Epidemiology of Sepsis in Siriraj Hospital 2007

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Background: *Sepsis remains a major health burden, and there is limited epidemiological report of sepsis in Thailand.*
Objective: *To determine the epidemiology, treatments, clinical courses and outcomes of sepsis patients.*
Material and Method: *All sepsis patients in medical wards at Siriraj Hospital were recruited from February 1 to July 31, 2007. The information from patients' medical records were retrieved and analyzed.*
Results: *From 3,451 patients, 201 (5.8%) were diagnosed as sepsis, and 38.8% of these developed septic shock. Among sepsis patients, 62.2% were community acquired, 40.8% had bacteremia, and gram negative bacteria were the common pathogen (51.7%). Appropriate antibiotics were given within 6 hours in 39%. Goal-directed therapy was achieved in only 11.5%. The mortality among sepsis and septic shock patients was 34.3% and 52.6%, respectively (p = 0.008). Risk factors for hospital mortality included higher maximum SOFA score, hospital-acquired infection, central nervous system dysfunction and receiving antibiotics after 6 hours of onset of sepsis.*
Conclusion: *Sepsis is still common and has contributed to high mortality. Goal directed therapy and appropriate antibiotics given within 6 hours might improve the outcome.*

Keywords: *Sepsis, Shock, Septic*

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Sepsis is defined as a systemic inflammatory response (SIRS) due to infection[1]. Sepsis remains a major health burden throughout the world in terms of morbidity, mortality and resource utilization. In the United States, sepsis ranks at the top in the 10 leading causes of death and costs as much as $50,000 per patient[2], resulting in an economic burden exceeding $16 billion annually[3]. From the recent epidemiological study of sepsis in the United States over the past 20 years, the incidence of sepsis continued to increase from 82.7 per 100,000 patients in 1979 to 240 per 100,000 patients in 2000[4] whereas a mortality rate was decreased from 27.8% to 17.9%. The epidemiological reports from the United States and Europe observed an increase of gram-positive and fungal infections in sepsis patients[5, 6]. However, several studies have reported an occurrence rate of sepsis varied from 4.5% to 21%[7-9] depending on different inclusion criteria, patient characteristics, severity of illness and hospital type, with associated mortality ranging from 20% to 53%[7-10]. The risk factors associated with mortality in sepsis patients included older age, active co-morbidities[10,11], organ dysfunction, development of septic shock, source of infections, type of micro-organisms and inappropriate antibiotics[12]. Early resuscitation and hemodynamic support in order to achieve goal-directed therapy[13], early initiation of appropriate antibiotic and corticosteroid therapy are important strategies to improve the outcome of sepsis. In addition, there is increasing evidence that statin use may have a role for decreasing severity and mortality in sepsis patients[14,15]. To our knowledge, there is no prior epidemiological report of sepsis in Thailand.

The present study was undertaken to determine the occurrence rate, the demographics, pattern of infections and causative pathogens, treatments, clinical courses and clinical outcomes of sepsis in the hospitalized patients in medical wards at Siriraj Hospital, Bangkok, Thailand.

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Material and Methods

This was a prospective observational cohort study undertaken in all medical wards at Siriraj Hospital from February 1 to July 31, 2007. The eligible subject was the hospitalized patient diagnosed with sepsis by the responsible healthcare personnel. The investigators (NA) assessed the eligible subject and the subject was included into the study if he/she met the definition of sepsis according to the ACCP/SCCM consensus conference definition[1]. Each study subject was followed until he/she left the hospital or died. The data collected were demographics, co-existing conditions, diagnosis, Acute Physiology and Chronic Health Evaluation (APACHE) II and the Sequential Organ Failure Assessment (SOFA) score at onset of sepsis, site of infections, causative organisms, treatment medications, clinical course and treatment outcome.

Definitions

Systemic Inflammatory Response Syndrome (SIRS) was defined as a syndrome with more than one of the following clinical findings: body temperature > 38°C or < 36°C, heart rate > 90 beats/min, hyper-ventilation evidenced by a respiratory rate of > 20 breaths/min or PaCO2 < 32 mmHg, and white blood cell count > 12,000 cells/mm^3 or < 4,000 cells/mm^3 or normal WBC count with > 10% immature forms.

Sepsis was defined as a systemic Inflammatory Response Syndrome (SIRS) due to infection[1].

Severe sepsis was defined as sepsis plus sepsis-induced acute organ dysfunction[6,16].

Acute organ dysfunction was defined as a Sequential Organ Failure Assessment (SOFA) score of $\geq$ 1 point[17,18].

Septic shock was defined as a systolic arterial pressure below 90 mmHg, a mean arterial pressure (MAP) < 60 mmHg, or a reduction in systolic blood pressure of > 40 mmHg from baseline, despite adequate volume resuscitation, in the absence of other causes for hypotension (after a crystalloid-fluid challenge of 20 to 30 ml /kg over a 30 min period)[6].

Septicemia was defined as a presence of microorganisms in the blood.

Culture proven infection was defined as an infection with positive cultures of clinical specimens taken from suspected site of infections.

Clinically suspected infection was defined as clinical sepsis without any microorganism isolated from the clinical specimens and the patient having received antibiotics[16].

Community-acquired infection was defined as an infection present on admission to the hospital or which developed within 48 hours of admission.

Hospital-acquired infection was defined as an infection that developed in the patient hospitalized $\geq$ 48 hours[19].

Healthcare-associated infection was defined as an infection in the patient who had hospitalization for $\geq$ 2 days in the preceding 90 days, was a resident in a nursing home or extended care facility, had home infusion therapy, had chronic dialysis within 30 days or had home wound care[20].

Goal-Directed Therapy was defined as the therapy aimed to achieve a central venous pressure (CVP) 8-12 mmHg, MAP $\geq$ 65 and $\leq$ 90 mm Hg, central venous oxygen saturation $\geq$ 70%, and urine output $\geq$ 0.5ml/kg/hr[13].

Appropriate antibiotics therapy was defined as a single or combined antibiotics regimen containing one or more antibiotics that had *in vitro* activity against the isolated causative pathogens[21].

Statistical analysis

Descriptive statistics were used to summarize the characteristics of the patients.

To compare data between different groups, Chi-square or Fisher's exact test for the categorical data and Student's t-test or Mann-Whitney U-test for the continuous data were used. A multivariate analysis of the predictive factors for mortality was performed by binary logistic regression method. A p-value of 0.05 or less was considered statistically significant.

Results

Occurrence rate and characteristics of sepsis patients

Sepsis was observed in 201 (5.8%) of 3,451 hospitalized patients in the medical wards during the study period. The characteristics of the patients are shown in Table 1. The mean age of the patients was 56.9 yrs and 63.2% were female. Chronic co-morbidities were presented in 88.6% (178/201) of the patients. The common chronic underlying diseases of sepsis patients included hypertension (20.9%), diabetes mellitus (19.4%), cerebrovascular diseases (16.4%), hematologic malignancy (13.9%) and coronary artery diseases (12.9%). Thirty-seven patients (18.4%) received HMG-CoA reductase inhibitors (statins) before hospitalization. Simvastatin was the most common statin prescribed (31/37, 83.7%).

Table 1. Characteristics of 201 sepsis patients

Characteristic	
Mean age ± SD (year)	56.9 ± 19.2
Gender	
Male	74 (36.8%)
Female	127 (63.2%)
Co-morbid diseases	178 (88.6%)
Hypertension	42 (20.9%)
Diabetes	39 (19.4%)
Cerebrovascular diseases	33 (16.4%)
Hematologic malignancy	28 (13.9%)
Coronary artery diseases	26 (12.9%)
Cancer	19 (9.5%)
HIV infection	19 (9.5%)
Chronic renal failure	15 (7.5%)
Cirrhosis	13 (6.5%)
Congestive heart failure	8 (4.0%)
SLE	8 (4.0%)
Receiving immunosuppressive agents	4 (2.0%)
COPD	2 (1.0%)
Others	28 (13.9%)
Prior statin therapy	37 (18.4%)
Undertermined	25 (12.4%)

Pattern of infections and causative pathogens

The pattern of infections and causative organisms are shown in Table 2. Most of infections (62.2%) were community acquired, and 27.9% and 10% were hospital acquired and healthcare-associated infections, respectively. The respiratory tract (36.3%) was the most common site of infection, followed by genito-urinary tract (18.9%) and gastrointestinal tract (17.4%). The microorganisms were isolated from 78.6% of the patients. Of these, 40.8% were septicemia in which the most common source of septicemia was the genito-urinary tract (26.8%). Gram negative bacteria were the most frequently identified pathogens (51.7%) and ESBL-negative *E. coli* was the most common organism among gram negatives. Gram positive bacteria were observed in 27.4% with MSSA was the most common organism among gram positives.

The site of infections and causative organisms in community, hospital and health care-associated infections are shown in Table 3. The most common site of infections in community-acquired infections and hospital-acquired infections was the respiratory tract whereas that of healthcare-associated infections was the genito-urinary tract. The most common causative pathogens in community-acquired infections and hospital-acquired infections were MSSA and *A. baumannii*,

Table 2. Pattern of infections and causative organisms in 201 sepsis patients

	n (%)
Type of infection	
Community-acquired	125 (62.2%)
Hospital-acquired	56 (27.9%)
Health care associated	20 (10.0%)
Sites of infections*	
Respiratory tract	73 (36.3%)
GU tract	38 (18.9%)
Abdominal	35 (17.4%)
Soft tissue	19 (9.5%)
CNS	10 (5.0%)
Bacteremia	11 (5.5%)
Endocarditis	5 (2.5%)
Systemic infection**	4 (2.0%)
Unknown	7 (3.5%)
Evidence of infection	
Culture proven infections	158 (78.6%)
with septicemia	82 (40.8%)
without septicemia	76 (37.8%)
Clinically suspected infections	43 (21.4%)
Causative organisms	
Single bacterial pathogen	129 (64.1%)
Gram negative bacteria	87 (43.2%)
Gram positive bacteria	42 (20.9%)
Mixed pathogens	17 (8.5%)
Mixed Gram positive and Gram negative bacteria	13 (6.5%)
Mixed Gram negative bacteria	3 (1.5%)
Mixed Gram negative and fungus	1 (0.5%)
Mycobacteria	8 (4.0%)
Fungus (*Cryptococcus neoformans*)	3 (1.5%)
Viruses	4 (2.0%)
Malaria	1 (0.5%)
Undetermined	39 (19.4%)
Type of bacteria	
Gram negative bacteria	104 (51.7%)
E. coli (ESBL negative)	23 (11.4%)
K. pneumoniae (ESBL negative)	16 (8.0%)
E. coli (ESBL positive)	15 (7.5%)
A. baumannii	14 (7.0%)
K. pneumoniae (ESBL positive)	7 (3.5%)
P. aeruginosa	7 (3.5%)
Salmonella spp.	4 (2.0%)
Aeromonas spp.	3 (1.5%)
Vibrio spp.	2 (1.0%)
Enterobacter spp.	2 (1.0%)
Proteus spp.	2 (1.0%)
A. baumannii & *P. aeruginosa*	2 (1.0%)
P. stutzeri	1 (0.5%)

* A patient had both respiratory and soft tissue infection
** Systemic infections included three patients with dengue hemorrhagic fever and a patient with malaria

Table 2. (Cont.)

	n (%)
Type of bacteria	
B. pseudomallei	1 (0.5%)
Unidentified non-fermentative gram negative rod	1 (0.5%)
Moraxella spp.	1 (0.5%)
K. pneumoniae (ESBL positive) & *P. aeruginosa*	1 (0.5%)
Citrobacter spp.	1 (0.5%)
E. coli & *K. pneumoniae* (ESBL negative)	1 (0.5%)
Gram positive bacteria	55 (27.4%)
MSSA	18 (9.0%)
MRSA	9 (4.5%)
S. pneumoniae	4 (2.0%)
E. faecalis	4 (2.0%)
Viridans streptococcus	3 (1.5%)
S. agalactiae	3 (1.5%)
Streptococcus group D	3 (1.5%)
S. pyogenes	2 (1.0%)
Streptococcus group G	2 (1.0%)
Alpha hemolytic streptococcus	2 (1.0%)
E. faecium	2 (1.0%)
Coagulase negative staphylococci	1 (0.5%)
S. bovis	1 (0.5%)
S. suis	1 (0.5%)

* A patient had both respiratory and soft tissue infection
** Systemic infections included three patients with dengue hemorrhagic fever and a patient with malaria

respectively. Both ESBL-negative *E. coli* and ESBL-positive *E. coli* were the most common causative pathogens in healthcare-associated infections.

Severity of sepsis and organ dysfunction

The severity of sepsis and organ dysfunction are shown in Table 4. Severe sepsis was observed in 90.5% of sepsis patients of which 38.8% had septic shock and 51.7% had severe sepsis without septic shock. The occurrence rate of severe sepsis and septic shock was 5.2% and 2.2% of the hospitalized patients in the medical wards, respectively. The Apache II scores were completed in 38% of all patients with the mean score was 25.5. The admission SOFA scores were completed in 24% of all patients with a median score of 7; the maximum SOFA scores were completed in 34.8% of all patients with a median score of 9. Of all sepsis patients, the median admission SOFA score and the median of maximum SOFA scores were 5 and 7, respectively.

Seventy percent of severe sepsis patients had two or more organ dysfunctions. The renal system was the most frequent place of organ dysfunction (occurred in 52.2%), followed by the central nervous system (45.8%) and the hematological system (44.8%), respectively. There were no significant difference in occurrence of septic shock between the patients who received statins and those did not received statins (48.6% vs. 41.0%, $p = 0.5$)

Antibiotic treatments of sepsis patients

The antibiotic treatments of sepsis patients are shown in Table 5. Antibiotics were administered in 199 patients (99%) and were initiated within 2 hours and 6 hours after onset of sepsis in 41.8% and 65.7%, respectively. Twenty-three patients (11.4%) received antibiotics after 24 hours of sepsis onset. Appropriate empirical antibiotics were given to 59.2% of the patients. Among the patients who received appropriate antibiotics, 42.9% and 66.5% of them received antibiotics within 2 hours and 6 hours after onset of sepsis, respectively; hence, appropriate empirical antibiotics were given within 6 hours in only 39% of sepsis patients. Septicemia patients received appropriate antibiotics more frequently than those who had no septicemia (76.8% vs. 47.9%, $p < 0.001$).

Supportive treatments of septic shock

The supportive treatments for septic shock are shown in Table 6. Fluid resuscitation was given to 93.6%, and vasoactive agents were given to 87.2% of the septic shock patients. The central venous catheters were inserted in 27% of the patients. The desired central venous pressure, mean arterial pressure and urine output were achieved according to early goal-directed therapy in only 11.5%. Corticosteroid was given to 56.4% of the septic shock patients. The treatments that were associated with hospital mortality in septic shock patients are shown in Table 7. The patients who received corticosteroid seemed to have lower mortality than those who did not receive corticosteroid (48.8% vs. 57.6%, $p = 0.6$). Furthermore, the mortality was significantly increased in the patients who did not achieve target urine output according to early goal-directed therapy (OR 4.1, 95% CI 1.39-12) and also was significantly increased in the patients who did not achieve goal-directed therapy within six hours after septic shock (57.4% vs.12.5%, $p = 0.04$)

Mortality and predictors of mortality

Among 201 patients, 69 patients died within

Table 3. Site of infection and causative organism in community, hospital and healthcare associated infections

	Community-acquired infection (n = 125)	Hospital-acquired infection (n = 56)	Healthcare-associated infection (n = 20)	Total
Site of infections				
Respiratory tract	38 (30.4%)	29 (51.7%)	6 (30.0%)	73
GU tract	15 (12.0%)	12 (21.4%)	11 (55.0%)	38
Abdominal	28 (22.4%)	7 (12.5%)	0 (0%)	35
Soft tissue	16 (12.8%)	3 (5.3%)	0 (0%)	19
Bacteremia	8 (6.4%)	1 (1.8%)	2 (10.0%)	11
CNS	8 (6.4%)	2 (3.6%)	0 (0%)	10
Endocarditis	4 (3.2%)	0 (0%)	1 (5%)	5
Unknown	4 (3.2%)	3 (5.4%)	0 (0%)	7
Systemic infection	4 (3.2%)	0 (0%)	0 (0%)	4
Causative organism				
Single bacteria	68 (54.4%)	42 (75.0%)	19 (95%)	129
Gram negative	34 (27.2%)	37 (66.1%)	16 (80.0%)	87
Gram positive	34 (27.2%)	5 (8.9%)	3 (15.0%)	42
Mixed pathogen	10 (8.0%)	7 (12.5%)	0 (0%)	17
Mycobacteria	8 (6.4%)	0 (0%)	0 (0%)	8
Fungus	3 (2.4%)	0 (0%)	0 (0%)	3
Virus	4 (3.2%)	0 (0%)	0 (0%)	4
Malaria	1 (0.8%)	0 (0%)	0 (0%)	1
Undetermined	31 (24.8%)	7 (12.5%)	1 (5.0%)	39
Type of common bacteria				
MSSA	16 (12.8%)	1 (1.8%)	1 (5.0%)	18
MRSA	2 (1.6%)	5 (8.9%)	2 (10%)	9
A. baumannii	1 (0.8%)	14 (25.0%)	1 (5.0%)	16
E. coli (ESBL negative)	12 (9.6%)	8 (14.3%)	4 (20%)	24
K. pneumoniae (ESBL negative)	12 (9.6%)	4 (7.1%)	1 (5.0%)	17
E. coli (ESBL positive)	1 (0.8%)	10 (17.8%)	4 (20%)	15

28 days. An overall mortality rate of the patients with sepsis was 34.3%. The univariate analysis of hospital mortality in all sepsis patients is shown in Table 8. The non-survivors were older (61.7 y vs. 54.5 y, $p = 0.012$) and had higher admission and maximum SOFA score (8.0 vs. 4.0, $p < 0.001$; 10.0 vs. 5.0, $p < 0.001$, respectively). The factors associated with hospital mortality in sepsis patients are shown in Table 9. The mortality rate increased significantly in the patients with coronary artery disease (OR 2.7, 95% CI 1.15-6.35) and diabetes mellitus (OR 2.3, 95% CI 1.15- 4.77). The patients with septic shock had significantly higher mortality than those without septic shock (52.6% vs. 24%, $p < 0.001$). The univariate analysis revealed an increased mortality among patients who had respiratory tract infection (OR 2.17, 95% CI 1.18-3.98) and hospital-acquired infection (OR 3.2, 95% CI 1.58-6.37). However, no difference in mortality was seen between the healthcare-associated infections and the community-acquired infections ($p = 0.9$). The patients with two or more organ dysfunctions had a significantly higher mortality than those with one or fewer organ dysfunctions (44.2% vs. 13.6%, $p < 0.001$) and the patients with cardiovascular, central nervous system or renal dysfunctions had a significantly higher mortality rate than those without such organ dysfunctions. No significant difference in mortality was seen between the patients with and without prior statins therapy (38.9% vs. 34.6%, $p = 0.77$). The patients who received antibiotics later than six hours of sepsis onset had a significantly higher mortality rate when compared with those who received antibiotics within six hours of sepsis onset (46.9% vs. 29.5%, $p = 0.023$). No difference in mortality rate was found among the patients who received antibiotic sooner than two or four hours.

Multivariate analysis of 28-day mortality in all sepsis patients is shown in Table 10. The factors that were independently associated with overall mortality were hospital-acquired infection, a higher

Table 4. Severity of sepsis and organ dysfunction in 201 sepsis patients

Sepsis syndrome	
Severe sepsis	182 (90.5%)
with shock	78 (38.8%)
without shock	104 (51.7%)
Apache II score, mean ± SD*	25.5 ± 6.2
Admission SOFA score (complete)**	7 (5-9)
Admission SOFA score (all)	5 (3-8)
Maximum SOFA score (complete)***	9 (6.7-14.2)
Maximum SOFA score (all)	7 (3-10)
Length of Hospital Stay (d), median (IQR)	17 (8-29.5)
Mortality rate	69 (34.3%)
Sepsis -related death	67 (97%)
Number of organ dysfunction	
0	19 (9.5%)
1	42 (20.9%)
2	50 (24.9%)
3	44 (21.9%)
4	23 (11.4%)
5	15 (7.5%)
6	8 (4.0%)
Type of organ dysfunction	
Renal†	105 (52.2%)
CNS	92 (45.8%)
Cardiovascular	79 (39.3%)
Respiratory††	68 (33.8%)
Hepatic†††	55 (27.4%)

Admission & maximum SOFA scores are shown in median (25% IQR-75% IQR)
* Complete APACHE II score in 77 patients (38%),
** Complete admission SOFA scores in 48 patients (24%),
*** Complete maximum SOFA scores in 70 patients (34.8%)
† Complete data of renal dysfunction in 198 patients (98.5%),
†† Complete data ofrespiratory dysfunction in 99 patients (49.3%),
††† Complete data of hepatic dysfunction in 136 patients (67.7%)

Table 5. Antibiotic treatment of sepsis in 201 patients

	n (%)
Antibiotic treatment	
Yes	199 (99%)
No	2 (1.0%)
Time from sepsis onset to the first dose of antibiotic(s)	
≤ 2 hr	84 (41.8%)
> 2 hr-4 hr	29 (14.4%)
> 4 hr-6 hr	19 (9.5%)
> 6 hr-24 hr	44 (21.9%)
> 24 hr	23 (11.4%)
Susceptibility of causative organism to antibiotic given in 24 hrs	
Susceptible	119 (59.2%)
Non susceptible	40 (19.9%)
Undertermined	40 (19.9%)
Time from sepsis onset to the first dose of antibiotic(s) (only in the patients who received appropriate antibiotic)	
≤ 2 hr	51 (42.9%)
> 2 hr-4 hr	14 (11.8%)
> 4 hr-6 hr	14 (11.8%)
> 6 hr-24 hr	27 (22.7%)
> 24 hr	13 (10.9%)

Table 6. Goal directed therapy for septic shock in the first 6 hrs

	n (%)
Fluid resuscitation	73 (93.6%)
Vasoactive agents	68 (87.2%)
Inserted central line	21 (26.9%)
Achieved target CVP	
Yes	15 (19.2%)
No	5 (6.4%)
Undetermined	1 (1.3%)
No central line was inserted	57 (72.1%)
Achieved target MAP	57 (73.1%)
Achieved target urine output	54 (69.2%)
Achieved goal-directed therapy	9 (11.5%)
Received corticosteroid	44 (56.4%)

maximum SOFA score, having central nervous system dysfunction and delayed initiation of antibiotics for more than six hours after sepsis onset.

Discussion

To our knowledge, this is the first prospective epidemiological study of sepsis in Thailand. The occurrence rate of sepsis in the patients hospitalized in the medical wards at Siriraj Hospital was 5.8%, which lay at the lower end of the 4.5% to 21% reported in the previous studies from other countries[5-7]. A lower occurrence rate may be explained by a difference in study population which we included only the patients in the general medical wards. Most of sepsis patients (90.5%) met the severe sepsis criteria and 38.8% of these patients developed septic shock; hence, the occurrence rate of severe sepsis was 5.2% and that of septic shock was 2.2%. The large proportion of the severe form of sepsis in our patients could be due to a delay in hospitalization of the patients.

Table 7. Association between treatment mode and hospital mortality in 76 patients with septic shock

Factors		Mortality	p-value	OR	95% CI
Fluid resuscitation	Yes	37/71 (52.1%)	1.000	1.38	0.17-12.7
	No	3/5 (60%)			
Achieved target CVP	Yes	7/14 (50%)	0.330	4.00	0.27-121.8
	No	4/5 (80%)			
Achieved target MAP	Yes	27/56 (48.2%)	0.300	1.99	0.62-6.57
	No	13/20 (65%)			
Achieved target urine output	Yes	22/52 (42.3%)	0.016	4.10	1.39-12.0
	No	18/24 (75%)			
Achieved goal-directed therapy	Yes	1/8 (12.5%)	0.042	9.40	1.10-80.0
	No	39/68 (57.4%)			
Received steroid	Yes	21/43 (48.8%)	0.600	1.42	0.52-3.93
	No	19/33 (57.6%)			

Table 8. Univariate analysis of hospital mortality in 201 sepsis patients

	Death (n = 69)	Survive (n = 128)	p-value
Mean age $\pm$ SD	61.7 $\pm$ 17.5	54.5 $\pm$ 19.8	0.012
Median LOS (IQR)	9.0 (4-25.5)	20.0 (12-34)	<0.001
Mean Apache II score $\pm$ SD	26.6 $\pm$ 6.8	24.0 $\pm$ 5.5	0.110
Admission SOFA score (complete)	7.0 (5-10)	7.0 (3.7-8.2)	0.200
Admission SOFA score (all)	8.0 (5-12)	4.0 (2-6)	<0.001
Maximum SOFA score (complete)	11.0 (8 -15.5)	8.0 (4-12)	0.003
Maximum SOFA score (all)	10.0 (6.5-14)	5.0 (2-8)	<0.001

Table 9. Factors associated with hospital mortality in 197 sepsis patients

Factor		Mortality	p-value	OR	95%CI
Gender	Male	21/72 (29.2%)	0.250	1.51	0.78-2.96
	Female	48/125 (38.4%)			
Co-morbid disease					
Coronary artery disease	Yes	14/25 (56%)	0.033	2.70	1.15-6.35
	No	55/172 (32%)			
Diabetes mellitus	Yes	20/39 (51.3%)	0.029	2.30	1.15-4.77
	No	49/158 (31%)			
Prior statin therapy	Yes	14/36 (38.9%)	0.770	1.20	0.5-2.7
	No	47/136 (34.6%)			
Sepsis syndrome					
Septic shock	Yes	40/76 (52.6%)	<0.001	3.52	1.9-6.5
	No	29/121 (24%)			
Severe sepsis	Yes	67/178 (37.6%)	0.036	5.13	1.1-22.9
	No	2/19 (10.5%)			
Septic shock		40/76 (52.6%)	0.008	2.13	1.2-3.8
Compare to all sepsis patients		69/201 (34.3%)			
Culture proven infection	Yes	54/154 (35.1%)	0.870	0.99	0.46-2.13
	No	15/43 (34.9%)			

Table 9. (Cont.)

Factor		Mortality	p-value	OR	95%CI
Septicemia	Yes	22/82 (26.8%)	0.037	0.50	0.27-0.92
	No	47/115 (40.9%)			
Site of infection					
Respiratory tract infection		33/71 (46.5%)	0.018	2.17	1.18-3.98
Non respiratory tract infection		36/126 (28.6%)			
Type of infection					
Community acquired	Yes	34/122 (27.9%)	0.011	0.44	0.23-0.84
	No	35/75 (46.6%)			
Hospital acquired	Yes	30/55 (54.5%)	<0.001	3.20	1.58-6.37
	No	39/142 (27.5%)			
Healthcare associated	Yes	5/20 (25%)	0.460	0.59	0.18-1.84
	No	64/177 (36.1%)			
Healthcare associated		5/20 (25%)	0.990	0.86	0.25-2.81
Community acquired		34/122 (27.9%)			
Causative organism					
Gram positive	Yes	14/42 (33.3%)	0.940	0.91	0.41-1.98
	No	55/155 (35.5%)			
Gram negative	Yes	33/87 (37.9%)	0.540	1.26	0.67-2.36
	No	36/110 (32.7%)			
Undetermined	Yes	13/39 (33.3%)	0.950	0.91	0.41-2.1
	No	56/158 (35.4%)			
Number organ dysfunction	≥ 2	61/138 (44.2%)	<0.001	5.00	2.2-11.4
	≤ 1	8/59 (13.6%)			
Type of organ dysfunction					
Respiratory	Yes	33/66 (50%)	0.600	0.70	0.28-1.86
	No	18/31 (58.1%)			
Hematological	Yes	34/88 (38.6%)	0.450	1.31	0.7-2.4
	No	35/108 (32.4%)			
Hepatic	Yes	19/52 (36.5%)	0.660	1.27	0.57-2.82
	No	25/80 (31.3%)			
Cardiovascular	Yes	38/76 (50%)	0.001	2.90	1.58-5.3
	No	31/121 (25.6%)			
CNS	Yes	53/90 (58.9%)	<0.001	8.15	4.1-16
	No	16/107 (15%)			
Renal	Yes	44/103 (42.7%)	0.026	2.08	1.1-3.8
	No	24/91 (26.4%)			
Appropriate antibiotic given within 24 hr	Yes	42/116 (36.2%)	0.890	1.09	0.57-2.08
	No	27/79 (34.2%)			
Time from sepsis onset to the first dose of antibiotic (all patients)					
Received antibiotics	> 6 hrs	31/66 (46.9%)	0.023	2.12	1.15-3.9
	≤ 6 hrs	38/129 (29.5%)			
Received antibiotics	> 4 hrs	34/84 (40.5%)	0.250	1.48	0.78-2.79
	≤ 4 hrs	35/111 (31.5%)			
Received antibiotics	> 2 hrs	39/112 (34.8%)	0.970	0.94	0.5-1.78
	≤ 2 hrs	30/83 (36.1%)			
Time from sepsis onset to antibiotic (only in the patients who receive appropriate antibiotic)					
Received antibiotics	> 6 hrs	17/40 (42.5%)	0.410	1.51	0.64-3.57
	≤ 6 hr	25/76 (32.9%)			
Received antibiotics	> 4 hrs	20/53 (37.7%)	0.900	1.13	0.49-2.59
	≤ 4 hrs	22/63 (34.9%)			
Received antibiotics	> 2 hrs	21/66 (31.8%)	0.350	0.64	0.28-1.48
	≤ 2 hrs	21/50 (42%)			

Table 10. Multivariate analysis, forward stepwise logistic regression for 28-day mortality in sepsis patients

	OR	95%CI for OR	p-value
Maximum SOFA score (all)	1.27	1.1-1.4	<0.001
Hospital-acquired infections	3.70	1.4-9.7	0.008
CNS dysfunction	3.36	1.4-7.96	0.006
Initiation of antibiotics after 6 hour	3.55	1.49-8.47	0.004

The common sources of infections in our sepsis patients were respiratory tract, urinary tract and intra-abdominal infections which were similar results to other previous studies. Gram negative bacteria were still the predominant causative agents in sepsis patient at Siriraj Hospital, particularly in hospital-acquired and healthcare-associated infections. This observation was different from other epidemiological studies in the United States and Europe which gram positives were the predominant organisms[2,4,6,8,12]. Invasive, fungal infections were identified in only 1.5% of culture proven sepsis, which was also lower than the observations from previous studies[3,22,23]. Among the patients with severe sepsis, the three most common organ dysfunction were renal, central nervous system and hematological; having more than one organ dysfunction was associated with an increase in mortality.

The guidelines from the Surviving Sepsis Campaign in 2008 recommend starting an antibiotic as soon as possible, preferably within the first hour of recognition of severe sepsis[21]. The results of our study indicated that antibiotic treatment within six hours after diagnosis of sepsis was associated with decreased mortality. No improvement in survival was found in those who received antibiotics within four or two hours when compared with those who received antibiotics within six hours. Corticosteroid and vasoactive agents were given to 56.4% and 87.2% of the septic shock patients, respectively. The mortality rate in the patients who received corticosteroid (48.8%) was less than that in the patients who did not receive corticosteroid (57.6%) with a relative risk reduction of 15.3%. However, this difference was not statistically significant due to the small sample. The result of study also revealed no statistical significance in septic shock and hospital mortality between the patients with or those without prior statin therapy. Goal-directed therapy was achieved only in 11.5% due to a low rate of central venous catheter insertion and monitoring during septic shock. In addition, hospital-acquired infection, the higher maximum SOFA score, and central nervous system dysfunction were risk factors for hospital mortality which were consistent with the previous studies[8,24]. The overall hospital mortality of sepsis patients was 34.3%, but rose to 52.6% in patients with septic shock, which was still high when compared with 17.9% for sepsis patients reported by Martin et al[4].

The limitations of our study included the low rate of complete data in the APACHE II score to assess severity of illness as well as lack of admission SOFA and maximum SOFA scores used to assess organ dysfunction, which was mostly due to lack of arterial blood gas and laboratory results assessing respiratory and liver functions. The analyses of data drawn from this study might not be generalized to all the sepsis patients since our data enrolled only the patients admitted to general medical wards in which most of patients have co-morbidities that might lead to a higher overall mortality.

In conclusion, sepsis is common among hospitalized medical patients and the mortality rate is still high. Goal-directed therapy and appropriate antibiotics given within six hours might improve the outcomes and should be emphasized.

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ระบาดวิทยาของเส็พสิสในโรงพยาบาลศิริราช 2550

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***ภูมิหลัง**: เส็พสิส (Sepsis) เป็นปัญหาสาธารณสุขที่สำคัญ แต่ยังไม่พบข้อมูลด้านระบาดวิทยาในประเทศไทย*
***วัตถุประสงค์**: เพื่อศึกษาระบาดวิทยา การรักษาและผลการรักษาของผู้ป่วยเส็พสิส*
***วัสดุและวิธีการ**: ผู้ป่วยที่รับไว้ที่ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์ศิริราชพยาบาลระหว่างเดือนกุมภาพันธ์ ถึงกรกฎาคม พ.ศ. 2550 ที่ได้รับการวินิจฉัยว่าเป็นเส็พสิส*
***ผลการศึกษา**: จากผู้ป่วย 3,451 ราย ที่รับไว้รักษาที่ภาควิชาอายุรศาสตร์ในช่วงที่ศึกษา มีผู้ป่วยเส็พสิส 201 ราย จึงมีอัตราป่วยร้อยละ 5.8 โดยพบภาวะช็อกจากเส็พสิส (septic shock) ร้อยละ 38.8, เป็นการติดเชื้อจากนอกโรงพยาบาลร้อยละ 62.2, มีการติดเชื้อในกระแสเลือด (bacteremia) ร้อยละ 40.8 และพบเชื้อกรัมลบเป็นเชื้อก่อโรคร้อยละ 51.7, ผู้ป่วยร้อยละ 39 ได้รับยาต้านจุลชีพที่เหมาะสมภายใน 6 ชั่วโมงหลังจากเริ่มมีอาการของเส็พสิส, มีผู้ป่วยเพียงร้อยละ 11.5 ที่ได้รับการรักษาแบบ ประคับประคองตามเป้าหมายของ goal directed therapy, อัตราเสียชีวิตในผู้ป่วยเส็พสิสทั้งหมดร้อยละ 34.3 และเพิ่มเป็นร้อยละ 52.6 หากมีภาวะช็อกจากเส็พสิส (p = 0.008), ปัจจัยที่สัมพันธ์กับการเสียชีวิตของผู้ป่วยเส็พสิส ได้แก่ การติดเชื้อที่เกิดในโรงพยาบาล (Hospital-acquired infection), มี maximum SOFA score สูง, มี central nervous system dysfunction และได้รับยาต้านจุลชีพช้ากว่า 6 ชั่วโมงหลังจากเกิดภาวะเส็พสิส*
***สรุป**: เส็พสิสยังคงพบบ่อยและมีอัตราเสียชีวิตสูง การรักษาประคับประคองตาม goal directed therapy และให้ยาต้านจุลชีพที่เหมาะสมอย่างรวดเร็วภายใน 6 ชั่วโมงน่าจะช่วยทำให้ผลการรักษาดีขึ้นได้*