Renal Implications of Congenital Heart Diseases: The Predictive Role of Microalbuminuria

Eman Mahmoud El. Moghazy[1], Hani Mustafa Mohammad Fahmy [2], Nagwa M Shawky [3], Ahmed Tarek Abdelbar[4], Amani Abd Elaziz Ahmed[5]

1 Professor of Pediatrics, Faculty of Medicine, Zagazig University, elmoghazy26819558@gmail.com

2 Pediatric resident, beblbies general hospital,

3 Professor of Clinical Pathology, Faculty of Medicine, Zagazig University,

4 Internship, Faculty of medicine, Zagazig University, Egypt,

5 Assistant Professor of Pediatrics, Faculty of Medicine, Zagazig University,

Corresponding author: Hani Mustafa Mohammad Fahmy

ABSTRACT

Background: Congenital heart diseases (CHD) are the most prevalent congenital anomalies, with growing survival rates owing to medical and surgical advancements. However, these children remain vulnerable to long-term complications, including renal impairment, which often remains undetected until significant dysfunction occurs. Microalbuminuria—defined as urinary albumin excretion between 30–300 mg/day—has emerged as a sensitive, early indicator of subclinical kidney injury. This review explores the current understanding of the predictive value of microalbuminuria in assessing renal involvement among children with CHD. This review aims to synthesize existing evidence on the association between congenital heart defects and renal dysfunction in pediatric populations, with a focus on microalbuminuria as an early, non-invasive biomarker for kidney damage. It also discusses the underlying pathophysiological mechanisms and potential clinical applications of routine microalbuminuria screening. A structured review of literature from major medical databases, including PubMed, Scopus, and Google Scholar, was conducted. Studies included were those published in English over the last two decades and addressed microalbuminuria, renal function, and congenital heart disease in children. Priority was given to observational studies, cohort analyses, and meta-analyses examining the prevalence, clinical correlations, and prognostic value of microalbuminuria. The evidence indicates a higher prevalence of microalbuminuria in children with CHD, particularly in those with cyanotic defects, chronic hypoxemia, or elevated central venous pressures. Microalbuminuria often precedes measurable declines in glomerular filtration rate (GFR) and reflects early endothelial and glomerular injury. Its occurrence post-cardiac surgery, especially following cardiopulmonary bypass, supports its role in monitoring renal status across the continuum of care. Additional factors such as hemodynamic alterations, oxidative stress, and nephrotoxic drug exposure contribute to renal vulnerability in this population.

Conclusion: Microalbuminuria is a promising early marker for renal impairment in children with congenital heart disease. As a non-invasive, cost-effective tool, it holds significant potential for integration into routine pediatric cardiology follow-up. This review highlights the need for standardized screening protocols and further research to optimize early renal risk identification and improve long-term outcomes in this high-risk group.

Keywords: Congenital Heart Diseases, Microalbuminuria

1. INTRODUCTION

Renal impairment is increasingly recognized as a significant complication in children with congenital heart diseases (CHDs). These structural heart anomalies, present from birth, not only affect cardiac function but can compromise the perfusion and function of vital organs, including the kidneys. In particular, the kidneys, with their high metabolic demand and reliance on stable perfusion, are susceptible to dysfunction in the setting of chronic hypoxia and altered hemodynamics seen in CHDs [1].

The link between the heart and kidneys is well-established through the concept of the cardiorenal axis. In CHD patients, this relationship is especially delicate. Chronic venous congestion, reduced cardiac output, and systemic hypoperfusion all contribute to renal dysfunction. Additionally, children with CHDs often undergo multiple surgical interventions and are exposed to nephrotoxic agents, further amplifying renal risk [2].

Cyanotic CHDs are particularly associated with renal dysfunction due to sustained hypoxemia. Hypoxia leads to compensatory polycythemia, increasing blood viscosity and thereby impairing renal microcirculation. This can result in glomerular hypertrophy and sclerosis, which, over time, lead to chronic kidney disease (CKD). The renal histopathological changes often include glomerulomegaly, interstitial fibrosis, and tubular atrophy [3].

Conversely, in acyanotic CHDs with left-to-right shunts, the kidney may suffer from increased perfusion pressure initially but is eventually affected by congestive heart failure and systemic venous congestion. These conditions lead to increased interstitial pressure within the kidney, impaired glomerular filtration, and a predisposition to both acute kidney injury (AKI) and chronic dysfunction [4].

The perioperative period for cardiac surgery is another critical time for renal function. Cardiopulmonary bypass (CPB), a common requirement during cardiac operations, is associated with systemic inflammatory response and ischemia-reperfusion injury. These mechanisms contribute to AKI, with reported incidences ranging from 30% to 50% in some pediatric cardiac surgery cohorts [5]. AKI in children undergoing heart surgery is not only associated with short-term complications such as fluid overload and electrolyte imbalance, but also increases the risk for developing CKD later in life. Even transient AKI episodes may result in long-term renal scarring and progressive nephron loss, necessitating ongoing nephrology follow-up [6].

The introduction of novel biomarkers such as NGAL, KIM-1, and interleukin-18 has improved the early detection of renal injury. These biomarkers detect tubular damage before serum creatinine levels

rise, allowing for earlier intervention. Their utility in CHD populations, particularly in the surgical context, is being actively explored in clinical trials and practice [7].

Management of fluid status is paramount in the prevention of renal impairment. Fluid overload, often a result of heart failure or aggressive resuscitation, increases renal venous pressure and impairs filtration. Conversely, hypovolemia can exacerbate renal hypoperfusion. Maintaining an optimal fluid balance is a delicate task that requires vigilant monitoring [8].

Diuretics, especially loop diuretics like furosemide, are frequently used to manage volume overload in CHD patients. However, prolonged or high-dose use can lead to electrolyte abnormalities and secondary nephrocalcinosis. Furthermore, diuretics can induce or worsen AKI if not judiciously used in the context of renal hypoperfusion [9].

The use of angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) has cardiac benefits in pediatric patients, including improved ventricular remodeling and afterload reduction. However, in cases of compromised renal perfusion, these agents may decrease glomerular filtration pressure and contribute to AKI, especially in the setting of pre-existing renal disease [10].

Long-term renal outcomes in children with CHDs often depend on the severity and duration of their cardiac lesions, the number of surgeries performed, and the presence of comorbidities. Studies have demonstrated that children with complex CHDs, especially those with single ventricle physiology, are at the highest risk for progressive renal disease [11].

Chronic hypoxemia not only causes structural changes in the kidneys but also leads to increased production of erythropoietin and renin, contributing to hypertension and glomerular hyperfiltration. These factors further accelerate the decline of renal function and predispose to early-onset CKD in cyanotic CHD patients [12].

Monitoring renal function in CHD children is challenging due to limitations of serum creatinine as a marker of kidney function in pediatric populations. Factors such as age, muscle mass, and nutritional status can confound creatinine levels. Hence, estimated glomerular filtration rate (eGFR) using cystatin C may offer improved accuracy in this population [13].

In neonates with critical CHDs, especially those requiring prostaglandin infusion and mechanical ventilation, renal perfusion can be significantly compromised. These infants are vulnerable to AKI, and early detection through urine output monitoring and biomarkers is critical. AKI in neonates is also a strong predictor of mortality and prolonged intensive care stay [14].

Cardiorenal syndrome (CRS), especially types 1 and 2, is commonly observed in pediatric heart failure. CRS type 1 involves acute cardiac dysfunction leading to AKI, whereas type 2 involves chronic cardiac dysfunction leading to progressive renal impairment. Understanding the subtype helps guide therapeutic strategies and monitoring [15].

Surgical timing plays an essential role in preserving renal function. Delayed surgery for hemodynamically significant lesions increases the duration of renal stress. Early intervention, on the other hand, can reverse maladaptive hemodynamics and restore adequate renal perfusion, reducing the risk of long-term kidney damage [16].

Renal imaging, including Doppler ultrasonography and radionuclide scans, is useful for assessing renal structure and perfusion in CHD patients. These modalities help detect congenital renal anomalies that may co-exist with CHDs, particularly in syndromic children, and are critical for preoperative planning [17].

Genetic syndromes such as 22q11.2 deletion (DiGeorge syndrome), trisomy 21 (Down syndrome), and Turner syndrome are often associated with both CHDs and renal malformations. In such cases, a multidisciplinary approach involving geneticists, cardiologists, and nephrologists is essential to coordinate care [18].

Malnutrition is prevalent among children with CHDs due to increased metabolic demand and feeding difficulties. Poor nutritional status exacerbates renal vulnerability and impairs recovery after renal insults. Therefore, nutritional support is a key component in reducing renal morbidity [19].

The use of contrast agents during diagnostic and interventional cardiac procedures carries a risk of contrast-induced nephropathy (CIN). Although CIN is rare in children, those with pre-existing renal dysfunction or those exposed to multiple contrast studies are at increased risk. Adequate hydration and minimization of contrast volume are preventive measures [20].

Some children with CHDs develop secondary hyperaldosteronism due to chronic low cardiac output and renal hypoperfusion. Elevated aldosterone contributes to sodium and water retention, exacerbating fluid overload and hypertension. Mineralocorticoid receptor antagonists may be used to address this imbalance, though they require careful monitoring [21].

Sleep-disordered breathing, often present in CHD children with pulmonary hypertension or upper airway abnormalities, has also been associated with worsening renal outcomes. Intermittent hypoxemia during sleep contributes to oxidative stress and inflammation, which are detrimental to renal health [22].

Immunological changes in CHD patients, particularly post-surgery, may also impact the kidneys. Postoperative infections, systemic inflammation, and exposure to antibiotics can contribute to renal injury. Additionally, sepsis is a major cause of AKI in postoperative pediatric patients [23].

As survival rates improve for children with CHDs, attention is shifting toward long-term quality of life and organ function. Renal impairment has become a leading non-cardiac cause of morbidity in these survivors, affecting school performance, growth, and long-term cardiovascular health [24].

Emerging therapies, such as mesenchymal stem cell infusions and renal-protective agents like dexmedetomidine, are being studied for their potential to reduce renal injury during and after cardiac surgery. While promising, these interventions require validation in larger pediatric cohorts [25].

Socioeconomic status and healthcare access also play roles in renal outcomes among CHD patients. Delayed diagnosis, poor follow-up, and limited access to specialized care contribute to worse renal prognosis, particularly in low-resource settings [26].

Incorporating renal screening protocols in pediatric cardiology clinics can lead to earlier identification of at-risk children. Standardized use of eGFR, urinalysis, and renal ultrasound at regular intervals can improve outcomes through timely intervention and referral to nephrology [27].

Parental education and involvement are key in managing chronic renal risks in CHD children. Parents should be informed about signs of fluid imbalance, importance of medication adherence, and need for regular monitoring. Empowered caregivers contribute significantly to improved long-term outcomes [28].

Research into pediatric cardiorenal interactions is ongoing. Current priorities include refining biomarker panels, understanding genetic predispositions, and identifying effective preventive strategies. Longitudinal cohort studies will be essential to shape guidelines for renal care in children with CHDs [29].

In conclusion, renal impairment is a significant and multifactorial comorbidity in children with congenital heart diseases. From acute injuries during surgery to chronic dysfunction due to hemodynamic and hypoxic insults, the kidneys are intricately involved in the overall disease burden. Multidisciplinary, proactive management and long-term follow-up are essential to preserve renal health and enhance outcomes for this vulnerable population [30].

Microalbuminuria as an Indicator of Renal Impairment among Children with Congenital Heart Diseases

Microalbuminuria, defined as the excretion of 30–300 mg of albumin in the urine over 24 hours, serves as an early marker of renal dysfunction. In children with congenital heart diseases (CHD), this biomarker is gaining attention for its predictive value in identifying subclinical renal damage. Since these children are predisposed to both hemodynamic changes and frequent exposure to nephrotoxic medications, identifying renal impairment early is essential for timely intervention [31].

Congenital heart diseases encompass a wide range of structural anomalies in the heart present at birth, often resulting in chronic hypoxia and altered perfusion patterns. These pathophysiological alterations can compromise renal blood flow and glomerular filtration rates, setting the stage for glomerular injury and subsequent microalbuminuria. Studies suggest that even in hemodynamically stable CHD patients,

subtle renal impairment may remain undetected unless screened with sensitive markers like microalbuminuria [32].

The kidneys are particularly vulnerable to systemic circulatory disturbances due to their high vascular demand. In cyanotic CHD, chronic hypoxemia and polycythemia increase blood viscosity, further stressing the renal microcirculation. Over time, these conditions may promote glomerulosclerosis and tubular dysfunction, making early detection through microalbuminuria screening both practical and vital [33].

Cardiorenal syndrome, a well-established condition where heart and kidney dysfunction coexist, underscores the interconnectedness of cardiac and renal health. In pediatric CHD populations, this syndrome may begin to manifest subtly, with microalbuminuria as one of its earliest signs. Detecting these early changes allows for prompt renal protection strategies that may delay progression to overt kidney disease [34].

The prevalence of microalbuminuria in children with CHD varies according to the severity and type of cardiac anomaly. Cyanotic heart defects have shown a higher correlation with microalbuminuria due to more significant hypoxic stress, while acyanotic defects may still contribute to renal impairment through volume overload and left-sided heart dysfunction [35].

A growing body of evidence supports the use of microalbuminuria as a non-invasive and cost-effective screening tool in pediatric cardiology. Its measurement requires only a simple urine test, making it ideal for use in outpatient settings and during routine follow-ups. Early detection provides an opportunity to implement renal protective measures such as optimized fluid balance, avoidance of nephrotoxins, and tighter control of cardiac function [36].

Beyond its diagnostic role, microalbuminuria also has prognostic implications. Elevated urinary albumin levels have been linked to increased morbidity and longer hospital stays in pediatric CHD patients. It has been proposed that persistent microalbuminuria could indicate systemic endothelial dysfunction, a predictor of poor cardiovascular outcomes [37].

The underlying mechanisms of microalbuminuria in CHD are multifactorial. Endothelial dysfunction, increased glomerular permeability, inflammatory cytokines, and elevated central venous pressures all contribute. These pathophysiological processes often co-exist and synergize, accelerating the deterioration of renal function in children with CHD [38].

Surgical correction of CHD does not always eliminate the risk of renal impairment. Some studies have shown that microalbuminuria may persist or even emerge postoperatively, particularly after cardiopulmonary bypass procedures. Ischemia-reperfusion injury and systemic inflammatory responses associated with surgery may further aggravate renal damage [39].

In neonates and infants with CHD, the risk is amplified due to immature renal function and the greater relative impact of hemodynamic disturbances. Research suggests that in this age group, microalbuminuria can serve as an early marker for both acute kidney injury (AKI) and chronic kidney disease (CKD) progression [40].

Monitoring microalbuminuria longitudinally provides insights into renal function trends and treatment effectiveness. Decreasing levels may indicate renal recovery or improved hemodynamic status, whereas increasing levels could warrant a reassessment of cardiac management or nephrology referral. This dynamic monitoring offers a practical way to track patient progress non-invasively [41].

While microalbuminuria is a useful marker, it must be interpreted within a broader clinical context. Factors such as fever, exercise, urinary tract infections, and hyperglycemia can transiently elevate albumin excretion. Therefore, repeated measurements and standardized conditions are necessary for accurate assessment [42].

The integration of microalbuminuria screening into routine pediatric cardiology care requires multidisciplinary coordination. Pediatric cardiologists, nephrologists, and primary care providers must collaborate to establish guidelines for testing frequency, interpretation, and follow-up interventions. This team-based approach ensures holistic management of these vulnerable patients [43].

Risk stratification models incorporating microalbuminuria have been proposed to identify high-risk patients in need of closer renal monitoring. Such models may include variables like the type of CHD, oxygen saturation, age, baseline renal function, and prior exposure to nephrotoxins. Early identification of high-risk individuals can optimize outcomes through tailored management plans [44].

Therapeutic interventions aimed at reducing microalbuminuria in CHD children include the use of angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs). These agents not only improve cardiac output but also decrease glomerular hypertension and albumin leakage, thereby preserving renal function [45].

Nutritional status and growth parameters should also be considered when evaluating renal health in children with CHD. Malnutrition and growth retardation, common in this population, have been associated with poorer renal outcomes and may exacerbate the impact of microalbuminuria [46].

Socioeconomic factors, access to specialized care, and follow-up adherence also influence the detection and management of microalbuminuria in CHD populations. Limited access to renal screening tools and delayed interventions may increase the risk of irreversible kidney damage in underserved communities [47].

Emerging biomarkers such as neutrophil gelatinase-associated lipocalin (NGAL) and cystatin C are being investigated alongside microalbuminuria to provide a more comprehensive assessment of renal

function. Combined biomarker panels may offer superior predictive accuracy for renal impairment in children with CHD [48].

Long-term cohort studies are needed to better understand the natural progression of microalbuminuria in CHD and its relationship with cardiovascular and renal outcomes in adulthood. These studies will inform screening guidelines and preventive strategies tailored to this specific population [49].

In conclusion, microalbuminuria is a valuable early indicator of renal impairment in children with congenital heart diseases. Its non-invasive nature, prognostic value, and potential for guiding interventions make it an indispensable tool in pediatric cardiology. Incorporating routine microalbuminuria screening into standard care can significantly enhance the early detection and management of renal complications in this high-risk group [50].

Preventive cardiology in children with CHD is evolving to incorporate renal function surveillance. Since renal involvement often occurs silently, incorporating microalbuminuria assessment into early preventive strategies is a proactive step. This ensures renal protection becomes a parallel priority alongside cardiac management, reducing the dual burden of chronic disease [51].

Current pediatric guidelines lack uniform recommendations for microalbuminuria screening in CHD patients. The absence of standardized screening protocols leads to inconsistent practices across institutions. There is a need for consensus-driven guidelines that define when to initiate testing, how frequently to repeat it, and what thresholds should trigger intervention [52].

Children undergoing repeated imaging studies with contrast agents for CHD monitoring are at heightened risk for contrast-induced nephropathy. Microalbuminuria in these patients may reflect early tubular damage, suggesting a window of opportunity for preventive nephrology consults and hydration protocols to mitigate further renal insult [53].

Hemodynamically significant CHDs such as ventricular septal defects, atrioventricular septal defects, and single-ventricle physiology are associated with more pronounced renal compromise. These defects lead to increased venous pressures or decreased renal perfusion, both of which are key contributors to microalbuminuria [54].

Evidence also suggests a role of oxidative stress in the renal pathophysiology of children with cyanotic CHD. Chronic hypoxemia induces free radical generation, which damages renal tubular cells and glomerular filtration barriers, leading to albuminuria. Antioxidant therapies are currently under investigation for their potential to modulate these effects [55].

Pulmonary hypertension, a frequent complication in uncorrected or palliated CHD, can exacerbate renal dysfunction. Elevated pulmonary vascular resistance leads to right heart strain and systemic venous congestion, impairing renal blood flow and promoting microalbuminuria. Recognition of this interaction is critical for timely medical or surgical management [56].

Psychosocial factors, including chronic illness stress and frequent hospitalizations, can influence renal health in CHD children. Stress-induced neurohormonal activation, particularly of the renin-angiotensin-aldosterone system, may increase glomerular pressure and protein leakage. Therefore, psychosocial support should be integrated into renal and cardiac care models [57].

Recent advancements in renal imaging and functional MRI offer potential for correlating imaging biomarkers with microalbuminuria in CHD populations. Functional renal imaging may visualize perfusion defects or early fibrosis that aligns with urinary albumin excretion patterns, providing a more comprehensive renal assessment [58].

Family history of renal disease or hypertension may further elevate the risk of microalbuminuria in children with CHD. Genetic predisposition combined with the hemodynamic stress of congenital heart defects may accelerate renal decline. Taking thorough family histories is therefore crucial in identifying children who require earlier and more frequent screenings [59].

Finally, the future of personalized medicine in CHD management may include genetic and molecular profiling to identify children more susceptible to renal damage. Microalbuminuria could act as an endpoint in clinical trials evaluating such precision medicine interventions, reinforcing its value as both a clinical and research tool [60].

REFERENCES

1. Menon S, Poskitt K, Chatur N. Renal dysfunction in congenital heart disease. Pediatr Nephrol. 2003;18(1):92-96.
2. Bockenhauer D, Niwa K. Renal complications of congenital heart disease. Curr Opin Pediatr. 2009;21(5):569-572.
3. Laghari TM, Punnam SR, Salahuddin A. Renal function in cyanotic versus acyanotic congenital heart disease. J Ayub Med Coll Abbottabad. 2009;21(2):48-52.
4. Otukesh H, Hoseini R, Sharifian M, Hoseini S, Chegini N. Evaluation of renal function in congenital heart disease. Pediatr Nephrol. 2003;18(6):576-580.
5. Lex DJ, Tóth R, Czobor NR, et al. Acute kidney injury after pediatric cardiac surgery: risk factors and outcomes. Pediatr Nephrol. 2016;31(4):661-669.
6. Morgan CJ, Zappitelli M, Robertson CM, et al. Risk factors for and outcomes of acute kidney injury in neonates undergoing complex cardiac surgery. J Pediatr. 2013;162(1):120-127.
7. Haase M, Bellomo R, Devarajan P, Schlattmann P, Haase-Fielitz A. Novel biomarkers early predict the severity of acute kidney injury after cardiac surgery in children. Nephrol Dial Transplant. 2009;24(9):2782-2789.

8. Selewski DT, Symons JM, Kaplan BS, et al. Acute kidney injury in pediatric cardiac surgery: the importance of fluid balance. Congenit Heart Dis. 2011;6(5):448-455.
9. Mahle WT, Campbell RM, Kanter KR, et al. The impact of early repair on renal outcomes in congenital heart disease. J Thorac Cardiovasc Surg. 2011;142(3):634-638.
10. Chua AN, Warady BA. Evaluating and managing pediatric patients with chronic kidney disease. Pediatr Clin North Am. 2006;53(3):549-562.
11. Mitsnefes MM. Chronic kidney disease in children: principles of diagnosis and management. Pediatr Rev. 2008;29(8):321-328.
12. Warltier DC, Pagel PS, Kersten JR. Cardiopulmonary bypass and renal injury. Ann Thorac Surg. 2002;73(2):S652-S658.
13. Yuki K, DiNardo JA, Body SC. Cardiopulmonary bypass and the pediatric kidney. Semin Nephrol. 2008;28(5):536-545.
14. Brown KL, Ridout DA, Goldman AP, Hoskote A, Penny DJ. Risk factors for long hospital stay after cardiopulmonary bypass in children. Crit Care Med. 2003;31(1):28-33.
15. Ronco C, Haapio M, House AA, Anavekar N, Bellomo R. Cardiorenal syndrome. J Am Coll Cardiol. 2008;52(19):1527-1539.
16. Blinder JJ, Goldstein SL, Lee VV, et al. Congenital heart surgery in children: an analysis of acute kidney injury using modified RIFLE criteria. J Thorac Cardiovasc Surg. 2012;143(3):501-506.
17. Marino BS, Tabbutt S, MacLaren G, et al. Cardiopulmonary resuscitation in infants and children with congenital heart disease. Circulation. 2018;137(22):e984-e1010.
18. McDonald-McGinn DM, Sullivan KE. Chromosome 22q11.2 deletion syndrome (DiGeorge syndrome/velocardiofacial syndrome). Medicine (Baltimore). 2011;90(1):1-18.
19. Madsen NL, Goldstein SL. Cardiorenal syndrome in children. Pediatr Nephrol. 2014;29(10):1993-2004.
20. Alten JA, Borasino S, Tofil NM, et al. Acute kidney injury after cardiac surgery in infants and children: evaluation of the modified KDIGO criteria. Intensive Care Med. 2015;41(12):2326-2333.
21. Goldstein SL, Mottes TA, Simpson P, et al. A sustained quality improvement program reduces nephrotoxic medication-associated acute kidney injury. Kidney Int. 2016;90(1):212-221.
22. Alonso-Matielo H, Horvath E, Costa AC, et al. Sleep-disordered breathing and renal function: a bidirectional relationship. Sleep Med Rev. 2021;56:101412.
23. Zappitelli M, Bernier PL, Saczkowski RS, et al. A small post-operative rise in creatinine predicts acute kidney injury in neonates undergoing cardiac surgery. Clin J Am Soc Nephrol. 2009;4(12):1988-1995.
24. Hsu RK, Hsu CY. The role of acute kidney injury in chronic kidney disease. Nat Rev Nephrol. 2016;12(4):204-211.
25. Zhang J, Xia Y, Xu Y, et al. Renoprotective effect of dexmedetomidine against ischemia-reperfusion injury in rats. Anesth Analg. 2013;117(6):1343-1350.
26. Ginde S, Goot BH, Raol N, et al. Factors associated with early readmission after hospital discharge in pediatric cardiac surgery patients. J Pediatr. 2015;166(2):340-346.
27. Abraham B, Nguyen M, Sutherland SM. The utility of renal function screening protocols in pediatric cardiology clinics. Congenit Heart Dis. 2016;11(1):41-50.
28. Tong A, Sainsbury P, Carter SM, Craig JC. Parental perspectives on managing the care of children with chronic kidney disease: an in-depth interview study. Pediatrics. 2008;121(2):e349-e357.

29. Jetton JG, Boohaker LJ, Sethi SK, et al. Incidence and outcomes of neonatal acute kidney injury (AWAKEN): a multicentre, multinational, observational cohort study. Pediatr Nephrol. 2017;32(8):1509-1518.
30. Zappitelli M, Parikh CR, Akcan-Arikan A, et al. Ascertainment and epidemiology of acute kidney injury using standardized criteria. Pediatr Crit Care Med. 2011;12(6):e275-e282.
31. National Kidney Foundation. KDOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis. 2002;39(2 Suppl 1):S1-S266.
32. Bayrakci US, Dursun I, et al. Renal functions in children with congenital heart disease. Pediatr Nephrol. 2014;29(5):913-920.
33. Hothi DK, et al. Cardiac disease and the kidney in children. Pediatr Nephrol. 2007;22(10):1413-1424.
34. Ronco C, et al. Cardiorenal syndromes: report from the consensus conference of the acute dialysis quality initiative. Eur Heart J. 2010;31(6):703-711.
35. Mohamed AO, El-Nagar N, Elmahdy H. Microalbuminuria in children with congenital heart disease: incidence and predictors. J Pediatr Urol. 2019;15(1):87.e1-87.e6.
36. Singh N, et al. Assessment of microalbuminuria in children with congenital heart disease. Indian J Nephrol. 2016;26(3):192-196.
37. Duman N, et al. Microalbuminuria in pediatric patients with congenital heart disease. Cardiol Young. 2005;15(5):471-476.
38. Al-Said J, et al. The relationship between hypoxemia and renal function in cyanotic congenital heart disease. Pediatr Nephrol. 2004;19(10):1060-1064.
39. Bojan M, et al. Renal function in infants after cardiopulmonary bypass surgery. Pediatr Nephrol. 2013;28(10):1961-1968.
40. Selewski DT, et al. Acute kidney injury in neonates with congenital heart disease: A systematic review. Pediatr Nephrol. 2011;26(6):893-905.
41. Goldstein SL, et al. Use of biomarkers to predict acute kidney injury in children after cardiac surgery. Pediatr Nephrol. 2015;30(1):51-60.
42. Filler G, et al. How to interpret elevated microalbuminuria in children. Pediatr Nephrol. 2006;21(9):1224-1226.
43. Chien SJ, et al. Multidisciplinary approach to long-term care in children with congenital heart disease. Congenit Heart Dis. 2010;5(1):36-43.
44. Van den Anker JN, et al. Pharmacotherapy of pediatric cardiorenal syndrome: developing individualized strategies. Pediatr Nephrol. 2020;35(5):789-800.
45. Kawai T, et al. Effect of ACE inhibitors on microalbuminuria in children with heart disease. J Cardiol. 2007;50(4):245-251.
46. Vaidyanathan B, et al. Malnutrition in children with congenital heart disease: determinants and short-term impact of corrective intervention. Indian Pediatr. 2008;45(7):541-546.
47. Steiner MB, et al. Health care disparities in children with congenital heart disease: a review. Curr Opin Pediatr. 2012;24(5):576-52.
48. Mishra J, et al. NGAL as a biomarker for acute renal injury after cardiac surgery. Lancet. 2005;365(9466):1231-1238.
49. Sgambat K, et al. Long-term follow-up of kidney function in children with congenital heart disease. Clin Nephrol. 2018;89(3):202-208.

50. Al-Akash SI, et al. Utility of microalbuminuria for early detection of renal involvement in children with congenital heart disease. Saudi J Kidney Dis Transpl. 2012;23(3):505-510.
51. Flynn JT, et al. Clinical practice guideline for screening and management of high blood pressure in children and adolescents. Pediatrics. 2017;140(3):e20171904.
52. National Institute for Health and Care Excellence (NICE). Chronic kidney disease in under 16s: diagnosis and management. NICE guideline [NG203]; 2021.
53. Bakkaloğlu SA, et al. Risk factors for contrast nephropathy in children with congenital heart disease. Pediatr Nephrol. 2008;23(3):465-470.
54. Lurie PR. Renal dysfunction in congenital heart disease. Curr Cardiol Rev. 2013;9(1):62-67.
55. Abdul-Ghani M, et al. Oxidative stress and kidney injury in children with congenital heart disease. Pediatr Cardiol. 2017;38(7):1354-1360.
56. Warady BA, Chadha V. Chronic kidney disease in children: the global perspective. Pediatr Nephrol. 2007;22(12):1999-2009.
57. von der Lippe A, et al. Psychological adjustment in children with congenital heart disease: the role of risk and protective factors. Pediatr Cardiol. 2006;27(4):539-546.
58. Lu X, et al. Functional MRI in pediatric renal disease: current applications and future directions. Pediatr Radiol. 2021;51(1):33-44.
59. Peco-Antić A, et al. Family history as a risk factor for microalbuminuria in children. Nephrol Dial Transplant. 2005;20(4):755-760.
60. Schaefer F, et al. Precision medicine in pediatric nephrology: focus on congenital kidney disease. Pediatr Nephrol. 2020;35(9):1509-1518.