Sultan Qaboos University Med J, November 2024, Vol. 24, Iss. 4, pp. 501–506, Epub. 27 Nov 24
Submitted 11 Mar 24
Revision Req. 2 May 24; Revision Recd. 31 May 24
Accepted 25 Jun 24
https://doi.org/10.18295/squmj.7.2024.044

CLINICAL & BASIC RESEARCH

Bloodstream Infection in Children Managed at a Tertiary Hospital in Oman

Nadiya Al Saeghi,[1] Marwah Al Thuhli,[1] Hajer Al Hamrashi,[2] Naema Al Shibli,[2,3]
Adil Al Wahaibi,[4] Badriya Al Adawi,[5] *Laila Al Yazidi[2,3]

abstract: ***Objectives:*** This study aimed to assess the local epidemiology and outcome of bloodstream infection (BSI) among Omani children. ***Methods:*** This retrospective study was conducted at Sultan Qaboos University Hospital, Muscat, Oman, over 5 years (2014–2018) and included laboratory-confirmed BSI among children aged 0–12 years old. Patients' demographic, clinical and laboratory data were extracted from the hospital's electronic records and used to assess BSI rates and outcomes. ***Results:*** A total of 1,253 positive blood cultures were identified, of which 592 (47.2%) were regarded as contaminants. Overall, 404 (32.2%) significant episodes of BSI were identified in 272 patients; 346 (85.6%) significant episodes were in children aged ≤5 years and 366 (90.6%) had comorbidities. The 5-year incidence of BSI was 13 per 1,000 admissions. Furthermore, 333 (82.4%) episodes were healthcare-related infections. Enterobacterales (n = 152; 37.6%) were the most common organisms identified followed by coagulase-negative staphylococci (n = 63; 15.6%). Approximately 40% of Gram-negative organisms were resistant to third-generation cephalosporins. The crude mortality rate at 30 days was 9.2%. Paediatric intensive care unit admission (crude odds ratio [COR] = 2.24, 95% confidence interval [CI]: 0.98–4.78) and the presence of graft-versus-host disease (COR = 7.99, 95% CI: 1.52–37.76) were associated with increased death within 30 days. The multivariate logistic regression analysis showed that *Pseudomonas aeruginosa* (adjusted odds ratio = 18.46, 95% CI: 3.96–97.84) was the only independent predictor of increasing 30-day mortality in this cohort. ***Conclusion:*** A high rate of hospital-related BSI was found in children in Oman, highlighting the need to optimise infection control strategies and the care of central vein access devices.

Keywords: Bloodstream Infection; Pediatrics; Oman.

Advances in Knowledge

- *Enterobacterales were the most common group of bacteria causing bloodstream infection (BSI) among Omani children, followed by coagulase-negative staphylococci.*
- *Two-thirds of children with BSI were ≤5 years of age and >90% had underlying co-morbidities.*
- *The majority of BSI episodes in this study were hospital-related BSI.*
- *High rates (35–40%) of resistance of Gram-negative organisms to third-generation cephalosporins.*
- *Pseudomonas aeruginosa was the only independent predictor of increasing 30-day mortality in this cohort.*

Application to Patient Care

- *This study reported a high rate of hospital-related BSI, which highlights the urgent need to optimise infection control strategies and the care of central vein access devices.*
- *Given the high rates of resistance to third-generation cephalosporins, a combination empirical therapy of a cephalosporin with an aminoglycoside is recommended for the first 24–48 hours of admission in patients with community-acquired septic shock.*

Bloodstream infection (BSI) causes significant morbidity and mortality in children, being associated with longer hospital stays and higher healthcare costs.[1,2] In North America and Europe, 2 million patients have BSI annually, with nearly 250,000 estimated to die due to BSI.[3] According to a retrospective cohort study conducted in the USA, the crude mortality rate for BSI patients was higher compared to non-BSI patients (5% versus 0.34%; P <0.001).[4]

There is a wide variation among the causative organisms of paediatric BSI in different countries.[5] For instance, *Escherichia coli* and methicillin-sensitive *Staphylococcus aureus* were the most commonly isolated pathogens among children in a multicentre study conducted in the USA.[6] Similarly, *S. aureus* was previously reported as the most common pathogen of bacteraemia in children in a study conducted at the University Hospital in Riyadh, Saudi Arabia.[7] While in Switzerland, the most frequent pathogens identified are *S. aureus*, followed by Enterobacterales.[8]

There is a dearth of data on the epidemiology and outcome of BSI among Omani children. One study on the central line linked bloodstream infection (CLABSI) in children receiving parenteral nutrition at Royal Hospital, Muscat, Oman, reported that the

[1]Department of Child Health, Al Nahda Hospital, Muscat, Oman; [2]Oman Medical Specialty Board, Muscat, Oman; Departments of [3]Child Health and [5]Microbiology & Immunology, Sultan Qaboos University Hospital, University Medical City, Muscat, Oman; [4]Department of Epidemiological Surveillance, Ministry of Health, Muscat, Oman
*Corresponding Author's E-mail: lailay@squ.edu.om

incidence of CLABSI was 14 cases per 1,000 catheter days with a mortality rate of 5.56%.[9] Therefore, the current study aimed to quantify the incidence of BSIs among children managed at Sultan Qaboos University Hospital (SQUH), Muscat, Oman, to assess the crude mortality associated with BSI and identify rates of antimicrobial resistance to guide empiric antibiotic choices, risk factors to refine and optimise mitigation strategies and community pathogens to inform public health strategies.

Methods

This retrospective study included laboratory-confirmed BSI in children managed at the Child Health Department at SQUH from January 2014 to December 2018. All positive blood cultures during the study period were extracted from the laboratory electronic database through the hospital information system.

Bacteraemia refers to the detection of an organism in a positive blood culture, which was deemed to be the causative agent responsible for the clinical illness. Commensal isolates were included if cultured on more than 1 occasion within 48 hours. Single positive cultures with commensals from peripheral or central lines were regarded as contaminants.

Primary BSI refers to a laboratory-confirmed BSI without an associated infection at another body site, while secondary BSI occurs when the BSI is linked to a site-specific tissue or organ infection elsewhere in the body. CLABSI was defined as a clinically significant BSI in a patient with either a current or recently removed central venous access device (CVAD) within 48 hours of the BSI diagnosis, without any other apparent primary infection site. Community-onset BSI was defined as the detection of a clinically significant pathogen in a blood culture obtained within 48 hours of admission. Conversely, instances where the blood culture was collected after the initial 48 hours of admission were classified as a healthcare-associated infection (HAI). A BSI episode was defined as 14 days after the first positive blood culture, excluding repeat positives of the same organism during this time. The purpose of employing this definition was to mitigate any potential overestimation of the number of episodes.[10]

Blood cultures were processed by the Microbiology Diagnostic Laboratory at SQUH. Blood culture bottles were incubated using the Bactec® automated microbial detection system (Becton Dickinson, Franklin Lakes, New Jersey, USA). Positive blood cultures were processed as per the standard operating procedures in the laboratory. Organism identification and susceptibility testing were performed using the BD Phoenix™ automated system (Becton Dickinson). The susceptibility interpretive breakpoints were based on the Clinical and Laboratory Standards Institute (CLSI) M100 document, which was in use for that year. During the last year of the study period, Bruker Biotyper, which uses matrix-assisted laser desorption ionisation time-of-flight technology, was introduced in the lab and was used for organism identification along with Phoenix™.

Institutional ethical approval was obtained to conduct this study from the Medical Research Ethics Committee (MREC) at Sultan Qaboos University.

Results

Between 2014 and 2018, 19,769 blood cultures were collected from children <13 years of age at SQUH, of which 1,253 (6.3%) positive blood culture episodes were identified. Among those, approximately half (n = 592, 47.2%) were excluded as they were contaminants, with the contamination rate being 3%. Furthermore, 251 positive blood cultures were repetitions and were therefore excluded from the analysis. A total of 404 (32.2%) episodes of bacteraemia in 272 patients were included in the final analysis. HAI comprised 82.4% of all BSIs, equating to an incidence rate of 11.1 per 1,000 patient days. Concurrently, community-onset bacteraemia constituted approximately 17.6% of the total cases.

The overall 5-year incidence of BSI was 13 per 1,000 hospital admissions. Table 1 presents the demographic and clinical data of the study population. Approximately two-thirds of the study population (n = 346, 85.6%) were ≤5 years of age; of whom 139 (34.4%) were infants were 1 month to 1 year old. Underlying comorbidities were identified in 366 (90.6%) patients, and prematurity-related complications were associated with 26.2% of the cases, followed by haematological malignancies (n = 90, 22.3%), gut-related pathologies (n = 71, 17.6%) and metabolic/genetic syndromes (n = 47, 11.6%). A total of 182 patients (45.0%) had central venous catheters. CLABSI was found to be the most common cause of bacteraemia (n = 193, 47.8%), followed by neonatal sepsis (n = 52; 12.9%) and sinopulmonary infection (n = 36, 8.9%), but no source was identified in 7.7% (n = 31) of the episodes. Overall, 62 patients with BSI required paediatric intensive care unit admission during the study period, of whom 37 died, accounting for a 30-day crude mortality of 9.2% [Table 1].

Among the isolates, 211 (52.2%) were Gram-negative bacteria, 168 (41.6%) were Gram-positive

Table 1: Characteristics of children with culture-proven bloodstream infection at the Sultan Qaboos University Hospital, Muscat, Oman (N = 404)

Characteristic	n (%)
Age group	
<1 month	76 (18.8)
1 month to 1 year	139 (34.4)
1–5 years	131 (32.4)
>5 year	58 (14.4)
Admitting speciality	
Nephrology	9 (2.2)
Surgery	11 (2.7)
Gastroenterology	71 (17.6)
Haematology/oncology	90 (22.3)
Immunology	9 (2.2)
Metabolic/genetic	47 (11.6)
Neonatology	106 (26.2)
Respiratory	8 (2.0)
Other	53 (13.1)
Diagnosis during episode of bacteraemia	
CLABSI	193 (47.8)
GI infection	24 (5.9)
MBI-LCBI	14 (3.5)
Neonatal intensive care	52 (12.9)
Sinopulmonary infection	36 (8.9)
Urosepsis	8 (2.0)
Febrile neutropenia	5 (1.2)
Meningitis	18 (4.5)
Osteoarticular infection	10 (2.5)
Primary bacteraemia	31 (7.7)
Skin and soft tissue infection	10 (2.5)
Other	3 (0.7)
Central line	
No	222 (55.0)
Yes	182 (45.0)
TPN	
No	225 (55.7)
Yes	179 (44.3)
PICU admission	
0	342 (84.7)
1	62 (15.3)
Death at 30 days	
No	367 (90.8)
Yes	37 (9.2)

CLABSI = central line-associated bloodstream infection; GI = gastrointestinal; MBI-LCBI = mucosal barrier injury laboratory-confirmed bloodstream infections; TNP = total parenteral nutrition; PICU = paediatric intensive care unit.

bacteria and 25 (6.2%) were Candida species. Enterobacterales (n = 152, 37.6%) were the most common organism identified, followed by coagulase-negative staphylococci (CoNS; n = 63, 15.6%) and *S. aureus* (n = 47, 11.6%). Similarly, *Enterobacterales* (37.5%), followed by CoNS (18.9%), were the most common causes of hospital-related BSI, whereas *Enterobacterales* (38.0%) followed by *Streptococcus pneumoniae* (16.9%) and *S. aureus* (12.7%), were the most common isolates in community-onset BSI.

Susceptibility testing revealed that about one-third of *S. aureus* (n = 15/47; 33%) isolates were methicillin-resistant *S. aureus* (MRSA). Approximately 94% and 100% of *Pseudomonas aeruginosa* isolates were susceptible to piperacillin-tazobactam and amikacin, respectively. Furthermore, third-generation cephalosporin susceptibility was around 60% for both *E. coli* (n = 18/29) and *Klebsiella pneumoniae* (n = 32/49), whereas gentamicin susceptibility was 86% and 80%, respectively [Table 2].

Univariate analysis was performed to identify factors associated with mortality within 30 days of confirmed BSI. The analysis indicated a statistically significant increase in mortality rates among children admitted to the paediatric intensive care unit (crude odds ratio [COR] = 2.24, 95% confidence interval [CI]: 0.98–4.78), those afflicted with graft-versus-host disease (COR = 7.99, 95% CI: 1.52–37.76) during episodes of bacteraemia, Gram-negative (COR = 3.12, 95% CI: 1.43–6.813) and *P. aeruginosa* infection (COR = 6.04, 95% CI: 2.67–13.69). The multivariate logistic regression analysis identified *P. aeruginosa* infection (adjusted odds ratio = 18.46, 95% CI: 3.96–97.84) as the only independent predictor increasing the risk of 30-day mortality following a confirmed BSI in children.

Discussion

The overall positivity rate of the BSI cultures in this study was 6.3%, which is higher than the rate of 4.8% reported in an Australian centre and lower than the rate of 12.3% observed in South Africa.[11,12]

The overall 5-year incidence of BSI was calculated at 13 cases per 1,000 admissions, which contrasts with the bacteraemia incidence of 19 and 4.8 cases per 1,000 reported by studies conducted in Qatar and Australia, respectively.[12,13] The overall contamination rate in the current study was approximately 3%, which falls within the acceptable range as per the guidelines of the CLSI.[10]

Remarkably, among the current cohort, healthcare-associated BSI accounted for more than two-thirds of all recorded BSI episodes. These results closely mirror a recent retrospective study conducted in Australia, which reported a prevalence of 71.8%.[12] This observation might signify an elevation in the usage of CVADs among patients presenting with comorbidities, constituting 45% of the study cohort.

Table 2: Antibiograms of study isolates of culture-proven bloodstream infection at Sultan Qaboos University Hospital, Muscat, Oman

	Number of isolates tested (% susceptible)											
Gram-negative organisms	**Ampicillin**	**Amoxicillin-clavulanate**	**Piperacillin-tazobactam**	**Cefuroxime**	**Ceftriaxone**	**Ceftazidime**	**Cefepime**	**Meropenem**	**Gentamicin**	**Amikacin**	**Trimethoprim-sulfamethoxazole**	**Ciprofloxacin**
E. coli (n = 29)	29 (28)	29 (55)	29 (93)	29 (62)	29 (62)	29 (62)	29 (62)	29 (100)	29 (86)	29 (100)	29 (62)	29 (76)
K. pneumoniae (n = 49)	49 (0)	49 (65)	49 (80)	49 (61)	48 (65)	49 (63)	47 (66)	49 (96)	49 (80)	49 (94)	49 (61)	49 (74)
P. aeruginosa (n = 33)			32 (94)			33 (85)	31 (81)	33 (94)	33 (97)	33 (100)		33 (100)
Gram-positive organisms	**Oxacillin**	**Erythromycin**	**Clindamycin**	**Trimethoprim-sulfamethoxazole**	**Ciprofloxacin**	**Rifampin**	**Gentamicin**		**Linezolid**		**Vancomycin**	
S. aureus (n = 39)	39 (67)	39 (80)	39 (87)	39 (87)	38 (84)	38 (100)	38 (97)		38 (100)		39 (100)	

This underscores the imperative to enhance infection control strategies and prioritise meticulous care of CVADs within the hospital.

Advancements in prenatal screening and infant immunisations have influenced the trends in bacteraemia. In the past, *S. pneumoniae*, *Haemophilus influenzae* type b and *Neisseria meningitidis* were the primary culprits.[14] However, the current study demonstrates a shift toward *Enterobacterales*, CoNS and *S. aureus* as the more common causative agents in paediatric bacteraemia cases. Moreover, the Specialist Advisory Committee on Antibiotic Resistance paediatric subgroup reported that CoNS were responsible for the highest number of isolates reported in all age groups, and there was a significant 34% increase in *E. coli* bacteraemia between 1998 and 2007; this is consistent with the present findings.[15] The overall rise in CoNS and Gram-negative bacteria observed in this study may correspond to a trend towards increased healthcare-associated infections.[14]

Susceptibility testing showed that 33% of the *S. aureus* isolates in this study were methicillin-resistant, which is higher than those in a recent similar study by Al Yazidi *et al.* from Australia, where they reported that 19% of the *S. aureus* isolates were MRSA.[12] Given that one-third of the *S. aureus* isolates in this cohort are MRSA, this study recommends giving anti-MRSA empiric antibiotic cover to patients presenting with sepsis when *S. aureus* sepsis is suspected. Only 60% of the *E. coli* and *K. pneumoniae* isolates were susceptible to third-generation cephalosporins, but 80–86% were susceptible to aminoglycosides. This is similar to data presented in a review of 15 paediatric studies from Africa, which showed that 11% of *E. coli* isolates were resistant to gentamicin and 30% of *K. pneumoniae* isolates were resistant to ceftriaxone.[11] In the current study, the empiric antibiotic therapy for community-acquired sepsis includes vancomycin and ceftriaxone, and for hospital-acquired sepsis, piperacillin-tazobactam is recommended for extra Gram-negative cover. Given that more than half of the isolates are *Enterobacterales*, it is strongly recommended to add an aminoglycoside to the third-generation cephalosporin for patients presenting with community-acquired sepsis pending culture results. The addition of an aminoglycoside in combination with piperacillin-tazobactam for hospital-acquired sepsis can be considered depending on how ill the patient is. Carbapenems should be considered when infection with a multi-drug-resistant organism is suspected.

The crude mortality rate in this cohort was high at 9.2% compared to a previous cohort in Australia, which reported a rate of 3.3%.[12] Conversely, a recently reported large multi-centre study from 59 US hospitals demonstrated a crude mortality rate of 13%.[3] These variations in crude mortality rates can likely be attributed to differences in case complexity, types of organisms involved and other host-related factors that influenced the outcomes of hospitalised patients. Therefore, this underscores the significance of conducting population-based studies to accurately assess the burden of BSI at a local level.

This is a single-centre, retrospective cohort study with several associated limitations such as selection bias and missing data. In addition, the results of this study may not necessarily reflect the experience at other tertiary, secondary and primary healthcare settings and might not completely assess the burden of BSI infection among Omani healthcare facilities. However, the authors believe that it is a good representation of the burden and outcome of BSI among children in a tertiary healthcare setting. Future work should include conducting a multi-centre study in Oman to assess the burden and outcome of BSI among children.

Conclusion

Most of the BSIs in this study were healthcare-related BSI, which highlights the need to optimise infection control strategies and CVAD care among patients. *Enterobacterales* are the most common cause of BSI in this cohort, and only 60% of the isolates are susceptible to third-generation cephalosporins. Adding an aminoglycoside to the BSI empiric antimicrobial cover is highly recommended.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

FUNDING

No funding was received for this study.

AUTHORS' CONTRIBUTION

NSae and MT played key roles in this project from its inception. They were responsible for writing the proposal, conducting data collection, assisting with analysis and drafting the initial manuscript. HH provided valuable support by assisting with data collection and revising the manuscript. AW contributed significantly to the project by assisting with data analysis and revising the manuscript. NShi, BA and LY served as the main supervisors of this study, providing guidance and expertise throughout the entire process. They were involved in the conceptualisation of the study, analysis of the data, revision of data collection methods and final revision of the manuscript. NSae

and MT contributed equally to the work and should both be considered first authors. All authors approved the final version of the manuscript.

ACKNOWLEDGEMENTS

The authors acknowledge all paediatricians and microbiology laboratory staff who helped to manage these children. A preliminary version of the abstract was presented at the OMSB Research Forum 2022/2023, Muscat, Oman.

References

1. Timsit JF, Ruppé E, Barbier F, Tabah A, Bassetti M. Bloodstream Infections in critically ill patients: An expert statement. Intensive Care Med 2020; 46:266–84. https://doi.org/10.1007/s00134-020-05950-6.
2. Elward AM, Hollenbeak CS, Warren DK, Fraser VJ. Attributable cost of nosocomial primary bloodstream infection in pediatric intensive care unit patients. Pediatrics 2005; 115:868–72. https://doi.org/10.1542/peds.2004-0256.
3. Goto M, Al-Hasan MN. Overall burden of bloodstream infection and nosocomial bloodstream infection in North America and Europe. Clin Microbiol Infect 2013; 19:501–9. https://doi.org/10.1111/1469-0691.12195.
4. Wang C, Hao W, Yu R, Wang X, Zhang J, Wang B. Analysis of pathogen distribution and its antimicrobial resistance in bloodstream infections in hospitalized children in East China, 2015–2018. J Trop Pediatr 2021; 67:fmaa077. https://doi.org/10.1093/tropej/fmaa077.
5. Kolesnichenko S, Lavrinenko A, Akhmaltdinova L. Bloodstream infection etiology among children and adults. Int J Microbiol 2021; 2021:6657134. https://doi.org/10.1155/2021/6657134.
6. Spaulding AB, Watson D, Dreyfus J, Heaton P, Grapentine S, Bendel-Stenzel E, et al. Epidemiology of bloodstream infections in hospitalized children in the United States, 2009–2016. Clin Infect Dis 2019; 69:995–1002. https://doi.org/10.1093/cid/ciy1030.
7. Al-Zamil FA. Bacteremia in Children at the University Hospital in Riyadh, Saudi Arabia. World J Pediatr 2008; 4:118–22. https://doi.org/10.1007/s12519-008-0023-9.
8. Buetti N, Atkinson A, Kottanattu L, Bielicki J, Marschall J, Kronenberg A, et al. Patterns and trends of pediatric bloodstream infections: A 7-year surveillance study. Eur J Clin Microbiol Infect Dis 2017; 36:537–44. https://doi.org/10.1007/s10096-016-2830-6.
9. AL Lawati TT, Al Jamie A, Al Mufarraji N. Central line associated sepsis in children receiving parenteral nutrition in Oman. J Infect Public Health 2017; 10:829–32. https://doi.org/10.1016/j.jiph.2017.01.022.
10. Clinical and Laboratory Standards Institute (CLSI). Principles and Procedures for Blood Cultures, 2nd ed. USA: Clinical and Laboratory Standards Institute, 2022.
11. Lochan H, Pillay V, Bamford C, Nuttall J, Eley B. Bloodstream infections at a tertiary level paediatric hospital in South Africa. BMC Infect Dis 2017, 17:750. https://doi.org/10.1186/s12879-017-2862-2.
12. Al Yazidi LS, Outhred AC, Britton PN, Kesson A. Culture-proven bloodstream infections at a specialist pediatric hospital. Pediatr Infect Dis J 2020; 39:500–6. https://doi.org/10.1097/INF.0000000000002605.
13. Khan FY, Elshafie SS, Almaslamani M, Abu-Khattab M, El Hiday AH, Errayes M, et al. Epidemiology of bacteraemia in Hamad General Hospital, Qatar: A one year hospital-based study. Trop Med Infect Dis 2010; 8:377–87. https://doi.org/10.1016/j.tmaid.2010.10.004.
14. Pai S, Enoch DA, Aliyu SH. Bacteremia in children: Epidemiology, clinical diagnosis and antibiotic treatment. Expert Rev Anti Infect Ther 2015; 13:1073–88. https://doi.org/10.1586/14787210.2015.1063418.
15. Sharland M; SACAR Paediatric Subgroup. The use of antibacterials in children: A report of the Specialist Advisory Committee on Antimicrobial Resistance (SACAR) paediatric subgroup. J Antimicrob Chemother 2007; 60:i15–26. https://doi.org/10.1093/jac/dkm153.