003
Systolic blood pressure (mmHg)							
< 90.0	25	(12.5)	25	(12.5)	50	(12.5)	0.005
≥ 90.0	175	(87.5)	175	(87.5)	350	(87.5)	0.132
Need for vasopressors	23	(11.5)	19	(9.5)	42	(10.5)	0.548

**Table 2.** The analysis of risk factors with sepsis via multiple regression analysis.

	Results	$\beta$ coefficient	R <sup>2</sup>	P
Comorbidities	Diabetes mellitus	0.12	2.3%	0.033
	Chronic kidney disease	0.14	2.3%	0.008
Clinical laboratory	Serum hemoglobin <10 g/dL	-0.28	7.1%	0.000
Characteristics	Serum albumin <3.5 g/dL	-0.11	7.1%	0.043
Organ dysfunctions	Systolic blood pressure <90 mmHg	-0.34	15.8%	0.001

## Discussion

Sepsis is commonly found in the emergency room and difficult to treat due to high complications; in this manner, it requires further diagnosis and precise clinical judgment including symptoms, records, physical examination or using anti-biotic medicine as an alternative plan in order to improve the treatment outcome.<sup>(13)</sup> In this research, recruited for the study were patients' records from in emergency room were divided into two groups, namely: culture-positive sepsis and culture-negative sepsis. However, all possible samples admitted through the ER were presumed in the same group due to approximately 1.6% of blood culture of patients with sepsis contributed therapeutic benefits.<sup>(14, 15)</sup>

Recently, several researches have been investigating and developing the methods in order to treat and diagnose sepsis condition effectively including identification of risk factors, associated symptoms prediction (gender, races, age, comorbidities, nursing home, vital sign at triage, blood culture).<sup>(16-19)</sup>

We found that male gender was significantly associated with sepsis, which was also reported by Melamed *et al.*<sup>(20)</sup> Moreover, the Asian male had higher mortality rate from sepsis than those in other

continents by 27%. This phenomenon could be further explained by the differences in genes, hormones and life styles.<sup>(20)</sup> On the other hand, the race that is associated with sepsis has not been obviously found plausible due to the low race distribution in our study.

According to the clinical characteristics, patients living in elder homecare services, present of long-term vascular access and diastolic blood pressure (DBP) had no association with sepsis, which was different from the study by Glickman *et al.*<sup>(18)</sup> This result might be assumed that elder homecare services and hygiene of the vascular access have met standard quality. Besides, 347 patients (86.8%) had DBP more or equal to 50 mmHg. It indicates that septic shock with at least 50 mmHg of DBP has higher survivability, which was coherent with the previous researches as well.<sup>(21)</sup> However, Holder *et al.*<sup>(17)</sup> found that DBP in sepsis patients (less than 52 mmHg) had higher likelihood of disease progression to a severe sepsis and septic shock within 96 hours of ER triage.<sup>(17)</sup> Also, we have not found any association with respiratory rate despite the clinical criteria of sepsis might be received from the data collected at ER triage, which have mostly shown the same value.<sup>(9)</sup>

Patients with diabetes mellitus have a higher risk of developing sepsis due to increased infection



rate in the urinary tract, pneumonia, tuberculosis and even cellulitis, increased mortality rate by 20% which basically defects the immune response to infection due to neutrophil dysfunction.<sup>(22)</sup> In addition, high blood glucose level typically serves as nutrient source for bacteria.<sup>(23)</sup> Mansur *et al.*<sup>(24)</sup> indicated that patients with diabetes have 1.65 times increased risk of sepsis. We also found diabetes significantly associated with sepsis. Moreover, Mansur *et al.*<sup>(24)</sup> also found chronic kidney diseases and alcohol dependence provide 2.25 times higher chance of sepsis, which are related to uremia. It impairs the functions of the white blood cells such as lymphocyte, monocyte, neutrophil and dendritic cells.<sup>(25)</sup> Whereas, alcohol-dependent patients with sepsis have a higher risk of infection than non-alcohol dependent one with 2.31 times increase in mortality rate.<sup>(26)</sup> Besides, in our study, those with alcohol dependence mostly had cirrhosis along with sepsis, which was one of the risks of sepsis development.<sup>(27)</sup> But relationships discovered in this study between these factors are not relevant that might explain from different races of the samples, i.e., age distribution and type of cirrhosis. This part of research was not obviously explained due to lack of collecting data of these diseases in details.

Regarding the aspects of laboratory characteristics, we also found the level of serum hemoglobin less than 10 g/dL and serum albumin less than 3.5 g/dL are associated with sepsis, which are commonly found in patients with multiple comorbidities. Particularly, anemia is a common condition in chronic kidney disease patients. In patients with diabetes mellitus, they tend to have complications from the disease and appetite loss from their medication. As for those affected by alcohol

dependence, they also suffered from liver disease simultaneously, which could directly suppress albumin production and caused hypoalbuminemia. The deflection could down regulated the immune system due to albumin affect the anti-inflammation. Remarkably, variables are correlated to prior reports in the literature.<sup>(17, 18)</sup> Oxygen nourishing cells and tissues throughout the body are necessary for survival from any conditions. In this case, serum lactate indicates the presence of tissue hypo-perfusion and hence indicates sepsis.<sup>(28)</sup> Regarding the organ dysfunctions aspect, lactate level of more than 2.1 mmol/L was associated with sepsis and they were connected to the previous study and Sepsis-3; both mentioned that patients with septic shock had been treated with vasopressors to maintain *mean arterial pressure* (MAP) of more than 65 mmHg and serum lactate level higher than 2 mmol/L; this gave greater hospital mortality burden up to 40%.<sup>(9, 29)</sup> Systolic blood pressure less than 90 mmHg was also associated with sepsis in our study. With SBP less than 90 mmHg was additionally correlated to DBP less than 52 mmHg and related to sepsis. Moreover, they showed a greater risk of a severe sepsis and septic shock at 96 hours after triage at ER.<sup>(17)</sup> The result was also consistent with qSOFA, using as a screening tool for sepsis, which was less than 100 mmHg in SBP.<sup>(9)</sup>

The association of variables could not be appropriately defined as risk factors. Thus, multiple regression analysis has been introduced to determine the associated risk factors with sepsis. In this regard, diabetes mellitus and chronic kidney disease have been found that their  $\beta$  coefficient were 0.12, 0.14, which obviously demonstrate positive association. Consequently, diabetes mellitus and chronic kidney

disease can lead to higher risks of sepsis. As for serum hemoglobin less than 10 g/dL, serum albumin less than 3.5 g/dL and systolic blood pressure less than 90 mmHg, their  $\beta$  coefficient were -0.28, -0.11, -0.34, which indicate negative association. In every decrease in serum hemoglobin (from less than 10 g/dL), serum albumin and SBP have from less than 3.5 g/dL, 90 mmHg, they increase the association with sepsis, respectively. Adjusted  $R^2$  of diabetes mellitus and chronic kidney diseases are 2.3%, and serum hemoglobin less than 10 g/dL, serum albumin less than 3.5 g/dL, were 7.10% indicating as low level of association compared to systolic blood pressure less than 90 mmHg (15.8%), which is the highest among all variables.

Several limitations of this study have been observed, however. Basically, this study was performed by collecting retrospective EMR despite the data were not completely acquired as we expected because patients with sepsis admitted via ER were not equally investigated. The data collection was performed randomly, which could not select in a certain patient. Consequently, some variables could be lower than expected, and thus affect the statistical analysis. Hence, the blood culture is one of a legitimate indicator for sepsis, at that period of time, without knowledge that the patients had true sepsis, since we only collected the retrospective data. There are possibilities that admitted patients in ER could express true negative results. Next limitations were the interpretation of sepsis. The latest version of Sepsis-3 does not involve low/middle income countries (LMIC) including Thailand.<sup>(9)</sup> As a result, it could interfere with the base population and affect the result of our study. Thus, we could not confirm

whether the new definition could be applied in our country. In addition, the specification of comorbidities was not collected in details, in which the different kinds of diseases could not be specified associated with sepsis. Lastly, all the collected data could not be implanted to other hospital beyond Somdech Phra Pinklao Hospital because the target population was limited, which were collected only from the medical records of this hospital.

This study might be used to advance further studies for ER practices in other hospitals in Thailand. Additionally, the increase of the sample size, variables and other clinical aspects could improve more understanding of the outcomes in this study in the future.

### Conclusion

Sepsis is a common ER encounter, which is lethal and the intervention should be as swiftly and efficiently as possible. Significantly associated risk factors were diabetes mellitus, chronic kidney disease, serum hemoglobin <10 g/dL, serum albumin <3.5 g/dL and systolic blood pressure <90 mmHg. SBP less than 90 mmHg was the most significant risk factor for development of sepsis. This research can be applied for the diagnosis and exclusion of the patients with sepsis in ER earlier and more effectively whether to invent new treatment guidelines or using antibiotics as initial treatment in ER to improve the survivability of the patient.

### References

1. Artero A, Zaragoza R, Nogueira JM. Epidemiology of severe sepsis and septic shock. *InTech* 2012:3-24.

2. Liu C, Bayer A, Cosgrove SE, Daum RS, Fridkin SK, Gorwitz RJ, et al. Clinical practice guidelines by the infectious diseases society of america for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children. *Clin Infect Dis* 2011; 52:e18-55.
3. Moran GJ, Krishnadasan A, Gorwitz RJ, Fosheim GE, McDougal LK, Carey RB, et al. Methicillin-resistant *S. aureus* infections among patients in the emergency department. *N Engl J Med* 2006;355:666-74.
4. Skiest DJ, Brown K, Cooper TW, Hoffman-Roberts H, Mussa HR, Elliott AC. Prospective comparison of methicillin-susceptible and methicillin-resistant community-associated *Staphylococcus aureus* infections in hospitalized patients. *J Infect* 2007;54: 427-34.
5. Brun-Buisson C, Meshaka P, Pinton P, Vallet B. EPISEPSIS: a reappraisal of the epidemiology and outcome of severe sepsis in French intensive care units. *Intensive Care Med* 2004; 30:580-8.
6. กระทรวงสาธารณสุข. แนวทางพัฒนาระบบบริการสุขภาพ (Service Plan) กระทรวงสาธารณสุข 5 สาขาหลัก (สูติ-นรีเวช ศัลยกรรม อายุรกรรม กุมารเวชกรรม และออร์โธปิดิกส์) ฉบับ 25 มีนาคม 56. นนทบุรี: กระทรวงสาธารณสุข;2556.
7. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. *Crit Care Med* 2013;41:580-637.
8. Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock: 2016. *Crit Care Med* 2017;45:486-552.
9. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA* 2016;315:801-10.
10. Edwards R, Hutson R, Johnson J, Sherwin R, Gordon-Strachan G, Frankson M, et al. Severe sepsis in the emergency department-an observational cohort study from the university hospital of the West Indies. *West Indian Med J* 2013;62:224-9.
11. Chase G, Klauber MR. A graph of sample sizes for retrospective studies. *Am J Public Health Nations Health* 1965;55:1993-6.
12. Phua J, Ngerng WJ, See KC, Tay CK, Kiong T, Lim HF, et al. Characteristics and outcomes of culture-negative versus culture-positive severe sepsis. *Crit Care* 2013;17:R202.
13. Heffner AC, Horton JM, Marchick MR, Jones AE. Etiology of illness in patients with severe sepsis admitted to the hospital from the emergency department. *Clin Infect Dis* 2010; 50:814-20.
14. Howie N, Gerstenmaier JF, Munro PT. Do peripheral blood cultures taken in the emergency department influence clinical management? *Emerg Med J* 2007;24:213-4.
15. Kelly AM. Clinical impact of blood cultures taken in the emergency department. *J Accid Emerg Med* 1998;5:254-6.
16. Capp R, Horton CL, Takhar SS, Ginde AA, Peak

- DA, Zane R, et al. Predictors of patients who present to the emergency department with sepsis and progress to septic shock between 4 and 48 hours of emergency department arrival. *Crit Care Med* 2015;43:983-8.
17. Holder AL, Gupta N, Lulaj E, Furgiuete M, Hidalgo I, Jones MP, et al. Predictors of early progression to severe sepsis or shock among emergency department patients with nonsevere sepsis. *Int J Emerg Med* 2016;9:10.
18. Glickman SW, Cairns CB, Otero RM, Woods CW, Tsalik EL, Langley RJ, et al. Disease progression in hemodynamically stable patients presenting to the emergency department with sepsis. *Acad Emerg Med* 2010;17:383-90.
19. Shapiro NI, Trzeciak S, Hollander JE, Birkhahn R, Otero R, Osborn TM, et al. A prospective, multicenter derivation of a biomarker panel to assess risk of organ dysfunction, shock, and death in emergency department patients with suspected sepsis. *Crit Care Med* 2009; 37:96-104.
20. Melamed A, Sorvillo FJ. The burden of sepsis-associated mortality in the United States from 1999 to 2005: an analysis of multiple-cause-of-death data. *Crit Care* 2009;13:R28
21. Benchekroune S, Karpati PC, Berton C, Nathan C, Mateo J, Chaara M, et al. Diastolic arterial blood pressure: a reliable early predictor of survival in human septic shock. *J Trauma* 2008 ;64:1188-95.
22. Kornum JB, Thomsen RW, Riis A, Lervang HH, Schonheyder HC, Sorensen HT. Type 2 diabetes and pneumonia outcomes: a population-based cohort study. *Diabetes Care* 2007; 30:2251-7.
23. Koh GC, Peacock SJ, Van der PT, Wiersinga WJ. The impact of diabetes on the pathogenesis of sepsis. *Eur J Clin Microbiol Infect Dis* 2012; 31:379-88.
24. Mansur A, Mulwande E, Steinau M, Bergmann I, Popov AF, Ghadimi M, et al. Chronic kidney disease is associated with a higher 90-day mortality than other chronic medical conditions in patients with sepsis. *Sci Rep* 2015;5: 10539.
25. Doi K, Leelahavanichkul A, Hu X, Sidransky KL, Zhou H, Qin Y, et al. Pre-existing renal disease promotes sepsis-induced acute kidney injury and worsens outcome. *Kidney Int* 2008;74:1017-25.
26. O'Brien JM Jr, Lu B, Ali NA, Martin GS, Abernethy SK, Marsh CB, et al. Alcohol dependence is independently associated with sepsis, septic shock, and hospital mortality among adult intensive care unit patients. *Crit Care Med* 2007;35:345-50.
27. Foreman MG, Mannino DM, Moss M. Cirrhosis as a risk factor for sepsis and death: analysis of the National Hospital Discharge Survey. *Chest* 2003;124:1016-20.
28. Bakker J, Schieveld SJ, Brinkert W. Serum lactate level as a indicator of tissue hypoxia in severely ill patients. *Ned Tijdschr Geneesk* 2000;144:737-41.
29. Lee SM, An WS. New clinical criteria for septic shock: serum lactate level as new emerging vital sign. *J Thorac Dis* 2016;8:1388-90.