Prevalent Bacterial Infections in Intensive Care Units of Shiraz University of Medical Sciences Teaching Hospitals, Shiraz, Iran

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(Received September 10, 2008. Accepted March 26, 2009)

SUMMARY: Intensive care unit (ICU)-acquired infections can bring some degree of morbidity and mortality to patients staying in the ICU. In this study, over a 6-month period, the prevalence of infections and mortality rates among ICU patients, the predominant organisms and their resistance patterns were determined in a cross-sectional study. Samples of all the patients hospitalized longer than 48 h in two Shiraz university teaching hospitals in Shiraz, Iran, were microbiologically cultured, and antimicrobial susceptibility was determined using the disk diffusion method. We studied 123 specimens from 89 patients aged 1 month to 80 years (38.3 ± 13.4), and among them 46 patients (51.7%; 95% CI, 41.3 - 62.1%) showed infection based on culture and clinical findings. Of these, 37 patients (41.6%) had more than one ICU-related nosocomial infection and 9 patients (10.1%) had only one ICU-related nosocomial infection. The overall mortality rate for ICU-acquired infections was 10.9% (5 patients). Gram-negative bacteria were significantly more involved in infections than were Gram-positive bacteria ($P < 0.05$). The most frequently reported infections were urinary tract infections. The most frequently isolated bacteria were Pseudomonas (39.1%), which was mainly sensitive to amikacin and ceftazidime. Our study results underscore the importance of specific measures for infection control in critically ill patients in ICUs in Shiraz, Iran, especially when using urinary catheters.

INTRODUCTION

The importance of the intensive care unit (ICU) is inestimable in the control and treatment of the most variable and severe illnesses of the human body. In spite of the invaluable and well-established role of the ICU in patient care, ICU-acquired infections bring some degree of morbidity and mortality to patients in the ICU as well as causing significant increases in costs (1-4). Hospital infection rates in ICUs have been documented to be the highest of all hospital-acquired infections in large multicenter studies in the United States and Europe (1,5,6). Infection rates in the ICU range from 12 to 45% and are the highest in surgical and burn ICUs and the lowest in coronary care units (2,7-9). This is related to the use of large numbers of invasive procedures and devices, such as endotracheal and tracheotomy tubes, in the former. Patient factors that contribute to susceptibility to infection include extremes of age, immune compromised state, malnutrition and severe underlying disease, and a high incidence of cross infection (2,3,7,8). The three most common nosocomial infections are ventilator-associated pneumonias, urinary tract infections (UTIs) and bloodstream infections (9,10). Data from the National Nosocomial Infections Surveillance System (NNIS) conducted between 1992 and 1997 from medical ICUs in the United States identified UTIs as the most frequent nosocomial infection (2,4). The nature of the ICU environment makes this area of the hospital a focus for the emergence and spread of many antimicrobial-resistant pathogens (9,10). Many antibiotic-resistant Gram-positive or Gram-negative bacteria including staphylococci, a wide variety of Enterobacteriaceae, Pseudomonas spp., Acinetobacter spp.
or Candida spp. pose a clinically significant danger of infection among ICU patients (11). One study showed that one-third of nosocomial infections could be prevented through infection control and watchful programs (12).

In view of the relevance and impact of such observations and also limited information about ICU-related infections in our hospitals in Shiraz, the biggest city in the south of Iran, it is crucial to know the prevalence rates and nature of such nosocomial infections to gain satisfactory results in managing these infections. Thus, in this cross-sectional study, we aimed to determine the prevalence rate of infections and frequency and susceptibility patterns of common infectious agents isolated from patients in the ICUs of the major teaching tertiary hospitals, in Shiraz, southwestern Iran.

METHODS

A total of eight ICUs in the two hospitals in Shiraz as the major southwest Iranian city were included in this study. Namazi and Faghihi hospitals are the two major referral and educational hospitals affiliated with Shiraz University of Medical Sciences. In a 6-month period from September 2006 to March 2007, 123 clinical samples were taken from all of 89 patients staying longer than 48 h in the ICUs of the two study hospitals. In agreement with the Centers for Disease Control and Prevention (CDC, Atlanta, Ga., USA) definitions, a patient was given a diagnosis of nosocomial infection when there was a medical diagnosis of an infectious focus that required the use of antimicrobial treatment (13). For each patient, data concerning demographics (age and gender), clinical status on admission to the ICU, and diagnostic and therapeutic interventions performed were collected on the day of study.

All clinical isolates were first identified by conventional methods in a routine microbiology laboratory. A positive
culture was defined as identification of an organism on Gram stain followed by growth of the organism in the appropriate culture medium (8,14).

The cultures employed included cultures of blood (more than two positive pairs of culture for the same pathogen), urine (more than 10,000 CFU when collected from a urinary catheter and 100,000 CFU of an isolate when not), bronchoalveolar lavage (more than 10,000 CFU for a single pathogen) and surgical wounds. Quantitative examination was done on the routine urine cultures to exclude normal flora and contaminants, and the presence of more than 10⁵ bacteria signified a UTI. All urine samples were cultured; even if the urinalysis was negative (2,8,14). Significant isolates were selected for identification and antimicrobial susceptibility testing using routine biochemical testing. Antibacterial susceptibility testing was done by Kirby-Bauer’s disk diffusion method for all of the isolated bacteria on Mueller-Hinton agar (Hi Media, Mumbai, India) to determine their resistance pattern against common antibiotics, following the standards of the Clinical Laboratory Standards Institute (CLSI, formerly National Committee for Clinical Laboratory Standards [NCCLS]) (15). Cefoxitin was included in our panel of antimicrobials to detect possible methicillin-resistant Staphylococcus aureus (MRSA) according to CLSI recommendation (16). Owing to the high risk of ICU infections, bacterial isolates showing intermediate susceptibility to an antimicrobial agent were categorized as resistant isolates for data analysis and presentation.

The recorded results were statistically analyzed, and the groups were compared by chi-square tests using SPSS, version 11.5. Differences between groups were considered statistically significant if P values were <0.05.

RESULTS

Among the 8 ICUs, 123 samples of 89 patients, 47 (62.7%) males, and 28 (37.3%) females with age ranging from 1 month to 80 years (average 38.3 ± 13.4 years) and hospitalization time of 15.1 ± 3.8 days, were studied. Of these, 46 patients (51.7%; 95% CI, 41.3-62.1%) showed infection based on culture and clinical findings, while 43 patients (48.3%) had no defined type. Of the 46 with infection, 37 patients (41.6%) had more than one ICU-related nosocomial infections and 9 patients (10.1%) had only one ICU-related nosocomial infection. The overall mortality rate for ICU-acquired infections after 6 weeks of follow-up was 10.9% (5 patients), and bacteremia with Gram-negative microorganisms was the cause of death.

The most frequent sites of infection were the urinary tract (84.7%) followed by the respiratory tract (65.2%), wounds (32.6%), blood (23.8%) and other sites (Table 1). As shown in Table 1, Gram-negative and Gram-positive bacteria were involved in 56 and 22 infections, respectively, and thus Gram negatives were more significantly involved (P < 0.05) in the infections observed. Mixed bacterial infection was observed in 11 (23.9%) infected patients. Yeast was isolated in 8 patients (19.5%). The most frequently isolated pathogen from wounds and urinary and respiratory tracts was Pseudomonas spp., and that for bloodstream infections was S. aureus (Table 1).

As shown in Table 2, most of our Gram-negative isolates were susceptible to ciprofloxacin and cephalosporin derivatives tested. The prevalent Pseudomonas isolates showed moderate to high sensitivity rates against all antibiotics tested. The most effective antibiotics for Pseudomonas isolates were amikacin and ceftazidime, with 88.9 and 77.8% susceptibility rates, respectively. Klebsiella spp. were mainly resistant to multiple antimicrobials but mostly susceptible to amikacin and ciprofloxacin. Most of our isolated staphylococci were resistant to cefoxitin (methicillin) and co-trimoxazole but were mostly susceptible to amoxicillin; however, coagulase-negative staphylococci (CoNS) were mostly resistant to vancomycin (66.7%). All of the isolated enterococci were sensitive to vancomycin, but they were mostly resistant to gentamicin. The details of antibiotic susceptibility patterns among isolated bacteria are depicted in Table 2.

Table 1. Microorganisms isolated from 97 samples of 46 patients with ICU-acquired infections according to the site of infection

<table>
<thead>
<tr>
<th>Microorganism</th>
<th>Urinary tract no. (%)</th>
<th>Respiratory tract no. (%)</th>
<th>Bloodstream no. (%)</th>
<th>Wound no. (%)</th>
<th>Other sites¹ no. (%)</th>
<th>Total no. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram-negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pseudomonas spp.</td>
<td>7 (15.2)</td>
<td>7 (15.2)</td>
<td>1 (2.2)</td>
<td>3 (6.5)</td>
<td>–</td>
<td>18 (39.1)</td>
</tr>
<tr>
<td>Acinetobacter spp.</td>
<td>4 (8.7)</td>
<td>3 (6.6)</td>
<td>–</td>
<td>1 (2.2)</td>
<td>1 (2.2)</td>
<td>9 (19.7)</td>
</tr>
<tr>
<td>Enterobacter spp.</td>
<td>3 (6.5)</td>
<td>–</td>
<td>–</td>
<td>1 (2.2)</td>
<td>1 (2.2)</td>
<td>5 (10.9)</td>
</tr>
<tr>
<td>Klebsiella spp.</td>
<td>2 (4.3)</td>
<td>4 (8.7)</td>
<td>2 (4.3)</td>
<td>1 (2.2)</td>
<td>–</td>
<td>9 (19.5)</td>
</tr>
<tr>
<td>E. coli</td>
<td>6 (13.0)</td>
<td>2 (4.3)</td>
<td>2 (4.3)</td>
<td>1 (2.2)</td>
<td>–</td>
<td>11 (23.8)</td>
</tr>
<tr>
<td>Other</td>
<td>4 (8.7)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>4 (8.7)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>26 (56.4)</td>
<td>16 (34.8)</td>
<td>5 (10.8)</td>
<td>7 (15.3)</td>
<td>2 (4.4)</td>
<td>56 (100)</td>
</tr>
<tr>
<td>Gram-positive</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S. aureus</td>
<td>1 (4.3)</td>
<td>3 (6.5)</td>
<td>3 (6.5)</td>
<td>2 (4.3)</td>
<td>–</td>
<td>9 (21.6)</td>
</tr>
<tr>
<td>CoNS</td>
<td>1 (2.2)</td>
<td>2 (4.3)</td>
<td>2 (4.3)</td>
<td>1 (2.2)</td>
<td>–</td>
<td>6 (13.0)</td>
</tr>
<tr>
<td>Enterococcus spp.</td>
<td>1 (2.2)</td>
<td>–</td>
<td>–</td>
<td>2 (4.3)</td>
<td>2 (4.3)</td>
<td>3 (6.5)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (2.2)</td>
<td>1 (2.2)</td>
<td>1 (2.2)</td>
<td>1 (2.2)</td>
<td>–</td>
<td>4 (8.8)</td>
</tr>
<tr>
<td>Subtotal</td>
<td>4 (10.9)</td>
<td>6 (13.0)</td>
<td>6 (13.0)</td>
<td>4 (8.7)</td>
<td>2 (4.3)</td>
<td>22 (46.8)</td>
</tr>
<tr>
<td>Mixed bacteria</td>
<td>5 (10.9)</td>
<td>4 (8.7)</td>
<td>–</td>
<td>2 (4.3)</td>
<td>–</td>
<td>11 (23.9)</td>
</tr>
<tr>
<td>Yeast</td>
<td>3 (6.5)</td>
<td>4 (8.7)</td>
<td>–</td>
<td>1 (4.3)</td>
<td>–</td>
<td>8 (18.9)</td>
</tr>
<tr>
<td>All isolates</td>
<td>38 (84.7)</td>
<td>30 (65.2)</td>
<td>11 (23.8)</td>
<td>14 (32.6)</td>
<td>4 (8.7)</td>
<td>97 (100)</td>
</tr>
</tbody>
</table>

¹: Cerebrospinal fluid, stool and peritoneal fluid.
CoNS, coagulase-negative staphylococci.
teria were significantly more involved in infections than were some recent studies (5,27). In our study Gram-negative bac-

Species of Gram-negative bacteria such as Pseudomonas, E. coli, Acinetobacter and Enterobacter and Gram-positive staphylococci were the most prevalent pathogens recovered from ICU patients in this study (Table 1). Regarding the bacte-

The ICUs are an area of considerable antibiotic use in which antibiotic-resistant organisms are prevalent. It is well-known that multidrug-resistant bacteria are becoming increasingly prevalent in the hospital environment as a result of the exten-

As shown in Table 2, Klebsiella spp. were mainly resistant to multiple antimicrobials. The high resistance of our Klebsiella isolates to the tested cephalosporin derivatives in our study is suggestive of the probable presence of extended-spectrum beta-lactamases (ESBLs) in our hospitals. Although the pres-

DISCUSSION

Nosocomial infections in ICUs have become increasingly problematic in recent years. Nevertheless, no records about the rates of infection in ICUs in our area are available. In this study, 51.7% of the clinically identified infections in the ICU were supported by positive cultures. These isolates might not necessarily have represented the cause of the infection; they may only have reflected possible contamination of the sample or the process of colonization. The prevalence of ICU-acquired infections is estimated to be between 12 and 45% (1,5,9,11,17). Higher rates of infection among ICU patients are mostly related to factors such as exposure to invasive procedures, underlying disease conditions, duration of stay in the ICU, infection sites and multidrug-resistant pathogens (18).

In this study, the overall mortality rate for ICU-acquired infections was 10.9% (5 patients), and bacteremia with aero-

It is well-known that multidrug-resistant bacteria are becoming increasingly prevalent in the hospital environment as a result of the extensive use of antibiotics. Antibiotic resistance among our Gram-

multiple antimicrobials. The high resistance of our Klebsiella isolates to the tested cephalosporin derivatives in our study is suggestive of the probable presence of extended-spectrum beta-lactamases (ESBLs) in our hospitals. Although the presence of ESBL-producing organisms was not confirmed in this study, its prevalence in our studied tertiary hospitals may be similar to other parts of the world where treatment of bacte-

The most frequently isolated pathogen in bloodstream infections was staphylococci, and for other infections it was Pseudomonas spp. In most of the other studies CoNS followed by S. aureus comprised the most prevalent bacteria isolated from bloodstream infections (9,32). For the other sites, similar results have been reported by other studies, except for UTI, which has been mostly caused by E. coli (9). Such a difference might be related to variables such as temperature, climate, environment and/or antibiotic use in our area.

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Table 2. Antimicrobial susceptibilities of isolated bacteria from studied patients with ICU-acquired infections

<table>
<thead>
<tr>
<th>Isolated bacteria</th>
<th>n</th>
<th>Cefazidine no. (%)</th>
<th>Amikacin no. (%)</th>
<th>Amoxicillin no. (%)</th>
<th>Ceftriaxone no. (%)</th>
<th>Cefazolin no. (%)</th>
<th>Cefoxitin no. (%)</th>
<th>Gentamicin no. (%)</th>
<th>Co-trimoxazole no. (%)</th>
<th>Vancomycin no. (%)</th>
<th>Ciprofloxacin no. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram-negative</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pseudomonas spp.</td>
<td>18</td>
<td>14 (77.6)</td>
<td>16 (88.9)</td>
<td>–</td>
<td>13 (72.2)</td>
<td>10 (55.5)</td>
<td>–</td>
<td>9 (69.2)</td>
<td>–</td>
<td>–</td>
<td>12 (66.7)</td>
</tr>
<tr>
<td>E. coli</td>
<td>11</td>
<td>3 (27.3)</td>
<td>7 (63.6)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>4 (36.4)</td>
<td>8 (72.7)</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Klebsiella spp.</td>
<td>9</td>
<td>3 (33.3)</td>
<td>7 (77.8)</td>
<td>4 (44.4)</td>
<td>4 (44.4)</td>
<td>–</td>
<td>5 (55.6)</td>
<td>5 (55.6)</td>
<td>–</td>
<td>–</td>
<td>6 (66.6)</td>
</tr>
<tr>
<td>Enterobacter spp.</td>
<td>5</td>
<td>1 (20.0)</td>
<td>2 (40.0)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>1 (20.0)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Acinetobacter spp.</td>
<td>9</td>
<td>2 (22.2)</td>
<td>8 (88.9)</td>
<td>5 (55.5)</td>
<td>6 (66.7)</td>
<td>3 (33.3)</td>
<td>2 (22.2)</td>
<td>4 (44.4)</td>
<td>–</td>
<td>–</td>
<td>7 (77.0)</td>
</tr>
<tr>
<td>Total</td>
<td>52</td>
<td>20 (38.5)</td>
<td>36 (69.2)</td>
<td>16 (30.7)</td>
<td>23 (44.2)</td>
<td>16 (30.7)</td>
<td>21 (40.4)</td>
<td>17 (32.7)</td>
<td>–</td>
<td>–</td>
<td>25 (48.1)</td>
</tr>
<tr>
<td>Gram-positive</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S. aureus</td>
<td>9</td>
<td>–</td>
<td>6 (66.7)</td>
<td>–</td>
<td>–</td>
<td>0</td>
<td>5 (55.5)</td>
<td>1 (11.1)</td>
<td>7 (77.8)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>CoNS</td>
<td>6</td>
<td>–</td>
<td>5 (83.3)</td>
<td>–</td>
<td>–</td>
<td>2 (33.3)</td>
<td>3 (50.0)</td>
<td>2 (33.3)</td>
<td>2 (33.3)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Enterococcus spp.</td>
<td>3</td>
<td>–</td>
<td>2 (66.7)</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>1 (33.3)</td>
<td>–</td>
<td>3 (100)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Total</td>
<td>18</td>
<td>13 (72.2)</td>
<td>9 (50.0)</td>
<td>3 (16.7)</td>
<td>12 (66.7)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

–, not done.
in Iran (32). However, other studies reported more frequent rates of vancomycin-resistant enterococci (VRE) in ICUs (9).

In a study in Shiraz, a colonization rate of 6.2% VRE was reported among chronic hemodialysis patients (41). In a recent study in Turkey neither staphylococci nor enterococci showed any vancomycin resistance (3).

In conclusion, the prevalence rate of ICU infections in Iran seems high; such a high prevalence in Iran could be attributed to many factors, including lack of financial support to medical facilities, inadequate number of trained personnel working in infection control, especially with regard to the procedures such as using urinary catheters, overcrowded wards and insufficient equipment and supplies. A comprehensive infection control program in Iran is in its infancy, compared with infection control programs in other countries, and so the occurrence of ICU-acquired infection can increase the morbidity and mortality rates in ICU patients. Our findings will be useful for the comparison of prevalence rates of infection and the implementation of strict infection control policy.

ACKNOWLEDGMENTS

This work was financially supported by Shiraz University research grant No. 84-SC-1772-C307 and Shiraz University of Medical Sciences research grant No. 2624.

The authors are grateful to Dr. E. Modjtahedi for his kind cooperation and Mr. M.R. Sarvaghad for his technical assistance.

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