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ORIGINAL RESEARCH
Neonatology

Frequency of nosocomial infections and affecting factors in neonatal congenital cardiac surgery: Experience of a cardiac surgery center

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ABSTRACT

Objective: Congenital heart diseases (CHD) are one of the most common causes of neonatal intensive care hospitalization. Nosocomial infections may cause increased mortality and morbidity in these cases. In this study, it was aimed to investigate the frequency and risk factors affecting the development of nosocomial infections in patients who underwent neonatal congenital heart surgery.

Material and Methods: This study was carried out retrospectively in newborns who were followed up in the pediatric cardiac intensive care unit and underwent cardiac surgery between November 1, 2021 and November 1, 2022. Cases with and without nosocomial infection were evaluated in terms of perinatal history, birth weight, presence of syndrome, degree of complexity of CHD, perioperative and postoperative factors, presence and duration of central venous catheter, mechanical ventilator, etc. The results were analyzed statistically.

Results: During the study, neonatal cardiac surgery was performed in 140 cases. 54 different nosocomial infections were detected in 40 (28%) cases. Bloodstream infection was the most common in 60%, followed by lower respiratory tract infection in 25% and wound infection in 15%. Of the detected infectious agents, 55% were gram (-) organisms, 30% were gram (+) organisms, and 15% were fungal organisms. The presence of independent risk factors associated with nosocomial infection was congenital syndromes (OR 6.1, CI 95% 1.3–18), central venous catheter time >10 days (OR 3.7, CI 95% 1.3–11.0), mechanical ventilation time >7 days (OR 6.6, CI 95% 2.1–20.1), and post-operative >6 blood product transfusions (OR 3.1, CI 95% 1.3–8.5). Mortality due to nosocomial infection was 25%.

Conclusion: Nosocomial infections are an important cause of mortality and morbidity in newborns undergoing congenital heart surgery. In particular, efforts should be made to prevent neonates from bloodstream and lower respiratory tract infections.

Keywords: Congenital heart surgery; neonatal; nosocomial infection.

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Konjenital kalp cerrahisi geçirmiş yenidoğanlarda nozokomiyal enfeksiyon sıklığı ve etkileyen faktörler: Bir kalp cerrahisi merkezi deneyimi

ÖZET

Amaç: Konjenital kalp hastalıkları yenidoğanın en sık yoğun bakımda yatış nedenlerinden biridir. Nozokomiyal enfeksiyonlar bu olgularda artmış mortalite ve morbiditeye neden olabilmektedir. Bu çalışmada, yenidoğan konjenital kalp cerrahisi yapılan olgularda nozokomiyal enfeksiyonların sıklığını ve gelişimini etkileyen risk faktörlerinin araştırılması amaçlandı.

Gereç ve Yöntemler: Bu çalışma, 1 Kasım 2021–1 Kasım 2022 tarihleri arasında pediatrik kardiyak yoğun bakımda izlendi ve kalp cerrahisi operasyonu yapılan yenidoğanlarda retrospektif olarak gerçekleştirildi. Nozokomiyal enfeksiyon gelişen ve gelişmeyen olgular perinatal öykü, doğum ağırlığı, sendrom varlığı, koroner kalp hastalığının kompleksite derecesi, perioperatif ve postoperatif faktörler, kateter varlığı ve süresi, mekanik ventilatör vb. durumlar açısından değerlendirildi. Sonuçlar istatistiksel olarak incelendi.

Bulgular: Bu dönemde, 140 olguya yenidoğan kalp cerrahisi operasyonu yapıldı. Kırk (%28) olguda 54 farklı nozokomiyal enfeksiyon saptandı. En sık %60 olarak kan akımı enfeksiyonu gözlenirken, bunu %25 olguda alt solunum yolu enfeksiyonu ve %15 olguda yara yeri enfeksiyonu takip etmekteydi. Saptanan enfeksiyon ajanlarının %55'ini gram-negatif mikroorganizmalar, %30'unu gram-pozitif mikroorganizmalar ve %15'ini fungal mikroorganizmalar oluşturmaktaydı. Nozokomiyal enfeksiyon ile ilişkili bağımsız risk faktörleri; sendrom varlığı (Odds Ratio [OR] 6,1, %95 Güven Aralığı [GA] 1,3–18), santral venöz kateter süresi >10 gün (OR 3,7, %95 GA 1,3–11,0), mekanik ventilasyon süresi >7 gün (OR 6,6, %95 GA 2,1–20,1) ve operasyon sonrası >6 kan ürünü transfüzyonu (OR 3,1, %95 GA 1,3–8,5) olarak saptandı. Nozokomiyal enfeksiyona bağlı ölüm %25 olarak tespit edildi.

Tartışma: Nozokomiyal enfeksiyonlar konjenital kalp cerrahisi geçiren yenidoğanlarda önemli mortalite ve morbidite nedenidir. Özellikle kan dolaşımı ve alt solunum yolu enfeksiyonlarının önlenmesine çaba gösterilmelidir.

Anahtar Kelimeler: Nozokomiyal enfeksiyon; yenidoğan; konjenital kalp cerrahisi.

INTRODUCTION

Congenital heart disease (CHD) is a common malformation with an overall incidence of 4–10/1000 live births. CHDs consist of different pathophysiologies, whether the blood flow is normal or there is arterial desaturation due to interruption or mixing of venous and/or arterial blood flow. 25% of cases require surgical or interventional, palliative or corrective procedures due to critical CHD during the neonatal period. These cases constitute one of the most common causes of neonatal morbidity and mortality (1, 2).

In the neonatal period, different complications may develop in organ systems due to the immaturity of the immune system, uncontrolled systemic inflammatory response as a result of interactions in the cellular and humoral systems in cases operated under cardiopulmonary bypass, and the complexity of the operation (3). Infections are one of the most important complications observed, and it has been stated in some studies that it can be seen at a rate of 20–50% after neonatal cardiac surgery (4, 5).

It has been reported in the literature that catheter-related and bloodstream infections, ventilator-associated pneumonia (VAP), nosocomial pneumonia, urinary system-related infections, and surgical site infections can be seen at different rates in these patients and may cause nosocomial infections. At the same time, it has been suggested that different conditions such as low birth weight, presence of cyanosis, malnutrition, use of blood products, sternal patency, surgical complexity, and length of catheter stay may affect the frequency of nosocomial infections (3–6).

In this study, it was aimed to determine the frequency of nosocomial infections and to evaluate the factors affecting the nosocomial infection in patients who underwent neonatal cardiac surgery in the pediatric cardiac intensive care unit.

MATERIAL AND METHODS

This study was carried out retrospectively in newborns who underwent cardiac surgery and were followed up in the pediatric cardiac intensive care unit between November 01, 2021 and November 01, 2022. The study was carried out in accordance with the Declaration of Helsinki after obtaining approval from the Local Ethics Committee (KAEK 2022/05/number 173).

Inclusion criteria were accepted as patients who were diagnosed with CHD by a pediatric cardiologist and underwent cardiac surgery in the neonatal period. Exclusion criteria were defined as patients who died within 48 h after the operation, those who had infection within the first 48 h after hospitalization, and premature patients.

Patients were divided into two groups as those with and without nosocomial infections. Nosocomial infections were defined according to the Centers for Disease Control and Prevention criteria and the National Healthcare Safety Network (7). The following infections were included: central line-associated blood stream infection, clinical sepsis, pneumonia, VAP, and surgical site infection. Sepsis was defined according to the proposed definition in the International Sepsis Forum definition of infection in the intensive care unit (8).

Table 1. General characteristics of the newborns included in the study

Parameters	Nosocomial infection (+) n=40	Nosocomial infection (-) n=100	p
Age/day	5 (3–9)	6 (4–8)	NS
Weight/gram	2900 (2700–3100)	3000 (2800–3200)	NS
Male	19 (47)	51 (51)	NS
APGAR			
1’	7 (6–8)	7 (6–8)	NS
5’	8 (7–9)	9 (8–10)	NS
Cesarean section	20 (50)	48 (48)	NS
Syndrome	9 (23)	4 (100)	**0.01**
STAT (≥III-IV)	36 (90)	92 (92)	NS
Cyanosis	23 (57)	62 (62)	NS
Single ventricle	12 (30)	35 (35)	NS

STAT: The Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery; NS: Not significant; Median (IQR) or n (%).

We have a clinical follow-up protocol in terms of nosocomial infection management. Patients referred from another center are initially followed up in isolated rooms until culture results are resulted. Infection team (doctors and/or nurses) check the patients every day. Tracheal aspiration, blood and urine tests are gathered periodically. In case of clinical sepsis, broad-spectrum antibiotics and pentoxifylline infusion (5 mg/kg/h 4-h infusion) are initiated. Antibiotic spectrum is modified according to the culture results and antibiograms.

A study form was prepared for each patient, including demographics, perinatal characteristics, type of the surgery, the characteristics of catheter and postoperative period, the characteristics of transfusion of total parenteral nutrition, isolated microorganisms, etc. The results were evaluated statistically.

Statistical Analysis

Continuous variables were described as median (ınterquartile range) according to their distributions, and categorical data were presented as frequency (%). For between-group comparison, t-tests or Mann-Whitney U-tests were used for continuous variables, and Chi-squared tests or Fisher’s exact tests for categorical data as appropriate. Odds ratio and 95% confidence interval were calculated. A multivariate logistic regression was used to identify the independent risk factors for nosocomial infection. Statistical significance was set at $p<0.05$.

RESULTS

There were 140 newborn cases during the study. Nosocomial infection was detected in 40 (28%) of these cases. The demographic characteristics of newborn patients with and without nosocomial infection are shown in Table 1.

Table 2. Distribution of microorganisms isolated in newborns with nosocomial infection

Type of microorganism	Blood culture	Tracheal aspirate	Needle aspiration of wound	p
Gram-negative	13	6	3	22
Acinetobacter baumannii	–	2	–	2
Enterobacter cloacae	1	1	–	2
Escherichia coli	2	–	–	2
Klebsiella pneumoniae	6	1	2	9
Pseudomonas aeruginosa	3	1	1	5
Serratia marcescens	1	1	–	2
Gram-positive	9	1	2	12
Enterococcus faecium	1	–	–	1
Staphylococcus aureus	3	1	1	5
Staphylococcus epidermidis	4	–	1	5
Staphylococcus hominis	1	–	–	1
Yeast	5	–	1	6
Candida albicans	4	–	1	5
Candida parapsilosis	1	–	–	1
Total	27	7	6	40

Fifty-four different nosocomial infections were detected. These were one infection in 28 cases, two infections in 10 cases, and three infections in two cases. While blood stream infection was the most common as 60% (sepsis n=22, catheter-related blood stream infection n=10). This was followed by lower respiratory tract infection in 25% of cases (VAP n=9, pneumonia n=4) and wound infection in 15% of the cases (n=8).

55% of the detected infectious agents were gram (-) organisms, 30% were gram (+) organisms, and 15% were fungal organisms. Gram (-) organisms were the most common agents detected in all three blood, lung, and wound swab cultures. Detected infections and sites of isolation are shown in Table 2.

Significant risk factors in the univariate analysis associated with postoperative nosocomial infections were non-cardiac congenital malformations, previous duration of hospital stay >7 days, chest drain, CVC indwelling time >14 days, duration of mechanical ventilation >7 days, number of transfusions (>5), and reinterventions (cardiac surgery) (Table 3).

Independent risk factors associated with nosocomial infection (OR 6.1, CI 95% 1.3–18) were presence of a syndrome, >10 days of duration of central venous catheter (OR 3.7, CI 95% 1.3–11.0), mechanical ventilation time >7 days (OR 6.6, CI 95% 2.1–20.1), and post-operative transfusion of >6 blood product (OR 3.1, CI 95% 1.3–8.5). The overall mortality was 15% (n=21/140). In 10 cases, the main cause of death was the NIs (10/40, 25%). Mortality was higher in patients with nosocomial infections than in patients without nosocomial infections (p=0.01).

Table 3. Univariate analysis of the risk factors associated with postoperative nosocomial infection

Factors	Nosocomial infection (+)		Nosocomial infection (-)		p
	n	%	n	%	
Pre- and perioperative factors					
Syndrome	9	23	4	4	**0.01**
Surgical prophylaxis	40	100	100	100	NS
Operative factors					
STAT (≥III-IV)	36	90	92	92	NS
Number of transfusions (>5)	30	75	50	50	**0.005**
Cardiopulmonary bypass (CPB)	32	80	85	85	NS
Duration of CPB (>100 min)	28	70	65	65	NS
Aortic cross-clamp (>50 min)	32	75	70	70	NS
Duration of the procedure (>130 min)	26	65	68	68	NS
Delayed sternal closure	10	25	20	20	NS
Postoperative factors					
Femoral vein	6	15	20	20	NS
Umbilical vein	6	15	10	10	NS
Jugular vein	28	70	70	70	NS
Central venous catheter indwelling time (>10 days)	24	60	13	13	**0.001**
Duration of MV (>7 days)	29	72	16	16	**0.001**
Duration of TPN (>10 days)	4	10	3	3	NS
Chest drain	34	80	81	81	NS
Delayed sternal closure (>3 days)	3	8	2	2	**0.04**

CPB: Cardiopulmonary bypass; MV: Mechanical ventilation; TPN: Total parenteral nutrition; NS: Not significant.

DISCUSSION

In this study, the frequency of nosocomial infections and risk factors for these infections in newborns who underwent congenital cardiac surgery were investigated. The frequency of nosocomial infection was 28% and most commonly associated with bacteremia with gram-negative microorganisms. We observed that having a genetic syndrome, central venous catheter indwelling time >10 days, mechanical ventilation duration >7 days, and ≥5 blood product transfusions significantly increased the nosocomial infection risk. Our study is one of the limited studies conducted in this specific patient subgroup.

Nosocomial infection is a significant health-care problem with serious morbidity and mortality, especially in countries with budgetary constraints; the greater cost of care for nosocomial infections may limit access to surgery for other patients with CHD. Due to the emergence of multidrug-resistant bacteria, the cost of newer broad-spectrum antibiotics is likely to become a major contributor to costs of care. Nosocomial infections may lead to death after cardiac surgery for CHD, which is even more critical in newborns (5, 9).

Sen et al. (10) evaluated the frequency of nosocomial infection in 14545 cases who underwent congenital heart surgery. Among them, 6.2% were neonatal cases. The rate of nosocomial infection in newborns was 25.3%, which was five times higher than in any other age groups. In Yu et al.'s (6) study, the nosocomial infection rate was 10.8% for all patient groups; according to the newborn, infant, and child subgroups were 32.9%, 15.4%, and 5.2%, respectively. Our nosocomial infection frequency was 28% and was consistent with the literature.

Infectious complications are among the main complications in the postoperative period in newborns with CHD. The infection might originate from various organ systems, such as the bloodstream, lower respiratory tract, urinary tract, and wound site (11). In a multicenter study, Pasquali et al. (12) stated that nosocomial infections originated from sepsis in 51%, wound infection in 35%, and pneumonia in 10%. Similarly, the most common hospital-acquired infection was bacteremia, occurring in 33 patients (47% of hospital-acquired infections episodes and 10% of the study patients), 18 definite and 15 probable (26 and 21% of episodes, respectively) in Levy et al.'s study. (13) Surgical wound infection developed in 26 of their patients (37% of hospital-acquired infections episodes and 8% of patients). In our study, the most common source of nosocomial infection was blood-borne infections, followed by lower respiratory tract infections.

In nosocomial infections, pathogenic microorganisms may grow in blood, tracheal, urine, and wound swab culture according to the unit's flora and infection characteristics. In the series of Garcia et al. (5), gram-positive cocci, especially S. aureus, are one of the principal etiologic agents. Mehta et al. (14) found similar results, but Levy (13) and Abou (15) reported a higher frequency of gram-negative microorganisms. Gram-positive cocci are common in catheter-related infections, gram-negative bacilli in urinary tract infections and late VAP. In our study, the most frequently produced agent was gram-negative microorganisms.

Independent risk factors affecting nosocomial infections have been described. Yu et al. (6) reported that STS risk grade, BMI, CPB duration, low lymphocyte/WBC, or high neutrophil/WBC ratio were independently associated with nosocomial infection in CHD infants after cardiac surgery. Furthermore, younger age at surgery, higher surgical complexity, lower oxygen saturation, and major medical illness were independent risk factors for infection in various studies. In a review by Dresbach et al. (4), the CVC indwelling time was an independent risk factor for bloodstream infection. The OR for CVC indwelling time 7–10 days was 6.2 and increased for >10 days (OR=14.3). In Garcia et al.'s (5) study, the independent risk factors associated with nosocomial infection were non-cardiac congenital malformations, CVC indwelling time >14 days, mechanical ventilation duration >7 days, and ≥5 blood product transfusions. In our study, having a genetic syndrome, CVC indwelling time >10 days, >5 blood product transfusions, and mechanical ventilator duration >7 days were independent risk factors.

The mortality rate was higher in patients with nosocomial infection. Magliola et al. (16) reported 14% and Abou et al. (15) reported 11% mortality rate in children with infection compared with 2% in children without infection. Pasquali et al. (12) also found a high mortality rate in patients with nosocomial infection (6% vs. 2.8%), and Garcia et al. (5) reported 17.8% mortality rate in their study. We calculated the mortality rate of 25% versus 11% in patients with and without nosocomial infection. Compared to other studies, the complexity of our patients' cardiac pathology may contribute to our high mortality levels.

Limitation

This is a single-center study with a limited number of patients. In addition, the patient's pathologies are heterogeneous and have different physiological consequences.

CONCLUSION

Nosocomial infections are significant causes of mortality and morbidity in newborns undergoing congenital heart surgery. In particular, bloodstream and lower respiratory tract infections are the most common nosocomial infections caused mainly by gram-negative organisms. Every effort should be taken to prevent correctable causes.

Ethics Committee Approval: The Başakşehir Çam and Sakura City Hospital Clinical Research Ethics Committee granted approval for this study (date: 26.05.2022, number: KAEK/2022.05.173).

Informed Consent: Written informed consent was obtained from the families of the patients who participated in this study.

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Authorship Contributions: Concept – DYÖ, STN, ŞM; Design – DYÖ, STN, ŞM, YÖ, İCT; Supervision – MÇ, ACH, BT, EÖ; Fundings – BT, MÇ, ACH, EÖ; Materials – DYÖ, STN, ŞM, BT, YÖ, İCT; Data collection and/or processing – EÖ, İCT, BT; Analysis and/or interpretation – DYÖ, STN, ŞM, YÖ, BT, İCT; Literature review – İCT, EÖ; Writing – DYÖ, STN, ŞM, İCT, EÖ; Critical review – ACH, MÇ, EÖ, İCT.

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