Hospital-acquired Infection: Prevalence and Outcome in Infants Undergoing Open Heart Surgery in the Present Era

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Abstract

Background: The aim of this study is to evaluate the causal relation between hospital-acquired infection (HAI) and clinical outcomes following cardiac surgery in neonates and infants and to identify the risk factors for the development of HAI in this subset of patients. **Materials and Methods:** After Ethics committee approval, one hundred consecutive infants undergoing open heart surgery (OHS) between June 2015 and June 2016 were included in this prospective observational study. Data were prospectively collected. The incidence and distribution of HAI, the microorganisms, their antibiotic resistance and patients' outcome were determined. The Centers for Disease Control and Prevention criteria were used for defining HAIs. Univariate and multivariate risk factor analysis was done using Stata 14. **Results:** Sixteen infants developed microbiologically documented HAI after cardiac surgery. Neonatal age group was found to be most susceptible. Lower respiratory tract infections accounted for majority of the infections (47.4%) followed by bloodstream infection (31.6%), urinary tract infection (10.5%), and surgical site infection (10.5%). *Klebsiella* (36.8%) and *Acinetobacter* (26.3%) were the most frequently isolated pathogens. HAI was associated with prolonged ventilation duration ($P = 0.005$), Intensive Care Unit stay ($P = 0.0004$), and hospital stay ($P = 0.002$). Multivariate risk factor analysis revealed that preoperative hospital stay (odds ratio [OR] 1.22, 95% confidence interval (CI) 1.6–1.39, $P = 0.004$), and prolonged cardiopulmonary bypass (CPB) (OR 1.03, 95% CI 1.01–1.05, $P = 0.001$) were associated with the development of HAI. **Conclusion:** HAI still remains a dreaded complication in infants after OHS and contributing to morbidity and mortality. Strategies such as decreasing preoperative hospital stay, CPB time, and early extubation should be encouraged to prevent HAI.

Keywords: Congenital heart surgery, hospital-acquired infection, infants, intensive care, neonates

Introduction

In recent years, there has been a dramatic improvement in the results of open heart surgeries (OHSs) for congenital heart diseases (CHDs) in infants and neonates due to advancement in surgical techniques, anesthesia, perfusion, and postoperative care. The sepsis-related morbidity and mortality still remains high, especially in infants after complex cardiac surgeries under cardiopulmonary bypass (CPB). Hospital-acquired infection (HAI) is a major contributing factor for prolonged mechanical ventilation, Intensive Care Unit (ICU), and hospital stays.

Identification of risk factors for the development of HAI is important to define the age group at highest risk, to develop strategies for preventing HAI, optimize antimicrobial therapy accordingly, and to direct empirical therapy in cases of presumed sepsis. This study was carried out to elucidate HAIs in infants after OHS and identify possible risk factors.

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Materials and Methods

Study design and setting

This prospective observational study was conducted in patients under 1 year of age, admitted to the cardiac surgical ICU (CSICU) of a tertiary care teaching hospital, after undergoing OHS for CHDs.

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Sample size: 100 consecutive infants with CHDs were included in this study.

Study period: The study was conducted for 1 year from June 2015 to June 2016.

Patient selection

One hundred consecutive patients admitted in CSICU after undergoing elective OHS were included in this study as per inclusion (all neonates and infants undergoing elective OHS for CHD with no preoperative evidence of infection) and exclusion (preoperative clinical or laboratory evidence of infection, closed heart procedures, suspected infective endocarditis, and parents refusing to participate in the study) criteria. The study was approved by the Institute's Ethics Board. Written informed consent was obtained from parents of these infants.

Infection classification

HAIs and infection site definitions were in agreement with the Center for Disease Control and Prevention definitions.[1]

Study protocol

All neonates and infants with congenital cardiac diseases who fulfill the inclusion and exclusion criteria were included in this study. Demographic data and disease profile were recorded. Standard anesthesia care was conducted in the operating room. Triple lumen central venous catheter insertion in the femoral/internal jugular vein, invasive arterial catheter insertion either in radial, or femoral arteries, and urinary catheterization were done under strict aseptic conditions in all the patients undergoing OHS. Surgical skin prep included combination of 10% povidone-iodine (Microshield PVP S, Schulke India Pvt Ltd.) and alcohol-based solution (Sterillium, Bode Chemie Hamburg, Germany). Surgical procedures were performed using standard CPB techniques. All patients were admitted to the CSICU for postoperative care. Samples were drawn from all possible sites of infection such as endotracheal secretions, blood, surgical wound, and urine for the first three consecutive days and thereafter as indicated if there was prolonged ventilation and CSICU stay because of suspected infection. Routine care was not altered as a result of this study.

Our antibiotic protocol included:

i. Injection cefazolin 30 mg/kg preoperatively, within 1 h of skin incision
ii. Injection cefazolin 30 mg/kg 8 hourly + injection amikacin 15 mg/kg once daily postoperatively
iii. Injection piperacillin + tazobactam 50 mg/kg 6 hourly and injection vancomycin 15 mg/kg 8 hourly, were started if sternum was kept open.

Antibiotics were continued in all the patients for period of 48 h and in cases of open sternum for 48 h poststernal closure in CSICU.[2] On suspicion of imminent sepsis in any patient, upgraded antibiotics were started as per the previous track record of detected microorganisms in our CSICU, after sending appropriate cultures. Antibiotics were later narrowed down as per the sensitivity reports.

Data analysis

The analysis was carried out using Stata 14 StataCorp. 2015. Stata Statistical Software: Release 14. College Station, TX: Stata Corp LP. Statistical analysis was performed using nonparametric tests: Mann–Whitney U test for continuous variables and Chi-square test for nominal variables. Both univariate and multivariate risk factor analysis was done by logistic regression. Statistically $P < 0.05$ was considered to be statistically significant.

Results

Data from 100 consecutive infants were prospectively collected over period of 1 year. The characteristics of the study population are reported in Table 1. The majority of the infants were male (81%). Mean age and weight of the study population was 5.4 ± 3.9 months (median = 5 months) and 4.9 ± 1.8 kg (median = 4.6 kg), respectively.

Among the data collected, HAI was detected in 16 patients. Sixteen patients developed 19 microbiologically documented infections in this study. Among them, nine (56.2%) were neonates. Out of the 100 consecutive patients, 4 died giving an all-cause mortality of 4% during the study. Three (3/16) infants died because of sepsis, giving 18.7% sepsis-related mortality. The first child was of 1 month age had underwent arterial switch operation (ASO) and ventricular septal defect (VSD) closure, had grown *Klebsiella* in endotracheal secretions and blood which was resistant to commonly used antibiotics except for colistin, and succumbed on day 38 to sepsis with multiorgan failure (MOF). Second child was 15 days old, underwent ASO (postballoon atrial septostomy [BAS]) and his blood culture was positive for *Klebsiella*, sensitive to colistin only. Despite starting colistin, the child succumbed on day 18 to septic shock. The third child was of 11 months and had underwent ASO and VSD closure, he too developed *Klebsiella* positive blood stream infection (BSI) and succumbed on day 15 to sepsis with MOF. Figure 1 describes the age-wise distribution of HAI.

Figure 2 shows the distribution of all the cardiac diseases in our cohort. Transposition of great arteries (TGA) (37%) and

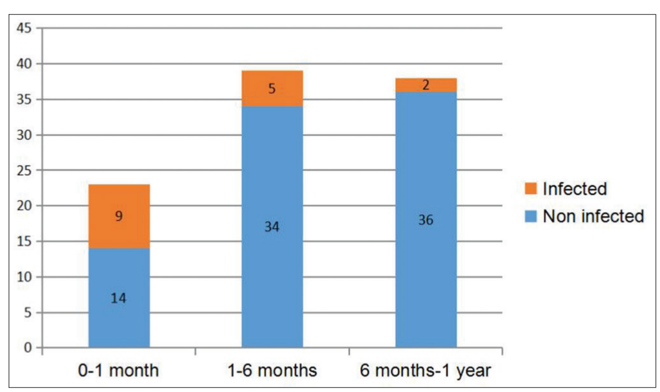

Figure 1: Age-wise distribution of hospital-acquired infection in numbers (*n*)

Table 1: Demographic and clinical characteristics of pediatric cardiac surgical patients with and without hospital-acquired infection

	Study population (*n*=100)	Mean±SD	
		With infection (*n*=16)	Without infection (*n*=84)
Demographic data			
Age (months)	5.4±3.9 (0.3-12)	3.1±3.7	5.8±3.8
Sex (male/female)	81/19	12/4	69/15
Weight (kg)	4.9±1.8 (2.1-10)	3.9±1.7	5.1±1.8
Height (cm)	59.3±7.4 (47-86)	55.5±7.7	59.9±7.1
Preoperative hospital stay (days)	7±6.6 (1-25)	7±6.6	2.9±3.3
Preoperative BAS (*n*)	12	7	5
Intraoperative variables			
CPB duration (min)	112.7±49.2 (37-230)	157.875±35.1	104±46.9
AOXCL (min)	66.6±28.1 (11-152)	80.3±22	64±28.5
Total surgical duration (min)	209.6±64.8 (75-420)	250.6±24.8	201.8±67.1
Surgical complexity score	2.8±0.7 (1-4)	3.4±0.5	2.9±2.2
Postoperative data			
TLC (1000/mm^3)	10.96±5.4	14.84±10.28	10.43±3.08
CRP	70.73±44.3	73.64±40.8	69.84±45.3
ESR	17.93±8.6	18.69±13.8	17.86±6.6
Open sternum (days)	0.7±0.9	1.5±0.9	0.53±0.8
Ventilation duration (h)	80.6±81.9 (2-400)	138.7±91.4	71.5±77
ICU stay (days)	8±6.8 (1-38)	14±8.9	7±5.8
Hospital stay (days)	17.1±17.6 (4-150)	35.3±8.2	13.6±8.2
Mortality	4	3	1

SD: Standard deviation; BAS: Balloon atrial septostomy; CPB: Cardiopulmonary bypass; AOXCL: Aortic cross clamp; TLC: Total leukocyte count; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; ICU: Intensive Care Unit

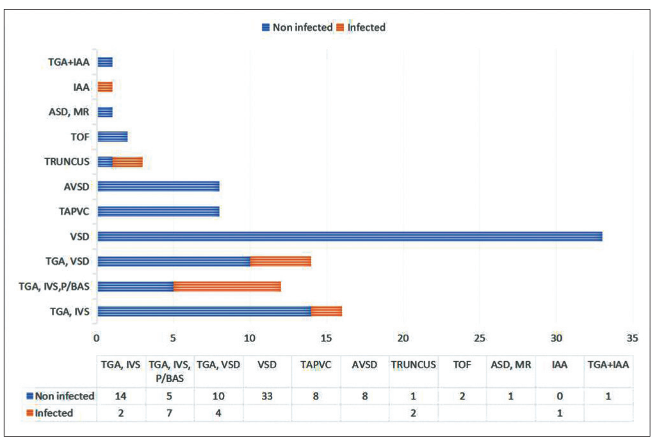

Figure 2: Diagnosis and distribution of infection. ASD: Atrial septal defect; AVSD: Atrioventricular septal defect; BAS: Balloon atrial septostomy; IAA: Interrupted aortic arch; MR: Mitral regurgitation; TAPVC: Total anomalous pulmonary venous connection; TGA: Transposition of great arteries; IVS: Transposition of great arteries with intact ventricular septum; TOF: Tetralogy of Fallot; VSD: Ventricular septal defect.

the VSD (33%) were the most common congenital defects in our cohort of patients. Out of 23 children with TGA and intact ventricular septum, 12 children underwent BAS preoperatively for desaturation and seven of these 12 children developed HAI postoperatively. Two patients with TGA and regressed left ventricle who underwent ASO were on extracorporeal membrane oxygenation for period of 72 h each, and both of them developed microbiologically documented infection. One had *Klebsiella* in endotracheal secretions, and the other one developed urinary candiduria. Two patients required cardiac massage in CSICU and one of them developed ventilator-associated pneumonia (VAP) with *Pseudomonas*. All these three patients recovered from sepsis. Totally 46 children in this study cohort had delayed sternum closure in the CSICU. 20 (43.5%) of them were neonates.

The incidence of VAP was highest in neonates, and it decreased as age increased, whereas the incidence of BSI was more in infants above 1 month age as illustrated in Figure 3. Most of the patients belonged to class 3 surgical complexity score (Society of Thoracic Surgeons-European Association of Cardiothoracic Surgeons congenital heart surgery mortality score) [Table 2].[3] VAP was the most common among all infections. Multiple infections were present in three patients as described in Table 3.

Table 4 delineates risk factors for HAIs according to univariate and multivariate analysis. HAI was also associated with increased morbidity in the form of prolonged ventilation duration (mean = 138.7 ± 91.4 vs. 71.5 ± 77 h, $P = 0.005$), ICU stay (14 ± 8.9 vs. 7 ± 5.8 days, $P = 0.0004$), and hospital stay (35.3 ± 8.2 vs. 13.6 ± 8.2 days, $P = 0.002$).

The microbes isolated in this cohort are described in Table 3 and Figure 4. The most commonly detected organisms from respiratory secretions were Gram-negative bacteria like

Klebsiella and *Acinetobacter*. *Klebsiella* was the leading Gram-negative bacteria isolated from blood cultures.

Acinetobacter was found to be sensitive to colistin (82%), cefoperazone-sulbactam (68%), piperacillin-tazobactam (40%), and resistant to other antibiotics such as cefotaxime, ceftazidime, amikacin, and ciprofloxacin (70%–80%). *Klebsiella* was found to be highly sensitive to colistin (100%) only and resistant to carbapenems, cefoperazone-sulbactam, and piperacillin-tazobactam (77%–100%). The resistance profile for *Escherichia coli* and *Pseudomonas* was also alarming, as they were sensitive to colistin, cefoperazone-sulbactam, and piperacillin-tazobactam mainly. Resistance profile of *Staphylococcus aureus* and *Staphylococcus* epidermidis was better than Gram-negative organisms, many were highly sensitive to linezolid, vancomycin, and teicoplanin but were found to be highly resistant to other antibiotics such as cephalosporins, quinolones, carbapenems, and piperacillin-tazobactam.

Table 2: Surgical complexity score

Score	Number of patients	Number of patients with HAI
1	0	0
2	36	0
3	43	9
4	21	7

HAI: Hospital-acquired infection

Table 3: Depicting the source of infection and pathogens involved

Source	Frequency (%)	Pathogens
VAP	9 (47.4)	*Klebsiella* (3), *Acinetobacter* (3), *Pseudomonas* (1), *Escherichia coli* (1), *Aspergillus* (1)
BSI	6 (31.6)	*Klebsiella* (4), *Acinetobacter* (2)
SSI	2 (10.5)	*Staphylococcus* species (2)
UTI	2 (10.5)	*Candida* (2)

VAP: Ventilator-associated pneumonia; BSI: Blood stream infection; SSI: Surgical site infection; UTI: Urinary tract infection

Discussion

In neonates and infants after cardiac surgery, HAIs are a frequent complication with its consequence of high morbidity and mortality. The diagnosis is sometimes difficult for two reasons, (i) it is not always possible for timely isolation of the causative pathogen from the right source, (ii) the clinical and laboratory signs of inflammation may be due to the inflammatory response associated with CPB.

The risk association for HAI is younger age,[4] lower body weight,[5] the need for preoperative treatment including catheterization laboratory procedures such as BAS,[6] use of antibiotics,[7] tracheal intubation, mechanical ventilation, stay in hospital before surgery, CPB-induced immune suppression/immunoparalysis,[8] complex intracardiac

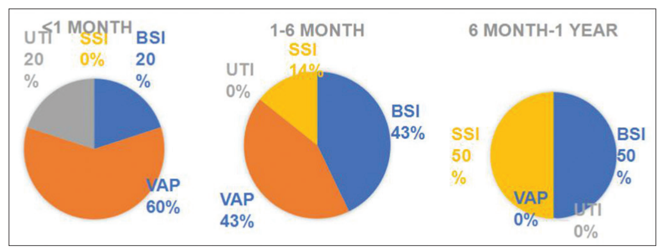

Figure 3: Site-wise distribution of HAI by age. BSI: Blood stream infection; VAP: Ventilator-associated pneumonia; SSI: Surgical site infection; UTI: Urinary tract infection

Table 4: Univariate and multivariate analysis of risk factors for hospital-acquired infection

	Univariate analysis		Multivariate analysis	
	P	OR (95% CI)	*P*	OR (95% CI)
Demographic data				
Age (months)	0.017	0.80 (0.67-0.96)		
Sex (male/female)	0.50	0.65 (0.18-2.30)		
Weight (kg)	0.021	0.61 (0.40-0.93)		
Preoperative hospital stay (days)	0.003	1.19 (1.06-1.35)	0.004	1.22 (1.06-1.39)
Preoperative BAS	0.002	12.28 (3.22-46.87)		
Intraoperative variables				
CPB duration (min)	0.001	1.02 (1.01-1.04)	0.001	1.03 (1.01-1.05)
AOXCL (min)	0.039	1.02 (1.00-1.04)		
Total surgical duration (min)	0.009	1.01 (1.00-1.02)		
Surgical complexity score	0.001	NA		
Postoperative data				
Open sternum (days)	0.001	2.62 (1.48-4.63)		
TLC (1000/mm^3)	0.03	1 (1.000016-1.000245)		
CRP	0.77	1.00 (0.99-1.01)		
ESR	0.91	1.00 (0.93-1.08)		

NA: OR couldn't be calculated since no event in Score 1 and 2. OR: Odds ratio; CI: Confidence interval; BAS: Balloon atrial septostomy; CPB: Cardiopulmonary bypass; AOXCL: Aortic cross clamp; TLC: Total leukocyte count; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate

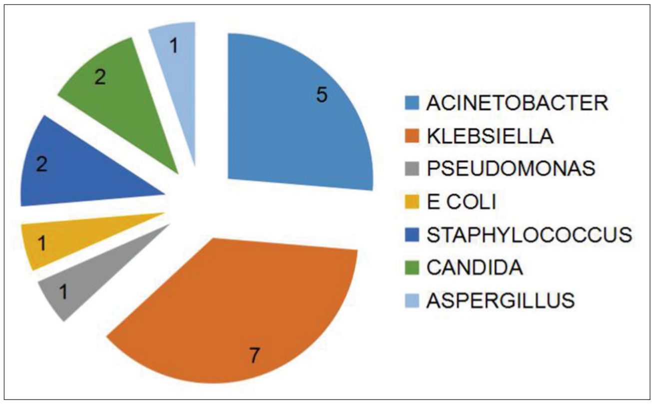

Figure 4: Microbial distribution

procedures, and need for open sternum in immediate postoperative period.[5,9] Children with left-to-right intracardiac shunts also commonly have poor feeding and failure to thrive leading to malnutrition and low immunologic competence preoperatively. On univariate analysis, neonates were found to be more susceptible than other infants raising a special concern for this age group. This could be due to their immature immune system, need for more preoperative hospital interventions, complex intracardiac repairs, CPB-induced immunoparalysis,[8] need for open sternum in the postoperative period[5,9] and prolonged ventilator support as well. Hypothermia as a risk factor for HAI has been described and compared in various studies,[6,10] but we had not used it for analysis since all our cases were performed under moderate hypothermia (28°C–32°C) except one case of interrupted aortic arch which was operated under deep hypothermic circulatory arrest.

In the present study, the microbiologically documented HAIs occurred in 16 of the 100 patients undergoing cardiac surgery. It is similar to the study by Levy *et al*.[5] from Israel. Our HAI rate (16%) is higher compared to the data from Rosanova *et al*.[11] with the incidence of 11%. Present HAI rate in our cohort of patients (16%) has decreased by almost 50% compared to a similar study (32%) in this institute in 2007.[6] Factors such as decreasing preoperative hospital stay, complete treatment and resolution of VAP before elective surgery, rational use of antibiotics, strict adherence to the infection control measures as per Institute guidelines, early enteral nutrition, and early sternal closure have led to decrease in HAI rate.

VAP (9% rate, 47.4% of total HAIs) was found to be the most common HAI followed by BSI (6% rate, 31.6% of total HAIs), surgical site infection (SSI) (2% rate, 10.5% of total HAIs), and urinary tract infection (UTI) (2% rate, 10.5% of total HAIs). This has improved from previous study results by Hasija *et al*.[6] It differs from the study of Levy *et al*.,[5] wherein the most common source of HAI was the bloodstream (47%), followed by SSI (37%) and pneumonia (4%). The relatively high rate of VAP in our study may be due to the relatively longer period of mechanical ventilation, and CSICU stay in view of the increasing number of complex surgeries under age of 1 year and predisposing lung infection from the preoperative period. BSI rate (6.3%) was similar to the retrospective cohort study of 192 patients by Shah *et al*.[12] Another prospective study by Abou Elella *et al*.[13] demonstrated 8.6% of BSI. Similarly, Mehta *et al*.[14] showed BSI rate of 7.0% (18 of 256 cardiac surgical procedures). A study by Allpress *et al*.[4] showed 2.3% of SSI in their cohort of 826 pediatric patients which is similar to our result. Nateghian *et al*.[15] found an incidence of 3.4% SSI in patients <18 years' age. Both these studies[4,15] showed that longer duration of surgery was an important risk factor for HAI, same was also observed in our study [Table 4]. The relatively low rate of SSI and UTI in our study might be due to the aseptic precautions taken during surgery, insertion, and postoperative sterile handling of all invasive monitoring devices, wound care, and rational use of antibiotics.

In the present study, most frequently isolated pathogens were *Klebsiella* (37%) and *Acinetobacter* (26%) [Figure 4], which was similar to what observed by Hasija *et al*.[6] except that the *Pseudomonas* incidence had decreased. A 4-year survey from Israel[16] showed coagulase negative *Staphylococcus* as the most common pathogen followed by *Klebsiella* spp., whereas the incidence of *Acinetobacter* was only 5%. Levy *et al*.[5] demonstrated *Klebsiella* as the most common organism but had low incidence of *Acinetobacter* (6%).

Klebsiella was responsible for most of the BSI and VAP. However, the organism most commonly responsible for BSI in other studies by Shah *et al*.[12] and Abou Elella *et al*.[13] was *Pseudomonas*. Interestingly, UTI was due to candida colonization only rather than any bacterial infection in our study. SSI was caused by *Staphylococcus aureus* and coagulase-negative *Staphylococcus*. This was similar to study by Allpress *et al*.,[4] wherein most common isolates were *Staphylococcus* spp. The most common isolates, *Klebsiella* and *Acinetobacter,* were found to be multidrug resistant. *Klebsiella*, grown in blood cultures, was especially highly resistant to most of the antibiotics except colistin. *Acinetobacter* was mainly sensitive to colistin and cefoperazone-sulbactam. As a whole, these Gram-negative microbes remain a major cause of HAI, becoming more and more multidrug resistant and difficult to treat.

Our study was different from others as it included exclusively neonates and infants with CHD and also higher number of complex cardiac surgeries were performed in this cohort of enrolled patients. HAI was more common in neonates with prolonged preoperative hospital stay, preoperative interventions, and undergoing complex cardiac repairs. Statistically significant difference in surgical duration, CPB time, and aortic cross-clamp time was observed between the groups with and without infection as was found in other studies.[11,16,17] However, in multivariate regression analysis, only CPB duration and preoperative hospital stay were statistically significant. Inflammatory markers such as C-reactive protein and erythrocyte sedimentation rate were not found to be useful in detecting HAI. This was probably because of CPB-induced inflammation was common to all the children in both groups. We did not use serum procalcitonin as a marker for sepsis in view of economic constraints. There was also statistically significant increase in ventilation duration, ICU and hospital stay, and mortality in patients with HAI compared to noninfected patients, same was observed by other studies too.[6,11,13,18] We also observed that the antibiotic resistance profile has changed over time for the worse with more and more drug-resistant pathogens, with more Gram-negative bacteria causing HAI, as has been reported by MacVane.[19] This suggests a need to decrease sources of infections such as invasive device days and provide more effective antibiotic prescribing practices to have the greatest overall impact on HAIs.

In a postoperative CSICU catering to neonates and infants, resources should be streamlined to save them from this preventable complication. Decisions should be taken at three levels: child care, staff, and ICU level.

Levels	Decisions to be taken to prevent hospital-acquired infection
Child care	Decrease preoperative hospital stay, care during preoperative interventions, early enteral feeding, and early chest closure post-OHS
Staff	Good hand washing practices, strict asepsis during handling the infants, and during application and maintenance of invasive devices, and implementation of VAP bundle[20]
ICU	Rational use of antibiotics, ICU-specific protocol implementation, antibiotic rotation and stewardship policies,[21] periodic cleaning, and disinfection of devices

ICU: Intensive Care Unit; OHS: Open heart surgery; VAP: Ventilator-associated pneumonia

Limitations of the study

Our study has some limitations. Firstly the sample size is small. Second, we have included only microbiologically documented cases labeled as HAI. Third, the study was performed in a single tertiary care high-volume teaching institute and results cannot be generalized.

Conclusion

In this era of improved surgical and perioperative care, HAI still remains a dreaded complication after pediatric cardiac surgery. The overall incidence of HAI and mortality was 16% and 4%, respectively. Mortality due to HAI was 18.7%. Preoperative hospital stay and increased CPB time were the risk factors identified in multivariate analysis. VAP was the most common type for HAI in infants. *Klebsiella* and *Acinetobacter* were the most common organisms isolated.

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Conflicts of interest

There are no conflicts of interest.

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