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Amanzholova A.[1, 2] ✉, Morenko M.[1], Baiko S.[3], Nigmatullina N.[4], Besbayeva G.[2], Khamitova Z.[5], Zhankorazova A.[5], Koichubayeva D.[2], Bekishev B.[2], Mustapayeva N.[4]
[1] Astana Medical University, Astana, Kazakhstan
[2] Corporate Fund University Medical Center "Heart Center", Astana, Kazakhstan
[3] Belarusian State Medical University, Minsk, Belarus
[4] Kazakh National Medical University named after S.D. Asfendiyarov, Almaty, Kazakhstan
[5] Nazarbayev University School of Medicine, Astana, Kazakhstan

# Risk Factors Associated with Cardiorenal Syndrome Type I in Children with Congenital Aortic Arc Pathology

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Contacts: aainamkoz7@gmail.com

**Abstract**

**Introduction.** Acute kidney injury (AKI) is one of the most serious postoperative complications in neonates undergoing surgical correction of congenital heart defects (CHD). Its development significantly worsens prognosis, increasing the incidence of complications and mortality. A particularly vulnerable group includes patients with congenital aortic arch pathology (CAP), who require complex interventions in the early neonatal period.

**Purpose.** To assess the prevalence, predictors, and clinical outcomes of type 1 cardiorenal syndrome (AKI associated with impaired cardiac function) in neonates with congenital aortic arch pathology who underwent surgical treatment.

**Materials and methods.** This retrospective cohort study included 95 neonates with CAP who underwent CHD correction at the "Heart Center" (Astana, Kazakhstan) between 2017 and 2024. Among a total of 402 pediatric patients with CHD, 15.6% developed AKI. The 95 neonates with CAP were divided into two groups: those with AKI (n=45) and those without (n=50). Demographic, intraoperative, and laboratory parameters were analyzed, including N-terminal prohormone of brain natriuretic peptide (NT-proBNP) levels, presence of sepsis, and duration of cardiopulmonary bypass (CPB).

**Results.** The development of AKI in neonates with CAP was significantly associated with elevated postoperative NT-proBNP levels and the presence of sepsis. The duration of CPB did not show a statistically significant correlation with AKI. Patients with AKI required prolonged mechanical ventilation, longer intensive care unit stays, and had higher mortality rates.
**Conclusion.** Early diagnosis and risk stratification for AKI in neonates with congenital aortic arch pathology are crucial for improving outcomes. NT-proBNP levels may serve as a potential biomarker for predicting the development of type 1 cardiorenal syndrome. Individualized perioperative management strategies are essential to reduce complications in this high-risk population.
**Keywords:** acute kidney injury, congenital heart defects, neonatal surgery, NT-proBNP, risk factors

Аманжолова А.К.[1, 2] ✉, Моренко М.А.[1], Байко С.В.[3], Нигматуллина Н.Б.[4], Бесбаева Г.К.[2], Хамитова З.К.[5], Жанкоразова А.К.[5], Койчубаева Д.К.[2], Бекишев Б.Е.[2], Мустапаева Н.М.[4]
[1] Медицинский университет Астана, Астана, Казахстан
[2] Корпоративный фонд UMC «Центр сердца», Астана, Казахстан
[3] Белорусский государственный медицинский университет, Минск, Беларусь
[4] Казахский национальный медицинский университет имени С.Д. Асфендиярова, Алматы, Казахстан
[5] Школа медицины Назарбаев Университета, Астана, Казахстан

# Факторы риска, ассоциированные с кардиоренальным синдромом I типа, у детей с врожденной патологией дуги аорты

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Контакты: aainamkoz7@gmail.com

**Резюме**

**Введение.** Острое повреждение почек (ОПП) представляет собой одно из наиболее серьезных послеоперационных осложнений у новорожденных после хирургической

коррекции врожденных пороков сердца (ВПС). Его развитие существенно ухудшает прогноз, увеличивая частоту осложнений и уровень летальности. Особенно уязвимой группой являются пациенты с врожденной патологией дуги аорты (ВПДА), требующие комплексных вмешательств в раннем неонатальном периоде.

**Цель.** Оценить распространенность, предикторы и клинические исходы развития синдрома кардиоренальной недостаточности 1-го типа (ОПП, связанное с нарушением функции сердца) у новорожденных с врожденной патологией дуги аорты, перенесших хирургическое лечение.

**Материалы и методы.** В ретроспективное когортное исследование были включены 95 новорожденных с ВПДА, которым была проведена хирургическая коррекция ВПС в Центре сердца (Астана, Казахстан) в период с 2017 по 2024 г. Из общего числа 402 детей с ВПС у 15,6% диагностировано ОПП. Пациенты с ВПДА были разделены на две группы: с развитием ОПП (n=45) и без него (n=50). Оценивались демографические, интраоперационные и лабораторные параметры, в том числе уровни N-концевого прогормона мозгового натрийуретического пептида (NT-proBNP), наличие сепсиса и длительность искусственного кровообращения (ИК).

**Результаты.** Развитие ОПП у новорожденных с ВПДА достоверно ассоциировалось с повышенными послеоперационными уровнями NT-proBNP и наличием сепсиса. Статистически значимой связи между продолжительностью ИК и развитием почечной недостаточности выявлено не было. Пациенты с ОПП нуждались в более длительной искусственной вентиляции легких, дольше находились в отделении интенсивной терапии, и летальность среди них была выше.

**Заключение.** Ранняя диагностика и стратификация риска развития ОПП у новорожденных с ВПДА имеют ключевое значение для улучшения исходов. Уровень NT-proBNP может рассматриваться как потенциальный биомаркер для прогнозирования развития синдрома кардиоренальной недостаточности 1-го типа. Индивидуализированные стратегии периоперационного ведения необходимы для снижения частоты осложнений в этой группе высокого риска.

**Ключевые слова:** острое почечное повреждение, врожденный порок сердца, неонатальная хирургия, NT-proBNP, факторы риска

## ■ INTRODUCTION

Acute kidney injury (AKI) is a critical and frequently encountered complication in neonates undergoing surgery for congenital heart defects (CHD). This condition poses significant challenges to postoperative management and healthcare systems due to its strong association with increased morbidity, mortality, and resource utilization. Reported incidence rates of AKI in this population vary widely, ranging from 15% to 64%, influenced by variations in diagnostic criteria, patient characteristics, and surgical factors [1–3]. Neonates are particularly vulnerable to AKI because of their immature renal physiology, limited nephron reserve, and heightened sensitivity to ischemic and inflammatory insults during the perioperative period [2, 4, 5].

The pathogenesis of cardiac surgery-associated AKI is multifactorial. While prolonged cardiopulmonary bypass (CPB) duration has traditionally been implicated, its significance as an independent risk factor varies across studies and was not statistically significant in our cohort. Nevertheless, CPB contributes to renal injury indirectly through mechanisms such as ischemia-reperfusion, systemic inflammation, and oxidative stress [3, 4, 6]. Additionally, sepsis and perioperative hemodynamic instability have consistently emerged as significant predictors of AKI, further exacerbating the systemic inflammatory response and endothelial dysfunction [5, 7].

The inclusion of N-terminal prohormone of brain natriuretic peptide (NT-proBNP) as a biomarker for cardiac dysfunction has provided a novel dimension to understanding the interplay between cardiac and renal systems in the perioperative setting. Elevated NT-proBNP levels are indicative of ventricular dysfunction and hemodynamic compromise, making it a promising tool for early risk stratification and management of neonates at risk for AKI [8, 9]. This biomarker underscores the relevance of the cardiorenal syndrome in this population, highlighting the necessity for integrated perioperative monitoring and management protocols [8, 10].

Despite advancements in surgical techniques and perioperative care, the prognosis for neonates with AKI remains poor. Studies consistently demonstrate prolonged mechanical ventilation, prolonged intensive care unit hospitalization, and higher mortality rates among affected neonates, reflecting the substantial burden of AKI on clinical outcomes [9, 11, 12]. Diagnostic criteria such as the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines have improved standardization, but their limited sensitivity for early detection in neonates highlights the need for additional markers. Emerging biomarkers, including urinary neutrophil gelatinase-associated lipocalin (NGAL) and serum cystatin-C, show promise in enhancing early diagnosis and guiding interventions [8, 9, 13].

This study seeks to evaluate the incidence, risk factors, and outcomes of AKI in neonates undergoing CHD surgery, focusing on the role of clinical and biochemical markers. By integrating contemporary diagnostic criteria and biomarker-driven risk stratification, this research aims to advance understanding of AKI pathophysiology and inform targeted interventions. Contextualizing these findings with existing literature underscores the critical need for multidisciplinary approaches to reduce AKI incidence and improve neonatal outcomes in this high-risk population.

## ■ PURPOSE OF THE STUDY

To assess the prevalence, predictors, and clinical outcomes of type 1 cardiorenal syndrome (AKI associated with impaired cardiac function) in neonates with congenital aortic arch pathology who underwent surgical treatment.

## ■ MATERIALS AND METHODS

### Study Design and Population

This retrospective cohort study was conducted at the CF "Heart Center" in Astana, Kazakhstan, from January 2017 to December 2024. The study included 402 pediatric patients who underwent congenital heart defect (CHD) correction with cardiopulmonary bypass (CPB). Acute kidney injury (AKI) developed in 15.6% of the patients (63 out of 402).

From this cohort, 95 neonates diagnosed with congenital aortic pathology (CAP) were included and divided into two groups:

- Main group: 45 children with CAP and AKI.
- Control group: 50 children with CAP and without AKI.

All patients underwent surgery within the neonatal period (1–40 days of life), and CAP was frequently observed in combination with other CHDs. The selection was based on the frequency of CAP and the capacity of the national cardiac surgical center.

**Inclusion and Exclusion Criteria**

Inclusion criteria:

- Neonates with a confirmed diagnosis of CAP.
- Scheduled corrective surgery for CAP.
- Written informed consent from parents or legal guardians.

Exclusion criteria:

- Preoperative AKI.
- Severe comorbid conditions, such as congenital defects in other organs or sepsis.
- Pre-existing chronic kidney disease.
- Refusal of parents or guardians to participate.
- Inability to undergo surgery due to medical contraindications.

**Ethical Considerations**

The study adhered to the principles outlined in the Declaration of Helsinki and was approved by the Institutional Review Board of Astana Medical University (Protocol No. 1234, dated December 15, 2020). Compliance with international Good Clinical Practice (GCP) standards, Joint Commission International (JCI) requirements, and Order No. 248 of the Ministry of Health of the Republic of Kazakhstan (dated December 11, 2020) was ensured. All participants' legal representatives provided informed consent.

**Data Collection**

Data were obtained through clinical, laboratory, and instrumental evaluations in the perioperative and early postoperative periods. Key parameters included:

- Clinical data: duration of catecholamine therapy, urine output, diuretic therapy, and mechanical ventilation (MV) time.
- Laboratory analysis: levels of lactate, creatinine, urea, alanine aminotransferase (ALT), aspartate aminotransferase (AST), C-reactive protein (CRP), and NT-proBNP.
- Hemodynamic data: left ventricular ejection fraction (EF) from echocardiographic monitoring.
- Complications: ANALYSIS of early postoperative complications, including cardiac arrhythmias, heart failure, pneumonia, respiratory distress syndrome, and AKI.

Urine output and serum creatinine were assessed before and after surgery. Renal replacement therapy (RRT) with peritoneal dialysis (PD) was initiated based on criteria such as reduced urine output, positive fluid balance, unresponsive lactic acidosis, hyperkalemia, or elevated nitrogenous waste products.

**Surgical Procedure**

All surgeries were performed under general anesthesia with CPB support, and the average surgery duration was 5 hours.

**AKI Assessment**

AKI was diagnosed and classified according to the neonatal KDIGO (Kidney Disease: Improving Global Outcomes) criteria, which included serum creatinine levels and urine output changes. Stages of AKI were analyzed to determine the severity of kidney dysfunction.

**Statistical Analysis**

Statistical analysis was performed using STATA version 18.0. Statistical significance was set at $p<0.05$.

Descriptive statistics: mean ± standard deviation (SD) or median (interquartile range) for continuous variables and counts (percentages) for categorical variables.

Comparative analyses:

- Parametric data: Independent samples t-test.
- Non-parametric data: Mann-Whitney U-test.
- Categorical variables: Fisher's exact test.

Correlation analyses:

- Pearson correlation for parametric data.
- Spearman correlation for non-parametric data.

This comprehensive approach allowed for an in-depth evaluation of perioperative risk factors and the development of predictive strategies for AKI in children with CHD undergoing surgical intervention for correction.

## RESULTS

Table 1 summarizes the preoperative clinical and biochemical characteristics of infants with and without postoperative acute kidney injury (AKI). There were no statistically significant differences in demographic parameters such as age at surgery ($p=0.895$), sex distribution ($p=0.578$), or weight before surgery ($p=0.448$) between the AKI and non-AKI groups. Although median preoperative urea levels were higher in the AKI group, this did not reach statistical significance ($p=0.051$). Notably, ferritin levels were significantly elevated in infants who developed AKI ($p=0.049$), suggesting a potential association with systemic inflammation or iron metabolism dysregulation. Other preoperative laboratory parameters, including creatinine, total protein, albumin, calcium, sodium, potassium, free hemoglobin, and NT-proBNP, as well as cardiac function assessed by LVEF, did not differ significantly between the groups.

Table 2 presents the postoperative clinical and biochemical parameters of infants with and without acute kidney injury (AKI). Infants who developed AKI exhibited significantly higher postoperative urea levels ($p=0.026$) and markedly elevated NT-proBNP concentrations ($p<0.001$), indicating a potential association with volume overload or cardiac dysfunction. Additionally, the AKI group demonstrated significantly larger right coronary artery (RCA) dimensions ($p=0.009$), which may reflect hemodynamic alterations or underlying structural differences. Postoperative albumin levels were paradoxically higher in the AKI group ($p=0.005$), potentially due to selective fluid management or

**Table 1**
**Parameters of infants with and without postoperative acute kidney injury before surgery**

| Parameters | No AKI (n=50) | AKI (n=22) | P-value |
|---|---|---|---|
| Age at surgery (d, median (IQR)) | 5.9 (5; 182) | 3.5 (1; 71) | 0.895 |
| Male (n, %) | 26 (52%) | 13 (59%) | 0.578 |
| Weight before surgery (kg, median (IQR)) | 4.1 3.4; 7.7) | 3.3 (3.1; 3.8) | 0.448 |
| Preoperative urea (mg/dL, median (IQR)) | 18.1 (11.4; 25.7) | 20.1 (14.8; 43.1) | 0.051 |
| Preoperative creatinine (mg/dL, median (IQR)) | 0.4 (0.3; 0.6) | 0.5 (0.4; 0.7) | 0.251 |
| Preoperative total protein (g/dL, median (IQR)) | 4.9 (0; 6.5) | 4.7 (4.4; 5.4) | 0.410 |
| Preoperative albumin (g/dL, median (IQR)) | 2.5 (0,0; 3.1) | 3.25 (2.5; 3.6) | 0.134 |
| Preoperative ferritin (ng/dL, median (IQR)) | 1.8 (0,0; 3.6) | 27.2 (21.6; 45.2) | 0.049 |
| Preoperative calcium (mg/dL, median (IQR)) | 0.9 (0.5; 1.3) | 1.1 (0.7; 1.5) | 0.201 |
| Preoperative sodium (mg/dL, median (IQR)) | 97.6 (56.2; 139.0) | 105.5 (66.1; 144.9) | 0.612 |
| Preoperative potassium (mg/dL, median (IQR)) | 3.3 (1.7; 4.9) | 3.3 (1.9; 4.7) | 0.989 |
| Preoperative free hemoglobin(mg/dL, median (IQR)) | 0.3 (0.1; 0.8) | 0.2 (0.0; 0.4) | 0.438 |
| Preoperative NT-proBNP (mg/dL, median (IQR)) | 7537 (6315; 8758) | 8801 (6901; 10700) | 0.693 |
| LVEF (%, median (IQR)) | 48.0 (36.6; 59.4) | 49.5 (35.9; 63.1) | 0.748 |

hemodilution in non-AKI patients. Furthermore, sepsis was observed exclusively in the AKI group ($p<0.001$), suggesting a strong correlation between systemic infection and kidney injury. Other parameters, including postoperative creatinine, electrolytes, calcium, total protein, ferritin, free hemoglobin, cardiopulmonary bypass (CBP) time, and left anterior descending artery (LAD) size, did not differ significantly between groups.

A comprehensive comparison of clinical and laboratory parameters between neonates with and without postoperative acute kidney injury (AKI) revealed several critical distinctions.

**Table 2**
**Parameters of infants with and without postoperative acute kidney injury after surgery**

| Parameters | No AKI (n=50) | AKI (n=22) | P-value |
|---|---|---|---|
| Weight at surgery (kg, median (IQR)) | 6.3 (2.5; 10.1) | 5.0 (0.1; 9.9) | 0.443 |
| Postoperative urea (mg/dL, median (IQR)) | 43.0 (19.2; 66.9) | 64.5 (34.2; 94.7) | 0.026 |
| Postoperative creatinine (mg/dL, median (IQR)) | 0.4 (0.3; 0.5) | 0.6 (0.4; 1.1) | 0.885 |
| Postoperative total protein (g/dL, median (IQR)) | 3.0 (1.1; 4.8) | 2.1 (0.7; 3.4) | 0.184 |
| Postoperative albumin (g/dL, median (IQR)) | 2.1 (0.7; 3.5) | 3.4 (2.8; 3.9) | 0.005 |
| Postoperative ferritin (ng/dL, median (IQR)) | 0.0 (0.0; 0.1) | 25.8 (8.4; 43.3) | 0.133 |
| Postoperative calcium (mg/dL, median (IQR)) | 1.2 (0.8; 1.5) | 1.1 (0.7; 1.5) | 0.508 |
| Postoperative sodium (mg/dL, median (IQR)) | 121.8 (90.0; 153.7) | 104.8 (60.4; 149.3) | 0.211 |
| Postoperative potassium (mg/dL, median (IQR)) | 3.5 (2.6; 4.3) | 3.0 (1.7; 4.3) | 0.281 |
| Postoperative free hemoglobin (mg/dL, median (IQR)) | 2.9 (1.1; 4.7) | 0.5 (0.1; 0.9) | 0.559 |
| Postoperative NT-proBNP (mg/dL, median (IQR)) | 7602 (6353; 8851) | 24017 (11985; 36048) | <0.001 |
| CBP time (min, median (IQR)) | 73.0 (63.7; 82.3) | 99.7 (87.2; 112.2) | 0.275 |
| LAD (mm, median (IQR)) | 7.9 (6.5; 9.2) | 8.8 (7.7; 9.9) | 0.069 |
| RCA (mm, median (IQR)) | 8.3 (6.3; 10.3) | 10.3 (8.6; 12.0) | 0.009 |
| Sepsis (yes, %) | 0 (0%) | 9 (41%) | <0.001 |
| ACVA (yes, %) | 4 (8.0%) | 3 (13.6%) | 0.457 |

Notes: ACVA – Acute Cerebrovascular Accident; AKI – acute kidney injury.

**Table 3**
**Clinical outcomes of patients (n=72)**

| Parameters | No AKI (n=50) | AKI (n=22) | p-value |
|---|---|---|---|
| Death (yes) | 3 (6%) | 11 (50%) | <0.001 |
| Ventilation days | 10.0 (0.9; 19.2) | 29.7 (12.8; 46.6) | <0.001 |
| Hospital days | 27.1 (14.4; 39.8) | 43.6 (25.2; 62.0) | 0.004 |
| Length of PICU, days | 12.9 (2.3; 23.6) | 33.9 (15.3; 52.5) | <0.001 |

Preoperative Parameters: While the majority of preoperative metrics, such as age at surgery, weight, and creatinine levels, did not differ significantly between the groups, a notable exception was ferritin. Ferritin levels were significantly higher in the AKI group compared to their non-AKI counterparts (p=0.049, table 1). This suggests a potential association between elevated ferritin, as a marker of inflammation or oxidative stress, and increased AKI risk. Although NT-proBNP levels were higher in the AKI group (table 1), this difference was not statistically significant.

Postoperative Parameters: Postoperative analysis demonstrated pronounced disparities. Patients with AKI exhibited significantly elevated urea levels (p=0.026, table 2) and NT-proBNP concentrations (p<0.001, table 2). Elevated NT-proBNP underscores the interplay between cardiac dysfunction and renal impairment in these patients. Additionally, serum albumin levels were higher in the AKI group (p=0.005, table 2). These findings align with established evidence linking hypoalbuminemia with adverse outcomes and emphasize the complex interplay of factors predisposing to AKI.

Hemodynamic and Structural Markers: The size of the right coronary artery (RCA) was larger in patients with AKI (p=0.009, table 2), suggesting potential underlying structural or hemodynamic variations in this cohort. No significant differences were observed for other parameters such as creatinine and calcium.

**Incidence of Complications**

Postoperative sepsis was significantly more prevalent in the AKI group, with 41% of affected patients experiencing this complication compared to 0% in the non-AKI group (p<0.001). This finding highlights the critical role of systemic inflammation and infection in the pathophysiology of AKI in this population. Acute cerebrovascular accidents occurred at similar frequencies between groups, with no significant difference observed (table 2).

The clinical impact of AKI was profound:

Mortality: Neonates with AKI experienced a significantly higher mortality rate (50%) compared to those without AKI (6%; p<0.001). This difference underscores the severe implications of AKI on patient survival.

Ventilation and Hospitalization Duration:

Mechanical ventilation was required for significantly longer durations in the AKI group (p<0.001, table 2). Similarly, the length of stay in the pediatric intensive care unit (p<0.001, table 2) and the total hospitalization period (p=0.004, table 2) were markedly extended for patients with AKI.

## ■ DISCUSSION

This study highlights the critical burden of acute kidney injury (AKI) in neonates undergoing congenital heart defect (CHD) surgeries, with an incidence rate of 15.6% in our

cohort. This finding is consistent with prior studies, which report AKI rates ranging from 15% to 64%, depending on the diagnostic criteria, population, and surgical complexity [1–3]. By identifying significant risk factors, including elevated NT-proBNP levels and sepsis, this research underscores the multifactorial etiology of AKI and its profound impact on postoperative outcomes.

Prolonged cardiopulmonary bypass (CPB) duration, a known risk factor for AKI due to ischemia-reperfusion injury, systemic inflammation, and oxidative stress, was observed in our AKI cohort. However, the difference between AKI and non-AKI groups was not statistically significant in this study. This discrepancy highlights the heterogeneity of AKI risk factors and suggests that additional perioperative conditions, including hemodynamic instability and inflammatory markers, may modulate AKI susceptibility [4, 8]. Nevertheless, minimizing CPB time remains an essential preventive strategy supported by the broader literature [6, 10, 14].

The role of NT-proBNP as a biomarker in AKI risk stratification is particularly noteworthy. Elevated postoperative NT-proBNP levels in the AKI group suggest a strong interplay between cardiac dysfunction and renal impairment, consistent with the pathophysiology of cardiorenal syndrome [9, 10]. NT-proBNP serves as a sensitive marker of ventricular dysfunction, reduced renal perfusion, and systemic congestion, underscoring its potential for early detection and risk assessment in high-risk neonates [8, 10, 13]. Incorporating NT-proBNP into perioperative monitoring protocols may provide an opportunity for timely intervention and improved outcomes.

Sepsis, identified in 41% of AKI cases, represents another critical factor exacerbating systemic inflammation, endothelial dysfunction, and renal injury [4, 5]. Previous studies have demonstrated that neonates are particularly vulnerable to infection-related complications due to their immature immune responses [5, 7, 15]. Our findings underscore the necessity for early recognition, prompt antibiotic therapy, and rigorous perioperative infection control measures to mitigate this significant risk factor.

From a clinical perspective, the consequences of AKI are severe and multifaceted. Neonates with AKI in this cohort experienced prolonged durations of mechanical ventilation, prolonged intensive care unit hospitalization, and significantly higher mortality rates compared to non-AKI patients. These findings mirror existing literature, where AKI has been consistently associated with longer hospital stays, increased resource utilization, and poorer long-term renal and cardiac outcomes [6, 11, 12]. This underscores the importance of comprehensive perioperative strategies, including individualized fluid management, close hemodynamic monitoring, and early renal replacement therapy, to improve survival and recovery trajectories in this high-risk population [16–18].

Our study also highlights the importance of biomarkers in advancing AKI diagnosis and management. Traditional markers like serum creatinine lack sensitivity for early detection, particularly in neonates with limited nephron reserves [1, 2, 11]. Emerging biomarkers, such as NT-proBNP, urinary NGAL, and serum cystatin-C, offer significant promise in improving early diagnosis and guiding targeted interventions [6, 8, 13]. Future studies should explore biomarker panels that integrate markers of cardiac dysfunction, systemic inflammation, and renal injury for comprehensive risk stratification.

Structural and hemodynamic parameters, such as coronary artery size, also emerged as potential contributors to AKI risk. Neonates with larger coronary arteries in the AKI group may reflect underlying hemodynamic or anatomical variations that predispose them

to renal complications. Further investigation into these parameters may yield valuable insights into the interplay between cardiac morphology and renal vulnerability [10, 19, 20].

Despite its strengths, this study has several limitations. Its retrospective design introduces inherent biases, and the exclusion of urine output data limits the comprehensiveness of AKI diagnosis. Additionally, the single-center design may reduce generalizability. Future multicenter prospective studies incorporating advanced biomarkers, detailed hemodynamic analyses, and long-term follow-up are essential to validate these findings and refine preventive strategies [12, 13, 18].

## ■ CONCLUSION

This study underscores the significant burden of AKI in neonates undergoing CHD surgery and its strong association with NT-proBNP levels, sepsis, and prolonged hospital stays. By integrating biomarker-based risk stratification, minimizing CPB duration, and implementing tailored perioperative care strategies, substantial improvements in AKI outcomes are achievable. These findings contribute to the growing body of evidence aimed at reducing AKI incidence, improving survival, and enhancing long-term recovery in this vulnerable population.

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