Nosocomial Bloodstream Infection in Songklanagarind Hospital: Outcome and Factors Influencing Prognosis

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Objective: *To determine epidemiology, microbiology, outcome, and factor influencing mortality in nosocomial bloodstream infection in Songklanagarind Hospital.*

Material and Method: *Retrospective study in adult patients who were hospitalized at Songklanagarind Hospital with positive blood culture after 48 hours of admission was conducted. The present study duration was between 1 August and 30 November 2008.*

Results: *There were 138 episodes of nosocomial blood stream infection in 117 patients, the prevalence of 11.6/1,000 admissions. The mean age of patients was 54.8 years (range 12 to 88 years) and males comprised of 60.9%. Hematologic malignancy was the most common underlying condition of the patients (27.5%) while 30.4% of patients had no underlying disease. The three common primary infections were lower respiratory tract (13.9%), urinary tract (12.4%) and skin and soft tissue (6.5%), whereas the unknown site of infection had accounted for 80 episodes (62.0%). The leading pathogens of nosocomial bacteremia were E. coli 17.4%, S. aureus 15.2%, K. pneumoniae 12.3% and P. aeruginosa 10.3%. Vanocomycin was dominantly sensitive to gram positive cocci, while about half (52.4%) of S. aureus had methicillin resistance. The variety of resistance had encountered for example P. aeruginosa (7.1%) to imipenem and majority of A. baumannii to aminoglycosides, fluoroquinolones and carbapenems. Overall mortality was 28.3% but mortality due directly to bacteremia was 13.8%. Univariate and multivariate analyses showed liver cirrhosis and lower respiratory tract infection to be associated with increased mortality.*

Conclusion: *The prevalence of nosocomial blood stream infection had slightly sideway down, while the mortality was stable, compared with several reports in the last two decades. The gram negative bacteria had a high proportion of antibiotic resistance.*

Keywords: *Nosocomial bloodstream infection, Outcome, Factors influencing prognosis*

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Blood stream infection reflects the immunologic failure to eradicate the organisms which disseminate in blood[1]. Nosocomial blood stream infection, which is almost always caused by multidrug-resistant organisms, has high morbidity and mortality and also presents a large scale economic burden[2]. The prevalence of nosocomial blood stream infection among all hospital-acquired infection was 11.6% in a large surveillances in Switzerland[3]. The mortality was as high as 27% over the 7-year surveillance in the United States[4]. In Thailand, the prevalence of nosocomial blood stream infection was 6.5% and most patients were found in intensive care units while the causative pathogens mostly were gram negative bacteria[5]. In Songklanagarind Hospital, the present study in 1987 reported a prevalence of nosocomial blood stream infection of 15.5/1,000 admissions with 37.2% of mortality and most of the patients were found in general medical wards[6]. The authors' previous study showed the prevalence had decreased to 12.7/1,000 admissions in the surveillance conducted in 2003, while the mortality decreased to 13.2%.

The epidemiologic study of blood stream infection in Songklanagarind Hospital was conducted to describe the characteristics of patients developing blood stream infection and identify factors influencing mortality.

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Material and Method

The medical records of the in-patients of Songklanagarind Hospital, age of 15 years or more, who developed the nosocomial blood stream infection between August and November 2008, were reviewed. The definition of blood steam infection was described as having at least one positive blood culture for causative bacteria within 48 hours of admission. Possible contaminant bacteria for example; coagulase negative staphylococcus, Bacillus species were also enrolled with specific criteria as CDC definition[7,8]. Sources of infections were described as surgical wound, upper respiratory tract, urinary tract, bone and joint, cardiovascular system, central nervous system, gastrointestinal system, lower respiratory tract, reproductive tract, skin and soft tissue, and catheter-related bacteremia.

The epidemiological data and outcome of the patients were analyzed. The outcome of patients was classified as survival, death directly from infection, which defined death within 7 days of diagnosis and death indirectly from infection, defined as death after 7 days following diagnosis. The Chi-square test with Yates' correction, Fisher's extract test for univariate analysis and multivariate logistic regression with odd ratios and 95% confident interval (CI) were used to identify factors associated with mortality. A p-value of less than 0.05 was considered statistical significance.

Results

The prevalence of nosocomial bacteremia during these periods was 11.6/1,000 admissions. The mean age of patients was 54.8 years with the range of 15 to 88 years. The three major underlying conditions were hematologic malignancy (21.9%), non-hematologic malignancy (17.1%) and diabetes mellitus (10.3%), while the remainder were chronic renal failure (5.1%), immunosuppressive agent (4.3%), cirrhosis (4.3%), human immunodeficiency virus infection (3.4%), other (6.3%) and no underlying condition (30.4%), as shown in Table 1. The mean length of hospital stay was 59.4 days, range of 5 to 669 days.

There were 138 episodes of nosocomial blood stream infection among 117 patients. The poly-microbial bacteremia accounted of 22 in 138 episodes (15.9%). The top four for causative organisms were *E. coli* (17.8%), *S. aureus* (15.2%), *K. pneumoniae* (12.3%) and *P. aeruginosa* (10.1%) and the others were *Enterobacter cloacae* (6.5%), *S. epidemidis* (6.5%), *A. baummanii* (4.3%), *Salmonella* species (3.6%), *Streptococcus* species (2.9%) and *Enterococci* species (2.2%).

The eight antibiotics, ampicillin, penicillin, erythromycin, imipenem, oxacillin, fosfomycin, vancomycin and fusidic acid, were tested for antibiotic resistance to gram positive cocci. Vancomycin was dominantly sensitive to gram positive cocci, while about half (52.4%) of *S. aureus* had methicillin resistance.

The nine antibiotics, amikacin, gentamicin, ampicillin, cefotaxime, ceftriaxone, ceftazidime, ciprofloxacin, sulperazon and imipenem, were tested for antibiotic susceptibility. The variety of resistance had encountered for example *P. aeruginosa* (7.1%) to

Table 1. Underlying condition and source of infection associated mortality rate, with univariate analysis

Variables	Total (%)	No of death (%)	Odds ratio	95% CI	p-value
Underlying condition (n = 117)					
Previous healthy	32 (27.4)	0	0	-	0.0048*
D M	12 (10.2)	3 (25.0)	2.00	0.497-8.343	0.3319
Chronic renal failure	6 (5.1)	2 (33.3)	2.97	0.492-17.921	0.2129
Cirrhosis	5 (4.3)	3 (60.0)	9.70	1.386-67.881	0.0049*
Human immunodeficiency	4 (3.4)	2 (50.0)	6.06	0.763-48.181	0.0519
Steroid usage	6 (5.1)	1 (16.7)	1.11	0.120-10.161	0.9291
Hematologic malignancy	32 (27.4)	7 (21.9)	1.88	0.652-5.445	0.2345
Solid organ malignancy	20 (17.1)	5 (25.0)	2.15	0.660-7.026	0.1925
Primary sit of infection (n = 43)					
Skin & soft tissue	6 (14.0)	1 (16.7)	1.11	0.120-10.161	0.9291
Lower respiratory tract	16 (37.2)	6 (37.5)	4.45	1.314-15.072	0.0086*
Gastrointestinal tract	7 (16.3)	1 (14.3)	0.91	0.102-8.136	0.9340
Urinary tract	14 (32.6)	0	0	-	0.0904

* Statistical significance, $p < 0.05$

imipenem and majority of *A. baumannii* to aminoglycosides, fluoroquinolones and carbapenems.

The largest proportion was unknown site of infection of 80 in 138 episodes (60.0%). The other primary infections were lower respiratory tract (18 in 138, 13.0%), urinary tract (16 in 138, 11.6%), skin and soft tissue (9 in 138, 6.5%), as demonstrated in Table 1, while the remainder of a few percent were catheter-related bacteremia, surgical site infection and cardiovascular system.

The majority of the subjects (86.2%) had fever, while half of the subjects (53.6%) had white cell count more than 10,000 cells per cu.mm^3 and most patients (81.2%) had normal neutrophil count. More than two-third (68.3%) had hypoalbuminemia, with nearly one-eleventh (13.8%) had serum creatinine more than 2 mg/dl.

The septic shock was among one-fifth (22.5%) of the subjects, while one-third (33.3%) were on mechanical ventilators. The empirical antibiotic scheme was given in 87.2% of cases, with three-fourth (74.6%) was treatment appropriate.

The overall mortality was 28.3%, while mortality due directly to bacteremia was 13.8%. The clinical variables and routine laboratory findings significantly associated in univariate analysis with mortality due directly to bacteremia were liver cirrhosis and lower respiratory tract infection, but in multivariate analysis liver cirrhosis and dependence on mechanical ventilator were identified as independent predictors of increased mortality, as demonstrated in Table 2.

Discussion

Although worldwide the prevalence of nosocomial bacteremia has been rising owing to the increased use of chemotherapy and invasive procedures, the prevalence in Thailand has shown a decreasing trend due to effective active surveillance and infection control[5]. In southern Thailand, the prevalence of nosocomial bacteremia in Songklanagarind Hospital, the only referral center in the region, also decreased from 15.5/1000 admissions in 1987 to 12.7 admissions in 2003[6].

Table 2. Factors associated mortality rate, with logistic regression model

Variable	Odds ratio	95% CI	p-value
Cirrhosis	17.5	2.431-125.979	0.004*
Mechanical ventilator	3.9	1.263-11.971	0.018*

* Statistical significance, $p < 0.05$

The ages of the presented patients, which were mostly in the range of 41-60 years, were lower than in previous studies[1,2,6]. These differences may reflect the greater bacterial virulence even in normal hosts or immunocompetent patients. It was interesting that the prevalence of nosocomial bacteremia in general medicine and surgery wards was higher than in ICU wards. This differs from previous reports of studies in developed countries[9]. The difference can be explained by the insufficient number of admission beds that necessitates some ICU-condition patients to be admitted in general wards. Although admitted in general wards, these patients receive the full scale of invasive procedures and monitoring. It is important that interventions as aggressive procedure, nasogastric intubation and mechanical ventilator have been identified as risk factors for nosocomial bacteremia in a previous study in the United States[11]. The mortality and length of hospital stay in the present study were as high as in previous reports[1,2,6].

The present microbiological study revealed 15.9% of polymicrobial infections, which is higher than the 8.5% recorded in our hospital report of 1987. The finding that 80% of causative organisms were gram negative bacilli and less than 20% gram positive cocci is in accordance with a previous national study[5]. The authors did not find vancomycin-resistant *Staphylococcus aureus*, which had been demonstrated in previous studies in Bangkok and Khon Kaen[11]. Although the present study was done in a tertiary care and referral hospital, the antimicrobial susceptibility testing showed a stable and slightly decreased broad-spectrum antibiotics resistant rate among causative bacteria compared with the authors' previous hospital report[6]. This finding is likely to be a result of the antibiotics policy in our hospital, which strictly controls the use of broad-spectrum antibiotics. A different pattern was seen for narrow-spectrum antibiotics: ceftriaxone-resistant gram negative bacilli in urinary tract infection showed an increasing trend, avoid the empirical antibiotics treatment adjusted in nosocomial bacteremia with evidences of urinary tract infections. However, the primary site of infection could not be identified in over 50% of the patients, reflecting greater attention paid by service-doctors to antibiotic treatment than to exploration of the source of infection.

The present study also showed liver cirrhosis and lower respiratory tract infection significantly

influenced mortality, in addition to the effects from other prognostic factors, liver cirrhosis has a significant impact on the mortality of patients with community-acquired bacteremia as previous report[12].

However, the present study had some limitations. First, the small number of patients was unable to represent the overall nosocomial bacteremia in Songklanagarind Hospital. Second, the failure to conduct susceptibility testing for some currently used broad-spectrum antibiotics caused limitation for empirical treatments and multiple drug resistance bacteria.

Nosocomial blood stream bacteremia has high mortality and poses a considerable economic burden although the prevalence in Songklanagarind Hospital has decreased. Active surveillance and infection controls appear to be effective in decreasing the prevalence and strict antibiotics control seems to minimize the severity of these problems.

Potential conflicts of interest

None.

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การติดเชื้อในกระแสเลือดจากโรงพยาบาลของโรงพยาบาลสงขลานครินทร์: ผลที่ได้รับและปัจจัยพยากรณ์ชักจูง

ธนภร หอทิวากุล, สมคิด นะกิจ, ศรัญญู ชูศรี, ขจรศักดิ์ ศิลปโภชากุล

วัตถุประสงค์*: เพื่อศึกษาระบาดวิทยา จุลชีววิทยา ผลที่ได้รับ และปัจจัยชักจูงการตายที่มีอิทธิพลต่อการตายในการติดเชื้อในกระแสเลือดจากโรงพยาบาลของโรงพยาบาลสงขลานครินทร์*

วัสดุและวิธีการ*: การศึกษาย้อนหลังในผู้ป่วยวัยผู้ใหญ่ที่รักษาในโรงพยาบาลสงขลานครินทร์ ที่มีผลเพาะเชื้อในเลือดได้ผลบวก เมื่ออยู่โรงพยาบาลผ่านพ้น 48 ชั่วโมงไปแล้ว ศึกษาระหว่างวันที่ 1 สิงหาคม ถึง 30 พฤศจิกายน พ.ศ. 2551*

ผลการศึกษา*: มีการติดเชื้อในกระแสเลือด 138 ครั้งในผู้ป่วย 117 คน ความชุก 11.6 ครั้งต่อการอยู่โรงพยาบาล 1,000 ครั้ง อายุเฉลี่ยของผู้ป่วย 54.8 ปี (อายุอยู่ระหว่าง 12 ถึง 88 ปี) เป็นผู้ชาย ร้อยละ 60.9 มะเร็งโลหิตวิทยาเป็นภาวะพื้นฐานที่พบบ่อยที่สุดเท่ากับร้อยละ 27.5 ขณะที่ร้อยละ 30.4 ไม่มีโรคพื้นฐาน การติดเชื้อปฐมภูมิที่พบบ่อยสามแหล่งได้แก่ ร้อยละ 13.9 ทางเดินหายใจส่วนล่าง ร้อยละ 12.4 ทางเดินปัสสาวะ และร้อยละ 6.5 ผิวหนัง และเนื้อเยื่ออ่อน ขณะที่ 80 ครั้ง (ร้อยละ 62.0) ไม่ทราบแหล่งติดเชื้อ การติดเชื้อในกระแสเลือดในโรงพยาบาลเชื้อตัวนำได้แก่ E. coli ร้อยละ 17.4, S. aureus ร้อยละ 15.2, K. pneumoniae ร้อยละ 12.3 และ P. aeruginosa ร้อยละ 10.3 แบคมีเรียกลมกรับบวกไวต่อยา vanomycin อย่างเด่นชัด ขณะที่ประมาณครึ่งหนึ่ง (ร้อยละ 52.4) ของ S. aureus ดื้อต่อยา methicillin ความแปรผันของการดื้อยามีตั้งแต่ P.aeruginosa ต่อยา imipenem และ A. baumannii ดื้อต่อยา aminoglycoside, fluoroquinolone และ carbapenems อัตราตาย โดยรวมร้อยละ 28.3 แต่อัตราตายการติดเชื้อแบคทีเรียในกระแสเลือดโดยตรงร้อยละ 13.8 การวิเคราะห์แบบ univariate และ multivariate พบว่าโรคตับแข็งและการติดเชื้อทางเดินหายใจส่วนล่างสัมพันธ์กับการตายเพิ่มขึ้น

สรุป*: อุบัติการณ์การติดเชื้อในกระแสเลือดในโรงพยาบาลลดลงเล็กน้อยขณะอัตราตายคงที่ เมื่อเปรียบเทียบกับสองทศวรรษก่อน แบคทีเรียกรัมลบดื้อยาในสัดส่วนสูง*