

Prevalence and antimicrobial resistance of health care associated bloodstream infections at a general hospital in Saudi Arabia

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ABSTRACT

الأهداف: تحديد مدى اتجاه التهاب مجرى الدم (HA-BSI) المرتبط بالرعاية الصحية بمستشفى خدمات ارامكو السعودية.

الطريقة: أجريت دراسة استطلاعية من عام 2002م إلى 2006م. كانت مصطلحات التهاب مجرى الدم (HA-BSI) مطابقة لمصطلحات شعبة مكافحة الأمراض والوقاية منها.

النتائج: كان العدد الإجمالي لحالات التهاب مجرى الدم HA-BSI-1103 حالة بمعدل سنوي متوسط 8.5 لكل 1000 من الحالات المسرحة من المستشفى وبنسبة 18 لكل 10,000 مريض في اليوم. وبلغت الحالات الأولية غير محددة السبب 38% مجمل الحالات، وبلغت نسبة التهاب الدم الناتجة عن تنبيب الوريد المركزي CLABSI حوالي 47% وكانت الباقي 15% حالات ثانوية. وارتفعت نسبة المعدل العام لالتهاب مجرى الدم لكل 1000 حالة من 7.8 إلى 11.9 مريض $p < 0.001$. واستمرت البكتيريا الثانوية بشكل مستقر خلال مدة الدراسة لدى 3/10,000 مريض $p = 0.41$. أما التهاب الدم الأولي فقد ارتفع من 6.9 إلى 10.6 لكل 10,000 مريض $p < 0.001$. وارتفعت نسبة التهاب الدم الناتج عن تنبيب الوريد المركزي CLABSI من 3.2 إلى 6 لكل 1000 مريض $p < 0.001$ ومن 7 إلى 11.8 لكل 10,000 مريض $p = 0.039$. الكريات العنقودية السالبة كانت السبب الرئيسي للالتهابات 23.7%، ثم الكريات العنقودية المذهبة 11.1%، ثم الإيشريكية القولونية 11.1%. كما شكلت المبيضات الفطرية 5% من كل الحالات، و الكليسيلا الرئوية 9%، والمقيحات الزرقاء 7.3%.

خاتمة: بقي معدل تجرثم الدم الثانوي مستقراً خلال فترة الدراسة الزمنية ولكن ارتفع التهاب الدم الأولي BSI والناتج عن تنبيب الوريد المركزي CLABSI مع مرور الوقت. وقد كانت الكريات العنقودية السالبة والكريات العنقودية المذهبة والإيشريكية القولونية من أكثر المكروبات انتشاراً.

Objectives: To determine the trend of health care associated blood stream infection (HA-BSI) at Saudi Aramco Medical Services Organization.

Methods: This prospective survey was conducted during the year 2002-2006. Definitions of HA-BSI infections

were based on the Centers for Disease Control and Prevention categories.

Results: There were a total of 1103 distinct episodes of HA-BSI with annual average rates of 8.5 per 1000 discharges and 18 per 10,000 patient-days. Of all episodes, 38% were primary, 47% were central line-associated bloodstream infection (CLABSI), and the remaining 15% were secondary bacteremias. The hospital wide BSI rate per 1000 discharges increased from 7.8 to 11.9 ($p < 0.001$). Secondary bacteremia remained relatively stable over the study period at 3/10,000 patient-days ($p = 0.41$). Primary BSI increased from 6.9 to 10.6 per 10,000 patient-days ($p < 0.001$). Hospital wide CLABSI increased from 3.2 to 6 per 1000 discharges ($p < 0.001$) and from 7 to 11.8 per 10,000 patient-days ($p = 0.039$). Coagulase negative staphylococcus was the leading pathogen (23.7%) followed by *Staphylococcus aureus* (11.1%) and *Escherichia coli* (11.1%). Of all episodes, candida caused 5%, *Klebsiella pneumoniae* (9%) and *Pseudomonas aeruginosa* (7.3%).

Conclusions: The rate of secondary BSI remained relatively stable over the study period. However, primary BSI and CLABSI increased over time. Coagulase negative staphylococcus, *Staphylococcus aureus*, and *Escherichia coli* were the most frequent microorganisms.

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Health care associated infections (HAI) significantly increase morbidity and mortality, increase healthcare costs, and prolong hospital stay.¹ Health care associated blood stream infections (HA-BSI) account for <10% of all HAI. However, HA-BSI may not increase mortality if there is a control for severity of illness,² and may increase mortality by 35% in prospective studies that did not use this control.³ Saudi Aramco Medical Services Organization (SAMSO) Antimicrobial Surveillance Program continues to monitor all HAI including pathogens causing BSI in addition to other objectives. Previously, we reported our results relating to pathogen-specific antimicrobial resistance rates over time. Those results were made available to be compared to local, national, regional, and international studies.⁴ We showed that there was an increase in methicillin (oxacillin) resistance in *Staphylococcus aureus* (MRSA).⁵ Those studies, however, were not specific for BSI pathogens. In addition, there is little data from Saudi Arabia documenting the prevalence and trend of HA-BSI. Few studies described central line related blood stream infections in pediatric patients^{6,7} and from fatal cases of BSI.⁸ The main objective of this study was to examine the annual rate of HA-BSI at SAMSO, identify the microorganisms responsible and document the pattern of antibiotic sensitivity.

Methods. This prospective study was conducted at SAMSO, which provides medical care for all Saudi Aramco employees and their dependents: spouses, children, and parents. There are approximately 370,000 individuals eligible for medical care. The main hospital, Dhahran Health Center (DHC), was initially constructed in 1944. Over the years, DHC has grown with a 380-bed referral hospital. Dhahran Health Center has 5 intensive care units (ICU) (cardiac, medical, surgical, pediatric, and neonatal)⁹ and an open-heart surgery was established in mid 2006. The study was approved by the Public Relation Department of Saudi Aramco on 6 October 2008 with the approval number of 10499.

The study included all HA-BSI throughout the hospital including patients in the ICU and the regular wards from January 2002 to December 2006. Those with repeat isolates were excluded from the study. All microbiological cultures were forwarded to a trained infection control practitioner on daily basis. The infection control practitioners using a standardized HAI-report form prospectively collected the clinical data. Data on central venous catheter days and utilization ratio were calculated for each ICU unit beginning in 2004.

These cultures were classified based on the Center for Disease Control and Prevention (CDC) definitions¹⁰ as

community-acquired or HAI by review of the available electronic and paper records of the patients. Nosocomial BSI was defined according to CDC as the presence of one (2 in case of potential skin contaminants) or more positive blood cultures at least 48 hours after admission, in association with clinical signs and symptoms.¹⁰ A new positive blood culture occurring more than 48 hours after the previous positive culture was classified as a separate episode of bacteremia except when clinical evidence suggested a common source or the same microorganism was recovered.¹¹ An episode of bacteremia was classified as a secondary, primary unknown source or central line-associated bloodstream infection (CLABSI).¹² Central line-associated bloodstream infection is a primary BSI in a patient that had a central line within the 48-hour period before the development of the BSI.¹³ In CLABSI, the central line is considered to be the most logical source for the positive blood culture. Secondary bacteremia is defined as the development of BSI after a documented infection with the same microorganism at another body site, including: urinary tract, lung, surgical site, or the skin.¹¹ A primary unknown BSI is any bacteremia in which an alternative source for the bloodstream invasion was not identified and was not CLABSI.

Blood cultures were processed at the microbiology laboratory of SAMSO, which is a certified laboratory by the College of American Pathologists. The microbiological identification methods and susceptibility testing followed the recommendation of the Clinical and Laboratory Standards Institute (CLSI) guidelines. The prevalence of antibiotic resistance was calculated as the percentage of any given microorganism with intermediate or full resistance divided by the total number of tested isolates for a particular antimicrobial agent. Unfortunately, confirmatory testing for the production of extended-spectrum β -lactamase (ESBL)-producing microorganisms among strains with resistance to third generation cephalosporin was not routinely carried out prior to the year 2007.

Descriptive statistics were used to calculate the incidence of HA-BSI and data was expressed per 1,000 admissions and per 10,000 patient-days. For comparison with other studies, we also calculated the device utilization ratio for central venous catheters. The device utilization ratio was calculated as the number of catheter days divided by the total number of patient-days in the ICU and was available for 2004-2006. Thus, the rate of CLABSI was expressed per 1000 device-days for this period. The rate was calculated as the number of CLABSI divided by the total number of central line days and expressed per 1000. Statistical analyses were performed using the statistical package for the social sciences (SPSS version 10.0). The trend of BSI rates

over time was determined using the linear trend analysis method and to show that a trend was statistically valid, the P value of the χ^2 for association had to be significant (<0.05). The results of 2-sample proportion tests assessed comparison between 2 resistance rates.

Results. During the study period there were a total of 1,103 episodes of nosocomial bacteremia. When only the first episode of bacteremia was included in the analysis, the mean age was 43.8 ± 29.4 years and the inter-quartile range was 14-71 years. There were 91 (8.2%) episodes in neonates, 187 (17%) cases in children (<18 years of age), and 825 (74.3%) in adults. The annual rate of bacteremia per 1,000 discharges and per 10,000 patient-days is shown in Figure 1. The hospital wide rate of BSI increased from 7.8-11.9 per 1000 discharges in 2002 and 2006 ($p<0.001$) and from 17.1-25 per 10,000 patient-days ($p<0.001$) (Figure 1). Of all the cases, 420 (38%) were primary episodes without an identifiable source, 517 (47%) were CLABSI and the remaining ($n=166$, 15%) were secondary episodes. Of the total episodes, 29 (2.6%) were surgery-related and 137 (12.4%) were organ-related episodes. The trend of the annual rates of each category is shown in Figure 2. Primary BSI increased from 6.9-10.6 per 10,000 patient-days ($p<0.001$) and from 3.1 to 4.9 per 1000 discharges ($p<0.001$) (Figure 2). The hospital wide CLABSI increased from 7-11.8 per 10,000 patient in days ($p=0.039$), and from 3.2 to 6 per 1000 discharges

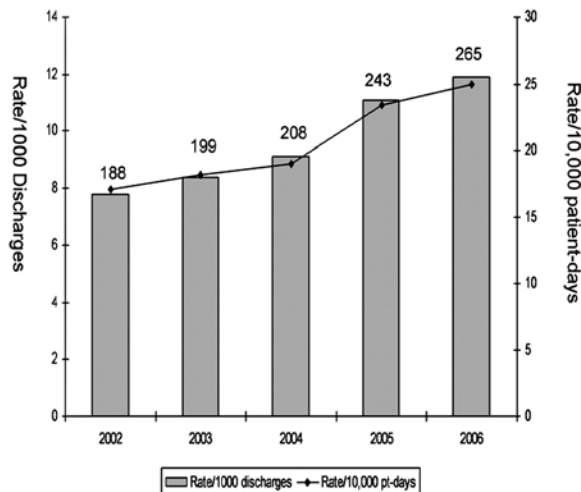


Figure 1 - A combination chart showing the annual rate of Health Care Associated Blood Stream Infection from 2002-2006. The bars show the rate per 1,000 discharges and the line shows the rate per 10,000 patient-days. Numbers above each column shows the total number of Health care associated blood stream infections in each year.

($p<0.001$) (Figure 2). Secondary bacteremia remained relatively stable over the study period at 3/10,000 patient-days ($p=0.41$) and 1.3/1000 discharges ($p=0.9$). For the ICU data from 2004-2006, the central venous catheter utilization ratio was 0.3 and the rate of CLABSI per 1000 device-days was 9.4 in 2004, 11.7 in 2005, and 8.2 in 2006. This change however, did not reach statistical significance ($p=0.083$).

Gram-negative bacilli accounted for 46% ($n=499$), gram positive cocci constituted 48.7% ($n=529$) and fungemia represented 5% ($n=57$). There was no major change over the study period in the type of micro-organisms. Coagulase negative staphylococcus (CoNS) was the number one to cause bacteremia ($n=261$, 23.7%) followed by *Staphylococcus aureus* (*S. aureus*) ($n=122$, 11.1%) and *Escherichia coli* ($n=121$, 11.1%). The rate of BSI due to *Klebsiella pneumoniae* (*K. pneumoniae*) was 9% ($n=99$), *Pseudomonas aeruginosa* (*P. aeruginosa*) was 7.3% ($n=81$), and *Acinetobacter calcoaceticus-baumannii* (*A. calcoaceticus*) complex constituted 5.3% ($n=59$) of all bacteremia. Of all candidemia cases, 52% ($n=29/56$) were due to *Candida albicans*.

Methicillin resistance was detected in 22% of *S. aureus* isolates ($n=27/122$) and in 71% of CoNS isolates ($n=65/92$). Among enterococcal isolates, resistance to penicillin G was 91% for *Enterococcus faecalis* ($n=31/34$) and none was vancomycin resistant. Antimicrobial resistance rates for the most common gram-negative bacteria causing HA-BSIs are shown in Table 1.

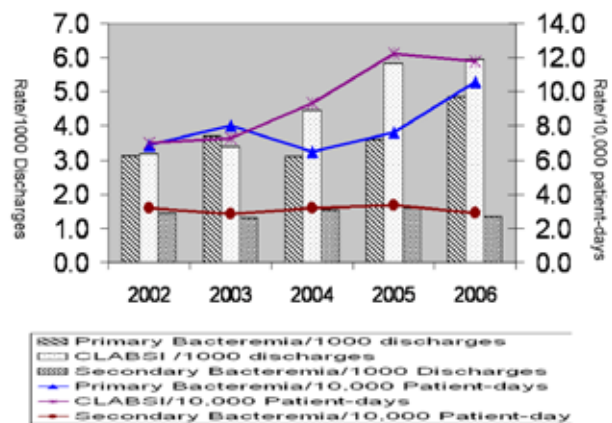


Figure 2 - A combination chart showing the annual rate of Health Care Associated Blood Stream Infection from 2002-2006 by Type of Bacteremia. The bars show the rate per 1,000 discharges and the lines show the rate per 10,000 patient-days. CLABSI - central line-associated bloodstream infection

Table 1 - Rates of antimicrobial resistance among most frequently isolated gram-negative microorganisms from patients with health care associated bloodstream infections (HA-BSI).

Microorganism	Ciprofloxacin n (%)	Imipenem n (%)	Gentamicin n (%)	Ceftriaxone n (%)
<i>Escherichia coli</i>	32/95 (33.7)	5/59 (8.5)	12/59 (2.3)	20/54 (37)
<i>Klebsiella pneumoniae</i>	28/78 (36)	6/46 (8.7)	11/48 (23)	11/44 (25)
<i>Pseudomonas aeruginosa</i>	21/61 (34.4)	2/34 (6)	8/36 (22)	-
<i>Acinetobacter calcoaceticus</i>	22/45 (49)	3/26 (11.5)	7/26 (27)	10/22 (45)
<i>Enterobacter cloacae</i>	9/26 (34.6)	3/14 (14.3)	0/13	3/10 (30)

The values indicate the percent (%) of resistant microorganisms and the values in parenthesis indicate the number of resistant isolates (intermediate and fully resistant) divided by the total number of tested isolates.

Discussion. The incidence of HA-BSI varies according to the type of the patients, the size of health care centers, and the length of hospital stay. Our data showed important differences compared to those reported from other hospitals.¹⁴ In the Surveillance and Control of Pathogens of Epidemiological Importance study, the rate of BSI was 60 cases per 10,000 hospital admissions.¹² In addition, the overall incidence of HA-BSI was 5.39 and 2.83 per 1000 patients in English teaching and non-teaching hospitals, respectively.¹⁵ In a recent study from Spain, the incidence of BSI increased from 16 episodes to 31.2/1000 admissions.¹⁶ We also showed an increase in the rate of HA-BSI from 17.1 to 25 per 10,000 patient-days. Our data showed that CLABSI is a considerable source of HA-BSI and accounted for 47% of all cases. This finding is similar to findings by other investigators.^{15,17} In a study by Taylor et al¹⁷ primary bacteremia accounted for 57% of all BSI and most of them must have been CLABSI. Similarly, Wisplinghoff et al¹² reported that intravascular devices were the most frequent predisposing factors for BSI. A clear trend in the reduction of BSI to a rate of 2.1 per 1000 catheter-days was reported.¹⁸ In a recent study from Kuwait, the mean CLABSI was 5.5/1000 central line days, however; the device utilization ratio was 0.88.¹⁹ In the current study, the rate of CLABSI per 1000 device-days in the ICU was around 9.7 per 1000 device-days and was closer to the 75th percentile of the National Healthcare Safety Network (NHSN). The central line utilization is one measure of invasive practices and is an extrinsic risk factor for HA-BSI. In addition, device utilization may serve as a marker for severity of illness of patients and the intrinsic susceptibility of those patients to infection.²⁰ However, the device utilization ratio in the major ICU in our hospital was 0.3 and this ratio is similar to the fiftieth percentile of the collective NHSN data.²¹ Similarly, in the International Nosocomial Infection Control Consortium (INICC) report, the device utilization was reasonably similar to that reported from ICUs in the CDC's NHSN.²² However, the rates of device-

associated nosocomial infections were markedly higher in the ICUs of the INICC hospitals than the NHSN report with a pooled rate of 9.2 per 1000 device-days.²² Thus, other measures such as introduction of alcohol-based hand hygiene and the implementation of the central line bundle were implemented to decrease CLABSI. Data from other institutions in different countries suggest that *Staphylococcus species*, *Klebsiella spp.* and *Pseudomonas spp.* are the predominant isolates of nosocomial BSI.^{16,23} Similarly, the dominance of gram-positive pathogens was documented in this study and previous studies.^{7,12,24} We found a relatively low rate (22%) of MRSA bacteremia among all *S. aureus* HA-BSI. We previously showed that of all *S. aureus* bloodstream infections, 31% were due to MRSA.⁵ This rate is much lower than a 60% rate in the National Nosocomial Infections Surveillance System (NNIS) report in 2004²¹ and is lower than rates (41%) reported from other USA hospitals.¹² However, the rate in the present study was higher than those reported from others parts of Europe (1.7-12.9%).²⁵ Less than 25% of BSIs were caused by MRSA in the United Kingdom,²⁶ and the incidence of MRSA bacteremia was 0.04 per 1,000 patient-days in France.²⁷ The proportion of BSIs due to *Candida species* in our study was 5% compared to a rate of 9% from the USA.¹² Similar to some studies, we found that 52% of candidemia cases were caused by *C. albicans*.^{9,12} These findings are slightly different from those reported in 2002 by NNIS System where non-albicans were more common.²⁸ The difference in these studies may be due to sample sizes and differences in the patient population.

We reported no vancomycin-resistant *Enterococcus spp* similar to a previous report from Saudi Arabia.⁷ This is in sharp contrast to Vancomycin resistance rates of 2% in *E. faecalis* and 60% in *E. faecium* reported from USA.¹² There are no published reports about VRE from Saudi Arabia apart from a recent description of 34 vancomycin-resistant *E. faecium*.²⁹

Among Gram-negative bacteria in this study, there was a high rate of resistance to fluoroquinolones

(33-50%), and lower resistance rates to imipenem (6-14%). In a study from UK and Ireland, imipenem non-susceptibility among *P. aeruginosa* from bacteraemias was 6-11%.³⁰ Imipenem resistant *E. coli* was almost zero and ciprofloxacin resistance was 8.2-25.6%.³¹ High resistance rates (16-22%) were reported in some countries,^{4,30-32} and lower rates of resistance were reported from other parts of the world.^{33,34} In a study of BSI from Germany, fluoroquinolone-resistant Enterobacteriaceae increased over time.³⁵ Similarly, imipenem resistance among *E. coli* increased from 1.4% (1 out of 70) in 2003 to 8.5% (5 out of 59) in this study.⁴ However, this increase did not reach statistical significance ($p=1.0$). On the other hand, the ceftriaxone resistance rate of *E. coli* increased significantly from 11% (11 of 148) in 2003 to 37% (20 of 54) in the present study ($p<0.001$).⁴ This is a disturbing finding and further strategies such as an antimicrobial improvement program were implemented to curtail this increase. The resistance rate of *A. calcoaceticus* to Imipenem in this study was 11.5% compared to earlier report of 3%.³⁶ The difference is related to the sample size and the source of the specimens. One of the limitations of the current study is that the presented data represent only one center experience and thus may limit the applicability to other centers. Another limitation is that there was no stratification of the BSI rates according to the type of the ICU. However, this study is important since it sheds light in areas of concern to health care professionals.

In conclusion, our data showed that primary episodes of HA-BSI were higher than the rate of secondary episodes and that CLABSI was a significant contributor to the overall BSI. While secondary BSI did not increase over the study period, primary BSI and CLABSI increased over the study period. We also showed high rates of fluoroquinolone and imipenem resistance among gram-negative microorganisms. The rate of MRSA bacteremia was 22% among all HA-BSI. These findings should be used to guide empirical therapy of HA-BSI in this population and adopting preventive measures to decrease CLABSI. Recently, we implemented the central line prevention bundle and developed antimicrobial improvement program to further decrease the development of resistance.

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Related topics

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