# Staphylococcus aureus bacteremia

**Daad H. Akbar,** MRCP (UK), Arab Board, **Maimona A. Mushtaq,** MRCP (UK), Arab Board, **Ahmed T. El-Tahawi,** MD, PhD, **Ahmed A. Bahnasy,** MSPH, PhD.

## ABSTRACT

**Objectives:** To study the episodes of *Staph.aureus* bacteremia diagnosed at King Abdulaziz University Hospital, to determine the source of infection, risk factors, the outcome of treatment and to compare our results with those reported in the literature.

**Methods:** A retrospective study in which the episodes of *Staph.aureus* bacteremia diagnosed at King Abdulaziz University Hospital, Jeddah, Kingdom of Saudi Arabia in the period from June 1996 to December 1998 were analyzed.

**Results:** A total of 103 episodes of *Staph.aureus* bacteremia were diagnosed in 95 patients with a mean age of 33.61 years (range 2 months to 90 years) and male:female ratio of 1.9:1. More than 50% of patients were Saudi nationals. Hospital-acquired infection was detected in 74% of the episodes versus 25% community-acquired. Methicillin resistant *Staph.aureus* was found in 29% of the episodes. Intravenous catheters and wounds were the main sources of bacteremic episodes (29% and 21%). The overall mortality was 32% with significant association with old age, diabetes mellitus and hemodialysis for renal failure. Risk factors such as surgical wounds, diabetes mellitus and malignancy, were more frequently associated with hospital-acquired than community-acquired bacteremia. Infective endocarditis was higher in patients with community-acquired bacteremia who had unknown source of infection.

**Conclusions:** As discussed in the text, our results are comparable with those reported in the literature. Insertion of intravenous catheters under aseptic precaution, better care and judicious limitation of patients length of exposure to central line, in addition to proper wound dressings could reduce the frequency of blood stream infections.

**Keywords:** *Staph.aureus*, bacteremia, sources, risk factors.

Information regarding the evolution, incidence, etiology and prognosis of blood stream infections suggests an increasing trend in the incidence of significant bacteremia as well as a shift in the etiology of their dreaded infection in recent years.[1] This is probably related to changes in the underlying diseases of susceptible populations, to more aggressive and invasive medical practice and to the presence of more virulent and difficult to treat microorganisms.[2] Gram-positive organisms represent more than 50% of all isolates of blood culture in different institutions which confirms the shift in the etiologic spectrum of bacteremia observed in recent years.[3-5] The most frequent microorganism isolated was *Stapylococcus aureus* (15%). The wide use of vascular catheters has contributed to the emergence of skin Staphylococcus organisms (such as *Staphylococcus epidermidis* and *Staphylococcus aureus*) as the leading cause of hospital-acquired bacteremia.[6] The most frequent observed predisposing factors to *Staph.aureus* bacteremia implies the rupture of the normal barrier, intravascular catheters, surgery and intubation. The second largest group involve factors that impair the general mechanism of defense such as the use of corticosteroids, cytotoxic therapy or neutropenia.[1]

The aim of this work is to study the sources, risk factors and outcome of treatment of *Staph.aureus* bacteremia at King Abdulaziz University Hospital (KAUH) and to compare our results with those reported in the literature.

**Methods.** The episodes of *Staph.aureus* bacteremia that were diagnosed at KAUH from June 1996 to December 1998 were reviewed. Blood for culture was obtained under aseptic precautions. At least 2 sets of blood cultures were collected before the start of antibiotics. Blood cultures were performed using the Bact/Alert Microbial Detection System (Organon Teknika, USA). Four mls of patient blood was added to 2 bottles containing 40 ml of broth culture media, one for aerobic and the other for anaerobic growth. Culture bottles were loaded into the instrument and remained there for 5 to 7 days or until designated positive. All bottles designated positive were smeared and sub cultured. Standard diagnostic microbiological methods of isolation of microorganism were used.[7] Detection of *Staph.aureus* in one or more blood cultures from the same patient within one week was defined as a single episode.[1] The records of all patients were reviewed for age, sex, ethnic origin, hospital unit in which bacteremia occurred, type of infection whether hospital or community acquired. Community-acquired is when positive blood cultures obtained at or within 48 hours of admission. While hospital - acquired defined as positive blood cultures >48 hours after admission.[1] The criteria used for inclusion of *Staph.aureus* isolated from blood culture were a potential source for blood stream infection and either clinical signs or suspicion of sepsis. A single positive blood culture with *Staph.aureus* was necessary for blood stream infection diagnosis. Blood stream infections were initially identified in the laboratory and further information on each episode was found in the medical records. Clinical sepsis (blood stream infection without positive blood culture) was not included. The blood stream infection was classified as catheter related, of unknown origin, or secondary to an infectious body site. Catheter related blood stream infection was diagnosed on isolation of the same *Staph.aureus* from the tip of the catheter and there was evidence of inflammation at the catheter insertion site from the blood of the patient with accompanying clinical symptoms of blood stream infection and no other apparent source of infection.[8] Blood stream infection occurring in the absence of an apparent portal of entry was classified as of unknown source. The susceptibility of *Staph.aureus* to methicillin was recorded as well as the sources of infection. The underlying conditions like diabetes mellitus, hemodialysis for renal failure, use of immunosuppressive agents (corticosteroid and cytotoxic), underlying malignancy, presence of skin ulcers and wounds as well as central or peripheral catheters were recorded. Secondary foci like infective endocarditis was recorded as well as the patients outcome (improvement or death) and duration of treatment.

***Method of statistic analysis.*** Descriptive statistics along with all analysis were carried out using Statistical Package for Social Sciences (SPSS 7.5). T-test and Chi-square were used appropriately. Logistic regression used to predict mortality from some important variables. Level of significance was set to be <0.05 throughout the study.

**Results.** Out of a total of 407 episodes of blood stream infection, 103 (25%) were positive for *Staph.aureus*. These episodes were diagnosed in 95 patients, 62 (65%) were males, with male:female ratio 1.9:1 and mean age of 33.6 (range 2 months - 90 years). More than 50% of the patients were Saudi nationals. The majority of the episodes occurred in the medical unit (including the intensive care unit) 45 (44%), followed by the pediatric unit 43 (42%), then the surgical unit 10 (10%), and last in the obstetric and gynecology unit 5 (5%). Hospital-acquired infection was detected more frequently than that from the community 77 (75%) versus 26 (25%) with a mean age of 33.89+/-29.46 years and 32.79+/-29.72 years (p 0.87). Methicillin resistant *Staph.aureus* was detected in 30 (29%) of the episodes. The source of infection is presented in Table 1. Hospital-acquired infections were catheter-related in 38% of the episodes, secondary to an infectious body site in 28% (mainly wounds), and of unknown origin in 34%. Table 2 demonstrates the risk factors to both hospital and community-acquired blood stream infection. Wounds, diabetes mellitus and malignancy were the factors most frequently identified in hospital-acquired infections. No significant differences were detected between community and hospital-acquired blood stream infection concerning the different risk factors. Three patients developed infective endocarditis as a secondary foci to blood stream infections, 2 had community-acquired

**Table 1 -** Source of blood stream infection.

| Source | Total N= 103 | | Community-acquired N = 26 | | Hospital-acquired N=77 | |
|---|---|---|---|---|---|---|
| | N | % | N | % | N | % |
| Intravenous catheters | 30 | (29) | 1 | (4) | 29 | (38) |
| Wounds | 22 | (21) | 2 | (8) | 20 | (26) |
| Unknown | 45 | (44) | 19 | (73) | 26 | (34) |
| Urinary tract | 2 | (2) | 1 | (4) | 1 | (1) |
| Respiratory tract | 4 | (4) | 3 | (12) | 1 | (1) |

**Table 2 -** Risk factors of blood stream infection.

| Risk factors* | Community-acquired | | Hospital-acquired | | P value |
|---|---|---|---|---|---|
| | N | % | N | % | |
| Diabetes mellitus | 9 | (36) | 16 | (64) | 0.16 |
| Malignancy | 5 | (36) | 9 | (64) | 0.13 |
| Hemodialysis | 2 | (33) | 4 | (67) | 0.60 |
| Immunosuppressive | 3 | (43) | 4 | (57) | 0.30 |
| Skin ulcers | 4 | (31) | 9 | (69) | 0.10 |
| Wounds | 3 | (11) | 24 | (89) | 0.10 |
| Intravenous catheters | 5 | (19) | 29 | (38) | 0.20 |
| *More than one risk factor was detected in one patient | | | | | |

infections and one hospital-acquired infection. These 3 patients had unknown portal of entry to the blood stream infections. Intravenous catheters and wounds presented in Table 2 were not the sources of blood stream infection in these patients but included in the Table as potential risk factors to infection. No cases of osteomyelitis were found as a source or complication of blood stream infection.

The mean duration of treatment of *Staph.aureus* bacteremia was 14.72+/-13.62 days. The overall mortality related to blood stream infection was 32%. No significant differences was observed in mortality between community and hospital-acquired infections (31% versus 32.5%) (p 0.91) on the other hand, mortality was significantly associated with old age, with a mean age of 45.78 +/-26.50 years for patients who died and 27.88+/-29.10 years for survivors (p 0.003). A logistic regression model to predict mortality for some variables is shown in Table 3. The odd ratio of mortality was about 3.9 times in patients with hemodialysis, and 3.3 times in patients with diabetes mellitus.

**Table 3 -** Logistic regression analysis to predict mortality from some variables.

| Variable | B | sig | Odd ratio |
|---|---|---|---|
| source | -.26 | 0.6 | 0.7 |
| MRSA | 0.74 | 0.1 | 2.0 |
| Type of infection | 0.20 | 0.7 | 1.2 |
| Diabetes mellitus | 1.18 | 0.04 | 3.3 |
| Hemodialysis | 1.30 | 0.2 | 3.9 |
| Immunosuppressive | 0.16 | 0.8 | 1.2 |
| Malignancy | 1.00 | 0.2 | 0.3 |
| Intravenous catheters | 0.50 | 0.2 | 1.6 |
| Infective endocarditis | 0.09 | 0.8 | 1.1 |
| Constant | -2.4 | 3.3 | - |

**Discusion.** Despite the availability of broad spectrum antibiotics, and current sophisticated therapeutic modalities, blood stream infections still carry high morbidity and mortality among hospitalized patients especially those with compromised host defenses.[2] The occurrence of blood stream infection has increased among hospitalized patients over the last decade.[9] In recent years gram-positive bacteria have emerged as important pathogens both in the community and hospital.[10] Bacteremia due to *Staph.aureus* has increased at KAUH. It was 13.5% in 1984,[11] in this study, there is almost a 54% rise which is similar to that observed by others.[12] In our study, hospital-acquired bacteremia was more common than community-acquired infection and this is in accordance with what has been reported by other investigators.[13-15] Bacteremic episodes occurred more in the medical unit than in the surgical and obstetric and gynecology units. The severity of the underlying conditions of many patients admitted to the Intensive Care Unit (ICU) and the need for multiple intravascular and other devices make such patients more vulnerable to blood stream infections. Infection computerized surveillance of an adult ICU in Sheffield, UK,[16] revealed bactermia to be the most common infection following respiratory tract and surgical wounds infections. Twenty nine percent of the *Staph.aureus* bacteremia in our study was due to MRSA. Among cases of *Staph.aureus* bacteremia reported in England and Wales,[17,18] the proportion due to MRSA has increased significantly from 2% in 1989 to 13% by 1995, 21% in 1996 and 32% in 1997. In the United States, approximately 25% of *Staph.aureus* bacteremia is caused by MRSA.[19] Patients colonized by MRSA are at risk of developing bacteremia which can lead to significant morbidity and mortality.[20] Our study as in other reports[21] showed that the presence of intravascular catheter was strongly associated with blood stream infections. It is important to document the source of infection and to determine the risk factors associated with bacteremia in order to develop guidelines for reducing the incidence of hospital-acquired infections. About 25% of endemic hospital-acquired blood stream infections are presumed to be preventable by the implementation of infection surveillance measures and strict control of procedure related infections.[12] As in other reports[22] our study did not identify osteomyelitis as a source or complication of the blood stream infection in pediatric patients. Diabetes mellitus, malignancy and surgical wounds were the risk factors most frequently associated with bacteremic episodes in this study. Diabetes has been present as an underlying disease in 8 to 36% of patients with Staphylococcal bacteremia.[23] Several immune mechanisms are defective in diabetic patients. Among these are a decrease in leukocyte chemotaxis and phagocytosis,

and diminished intracellular killing. Both the underlying malignancy and intensive myelosuppressive treatment have contributed to an increase in the number of patients susceptible to nosocomial infections. Patients having neutropenia for more than 3 days are at higher risk of blood stream infection than patients with a history of neutropenia for a shorter period.[24] Bacteremia of unknown source was reported in 44% of our patients in general and 34% of hospital-acquired bacteremia. In the study that was carried out by Spencer in 1999[16] no focus of infection could be found in about 30% of hospital-acquired bacteremia.

The over all mortality in our study was 32% which is similar to the 35% estimated attributable mortality rate reported by Pittet et al.[25] High mortality rate was significantly associated with old age, as reported by others,[26] and underlying disorders like diabetes and hemodialysis for renal failure. We did not find a significant association between mortality and the source of infection unlike other series,[27,28] that found high mortality with bacteremia of unknown source. In over half of the bacteremic episodes in our study, the main site of infection was a vascular site or an infected surgical wound. The knowledge of modifiable risk factors is useful in the development of strategies that may contribute to the prevention of blood stream infections, e.g guide lines for intravascular catheter care and surgical wounds.

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