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

Thanaporn Hortiwakul MSc*, Somkid Nagij MD*, Sarunyou Chusri MD*, Khachornsakdi Silpapojakul MD*

*Department of Internal Medicine, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla, Thailand

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 bacteraemia were E. coli 17.4%, S. aureus 15.2%, K. pneumoniae 12.3% and P. aeruginosa 10.3%. Vancomycin 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 bacteraemia 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

J Med Assoc Thai 2012; 95 (2): 170-4
Full text. e-Journal: http://www.jmat.mat.or.th
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 polymicrobial bacteremia accounted of 22 in 138 episodes (15.9%). The top four for causative organisms were \textit{E. coli} (17.8%), \textit{S. aureus} (15.2%), \textit{K. pneumoniae} (12.3%) and \textit{P. aeruginosa} (10.1%) and the others were \textit{Enterobacter cloacae} (6.5%), \textit{S. epidemidis} (6.5%), \textit{A. baumannii} (4.3%), \textit{Salmonella} species (3.6%), \textit{Streptococcus} species (2.9%) and \textit{Enterococcus} 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 \textit{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 \textit{P. aeruginosa} (7.1%) to

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

* 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 bacteraemia, 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 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 bacteraemia was 13.8%. The clinical variables and routine laboratory findings significantly associated in univariate analysis with mortality due directly to bacteraemia 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 bacteraemia 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\(^9\). In southern Thailand, the prevalence of nosocomial bacteraemia 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\(^6\).

The ages of the presented patients, which were mostly in the range of 41-60 years, were lower than in previous studies\(^1,2,9\). These differences may reflect the greater bacterial virulence even in normal hosts or immunocompetent patients. It was interesting that the prevalence of nosocomial bacteraemia 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 bacteraemia 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\(^1,2,9\).

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 bacteraemia 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

<table>
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<tr>
<th>Variable</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Cirrhosis</td>
<td>17.5</td>
<td>2.431-125.979</td>
<td>0.004*</td>
</tr>
<tr>
<td>Mechanical ventilator</td>
<td>3.9</td>
<td>1.263-11.971</td>
<td>0.018*</td>
</tr>
</tbody>
</table>

* Statistical significance, p < 0.05
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.

References

การติดเชื้อในกระแสเลือดจากโรงพยาบาลของโรงพยาบาลสงขลานครินทร์: ผลที่ได้รับและปัจจัยพยากรณ์ซ้ำซ้อน

ธนภร หอทิวากุล, สมคิด นาภี, ศรัญญู ชูศรี, จรรยาคิค ศิลปโภชากุล

วัตถุประสงค์: เพื่ศึกษาระบบการตรวจจุดเชื้อไข้, จุดซึ่งมีการตรวจพบการตายที่มีอัตราส่วนต่อการตายในการติดเชื้อในกระแสเลือดจากโรงพยาบาลสงขลานครินทร์

วัสดุและวิธีการ: การศึกษาข้อมูลในผู้ป่วยผู้ป่วยที่มีการติดเชื้อในกระแสเลือดจากโรงพยาบาลสงขลานครินทร์ที่มีผลเพาะเชื้อในเลือดโดยมีผลเพาะเชื้อในเลือดได้แล้ว ภายใน 48 ชั่วโมง ศึกษาระหว่างวันที่ 1 สิงหาคมถึง 30 พฤศจิกายน พ.ศ. 2551

ผลการศึกษา: มีการติดเชื้อในกระแสเลือด 138 ครั้งในผู้ป่วย 117 คน ความชุก 11.6 ครั้งต่อการอยู่โรงพยาบาล 1,000 ครั้ง อายุเฉลี่ยของผู้ป่วย 54.8 ปี (ตั้งแต่ 12 ถึง 88 ปี) เป็นผู้ชาย 60.9 ละผลิตภัณฑ์ ซึ่งมีการเพาะเชื้อในกระแสเลือด 27.5 ขณะที่การศึกษา 30.4 ไม่มีโรคพื้นฐาน การติดเชื้อไวรัสและที่พบบ่อยตามแหล่งได้แก่ กระเพาะ 13.9 ทางเดินหายใจ 13.4 ทางเดินปัสสาวะ และกระเพาะ 6.5 ความแปรผันของการติดเชื้อในกระแสเลือดในโรงพยาบาลลดลง 138 ครั้ง กระทั่ง E. coli 17.4, S. aureus 15.2, K. pneumoniae 12.3 และ P. aeruginosa 10.3 แบคทีเรียกรัมลบในสัดส่วนสูง

การติดเชื้อในกระแสเลือดโดยตรง 13.8 การวิเคราะห์แบบ multivariate และ univariate พบว่า โรคตับแข็งและการติดเชื้อทางเดินหายใจอยู่ในระดับที่สูงกว่าเปรียบเทียบกับการตายเพิ่มขึ้น

สรุป: ผลการศึกษาการติดเชื้อในกระแสเลือดจากโรงพยาบาลลดลงส่วนที่ค่อนข้างสูง แต่ยังคงมีอัตราการตายสูงในบางกลุ่มเป้าหมาย