Received: 25 January 2019 | Revised: 16 March 2019 | Accepted: 10 April 2019

DOI: 10.1111/chd.12779

ORIGINAL ARTICLE

Congenital Heart Disease WILEY

Health care-associated infections are associated with increased length of stay and cost but not mortality in children undergoing cardiac surgery

Sarah Tweddell MD, MS | Rohit S. Loomba MD | David S. Cooper MD, MPH | Alexis L. Benscoter DO

Division of Cardiology, Department of Pediatrics, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio

Correspondence
Sarah Tweddell, MD, Department of Pediatrics, Cincinnati Children's Hospital Medical Center, 3333 Burnet Avenue, MLC 2003, Cincinnati, OH 45229.
Email: sarah.tweddell@cchmc.org

Abstract

Introduction: Health care-associated infections (HAIs) increase mortality, length of stay, and cost in hospitalized patients. The incidence of and risk factors for developing HAIs in the pediatric population after cardiac surgery have been studied. This study evaluates the impact of HAIs on length of stay, inpatient mortality, and cost of hospitalization in the pediatric population after cardiac surgery.

Methods: The Kids' Inpatient Database was queried for analysis. Patients under 18 years of age who underwent cardiac surgery from 1997 to 2012 were included. HAIs were defined as central line-associated blood stream infections, catheter-associated urinary tract infections, ventilator-associated pneumonias, and surgical wound infections. Univariate analysis compared admissions with and without a HAI. Next, regression analysis was done to determine patient factors independently associated with a HAI, and to determine what specific HAIs were independently associated with our primary outcomes.

Results: In total 46 169 admissions were included, 773 (1.6%) of which had a HAI. Regression analysis showed younger age ($P < .001$), heart failure (OR 1.2, 95% CI 1.1-1.4, $P = .03$), and acute kidney injury (AKI; 2.7, 2.0-3.6, $P < .001$), among others were all independently associated with a HAI.

The presence of HAI was associated with increased length of stay (median 29 vs 6 days, $P < .001$), total cost (median $271 884 vs $88 385, $P < .001$), and inpatient mortality (6.1% vs 2.5%, $P < .001$) by univariate analysis. Regression analysis demonstrated that each HAI were independently associated with increased length of stay and increased total charges for the hospital stay. However, HAI, was not associated with increased mortality after regression analysis.

Conclusions: The incidence of HAIs in this analysis was low (1.6%) but contributed significantly to length of stay and cost. No individual HAI was associated with increased mortality. Potential modifiable risk factors include age and prevention of AKI.

KEYWORDS

catheter-associated urinary tract infection, central line-associated blood stream infection, health care-associated infection, pediatric cardiac surgery, surgical wound infection, ventilator-associated pneumonia

1 | INTRODUCTION

Health care-associated infections (HAIs) are an important preventable cause of increased morbidity and mortality in the United States. In both the adult and pediatric populations, they have been associated with increased cost of hospitalization and length of hospital stay (LOS).[1-4] HAI reduction has become an important target for quality improvement and patient safety in the recent years as they impact both patient outcomes and financial reimbursement.

The most common HAIs in the pediatric population include central line-associated bloodstream infections (CLABSIs), ventilator associated pneumonia (VAP), and catheter-associated urinary tract infections (CAUTIs).[5] CLABSIs, in particular, have been the focus of much research in pediatrics. They have been shown to increase the LOS by 19-21 days and cost of hospital admission up to $70 000 in the pediatric population.[2,3] With ongoing efforts to decrease the incidence of CLABSIs and CAUTIs at the national level, the rate of both has downtrended.[3,6]

Approximately 40 000 infants are born with congenital heart disease per year in the United States, with about 25% requiring surgery within their first year of life.[7,8] If there are complications of surgery, the total cost of hospitalization may increase by >$50 000.[9-11] Complications have been shown to increase postoperative length of stay, which also contributes significantly to the overall cost of hospitalization.[11] Among these complications are HAIs. Of all, the children who require surgical correction for both congenital and acquired heart disease, 2.7%-8% of these patients will be diagnosed with a HAI during their postoperative course.[10,12,13] In the general pediatric and adult critical care populations, postoperative HAIs have been associated with increased mortality, length of stay, and costs. There is little data published regarding the influence of HAI on the pediatric cardiac population; however, studies have shown an association of postoperative complications with increased cost, length of stay, and mortality.[10,12,14]

The aim of this study was to determine the impact of HAIs on resource utilization and patient outcomes in the pediatric cardiac surgery population. This study focused on the impact of CLABSIs, CAUTIs, ventilator-associated pneumonias (VAPs), and surgical wound infections (SWIs) on the total cost of hospitalization, LOS, and morbidity and mortality.

2 | METHODS

2.1 | Study design and data collection

We performed a retrospective analysis using the Healthcare Cost and Utilization Project Kids' Inpatient Database (KID). KID is the largest publicly available all-payer pediatric inpatient care database in the United States and is an undertaking of the Agency for Healthcare Research and Quality. All patients under 18 years of age who underwent cardiac surgery from 1997 to 2012 were included due to availability and coding strategy. The patients were then screened for presence or absence of HAIs using International Classification for Diseases, 9th Revision, Clinical Modification (ICD-9) diagnostic codes for CLABSI (999.32), CAUTI (996.64), VAP (997.31), and SWI (998.59). Specific HAI with corresponding ICD-9 codes are listed in the Appendix. Sepsis, osteomyelitis, and nonventilator-associated pneumonia were not included as these diagnoses are not consistently associated with devices or procedures and may overlap with the ICD-9 codes queried. Mediastinitis was also excluded from this analysis due to the evidence from Southern et al demonstrating there is likely significant overlap in ICD-10 coding for SWIs.[15] Total hospital charges, LOS, and mortality data were collected for all patients. General demographic data, including age, cardiac lesion, and cardiac repair were also collected for all patients.

2.2 | Outcome measures

Our two main outcomes of interest were total hospital cost and LOS, as these have been shown to be most impacted by the development of HAIs. In hospital, mortality was also assessed.

2.3 | Statistical analysis

Statistical analysis was performed using SPSS Version 23.0 (IBM, Chicago, IL). Univariate analysis was conducted comparing characteristics between admissions of patients with and without HAI. Next, regression analysis was performed to determine the patient characteristics, comorbidities, cardiac lesions, and cardiac surgeries that were independently associated with a HAI using HAI as the dependent variable. Regression analysis was also used to identify the specific HAIs that were independently associated with an increased LOS, increased total charges, or increased inpatient mortality, using the individual HAI components as independent variables. Finally, regression analysis using mortality as the dependent variable and the aggregate outcome of HAI found that HAI was not independently associated with inpatient mortality.

3 | RESULTS

A total of 46 169 admissions were included in the data set. Of these, 773 (1.6%) developed a HAI. Characteristics of patients with HAI included younger age with a median age of 6 months compared to 12 months in those without an HAI ($P < .001$). Race did not appear to correlate with development of HAI (Table 1).

Those with a HAI were more likely to have heart failure (OR 1.6, 95% CI 1.4-1.9, $P < .001$), and arrhythmia not including atrioventricular block (OR 2.1 95% CI 1.5-2.9, $P < .001$). Cardiac lesions associated with increased likelihood of HAI (Table 1) were most commonly hypoplastic left heart syndrome (OR 3.1 95% CI 2.6-3.7, $P < .001$) and common arterial trunk/truncus arteriosus (OR 2.4 95% CI 1.6-3.5, $P < .001$). Table 2 shows the results of factors associated with HAI by regression analysis, with acute kidney injury (AKI; 2.7, 2.0-3.6, $P < .001$) being the greatest factor independently associated with a HAI.

The cardiac surgeries associated with HAI (Table 1) were most frequently common arterial trunk complete repair (OR 3.4 95% CI

TABLE 1 Patient characteristics associated with HAI

	No HAI (*n* = 45 396)	HAI (*n* = 773)	Odds ratio (95% CI)	*P* value
Age (years)	1 (0-17)	0.5 (0-17)	–	<.001
Race			–	.522
White	19 531 (53.4)	354 (54.0)		
Black	4420 (12.1)	71 (10.8)		
Hispanic	8181 (22.4)	144 (22.0)		
Asian or Pacific Islander	1507 (4.1)	25 (3.8)		
Native American	295 (0.8)	3 (0.5)		
Other	2667 (7.3)	58 (8.9)		
Heart failure	8532 (18.8)	218 (28.2)	1.6 (1.4-1.9)	<.001
Arrhythmia (not including AV block)	1107 (2.4)	39 (5.0)	2.1 (1.5-2.9)	<.001
Atrioventricular block	898 (2.0)	10 (1.3)	0.6 (0.3-1.2)	.173
Cardiac lesion				
Double outlet right ventricle	2435 (5.4)	62 (8.0)	1.5 (1.1-1.9)	.001
Atrioventricular septal defect	4678 (10.3)	101 (13.0)	1.3 (1.0-1.6)	.013
PAPVR	834 (1.8)	*** (***)	0.5 (0.2-1.0)	.054
TAPVR	1117 (2.5)	29 (3.7)	1.5 (1.0-2.2)	.023
Coronary artery anomaly	707 (1.6)	17 (2.2)	1.4 (0.8-2.3)	.156
Atrial septal defect	18 527 (40.8)	237 (30.6)	0.6 (0.5-0.7)	<.001
TOF	4722 (10.4)	82 (10.6)	1.0 (08-1.2)	.862
Ventricular septal defect	13 319 (29.3)	225 (29.1)	0.9 (0.8-1.1)	.871
Pulmonary atresia	1134 (2.5)	37 (4.8)	1.9 (1.4-2.7)	<.001
Tricuspid atresia	1606 (3.5)	41 (5.3)	1.5 (1.1-2.0)	.009
Ebstein anomaly	346 (0.8)	*** (***)	1.3 (0.6-2.7)	.391
HLHS	3321 (7.3)	155 (20.0)	3.1 (2.6-3.7)	<.001
Transposition	1518 (3.3)	48 (6.2)	1.9 (1.4-2.5)	<.001
ccTGA	322 (0.7)	*** (***)	1.4 (0.7-2.9)	.288
CAT	737 (1.6)	30 (3.9)	2.4 (1.6-3.5)	<.001
Cardiac surgery				
Valvuloplasty, no VR	3304 (7.3)	43 (5.6)	0.7 (0.5-1.1)	.067
Valvuloplasty with VR	3757 (8.3)	21 (2.7)	0.3 (0.2-0.4)	<.001
Septal defect repair	23 098 (50.9)	259 (33.5)	0.4 (0.3-0.5)	<.001
TOF, complete repair	3329 (7.3)	54 (7.0)	0.9 (0.7-1.2)	.706
CAT, complete repair	437 (1.0)	25 (3.2)	3.4 (2.2-5.1)	<.001
TAPVR repair	1209 (2.7)	32 (4.1)	1.5 (1.1-2.2)	.012
dTGA, ASO	592 (1.3)	31 (4.0)	3.1 (2.1-4.5)	<.001
dTGA, atrial switch	223 (0.5)	*** (***)	0.5 (0.1-2.1)	.356
RV-PA conduit	1505 (3.3)	64 (8.3)	2.6 (2.0-3.4)	<.001
Blalock-Tausig shunt	92 (0.2)	*** (***)	3.8 (1.6-8.8)	.001
Glenn	3775 (8.3)	136 (17.6)	2.3 (1.9-2.8)	<.001
Fontan	3457 (7.6)	74 (9.6)	1.2 (1.0-1.6)	.043
Heart transplant	620 (1.4)	27 (3.5)	2.6 (1.7-3.8)	<.001

Abbreviations: ASO, arterial switch operation; AV, atrioventricular; CAT, common arterial trunk; ccTGA, congenitally corrected transposition of the great arteries; CI, confidence interval; dTGA, dextro-transposition of the great arteries; HLHS, hypoplastic left heart syndrome; OR, odds ratio; PAPVR, partial anomalous pulmonary venous return; TAPVR, total anomalous pulmonary venous return; TOF, tetralogy of Fallot; VR, valve replacement.

Numbers reported in parenthesis represent percentages (%).

***Represents an absolute frequency less than 10 which per database policies cannot be explicitly reported.

TABLE 2 Factors associated with HAI by multivariate regression analysis

Factor	Odds ratio (95% CI)	*P* value
Older age	0.8 (0.8-0.8)	<.001
Heart failure	1.2 (1.0-1.4)	.034
Arrhythmia	1.7 (1.1-2.5)	.004
Atrioventricular septal defect	1.4 (1.1-1.8)	.01
Pulmonary atresia	1.7 (1.1-2.4)	.005
Hypoplastic left heart syndrome	1.8 (1.3-2.3)	<.001
Acute kidney injury	2.7 (2.0-3.6)	<.001

Abbreviation: HAI, health care-associated infection.

2.2-5.1, $P < .001$), arterial switch operation (OR 3.1 95% CI 2.1-4.5, $P < .001$) and Blalock-Tausig Shunt (OR 3.8 95% CI 1.6-8.8, $P = .001$).

The presence of any HAI was associated with increased LOS (median 29 vs 6 days, $P < .001$), increased total charges for the hospitalization (median $271 884 vs $88 385, $P < .001$), and increased inpatient mortality (6.1% vs 2.5%, $P < .001$) by univariate analysis. While any HAI was associated with increased mortality using univariate analysis (OR 2.5 95% CI 1.9-3.4, $P < .001$), no HAI, specific or in aggregate were associated with increased mortality after multivariate regression analysis (OR 1.3 95% CI 0.9-1.8, $P = .157$). Odds of mortality with HAI was noted to decrease by 3.4% with each subsequent year, demonstrating lower mortality over the course of the study period. Regression analysis demonstrated that HAIs were all independently associated with increased length of stay (Table 3). There was no effect of year on the length of stay.

4 | DISCUSSION

Our study indicates that development of any HAI, specifically CLABSI, CAUTI, VAP, and SWI, contributes significantly to both total hospital charges and LOS, with a median increase of approximately $183 500 and 23 days, respectively. Additionally, each individual type of HAI was independently associated with increase in both total hospital charges and LOS. Although the presence of any HAI was associated with increased mortality by univariate analysis, remarkably, no specific HAI or HAIs in aggregate were associated with increased in mortality after multivariate regression. These findings indicate that an increase in mortality associated with HAI by univariate analysis may be a result of confounding variables, such as early mortality. Pasquali and colleagues, in a linked clinical (STS-CHS) and resource utilization (PHIS) dataset, similar to the KID database, evaluated the impact of postoperative complications (including infection) following congenital heart disease surgery, and found an increase in hospital LOS and cost, but not mortality at the hospital level.[10] Our study also noted that mortality in those with HAI did decrease over the study period with the odds of mortality decreasing by 3.4% with each subsequent year.

TABLE 3 Impact of health care-associated infections on admission characteristics

Type of HAI	Length of stay (days)	*P* value	Total charges (USD)	*P* value
CLABSI	39	<.001	980 347	<.001
VAP	39.1	<.001	372 585	<.001
SWI	19.2	<.001	135 399	<.001
CAUTI	19.2	<.001	129 309	.038

Abbreviations: CAUTI, catheter-associated urinary tract infection; CLABSI, central line-associated bloodstream infection; HAI, health care-associated infection; SWI, surgical wound infection; VAP, ventilator-associated pneumonia.

Compared to other studies in both the general pediatric population and the postoperative pediatric cardiac surgery population, the incidence of HAIs in our study was quite low at 1.6%. However, our study is consistent with previous studies in postoperative pediatric cardiac surgical patients in that HAIs were more common in younger patients, particularly infants, and in patients undergoing higher risk procedures.[11,16] It has also been shown in recent studies of cardiac patients that complications contribute to increased cost and hospital LOS.[9-11,14,17] It is no surprise that HAIs, which can be a serious postoperative complication, resulted in increased hospital charges and length of stay. While our study did not show an association with increased mortality, our data are consistent with other studies regarding the impact of HAIs on hospital charges and length of stay. In particular, we were able to provide the magnitude of impact on hospital charges and length of stay by HAI type, which has not been demonstrated in previous studies for this population.

Interestingly, this study showed that patients who developed a HAI were 2.7 times more likely to have AKI. By the nature of our study, we are unable to comment as to if the development of a HAI causes increased risk of development of AKI or if AKI places patients more at risk for development of a HAI. It is known that AKI can occur in up to 30%-50% of patients after cardiac surgery requiring cardiopulmonary bypass, and contributes to LOS, cost of hospitalization, and mortality.[18] One possibility is that patients with HAI are at increased risk of developing AKI due to hemodynamic compromise, which results in increased morbidity and mortality. In contrast, prior development of AKI may increase the LOS and morbidity, which, in turn, may increase the duration of ICU therapy and monitoring devices, making HAI more likely to occur. This association warrants further investigation in future studies as a potentially modifiable risk factor for, or as a consequence of, hospital acquired infection.

Another interesting point of note is that of all the studied HAIs, CLABSI increased the total charges of hospitalization by a greater magnitude than the other HAIs. This discrepancy in resource utilization highlights the importance of prioritizing identification, treatment, and prevention of CLABSI in quality

improvement initiatives over other HAIs. This would potentially allow for efforts to be focused on the HAI on which interventions in reduction or early detection may have the greatest impact on resource utilization.

5 | LIMITATIONS

KID relies on ICD-9 coding, which creates several serious limitations for this study. First, ICD-9 codes for the HAIs included in this study did not exist prior to 2008. Therefore, the rates of HAIs in this study may be falsely lower, because the data may not have been captured prior to 2008. Relying on ICD-9 codes in itself may contribute to lower reported rates of HAIs, as the infections may not have been appropriately coded or coded at all. Lastly, there are also shortcomings of ICD-9 coding in pediatrics. Several of the included codes have not been validated in the pediatric population.

Due to the limitations of the KID, it cannot be determined when the HAI occurred in relation to the hospital stay. Without this information, it is impossible to know how much of each patient's LOS and total hospital cost were attributable to the development of a HAI. Additionally, the database is not designed to assess for possible risk factors that may have contributed to the development of a HAI, such as chronic medical conditions and surgical prophylaxis methods.

An additional limitation to this study is the inability to generalize differences in length of stay and hospital charges among centers with different surgical volumes, costs, payers, patient populations, and hospital practices.

An additional limitation is that we were unable to include more recent data. Newer data for the database are limited at the moment and that which is published is coded with ICD-10 codes which makes it difficult and problematic to combine the datasets from the older iterations.

Another limitation was that data regarding frequency of specific HAI was not included. This was intentionally excluded from the manuscript as it was a large amount of additional data that we felt would not add to the primary focus of the manuscript which was to determine the effect of HAI on hospital outcomes. It was felt that too much data may detract from the primary focus of the manuscript and dilute the message related to this.

6 | CONCLUSIONS

Although many centers are conducting quality improvement initiatives to reduce the rate of HAIs across all patients, similar to recent published studies, this study demonstrates the burden of HAIs on resource allocation and, more importantly, negative effects on patient outcome and emphasizes the need for continued improvement in HAI reduction. These data support ongoing efforts for prevention and mitigation of HAIs.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest with the contents of this article.

AUTHOR CONTRIBUTIONS

Conception and design of the study: Tweddell, Loomba, Cooper, Benscoter
Acquisition of data: Loomba
Analysis and/or interpretation of the data: Tweddell, Loomba, Cooper, Benscoter
Drafting of the manuscript: Tweddell
Critically revised the paper: Tweddell, Loomba, Cooper, Benscoter

ORCID

Sarah Tweddell https://orcid.org/0000-0003-3008-0235
Rohit S. Loomba https://orcid.org/0000-0002-9116-2835

REFERENCES

1. Warren DK, Quadir WW, Hollenback CS, Elward AM, Cox MJ, Fraser VJ. Attributable cost of catheter-associated bloodstream infections among intensive care patients in a nonteaching hospital. *Crit Care Med*. 2006;34(8):2084-2089.
2. Goudie A, Dynan L, Brady PW, Rettiganti M. Attributable cost and length of stay for central line-associated bloodstream infections. *Pediatrics*. 2014;133:e1525-e1532.
3. Wilson MZ, Rafferty C, Deeter D, Comito MA, Hollenbeak CS. Attributable cost of central line-associated bloodstream infections in a pediatric hematology/oncology population. *Am J Infect Control*. 2014;42:1157-1160.
4. Stevens V, Geiger K, Concannon C, Nelson RE, Brown J, Dumyati G. Inpatient costs, mortality and 30-day re-admission in patients with central-line-associated bloodstream infections. *Clin Microbiol Infect*. 2014;20:O318-O324.
5. Klevens RM, Edwards JR, Richards CL, et al. Estimating health care-associated infections and deaths in U.S. hospitals, 2002. Public Health Rep. 2007;122:160–166.
6. Davis KF, Colebaugh AM, Eithun BL, et al. Reducing catheter-associated urinary tract infections: a quality improvement initiative. *Pediatrics*. 2014;134:857-864.
7. Hoffman J, Kaplan S. The incidence of congenital heart disease. *J Am Coll Cardiol*. 2002;39:1890-1900.
8. Reller MD, Strickland MJ, Riehle-Colarusso T, Mahle WT, Correa A. Prevalence of congenital heart defects in Atlanta, 1998-2005. *J Pediatr*. 2008;153:807-813.
9. Pasquali SK, Jacobs ML, He X, et al. Variation in congenital heart surgery costs across hospitals. *Pediatrics*. 2014;133:e553-3560.
10. Pasquali SK, He X, Jacobs ML, et al. Hospital variation in postoperative infection and outcome after congenital cardiac surgery. *Ann Thorac Surg*. 2013;96(2):657-663.
11. Pasquali SK, He X, Jacobs ML, et al. Excessive costs associated with complications and prolonged hospital stay after congenital heart surgery. *Ann Thorac Surg*. 2014;98:1660-1666.
12. Levy I, Ovadia B, Erez E, et al. Nosocomial infections after cardiac surgery in infants and children: incidence and risk factors. *J Hosp Infect*. 2003;53:111-116.

13. Sohn AH, Schwartz JM, Yang KY, Jarvis WR, Guglielmo BJ, Weintrub PS. Risk factors and risk adjustment for surgical site infections in pediatric cardiothoracic surgery patients. *Am J Infect Control*. 2010;38:706-710.
14. Barker GM, O'Brien SM, Welke KF, et al. Major infection after pediatric cardiac surgery: a risk estimation model. *Ann Thorac Surg*. 2010;89(3):843-850.
15. Southern DA, Doherty C, De Souza MA, et al. Charts versus discharge ICD-10 coding for sternal wound infection following coronary artery bypass grafting. *Perspect Health Inf Manage*. 2015;12(Summer):1e.
16. Turcotte RF, Brozovich A, Corda R, et al. Health care associated infections in children after cardiac surgery. *Pediatr Cardiol*. 2014;35:1448-1455.
17. Kansy A, Jacobs JP, Pastuszko A, et al. Major infection after pediatric cardiac surgery: external validation of risk estimation model. *Ann Thorac Surg*. 2012;94(6):2091-2095.
18. Dent CL, Ma Q, Dastrala S, et al. Plasma neutrophil gelatinase-associated lipocalin predicts acute kidney injury, morbidity and mortality after pediatric cardiac surgery: a prospective uncontrolled cohort study. *Crit Care*. 2007;11:R127.

How to cite this article: Tweddell S, Loomba RS, Cooper DS, Benscoter DO AL. Health care-associated infections are associated with increased length of stay and cost but not mortality in children undergoing cardiac surgery. *Congenital Heart Disease*. 2019;14:785–790. https://doi.org/10.1111/chd.12779

APPENDIX

Healthcare-associated infection ICD-9 codes

Healthcare-associated infection	ICD-9 code
Central line-associated bloodstream infection	999.32
Catheter-associated urinary tract infection	996.64
Surgical wound infection	998.59
Ventilator-associated pneumonia	997.31