International Journal of Science and Research (IJSR)
ISSN: 2319-7064
ResearchGate Impact Factor (2018): 0.28 | SJIF (2018): 7.426

The Characteristics of Staphylococcus Aureus Bloodstream Infections among Children in Pediatric Ward Sanglah Hospital

Carissa Lidia[1], I Wayan Gustawan[2], I Made Gede Dwi Lingga Utama[3], Ni Nengah Dwi Fatmawati[4]

Udayana University, Medical Faculty, Department of Child Health, Department of Clinical Microbiology, Sanglah Hospital, Denpasar, Indonesia

Abstract: ***Objective: To determine the characteristics of Staphylococcus aureus bloodstream infections among children. Method: A cross sectional study conducted in Pediatric Ward Sanglah Hospital. This study performed a retrospective review of medical records from pediatric patients who were proven to have Staphylococcus aureus infection through microbiological examination from blood culture samples while undergoing treatment. Result: There were total of 30 pediatric patients who were proven to have Staphylococcus aureus bloodstream infection. Nineteen (63%) cases were male. The most common age group was 12-18 years old (36.7%). Malnourished was found in 53% of the patients. Malignancy, pneumonia, and chronic kidney disease were found in 8 (26.7%), 5 (16.7%), and 5 (16.7%) subjects as the major comorbidities. Twenty three cases (76.7%) were community-acquired infections while 7 cases (23.3%) were hospital-acquired infections. The average length of stay before Staphylococcus aureus infection was 9.77 (SD 10.67) days with average total length of stay was 21.97 (SD 17.53) days. Most subjects used medical devices with an average duration of use of each medical device was more than 10 days. Antibiotics that were given before infection, most of the time, were Cefepime, Amikacin, and Cefixime with an average duration of use of each antibiotic was more than 7 days. Infections due to methicillin-resistant Staphylococcus aureus occured in two patients. Mortality rate for this study was 33%. Conclusion: The majority of our patients were adolescents with malnourished in more than 50% of cases. Malignancy, pneumonia, and chronic kidney disease as the major comorbidities in this study. Underlying medical conditions and medical devices used may be considered to be related to infection.***

Keywords: *Staphylococcus aureus* infection, children

1. Introduction

Staphylococcus aureus is recognized as an important cause of invasive disease in children [1],[2]. *Staphylococcus aureus* remains a major cause of bacteremia and is associated with severe morbidity and mortality in all age groups. *Staphylococcus aureus* is a frequent cause of hospital-acquired bacteremia, with patients admitted to neonatal and pediatric intensive care units at the highest risk [3],[4]. *Staphylococcus aureus* represented the third most commonly isolated blood culture organism (12%) in the pediatric population from 2000 to 2006, following *Streptococcus viridans* (23%) and *Streptococcus pneumonia* (16%), with a prevalence similar to *Escherichia coli*. The proportion was significantly higher in the nosocomial and healthcare-associated groups [5].

While nosocomial infections due to methicillin-resistant *Staphylococcus aureus* (MRSA) have been recognized in many jurisdictions for decades, in recent years, severe invasive infections due to MRSA strains have increasingly been reported in patients, including children, without significant previous healthcare exposure [6].

Antibiotics have played a major role since the 20th century on reducing the morbidity and mortality associated with common infectious diseases and have therefore had an important impact on health care and human longevity [7]. Antibiotics and other antimicrobial agents are invaluable life savers, particularly in resource-limited countries where bacterial infections are predominant in both adults and childhood illness, contributing to the sustainable use of antibiotics which is the most important drugs of choice in the therapeutic arsenal [8]. *Staphylococcus aureus* is one of the most common organisms isolated from children with healthcare–associated infections, regardless of whether these infections had their onset in the community or were acquired in the hospital. Thus, the initial empiric treatment of an invasive infection in a child almost always includes an antibiotic effective against *Staphylococcus aureus* [9].

Although *Staphylococcus aureus* is one of the most frequent causes of pediatric bacteremia, there are few studies describing characteristics of *Staphylococcus aureus* bloodstream infections in pediatric populations. Therefore, we aimed to describe the characteristics and antibiotic susceptibility patterns of *Staphylococcus aureus* bloodstream infections among children in Pediatric Ward Sanglah Hospital

2. Methods

The design of this study was a cross sectional study and conducted in Pediatric Ward of Sanglah Hospital. We performed a retrospective review of medical records from pediatric patients who were proven to have *Staphylococcus aureus* infection through microbiological examination from blood culture samples. The inclusion criteria was pediatric patients who were proven to have *Staphylococcus aureus* bloodstream infection while undergoing treatment in Pediatric Ward Sanglah Hospital during January 2017 until December 2018. *Staphylococcus aureus* identification and the antimicrobial susceptibility testing (AST) were performed using VITEK-2 Compact (Biomerieux, France).

The exclusion criteria was subjects with incomplete medical records data. Sample in this study determined using total population sampling with total of 30 samples.

3. Results

There were total of 30 pediatric cases who were proven to have *Staphylococcus aureus* bloodstream infection from January 2017 to December 2018. Nineteen (63%) cases were male. The most common age group was 12-18 years old (36.7%) with the most common nutritional status was malnourished (53%). Six (20%) neonates developed *Staphylococcus aureus* bloodstream infection, of which 3 cases were complicated by prematurity. All cases had comorbidities, including 8 (26.7%) with malignancy, 5 (16.7%) with pneumonia, and 5 (16.7%) with chronic kidney disease. The average length of stay before *Staphylococcus aureus* bloodstream infection was 9.77 (SD 10.67) days with average total length of stay was 21.97 (SD 17.53) days. Twenty three cases (76.7%) were community-acquired infections while 7 cases (23.3%) were hospital-acquired infections. Subject characteristics were shown in Table 1.

Table 1: Subject Characteristics

Characteristics	n = 30
Age, n (%)	
0-28 days	6 (20)
29 days-24 months	5 (16.7)
2-12 years	8 (26.7)
12-18 years	11 (36.7)
Sex, n (%)	
Male	19 (63.3)
Female	11 (36.7)
Nutritional status, n (%)	
Malnourished	16 (53.3)
Well nourished	12 (40)
Overweight / Obese	2 (6.7)
Comorbidity, n (%)	
Pneumonia	5 (16.7)
Malignancy	8 (26.7)
Prematurity	5 (16.7)
Intracranial Infection	3 (10)
Combustio	1 (3.3)
Chronic Kidney Disease	5 (16.7)
Septic arthritis	3 (10)
Congenital Heart Disease	1 (3.3)
HIV infection	1 (3.3)
Length of stay before infection, mean (SD), days	9.77 (10.67)
Total length of stay, mean (SD), days	21.97 (17.53)
Outcome, n (%)	
Alive	20 (66.7)
Death	10 (33.3)

Most subjects used medical devices with an average duration of use of each medical device was more than 10 days. The most used medical devices was peripheral venous catheter with an average usage for 19 (SD 16.19) days. The length of use of medical devices were shown in Table 2.

Table 2: The Length of Use of Medical Devices

Medical Devices	n	Mean (SD), days
Endotracheal Tube	6	10.17 (7.25)
Non Invasive Ventilation	5	12.20 (12.23)
Central Venous Catheter	8	20.38 (18.79)
Peripheral Venous Catheter	28	19.07 (16.19)
Nasogastric Tube	10	11 (9.14)
Endotracheal Tube	6	15.50 (10.24)

The most used antibiotics before infection was Cefepime, Amikacin, and Cefixime with an average duration of use of each antibiotic was more than 7 days. History of antibiotics before *Staphylococcus aureus* bloodstream infection were shown in Table 3.

Table 3: History of Antibiotics Before Infection

Antibiotics	n	Mean (SD), days
Ampicillin	3	9.67 (3.78)
Amikacin	4	7.75 (4.92)
Cefepime	5	7 (2.23)
Ceftriaxone	3	6 (1.73)
Cefotaxime	1	9
Cefazoline	1	8
Cefixime	4	8.25 (0.95)
Amoxicillin	1	4
Clindamycin	1	14

Antibiotic susceptibility testing of *Staphylococcus aureus* infection from blood culture samples showed that 100% of isolates were still sensitive to Vancomycin and Linezolid.

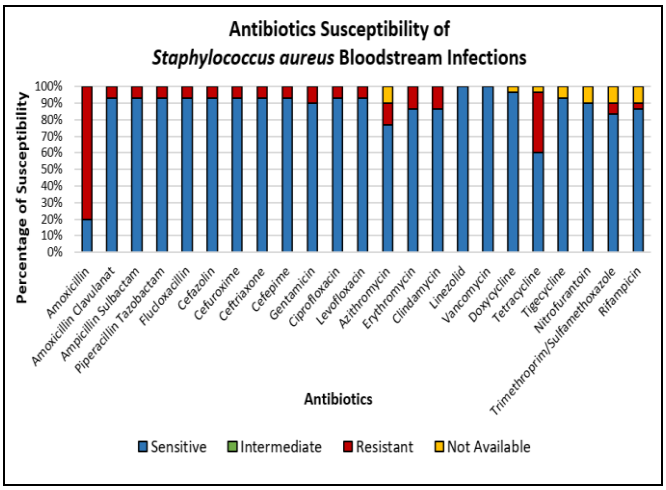

Figure 1: Antibiotics Susceptibility of *Staphylococcus aureus* Bloodstream Infections

4. Discussion

More than 100 years after its discovery, *Staphylococcus aureus* remains one of the most common and troublesome of bacteria causing disease in humans, despite the development of effective antibacterials and improvement in hygiene. *Staphylococcus aureus* is one of the most common skin commensals, yet possesses the ability to cause a range of different infections ranging from trivial to life threatening [10].

Staphylococcus aureus is an aerobic, non-spore-forming, Gram-positive coccus belonging to the Micrococcaceae family, which is found in air, fomites, and dust, and commonly colonizes humans and animals. It can be distinguished from other *Staphylococcal* species on the basis

of the yellow pigmentation it produces, β-hemolysis on blood agar, and positive results of coagulase, mannitol fermentation, and deoxyribonuclease tests [10].

Humans are a natural reservoir of *Staphylococcus aureus*, with 25-50% of the general population being nasal carriers and 10-20% being persistently colonized [10]. A recent Canadian population-based study covering almost a million residents in and around Calgary reported that the annual incidence of invasive *Staphylococcus aureus* infection was 28.4/100000 population, which is comparable to invasive *Pneumococcal* disease and 5- to 10-fold higher than invasive *group A or group B Streptococcal* disease [11].

Study conducted by Otto Vanderkooi (2011) reported that the risk for developing *Staphylococcus aureus* bacteremia was related to age, with the risk being highest in the neonatal period (younger than 30 days) with an increased risk in male children [6]. Similarly, a recent Canadian population-based study reported that *Staphylococcus aureus* infection was more common in males, infants <1 year of age, and adults over 65 years old [10]. We found the most common age group in our study was 12-18 years old (36.7%). Neonatal patients accounted for 6 (20%) cases of the total number of patients in the study.

Individuals with primary skin disorders (such as atopic dermatitis, contact dermatitis, and psoriasis), underlying diseases (such as diabetes mellitus and AIDS), those undergoing hemodialysis, and surgical patients, have higher carriage rates of up to 100% [10]. In this study, all cases had underlying disease in the form of malignancy (26.7%), pneumonia (16.7%), and chronic kidney disease (16.7%) who routinely undergo hemodialysis.

The presence of an indwelling catheter has been consistently shown to be a major risk factor for invasive *Staphylococcal* infections. The mean incidence of catheter-related bloodstream infection in hospitalized pediatric patients is 2.4 episodes per 1000 days. *Staphylococcus aureus* is responsible for around one-third to one-half of all catheter-associated bacteremias, and is generally more aggressive and associated with more complications than *coagulase-negative staphylococci*. The presence of a long-term catheter, as in patients on long-term hemodialysis, increases the risk of catheter-related bacteremia, which is mostly due to *coagulase-negative staphylococci* or *Staphylococcus aureus* [12]. There were 6 cases in our study used indwelling catheter with an average duration for 11 days. It is important to note that most of the patients who have indwelling catheters are either very ill (such as those admitted to the pediatric or neonatal intensive care unit or children with severe burns) or have serious underlying disease (such as immune deficiency due to various causes including chemotherapy for malignancy) [13],[14]. In this study, there were 8 (26.7%) patients with malignancy who undergo chemotherapy for their illness.

Staphylococcus aureus remains one of the major pathogens responsible for causing human disease and death in all age groups. In the pre-1940s era, mortality due to *Staphylococcus aureus* bloodstream infections was reported to be over 80%, and, although the discovery of Penicillin resulted in a dramatic decrease in mortality due to invasive *Staphylococcus aureus* infections, it still remains around 25%, with reported mortality rates of 11–43% over the past 25 years [11]. In this study, 10 (33%) patients died.

Despite all advances in the prevention and management of infections (including improved hygiene, more aggressive treatment, and new antibacterial families), the incidence of both community-acquired and hospital-acquired *Staphylococcal* infections over the past 20 years continues to rise, with little change in mortality rates. This increase parallels more widespread use of invasive procedures, increasing severity of illness in the hospitalized population, poor compliance with infection control practices, increasing selection of antibacterial-resistant strains, intravenous drug abuse, and an increasing prevalence of diabetes [11]. Children exposed to frequent and/or multiple hospital infections are also at high risk of developing *Staphylococcal* infections, particularly in intensive care units [13],[15]. One 6-month prospective European study of 20 pediatric units in eight countries reported a 2.5% overall incidence rate of nosocomial infection, ranging from 1% in the general pediatric ward to almost 25% in the pediatric intensive care unit, and *Gram-positive cocci* (including *Staphylococcus aureus*) accounted for 31% of all confirmed infections [15]. In our study we found 23 cases (76.7%) were community-acquired infections while 7 cases (23.3%) were hospital-acquired infections.

Numerous studies have consistently shown that people who are colonized with *Staphylococcus aureus* are at higher risk for subsequent development of *Staphylococcal* infections. Other predisposing factors for developing *Staphylococcal* infections include immunodeficiency, diabetes, chronic granulomatous disease, defects in the mucocutaneous barriers produced by trauma including surgery, foreign surfaces (sutures, shunts, intravascular catheters), and burns. The risk of infection was highest in patients on hemodialysis and in those with HIV infection, although solid organ transplantation, heart disease, cancer, illicit intravenous drug use, alcohol abuse, diabetes, stroke and chronic obstructive pulmonary disease were also important risk factors [16]. Our study reported that there were 5 (16.7%) patients with routine hemodialysis and there was 1 (3.3%) patient with HIV infection.

The past 2 decades have seen a dramatic rise in the incidence of MRSA infections, not only in adults but also in children [17]. Previous assumptions that methicillin resistance was restricted to a selected subgroup of patients with well defined risk factors – namely, prolonged or frequent hospital admissions, the presence of indwelling catheters, invasive or surgical procedures, critical care unit stay, prolonged or recurrent antibacterial exposure, endotracheal intubation, tracheotomy, chronic illnesses, and malignancies – have been challenged by reports of community-acquired MRSA in adults and children who have not been exposed to any of the above risk factors [18]. We found infections due to MRSA occured in two patients in our study.

For severe infections due to MRSA, intravenous Vancomycin remains the antibacterial of choice. Intravenous Clindamycin may also be used as an alternative or an adjunct to Vancomycin. Both have the advantage of covering for *Streptococcus pyogenes* infections – the second most common cause of skin and soft tissue infection. The use of Teicoplanin for the treatment of serious multi-resistant Gram-positive infections is increasing because of its once daily administration and the option to change to the oral route once the patient is improving. Linezolid is a new class of antibacterial that is currently showing great promise for the treatment of multi-resistant infections [19],[20]. Linezolid has been shown to be as effective as the cephalosporins for the treatment of *Staphylococcus aureus* infections in children, with the added advantage of being highly effective against MRSA infections [21]. In this study, antibiotic susceptibility testing of *Staphylococcus aureus* infection from blood culture samples showed that 100% of isolates were still sensitive to Vancomycin and Linezolid.

This study has limit in terms of it design as a descriptive study and using cross-sectional approach so that patients progressed can't be followed either forward or backward. A limitation of using administrative data is that they do not allow for case follow-up and, thus, sequelae related to *Staphylococcus aureus* bacteremia cannot be determined. The exact length of treatment (intravenous portion followed by oral step down) cannot be determined. It is possible that not all potential risk factors associated with invasive *Staphylococcal* infection would be identified using administrative data. Further studies are needed to see predictive factors that significantly influence the occurrence of *Staphylococcus aureus* infection in children who receive treatment at Pediatric Ward, especially at NICU and PICU.

References

[1] B.A. Suryati, M. Watson, "Staphylococcus aureus bacteraemia in children: A 5-year retrospective review," J Paediatr Child Health, 38:290-4, 2002.
[2] K.B. Laupland, D.L. Church, M. Mucenski, L.R. Sutherland, H.D. Davies, "Population-based study of the epidemiology of and the risk factors for invasive *Staphylococcus aureus* infections," J Infect Dis, 187:1452-9, 2003.
[3] D. Isaacs, S. Fraser, G. Hogg, H.Y. Li, "*Staphylococcus aureus* infections in Australasian neonatal nurseries," Arch Dis Child Fetal Neonatal, 89:331-5, 2004.
[4] H. Wisplinghoff, H. Seifert, S.M. Tallent, T. Bischoff, R.P. Wenzel, M.B. Edmond, "Nosocomial bloodstream infections in pediatric patients in United States hospitals: Epidemiology, clinical features and susceptibilities," Pediatr Infect Dis J, 22:686-91, 2003.
[5] K.B. Laupland, D.B. Gregson, O.G. Vanderkooi, T. Ross, J.D. Kellner, "The changing burden of pediatric bloodstream infections in Calgary, Canada, 2000-2006," Pediatr Infect Dis J, 28:114-7, 2009.
[6] O.G. Vanderkooi, D.B. Gregson, J.D. Kellner, K.B. Laupland, "Staphylococcus aureus bloodstream infection in children: A population-based assessment," Paediatr Child Health, 16(5):276-80, 2011.
[7] World Health Organization (WHO), "Antimicrobial resistance: Global report on surveillance," WHO report, Geneva, 2014.
[8] G.E. Ekambi, C.O. Ebongue, I.C. Penda, E.N. Nga, E.M. Mpondo, C.E. Moukoko, "Knowledge, Practices, and Attitudes on Antibiotics Use in Cameroon: Self-medication and Prescription Survey among Children, Adolescents and Adults in Private Pharmacies," Plos One, 14(2):1-17, 2019.
[9] S.L. Kaplan, "*Staphylococcus aureus* Infections in Children: The Implications of Changing Trends," Pediatrics, 137(4):1-4, 2016.
[10] S. Ladhani, M. Garbash, "*Staphylococcal* Skin Infections in Children," Pediatr Drugs, 7(2):77-102, 2005.
[11] K.B. Laupland, D.L. Church, M. Mucenski, et al, "Population-based study of the epidemiology and the risk factors for invasive *Staphylococcus aureus* infections," J Infect Dis, 187:1452-9, 2003.
[12] B.F. Gonzalez, J. Carratala, A. Mykietiuk, et al, "Predisposing factors and outcome of *Staphylococcus aureus* bacteremia in neutropenic patients with cancer," Eur J Clin Microbiol Infect Dis, 20:117-9, 2001.
[13] S.M. Hudome, M.C. Fisher, "Nosocomial infections in the neonatal intensive care unit," Curr Opin Infect Dis, 14:303-7, 2001.
[14] D.K. Benjamin, W. Miller, H. Garges, et al, "Bacteremia, central catheters, and neonates: when to pull the line," Pediatrics, 107:1272-6, 2001.
[15] J. Raymond, Y. Aujard, "Nosocomial infections in pediatric patients: a European multicentre prospective study. European Study Group," Infect Control Hosp Epidemiol, 21:260-3, 2000.
[16] S.S. Huang, R. Plat, "Risk of methicillin-resistant *Staphylococcus aureus* infection after previous infection or colonization," Clin Infect Dis, 36:281-5, 2003.
[17] M.M. Nakamura, K.L. Rohling, M. Shashaty, et al, "Prevalence of methicillin-resistant *Staphylococcus aureus* nasal carriage in the community pediatric population," Pediatr Infect Dis J, 21:917-22, 2002.
[18] F.M. Hussain, V.S. Boyle, R.S. Daum, "Community-acquired methicillin resistant *Staphylococcus aureus* colonization in healthy children attending an outpatient pediatric clinic," Pediatr Infect Dis J, 20:763-7, 2001.
[19] A.L. Frank, J.F. Marcinak, P.D. Mangat, et al, "Clindamycin treatment of methicillin-resistant *Staphylococcus aureus* infections in children," Pediatr Infect Dis J, 21:530-4, 2002.
[20] D.L. Steven, D. Herr, H. Lampiris, et al, "Linezolid versus Vancomycin for the treatment of methicillin-resistant *Staphylococcus aureus* infections," Clin Infect Dis, 34:1481-90, 2002.
[21] K. Wible, M. Tregnaghi, J. Bruss, et al, "Linezolid versus cefadroxil in the treatment of skin and skin structure infections in children," Pediatr Infect Dis J, 22:315-23, 2003.