

# Impact of Bloodstream Infection on the Outcome of Children Undergoing Cardiac Surgery

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**Abstract** Bloodstream infections (BSIs) are a main cause of nosocomial infection in the critical care area. The development of BSI affects the surgical outcome and increases intensive care unit (ICU) morbidity and mortality. This prospective cohort study was undertaken to determine the incidence, etiology, risk factors, and outcome of BSI for postoperative pediatric cardiac patients in the pediatric cardiac ICU setup. All postoperative pediatric patients admitted to the pediatric cardiac ICU from January 2007 to December 2007 were included in the study. Data were prospectively collected using a standardized data collection form. Patients with BSI (group 1) were compared with non-BSI patients (group 2) in terms of age, weight, surgical complexity score, duration of central line, need to keep the chest open postoperatively, and the length of the pediatric cardiac ICU and hospital stay. Of the 311 patients who underwent cardiac surgery during the study period, 27 (8.6%) were identified as having BSI (group 1). The 311 patients included in the study had a total of 1,043 central line days and a catheter-related BSI incidence density rate of 25.8 per 1,000 central line days. According to univariate analysis, the main risk factors for the development of BSI after pediatric cardiac surgery were lower patient weight ( $p = 0.005$ ), high surgical complexity score ( $p < 0.05$ ), open sternum postoperatively ( $p < 0.05$ ), longer duration of central lines ( $p < 0.0001$ ), and prolonged pediatric cardiac ICU and hospital stay

( $p < 0.0001$ ). Gram-negative organisms were responsible for 67% of the BSI in the pediatric cardiac ICU, with pseudomonas (28%) and enterobacter (22%) as the main causative organisms. The mortality rate in the BSI group was 11% compared with 2% in the non-BSI group. In our pediatric cardiac ICU, BSI developed in 8.6% of the children undergoing cardiac surgery, mainly caused by a Gram-negative organism. The main risk factors for BSI in the postoperative pediatric cardiac patient were high surgical complexity, open sternum, low body weight, longer duration of central line, and prolonged pediatric cardiac ICU stay.

**Keywords** Bloodstream infection · Pediatric cardiac surgery

## Introduction

Hospital-acquired infections are a major cause of morbidity and mortality for pediatric patients undergoing cardiac surgery. The development of these infections hinders the surgical result and affects the outcome for children undergoing cardiac surgery. In addition, their impacts are overwhelming, both emotionally and financially [1].

Bloodstream infections (BSIs) represent a major cause of hospital-acquired infections for pediatric intensive care unit (PICU) patients [2]. The information about BSIs and their consequences for postoperative cardiac children managed in the specialized pediatric cardiac intensive care unit (PCICU) is limited. The majority of currently published data about BSI does not stratify the rate or risk factors for postoperative pediatric patients [1, 2]. Furthermore, studies have demonstrated that more than 90% of BSIs are associated with the use of intravascular catheter

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devices, which increase morbidity, mortality, resources utilization, and medical costs [3].

In the past, most pediatric patients undergoing cardiac surgery received care in general PICUs or in mixed adult–pediatric cardiothoracic units. However, in the past decade, an increasing number of specialized PCICUs have been established. The characteristic features of these specialized units in terms of their infection rate, type of infection, general complications, and outcome are not clearly outlined.

Traditionally, many general pediatric and adult ICUs have reported Gram-positive organisms as the main cause for BSIs [4]. However, recently emerging data from specialized pediatric cardiac units have reported a shift in the spectrum of organisms causing BSIs from those reported previously in either adult cardiothoracic surgical units or general PICUs [1]. Gram-negative organisms seem to take over the lead in many ICU reports about BSIs and catheter-related blood stream infections (CRBSIs) [5, 6].

To understand better the current status of BSI among children undergoing cardiac surgery in the specialized PCICU, we designed our study to determine the incidence, etiology, main risk factors, and outcome of BSIs for postoperative cardiac children admitted to the PCICU.

## Patients and Methods

The PCICU of the Cardiac Sciences Department at King Abdulaziz Cardiac Center consists of nine beds. The average annual number of medical–surgical admissions is approximately 400 patients, about 80% of whom undergo postcardiac surgeries.

All patients admitted between 1 January and 31 December 2007 were prospectively studied for the development of BSIs after their cardiac surgery. The patients were divided into two groups, namely, the patients in whom BSI developed (group 1) and the patients who did not experience BSI (group 2). Data were prospectively collected using a standardized data collection form. Demographic, clinical, and microbiologic data were collected from the patients' medical records and from the microbiology laboratory records. The study was approved by our hospital research committee. The two groups were compared for age, weight, surgical complexity score, central line duration, whether the patient's chest was open or closed postoperatively, and the length of the PCICU and hospital stay.

Due to the wide variety of cardiothoracic surgical procedures, we grouped our patients based on their surgical complexity score according to a previously published scoring system described by previous investigators [7, 8]. This scoring system categorizes procedures according to

the severity of cardiac lesion and complexity of cardiac repair as shown in the Appendix.

All the patients undergoing cardiac surgery had percutaneously placed central lines either before or at the time of surgery. The catheters were arbitrarily placed by either the intensivist in the PCICU before surgery or by the anesthesiologist at the time of surgery. The current study did not examine the effects of operator background or site of insertion on the BSI rate. Transthoracic and transatrial lines were placed by surgeons and used exclusively for hemodynamic monitoring. None of the patients had antibiotic-impregnated catheters.

All the patients undergoing cardiac surgery were treated with intravenous cefazolin at a dose of 100 mg/kg/day in three divided doses, starting 30 min before surgery and continuing until the chest tubes were removed after surgery. For the patients with an open chest postoperatively, intravenous ceftazidime and vancomycin were used as a prophylaxis and continued until the chest was closed (48–72 h postoperatively).

All catheters were checked routinely, and the site of skin entry was examined frequently. The catheters were covered with sterile transparent adhesive cover after initial insertion. Routine change of central lines has not been adapted as a policy in our unit unless there is a specific indication for that such as local inflammation, leakage, suspected infection, or catheter malfunction. Changing the line “over the wire” generally was avoided, and a different new site was preferentially chosen in the vast majority of cases.

Although no specific protocol for accessing the central line was followed, maximal infection control awareness was applied when central catheters were accessed or dressings were changed. Dressings for all percutaneously inserted catheters were completed under aseptic technique and renewed every third day or sooner if needed.

## Definition

For the purpose of the study, the following definition was adopted from the National Healthcare Safety Network (NHSN) [9]. Any BSI that developed within the PCICU or 48 h after discharge was considered ICU associated.

## Catheter-Related BSI

Bacteremia/fungemia in a patient with an intravascular catheter was considered to be catheter-related based on at least one positive blood culture obtained from a peripheral vein, clinical manifestations of infection (fever  $>38^{\circ}\text{C}$ , chills, and/or hypotension), and no apparent source for BSI except the catheter. One of the following needed to be present: a positive semiquantitative culture ( $>15$  colony-forming units [CFUs] per catheter segment) or a

quantitative culture (>103 CFUs per catheter segment) whereby the same organism is isolated from the catheter and peripheral blood, simultaneous quantitative blood cultures with more than a 5:1 ratio of central venous catheter (CVC) blood to peripheral blood, a differential of CVC culture versus peripheral blood culture positivity of more than 2-h culture.

The CRBSI incidence density rate (i.e., catheter-related BSI rate per 1,000 central line days) is calculated by dividing the number of catheter-related BSIs by the number of central line days and multiplying the result by 1,000 [9].

**Device Utilization Ratio**

The device utilization ratio is calculated by dividing the number of central line days by the number of patient days and multiplying the result by 100 [10].

**Statistical Analysis**

Continuous variables were analyzed by Student’s *t* test and the discrete variables by Fisher’s exact test. A *p* value less than 0.05 was considered statistically significant. Data were analyzed with SPSS software (SPSS) for comparison of data and risk factors using univariate analysis and multiple regression analysis.

**Results**

A total of 311 pediatric patients underwent cardiac surgery during the study period. Of these patients, 27 (8.6%) experienced CRBSI during their PCICU stay. All the patient characteristics and risk factors for the development of BSI are shown in Table 1.

The CRBSI density rate was 25.8 per 1,000 central line days, for a device utilization ratio of 47%. Of the 27 patients with CRBSI, 18 (67%) had Gram-negative organisms, 7 (26%) had Gram-positive organisms, and 2 (7%) had fungal infections (Table 2). The main causative organisms were *Pseudomonas* (28%), *Enterobacter* (22%), and Gram-positive bacteria, mainly coagulase-negative *Staphylococcus* (6/27, 22%). Only one patient had methicilline-resistant *Staphylococcus* (MRSA) infection (Table 2).

The median time for the development of BSI in our patient population was 7 days after cardiac surgery. There was more than a fourfold increase in the BSI incidence rate between the lowest surgical risk category (category 1) and the highest surgical risk category (category 4), as shown in Fig. 1.

Three patients in group 1 died (11%) compared with six patients in group 2 (2%). All the deceased patients in the

**Table 1** Patient characteristics and univariate analysis of 311 post-cardiac surgery patients with and without bloodstream infection (BSI)

Characteristics	BSI ( <i>n</i> = 27) <i>n</i> (%)	No BSI ( <i>n</i> = 284) <i>n</i> (%)	<i>p</i> Value
Gender			
Male	16 (59)	136 (45)	
Female	11 (41)	148 (55)	
Age (months)			
Median	1.8	7.15	
Range	0.2–14.3	0.1–140	0.014
Weight (kg)			
Median	3.3	4.7	0.0013
Range	1.8–6.5	2–39	
Surgical complexity (mean)	3	2	0.0023
Category			
1	4 (15)	103 (36)	0.04
2	3 (11)	38 (13)	0.97
3	9 (33)	93 (33)	0.95
4	11 (41)	50 (18)	0.01
Open sternum	19 (70)	5 (2)	0.05
Mean central line days	17	3	0.0001
Mean PCICU stay	23	6	0.0001
Mean hospital stay	34	11	0.0001
Mortality	3 (11)	6 (2)	0.04

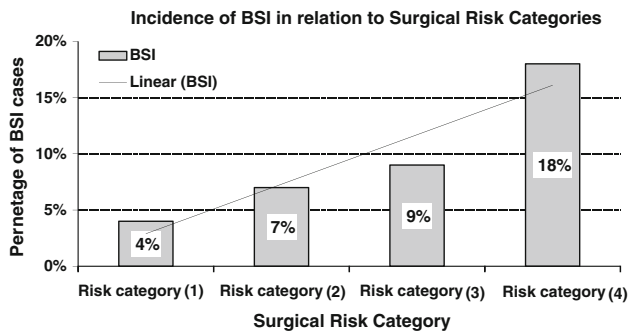
PCICU pediatric cardiac intensive care unit

**Table 2** Causative organisms of catheter-related blood stream infection (CRBSI) in pediatric cardiac intensive care unit (PCICU)

Causative organism	Patients <i>n</i> (%)
Gram-negative bacteria	18/27 (67)
<i>Pseudomonas</i>	5/18 (28)
<i>Enterobacter</i>	4/18 (22)
<i>Klebsiella</i>	2/18 (11)
Others	7/18 (39)
Gram-positive bacteria	7/27 (26)
Coagulase-negative <i>Staphylococcus</i>	6/7 (86)
MRSA	1/7 (14)
Fungal	2/27 (7)

MRSA methicilline-resistant *Staphylococcus*

BSI group (group 1) were younger than 6 months and had a body weight less than 4 kg. Two of the three patients were in the highest surgical risk category (category 4). The first patient was 1.6 months old, weighed 2.3 kg, and had a diagnosis of interrupted aortic arch, pulmonary atresia, ventricular septal defect (VSD), and patent ductus arteriosus (PDA). He underwent systemic-to-pulmonary



**Fig. 1** Incidence of bloodstream infection (BSI) among postoperative cardiac children in relation to different surgical risk categories

shunt and aortic arch repair. His hospital course was complicated with the development of CRBSI involving coagulase-negative staphylococci 10 days after surgery associated with severe hemodynamic failure that led to his death 18 days after surgery.

The second patient was 3 months old, weighed 3.8 kg, and had VSD, PDA, and tricuspid valve regurgitation. He underwent pulmonary artery banding and PDA ligation. During his postoperative ICU stay, persistent chylothorax was observed, and total parenteral nutrition was initiated. Subsequently, CRBSI with yeast developed 12 days after surgery. The child did not recover and died 23 days after surgery (11 days after BSI).

The third patient was a 2-month-old baby (weight, 2 kg) with Shone's complex and coarctation of the aorta who underwent coarctation repair. *Candida albicans* BSI developed 15 days after surgery, which progressed to refractory septic shock and multiple organ failure. The child died 29-days after surgery (11 days after *Candida* BSI).

Univariate analysis demonstrated that younger patient age ( $p < 0.05$ ), lower body weight ( $p < 0.005$ ), a high surgical complexity score ( $p < 0.05$ ), the need to keep an open sternum postoperatively ( $p < 0.05$ ), longer duration of central lines ( $p < 0.0001$ ), and prolonged PCICU and hospital stay ( $p < 0.0001$ ) are associated with a statistically significant increased risk of BSI infection. The difference in the mortality rates between groups 1 (11%) and 2 (2%) also was statistically significant ( $p = 0.04$ ). Due to the small number of deceased patients in each group, comparison of mortality between the four risk categories in the two groups did not show a statistically significant difference. In the multivariate analysis, prolonged hospital stay was the only independent variable associated with increased risk of BSI development.

## Discussion

Children undergoing cardiac surgery represent a special type of ICU patient. Many of them are infants and neonates

requiring cardiopulmonary bypass and various invasive procedures. Some of the pediatric cardiac patients with ductus-dependent lesions may present in a suboptimal compromised condition that requires urgent palliation or imminent surgical repair. Malnutrition, poor feeding, and failure to thrive also are common findings in children with congenital heart disease, particularly those associated with left-to-right shunting. Furthermore, the use of cardiopulmonary bypass during open heart surgery is associated with a systemic inflammatory response that has many negative effects on the immunologic system [11]. As a result, pediatric patients undergoing cardiac surgery may be exposed to a significantly higher risk of infection than other noncardiac patients.

Some published reports describe different types of nosocomial infection such as BSI and ventilator-associated pneumonia in general pediatric intensive care patients [2, 12]. However, there is less information about BSI in children undergoing heart surgery and managed in a specialized PCICU. Because the PCICU population is notably distinctive and different from the population of other critical care units, the risk factors and outcome of BSI in this subgroup of patients might be different in essence. In our prospective cohort study, the incidence of BSI after pediatric cardiac surgery was 8.6%. In a small number of published studies, the incidence of BSI in postoperative cardiac patients ranges from 6 to 8% [1, 6, 13].

In our study, CRBSIs were responsible for the vast majority of BSIs, with an incidence density rate of 25.8 per 1,000 central line days. Central lines and invasive monitoring are widely used for postoperative cardiac children, who frequently tend to be infants or neonates requiring high-risk complex cardiac repair. In our group of patients, 50% of our postoperative cardiac patients were younger than 6 months, and more than 50% were in surgical risk category 3 or 4 (Table 1). The combination of young age, lower body weight, and high-risk surgical category in our cohort group may have synergistically intensified the risk of BSI and could explain in part the high incidence density rate of CRBSI in our patients.

A lower CRBSI rate has been reported by some other investigators, but for general PICU patients. These rates have ranged from 13.8 to 20 per 1,000 catheter days [2, 12].

On the other hand, the National Nosocomial Infections Surveillance System (NNIS) surveyed 161,314 patients from 54 general PICUs in the United States and found a mean CRBSI rate of 6.6 per 1,000 central line days [14]. Although the NNIS infection rate is much lower than ours, their patient population consists of general pediatric ICU patients rather than a distinctive group of postoperative cardiac patients. We postulate that the relatively high BSI rate in our study population may be attributable to multiple

factors that include a different patient population, extensive use of invasive devices, a high percentage of neonates undergoing complex cardiac surgery, and the relative malnourished status of many of our patients [2, 15].

Some intrinsic factors related specifically to our PCICU cannot be ruled out and possibly could have contributed to the development of BSI in our unit. Several of our cardiac cases had delayed referral for logistic reasons that ultimately affected their medical conditions and vulnerability for infection.

Some additional factors also may affect the incidence of CRBSI among postoperative cardiac patients such as the site of catheter insertion, the type of catheter used, and whether the route of insertion is percutaneous or that of a transthoracic intracardiac surgically placed line. Transcardiac lines such as right atrial, left atrial, and pulmonary arterial lines are reported to have a relatively low rate of infections [8]. In our practice, we use the intracardiac line for hemodynamic monitoring and the percutaneous line for medications, fluid administration, and vasoactive drug infusions. Transthoracic monitoring catheters generally are accessed less frequently than percutaneous catheters, which may explain why their infection rate generally is lower than that of percutaneously placed catheters. Transthoracic lines, however, are associated with different types of complications such as serious bleeding, infective endocarditis, and intracardiac thrombus formation [8].

Furthermore, the type and complexity of cardiac surgery in particular seem to play an important role in BSI development. In simple straightforward surgical cases such as those involving ventricular septal defects and atrial septal defects, the infection rate is low (4%), whereas in high-risk complex cardiac cases such as Norwood palliation cases (category 4), the BSI rate multiplies, reaching almost 18%. Although not definite, there appears to be a linear relationship between the increase in BSI rate and the increase in the surgical risk category that applies to postoperative pediatric cardiac patients (Fig. 1).

The array of causative microorganisms for CRBSI in our PCICU is different from that reported in the NNIS data [14]. Gram-negative organisms were predominant in 67% of our patients, whereas NNIS reported Gram-positive microorganisms, mainly coagulase-negative staphylococci, as the primary etiology for CRBSI [12]. Other investigators from specialized PCICUs and some general pediatric ICUs have reported results similar in essence to our findings [1, 5, 12].

The appearance of Gram-negative organisms as the primary cause for CRBSI may have multiple reasons that need to be analyzed and studied. The authors of a recently published study [4] found that BSI caused by Gram-negative organisms in the PICU were associated with many

factors including transfer from another facility, the presence of congenital heart disease, failure to thrive, genetic syndrome, age of 30 days or less, administration of total parenteral nutrition, administration of prednisone, and blood transfusion. Many of these factors that they reported are commonly seen in postoperative cardiac cases. Other types of nosocomial infection also may increase the risk of BSI development, particularly with Gram-negative organisms. Studies have reported a 30% incidence of ventilator-associated pneumonia among intubated pediatric ICU patients, predominantly with Gram-negative organisms [16]. Secondary bacteremia may develop in association with different types of nosocomial infections. In one study, secondary bacteremia occurred in 10.6% of children with a diagnosis of nosocomial infections. Skin wound infection, pneumonia, and urinary tract infection were the main primary sources of secondary bacteremia associated with nosocomial infection [17]. Our study did not look specifically for such association between BSI and other types of nosocomial infections such as ventilator-associated pneumonia, urosepsis, or wound infection. Further research and investigation are needed to evaluate the exact risk of BSI and its link with BSI and different types of hospital-acquired nosocomial infection, particularly with Gram-negative organisms.

Additionally, the increased prevalence of Gram-negative organisms also may be attributed to the common current practice of using prophylactic antibiotics that cover primarily Gram-positive organisms in the postoperative period [12, 18]. The main aim for the use of prophylaxis is to prevent wound infection at the surgical site caused primarily by Gram-positive organisms. Studies have demonstrated that prolonged antibiotic use after surgery induces antimicrobial resistance and may facilitate the colonization of foreign devices with antimicrobial-resistant organisms [19]. Whether changing the selection of postoperative antibiotics prophylaxis or their duration can minimize or alter the spectrum of organisms causing BSI remains uncertain. This observation requires further studies and analysis for assessment of its validity, legitimacy, and occurrence in other PCICUs.

Notably, the mortality rate in the BSI group was 11% compared with only 2% in the non-BSI group. Although the overall mortality was distinctly and statistically different between the two study groups, comparative sub-analysis of the mortality results in each risk category did not show a statistically significant difference. Additionally, unlike the linear relationship between a higher surgical risk category and increased risk of BSI, the mortality did not follow a clearly similar trend. This might be due to the limited small number of deceased patients within each risk category. Nevertheless, the almost sixfold overall increase in mortality among postoperative cardiac children with BSI

reflects the major impact of infection development on children undergoing cardiac surgery.

## Conclusion

High surgical complexity, open sternum, low body weight, longer central line duration, and prolonged PCICU stay were the main risk factors for BSI among postoperative pediatric cardiac patients. Gram-negative organisms were the main cause for BSI in our unit. The BSI rate increases as the surgical risk category increases, and BSI has led to a sixfold increase in mortality for infected patients. Comorbidity and increased ICU resource utilization likely are significant consequences of BSI.

Our study had some limitations, which may include inability to study all the possible risk factors for BSI, the possibility that the BSI development leads to prolonged PCICU and hospital stays instead of being a result of these

two factors, and limitation of our study to a single-center experience versus a multicenter study. Nevertheless, we believe the study highlights the impact of BSI on children undergoing cardiac surgical repair, particularly high-risk complex repair. It also helps to establish a baseline clinical benchmark for monitoring BSI incidence, type, and outcome for postoperative cardiac patients managed in specialized PCICUs. Last but not least, the study also will help in assessing any future measures considered to minimize BSI in critically ill cardiac children.

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## Appendix

See Table 3.

**Table 3** Complexity categories of cardiovascular surgical procedures [20]

Category 1	Category 2	Category 3	Category 4
Patent ductus arteriosus closure weight >1,500 g	Multiple VSD	Blalock–Taussing/other shunts	Patent ductus arteriosus closure weight <1,500 g
Coarctation of aorta repair	Tetralogy of Fallot with transannular patch	Complete A–V canal repair	Aortic arch anomaly repair
Blalock–Henlon septotomy	Bidirectional Glenn anastomosis	Tetralogy of Fallot (with right ventricular to pulmonary conduit)	Banding of pulmonary artery
Aortic valvulotomy	Aortopulmonary window repair	Tetralogy of Fallot with other intracardiac procedures	Waterstone or central shunt
Vascular ring repair	Aortic root repair	Reconstruction of right ventricular outflow tract with or without shunt	Pulmonary valvotomy (not open heart)
Atrial septal defect, secundum ASD	Mitral valve repair	Fontan operational/total cavopulmonary deviation	Other op for CHF without extra corporeal connection
Corticatriatum or supra-valvular mitral stenosis	Rastelli repair/intraventricular tunnel repair	Ebstein malformation repair	Total anomalous pulmonary venous connection
Single VSD		Aortoventriculoplasty	Truncus arteriosus repair
VSD & aortic incompetence		Aortic valvotomy, open Mitral valve replacement	Anomalous left coronary from pulmonary artery
Tetralogy of Fallot without transannular patch		Arterial switch with or without other cardiac procedures	Aortic valve replacement (other)
Pulmonary valvotomy		Other operations for CHF with extra corporeal	Other ops for left ventricular outlet obstruction
Coronary fistula closure			Hypoplastic left heart of aortic atresia (Norwood, other)
Aortic valve replacement			Mitral valve replacement, creation or enlargement of ASD
Aortic stenosis (subvalvular, supra-valvular)			Mustard/Senning repair of transposition of great arteries
Cardiac Arrhythmia surgery			LV–PA conduit with or without other cardiac procedures
			Other procedures for transposition of great arteries or double outlet of right ventricle or septation (primary or staged), single ventricle procedures
			Other procedures for single ventricle

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