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CARDIOVASCULAR COMPLICATIONS IN CHILDREN WITH CHRONIC KIDNEY DISEASE: PREVALENCE AND CLINICAL CHARACTERISTICS

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ABSTRACT

Cardiovascular disease is a leading cause of morbidity and premature mortality in children with chronic kidney disease (CKD) although the burden often remains clinically silent until advanced stages of renal dysfunction. Early recognition of cardiovascular abnormalities in pediatric CKD is therefore crucial for early risk stratification and intervention. We performed a hospital-based, cross-sectional observational study in a pediatric nephrology unit of a tertiary care teaching hospital between January 2022 and December 2024. Children aged 2–18 years with CKD stages 2–5 were enrolled consecutively. Assessment in the clinic comprised anthropometry, blood pressure measurement, electrocardiography, transthoracic echocardiography, and carotid intima-media thickness (cIMT) results. Laboratory measurements were hemoglobin, serum creatinine, calcium, phosphate, albumin, and intact parathyroid hormone. The main outcome was the presence of any cardiovascular complication, defined as hypertension, left ventricular hypertrophy (LVH), diastolic dysfunction, systolic dysfunction, arrhythmia or conduction abnormality, pericardial effusion or elevated cIMT. Logistic regression analyses were performed univariable and multivariable for associated factors. The mean age was 10.9 ± 4.1 years and 57.4% were male. The overall prevalence of any cardiovascular complication was 62.8%. Hypertension was found in 48.9%, LVH in 31.9%, elevated cIMT in 27.7%, diastolic dysfunction in 18.1%, electrocardiographic abnormalities in 12.8%, pericardial effusion in 8.5%, as well as systolic dysfunction in 6.4%. The burden increased progressively with CKD stage, from 33.3% in stage 2 to 84.6% in stage 5. The estimated glomerular filtration rate and hemoglobin levels were significantly lower in children with cardiovascular complications, and serum phosphate and parathyroid hormone concentrations were higher. On multivariable analysis, CKD stage 4–5 (adjusted odds ratio [aOR] 3.41, 95% CI 1.29–9.03), uncontrolled hypertension (aOR 4.12, 95% CI 1.56–10.89), anemia (aOR 2.97, 95% CI 1.14–7.74), and hyperphosphatemia (aOR 3.25, 95% CI 1.19–8.87) were independently associated with cardiovascular complications. Cardiovascular problems were common in children with CKD and were disproportionately present in those with advanced disease. Hypertension, LVH and vascular remodeling were the most prevalent phenotypes. These results provide a basis for initiating cardiovascular monitoring in addition to early management of CKD and the development of the kidneys, particularly with respect to controlling blood pressure and anemia control and management of the mineral and bone abnormalities of CKD.

KEYWORDS: chronic kidney disease; children; cardiovascular complications; left ventricular hypertrophy; hypertension; carotid intima-media thickness; pediatric nephrology

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1. INTRODUCTION

The development of cardiovascular risk trajectories in children with chronic kidney disease is different than that in adults, not because vascular nor myocardial injury are absent, but because these impairments often start quietly and develop before overt atherosclerotic disease becomes clinically apparent. Registry-based survival data suggests that, relative to adult kidney failure, children with kidney failure, despite significant advances in renal replacement therapy and transplantation, are experiencing considerable premature death, and cardiovascular causes account for a significant portion of long-term excess deaths [1,2]. These issues have now been elucidated in pediatric nephrology studies as well, indicating that this burden goes well beyond renal failure itself. Consequently, cardiovascular remodeling can be established in earlier stages of CKD, typically while children are still asymptomatic and pre-dialysis [3,4].

The predominant pediatric phenotypic structure is not ischemic coronary disease, as in older age, but a syndrome of hypertension, left ventricular hypertrophy, diastolic dysfunction, carotid intima-media thickening, arterial stiffening and, in the advanced years, vascular calcification [3,4]. These abnormalities develop during a time of maturation that is marked by somatic growth, pubertal hormonal change, altered body composition, and kidney-specific metabolic disturbances. The outcome is a unique cardiorenal environment characterized by elevated pressure load, anemia, chronic inflammation, sodium, and water retention, disordered mineral metabolism, increased fibroblast growth factor 23, and uremic toxin accumulation, all of which interact with an immature cardiovascular system [3,4]. This biological context is significant because it suggests that pediatric CKD represents a distinct opportunity for prevention, as structural cardiovascular injury may be detected prior to the establishment of irreversible clinical endpoints [3].

The concept has been sharpened and made more evident by large multicenter cohorts. The Chronic Kidney Disease in Children study found a high prevalence of under-recognized blood pressure abnormalities such as masked hypertension and abnormal ambulatory patterns, even in mild-to-moderate CKD [5-9]. These blood pressure phenotypes are of clinical importance because the pattern of masked or uncontrolled hypertension follows that of target-organ injury, particularly left ventricular hypertrophy [6-9,14]. Echocardiography studies additionally demonstrate that myocardial remodeling starts early. Indeed, foundational work by Mitsnefes et al. showed increased left ventricular mass and altered systolic or diastolic performance in children with chronic renal insufficiency [10,11], while later longitudinal data demonstrated that optimization of blood pressure may promote regression of left ventricular hypertrophy [15]. In a similar vein, research reports using the ESCAPE and KNOW-Ped networks demonstrated that abnormal cardiac geometry is common across pediatric CKD cohorts [12,16,17], and differences in prevalence estimates result from different indexing criteria as well as differential diagnosing of subpopulations of children [12,16,17].

Vascular injury has been characterized with similar consistency. Litwin et al. demonstrated altered morphologic properties of large arteries in children with chronic renal failure and after transplantation [23]. Shroff and colleagues linked dialysis-associated mineral dysregulation to vascular damage and later showed mechanistically that dialysis may accelerate medial vascular calcification through vascular smooth-muscle-cell apoptosis [24,25]. More recent work has extended this phenotype to arterial stiffness, increased carotid intima-media thickness, and coronary calcification in adolescents and young adults with advanced CKD [26-28]. Such findings are clinically important because they suggest that pediatric CKD does not merely predict adult cardiovascular disease at a distance; it already contains measurable cardiovascular disease biology during childhood [3,4,26,27].

As much as this literature is gaining traction, several important uncertainties persist that we are interested in addressing. First, known estimates of prevalence of cardiovascular complications vary greatly by study setting, CKD stage distribution, dialysis exposure, imaging modality, and the thresholds used to define abnormalities. Second, single phenotypes have been reported independently, e.g. left ventricular hypertrophy alone or carotid intima-media thickness alone, and, so also, the underlying clinical landscape of cardiovascular involvement is not known. Thirdly, several of the most informative cohorts overlap in ways making it simpler to interpret the narratives rather than pooling data in more quantitative formats. Ultimately, the latest pediatric care of CKD is starting to focus on ambulatory blood pressure monitoring, mineral-bone disorder control, and earlier transplantation, but it is unclear what the evolving practice has done to the observed cardiovascular phenotype in the different studies we reviewed [3,4,9,26,27].

This systematic overview followed by an

exploratory meta-analysis of pediatric CKD in turn concentrated specifically on cardiovascular complications. The aim was to summarize the burden of crucial cardiovascular abnormalities, focusing on left ventricular hypertrophy because it was the most consistently reported and clinically interpretable phenotype. Secondary objectives were to summarize the clinical features of these populations and identify recurrent correlates of cardiovascular injury, including CKD severity, hypertension, anemia, and mineral-metabolic disturbances. It was hypothesized that cardiovascular abnormalities would be common in pediatric CKD populations, would increase with disease severity and dialysis exposure, and would cluster around potentially modifiable risk factors [3,4,6,12,24-27].

2. METHODS

2.1. Study Design

This was a hospital-based cross-sectional observational study conducted to evaluate the prevalence and clinical characteristics of cardiovascular complications in children with chronic kidney disease. The study was designed to assess both the burden and pattern of cardiovascular abnormalities and to identify clinical and biochemical factors associated with their presence.

2.2. Study Setting and Duration

The study was carried out in the Department of Pediatric Nephrology of a tertiary care teaching hospital. Participant recruitment and data collection were performed over a three-year period from January 2022 to December 2024.

2.3. Study Population

The study population consisted of children aged 2–18 years with established chronic kidney disease stages 2–5 who were evaluated either during outpatient follow-up visits or inpatient admissions. Chronic kidney disease was defined as kidney damage or reduced kidney function persisting for at least 3 months, and CKD stage was determined according to estimated glomerular filtration rate.

2.3. Eligibility Criteria

2.3.1. Inclusion Criteria

Children were eligible for inclusion if they met all of the following criteria:

1. Age between 2 and 18 years.
2. Diagnosis of CKD stage 2–5 for at least 3 months.
3. Availability of complete cardiovascular evaluation during the study period, including electrocardiography, echocardiography, and carotid ultrasonography.

2.3.2. Exclusion Criteria

Children were excluded if they had any of the following:

1. Congenital heart disease.
2. Primary cardiomyopathy.
3. Acute kidney injury.
4. Sepsis or acute intercurrent illness at the time of assessment.
5. Active malignancy.
6. Previous kidney transplantation.
7. Incomplete echocardiographic or laboratory data.

2.4. Sampling Method and Sample Size

Eligible children were enrolled consecutively during the study period. A total of 108 children were screened for eligibility. Fourteen were excluded because of congenital heart disease (n = 4), prior renal transplantation (n = 3), acute intercurrent illness (n = 2), or incomplete cardiovascular assessment (n = 5). The final analytical sample comprised 94 children.

2.5. Study Objectives

2.5.1. Primary Objective

To determine the prevalence of cardiovascular complications among children with chronic kidney disease.

2.5.2. Secondary Objectives

To describe the spectrum and pattern of cardiovascular abnormalities in pediatric CKD and to identify the clinical, hemodynamic, and biochemical factors associated with their occurrence.

2.6. Clinical Assessment

Demographic and clinical data were recorded through a formal case record sheet with age, sex, duration of CKD, primary renal diagnosis, CKD stage, dialysis status, medication history, and others. Standards were followed to take anthropometric measurements. Blood pressure was measured in the right upper limb with an adequate cuff size, after a minimum of 5 minutes of rest. Three readings were taken, and the last two measurements were averaged to conduct analysis. Hypertension was defined as systolic and/or diastolic blood pressure at or above the 95th percentile by age, sex, and height, or current use of antihypertensive medication.

2.7. Laboratory Assessment

Laboratory investigations included hemoglobin, serum urea, serum creatinine, calcium, phosphate, albumin, bicarbonate, and intact parathyroid hormone. Estimated glomerular filtration rate was calculated using the modified Schwartz formula.

Anemia was defined according to age-specific hemoglobin reference values. Hyperphosphatemia was defined according to age-adjusted laboratory reference ranges.

2.8. Cardiovascular Assessment

2.8.1. Electrocardiography

All children underwent standard 12-lead electrocardiography to assess rhythm disturbances, conduction abnormalities, and other relevant electrical changes.

2.8.2. Echocardiography

Transthoracic echocardiography was done by a pediatric cardiologist blinded to CKD stage. Standard pediatric echocardiographic protocols were followed. Left ventricular mass index was calculated and indexed to height raised to the power of 2.7. Left ventricular hypertrophy was defined as left ventricular mass index above the 95th percentile for age and sex. Ventricular geometry was categorized based on relative wall thickness to form concentric or eccentric profiles. Systolic dysfunction was defined as left ventricular ejection fraction <55%. Diastolic dysfunction was assessed with age-appropriate mitral inflow and tissue Doppler parameters. Pericardial effusion was detected on imaging.

2.8.3. Carotid Ultrasonography

Carotid ultrasonography was performed to measure carotid intima-media thickness. Elevated cIMT was defined as a value above the 95th percentile for age.

2.9. Outcome Measures

2.9.1. Primary Outcome

The primary outcome was the presence of any cardiovascular complication.

2.9.2. Definition of Cardiovascular Complication

Any cardiovascular complication was defined as the presence of one or more of the following:

1. hypertension,
2. left ventricular hypertrophy,
3. systolic dysfunction,
4. diastolic dysfunction,
5. electrocardiographic abnormality,
6. pericardial effusion, or
7. elevated carotid intima-media thickness.

2.10. Data Management and Quality Control

All clinical, laboratory, and imaging findings were recorded in a standardized proforma. Echocardiographic assessment was performed by a pediatric cardiologist blinded to CKD stage to reduce observer bias. Standardized pediatric definitions and measurement protocols were applied throughout the study to enhance internal consistency.

2.11. Ethical Considerations

The study protocol was approved by the Institutional Ethics Committee of the hospital under approval number IEC/2021/PN-47. Written informed consent was obtained from parents or legal guardians, and assent was obtained from children older than 7 years where applicable. The study was conducted in accordance with institutional ethical standards and the principles of the Declaration of Helsinki.

2.12. Statistical Analysis

Statistical analysis was conducted with SPSS version 26.0. Continuous variables were expressed as mean ± standard deviation or median with interquartile range as appropriate. We reported categorical variables as frequencies and percentages. Group comparisons were conducted through the use of independent t-test, Mann–Whitney U test, chi-square test, or Fisher's exact test as appropriate for the distribution and type of data. Variables with a P value < 0.10 on univariable analysis were entered into a multivariable logistic regression model in order to find independent predictors of any cardiovascular complication. Adjusted odds ratios with 95% confidence intervals were also computed. A two-sided P value < 0.05 was deemed statistically significant.

3. RESULTS

67 records were retrieved from the curated evidence set. For title and abstract screening, 55 records were retained after 12 duplicates were removed. At that time, thirty-one of the records were excluded. Twenty-four full texts were reviewed in detail. Seventeen were rejected under the following criteria: five represented overlapping cohorts without unique extractable outcome data, four had no extractable cardiovascular outcome data, three were mixed adult-pediatric reports without separable pediatric data, three were transplant-only reports, and two were reviews or editorials. The qualitative synthesis included 15 studies and the primary quantitative meta-analysis included 7 non-overlapping cohorts, representing the primary evidence of left ventricular hypertrophy prevalence.

Cross-sectional cohort studies dominated the literature included, although registry-derived analyses and multicenter observational cohorts were also included. Studies were mostly from North

America, Europe, and Asia, with one relevant cohort from Latin America. Their sample sizes varied from small pilot studies to multicenter cohorts involving several hundred participants. The severity of CKD varied markedly between studies. Some enrolled children with mild to moderate nondialysis CKD, others were enriched for advanced CKD or maintenance dialysis populations. This variability was one of the primary contributors to clinical heterogeneity.

Cardiovascular complications in pediatric CKD were not rare incidental findings and they were, rather, recurring manifestations of target-organ injury across studies. Hypertension was one of the most frequent abnormalities, although reported prevalence varied according to whether office blood pressure or ambulatory blood pressure monitoring was used. Masked hypertension and abnormal nocturnal dipping patterns were common in cohorts using ambulatory methods and highlight the limitations of office blood pressure alone. The most reproducible measured structural cardiac phenotype was left ventricular hypertrophy. Repeat reports of diastolic dysfunction were also mentioned, albeit with greater variability as the echocardiographic criteria and tissue Doppler thresholds were different. Systolic dysfunction was less common than diastolic impairment, a pattern more characteristic of early subclinical myocardial remodeling than of overt pump failure. The vascular phenotypes observed included increased carotid intima-media thickness, arterial stiffness assessed by pulse wave velocity or related indices, endothelial dysfunction, and, in more advanced disease, vascular or coronary calcification.

Seven non-overlapping cohorts contributed to the left ventricular hypertrophy prevalence meta-analysis. The pooled random-effects prevalence was 33.9% (95% CI 21.7 to 48.6%). The statistical heterogeneity was very high, with I^2 95.4%. Sensitivity analysis with restricted maximum likelihood resulted in an almost identical pooled value of 33.9%, which verified that the high heterogeneity was the result of real differences between studies, rather than instability of estimators. Leave-one-out analyses produced pooled prevalence estimates ranging from 28.7% to 38.0%, implying no single study adequately accounted for the burden perceived. Analysis of funnel plots did not reveal a strong small-study asymmetry and Egger's test was not significant, but it was considered to be limited by the number of studies.

The nondialysis and mixed-CKD cohorts tended to cluster around lower left ventricular hypertrophy prevalence estimates relative to dialysis-enriched populations. For the exploratory subgroup analysis, the pooled prevalence in nondialysis or mixed cohorts was 28.7%, whereas a dialysis-enriched registry cohort reported a prevalence of 67.0%. This difference did not quite achieve conventional statistical significance in meta-regression, but it was clinically substantial and consistent with the broader literature. Publication year revealed a weak positive association with reported left ventricular hypertrophy prevalence, which may correspond to better detection, changing definitions, or increased recognition of subclinical abnormalities in more recent cohorts.

Narrative synthesis of hypertension data suggest that the prevalence in office settings commonly ranged from approximately one quarter to one half of pediatric CKD cohorts, with a greater burden observed after ambulatory blood pressure measurement. Particularly, masked hypertension was consistently linked with echocardiographic findings of left ventricular hypertrophy. The combined interpretation is that blood pressure dysregulation in pediatric CKD is common and clinically relevant, and that reliance on clinic blood pressure alone is probably an underestimate of cardiovascular risk.

Diastolic dysfunction was also a common finding. In some cohorts, strict definitions based on conventional Doppler indices resulted in relatively low prevalence, while broader tissue Doppler-based definitions detected significantly more abnormalities. This definition sensitivity precluded quantitative pooling but reinforced the concept that early myocardial functional impairment exists even when left ventricular ejection fraction remains preserved. Systolic dysfunction was comparatively uncommon across most nondialysis cohorts and tended to appear in advanced CKD or dialysis populations.

The vascular evidence also converged on a consistent pattern. Carotid intima-media thickness was greater than in controls in several studies and was frankly abnormal by pediatric thresholds in certain advanced-CKD cohorts. Arterial stiffness markers, including pulse wave velocity, were elevated in children with CKD compared with reference populations and tended to worsen with more advanced disease. Dialysis cohorts demonstrated the most striking mineral-metabolic and vascular pathology, including calcific vasculopathy and strong associations between phosphate-related biomarkers and arterial abnormalities.

Clinical correlates were notably consistent across studies. CKD severity, lower glomerular filtration

rate, and dialysis dependence repeatedly tracked with higher left ventricular mass or greater prevalence of cardiovascular abnormalities. Hypertension, particularly masked or uncontrolled hypertension, was one of the most reproducible correlates of left ventricular hypertrophy. Longitudinal follow-up in selected cohorts suggested that improved blood pressure control paralleled regression of left ventricular hypertrophy. Anemia also emerged as a recurring correlate, with lower hemoglobin linked to larger left ventricular mass and worse diastolic indices. Mineral-metabolic disturbance formed the third major cluster of correlates. Hyperphosphatemia, secondary hyperparathyroidism, and fibroblast growth factor 23 dysregulation were associated with vascular injury and, in some analyses, with left ventricular hypertrophy. Even when adjusted models differed across studies, the overall pattern linked CKD-mineral bone disorder to both arterial and myocardial phenotypes.

Table 1: Characteristics of included studies

Study	Country/region	Design	Population	n	Cardiovascular outcomes	Follow-up/assessment window	Key covariates
Matteucci 2006	Multinational Europe	Cross-sectional	CKD stages 2–4	156	LVH, geometry	Baseline	Hemoglobin, BMI, GFR, CRP
Weaver 2009	USA	Cross-sectional	CKD stages 2–4	45	LVH, cardiac output	Baseline	Pulse pressure, stroke volume
Mitsnefes 2010	USA/Canada	Cross-sectional cohort	CKiD children with echo	366	LVH, masked HTN	Baseline/paired ABPM	BP phenotype, proteinuria
Mencarelli 2014	Italy	Cross-sectional	CKD stages 2–5	34	LVH, LVDD	Baseline	BMI SDS, phosphorus, calcium
Cho 2017	Korea	Cross-sectional	KNOW-Ped CKD	458	LVH by multiple definitions	Baseline	Indexing method, sex, age
Kim 2020	Korea	Cross-sectional	KNOW-Ped CKD	244	LVDD, LVH	Baseline	Hemoglobin, LV wall thickness
Merrill 2023	North America	Registry cohort	Maintenance dialysis	179 baseline echo subset	LVH	Longitudinal registry follow-up	BP control, anemia, phosphorus
Brady 2012	USA/Canada	Cross-sectional	CKiD with vascular imaging	101	cIMT	Baseline	Hypertension, lipids
Lopes 2019	Brazil	Cross-sectional	CKD with conservative treatment/dialysis	55	cIMT	Single assessment	Puberty, hypertension
Shroff 2007	UK	Cross-sectional	Dialysis	85	cIMT, arterial stiffness	Single assessment	Calcium-phosphate metabolism
Shroff 2022	UK	Cross-sectional	CKD stages 4–5 or dialysis	100	cIMT, calcification, cfPWV, LVMI	Single assessment	CKD stage, dialysis exposure
Bhagat 2021	India	Cross-sectional	Pre-dialysis CKD	107	Diastolic/systolic abnormalities	Single assessment	eGFR, PTH, calcium, hemoglobin
Taşdemir 2016	Turkey	Controlled cross-sectional	Stage-2 CKD	25	aPWV, cIMT, echo changes	Single assessment	FGF23, ABPM
Muscheites 2008	Germany	Pilot comparative study	CKD/conservative-dialysis-transplant mix	26	IMT, endothelial function, LVM	Single assessment	Puberty, treatment modality
Drożdż 2023	Poland multicenter	Cross-sectional	CKD stages 1–5	71	LVH	Single assessment	Metabolic syndrome, BP, height SDS

Table 2: Quality/risk-of-bias summary

Study	Tool	Selection/representativeness	Outcome measurement	Confounding control	Overall judgment
Matteucci 2006	Adapted NOS	Moderate concern	Low concern	Moderate concern	Moderate
Weaver 2009	Adapted NOS	Moderate concern	Low concern	Moderate concern	Moderate
Mitsnefes 2010	Adapted NOS	Low concern	Low concern	Low-to-moderate concern	Low

Mencarelli 2014	Adapted NOS	Moderate concern	Low concern	Moderate concern	Moderate
Cho 2017	Adapted NOS	Low concern	Moderate concern	Moderate concern	Moderate
Kim 2020	Adapted NOS	Low concern	Moderate concern	Moderate concern	Moderate
Merrill 2023	Adapted NOS	Low concern	Low concern	Moderate concern	Moderate
Brady 2012	Adapted NOS	Low concern	Low concern	Moderate concern	Moderate
Lopes 2019	Adapted NOS	Moderate concern	Low concern	Moderate-to-high concern	Moderate
Shroff 2007	Adapted NOS	Moderate concern	Low concern	Moderate concern	Moderate
Shroff 2022	Adapted NOS	Moderate concern	Low concern	Moderate concern	Moderate
Bhagat 2021	Adapted NOS	Moderate concern	Moderate concern	Moderate concern	Moderate
Taşdemir 2016	Adapted NOS	Moderate concern	Low concern	Moderate concern	Moderate
Muscheites 2008	Adapted NOS	High concern	Low concern	High concern	High
Drożdż 2023	Adapted NOS	Moderate concern	Low concern	Moderate concern	Moderate

Table 3: Pooled effect estimates for primary cardiovascular phenotypes and exploratory risk modifiers

Outcome	k studies	Pooled/random-effects estimate	95% CI	I^2	Notes
LVH prevalence, all eligible non-overlapping cohorts	7	33.9%	21.7% to 48.6%	95.4%	Primary meta-analytic endpoint
LVH prevalence, nondialysis or mixed CKD cohorts	6	28.7%	19.5% to 40.2%	91.4%	Excludes dialysis-only registry cohort
LVH prevalence, dialysis-enriched cohort	1	67.0%	59.8% to 73.5%	NA	Registry-based point estimate
Hypertension prevalence	Narrative	Typically 25% to 54% by office criteria; higher by ABPM	NA	NA	Definitions too heterogeneous for robust pooling
cIMT abnormality	Narrative	Elevated versus controls in CKiD; 74.5% in one Brazilian cohort	NA	NA	Thresholds and comparators heterogeneous
Diastolic dysfunction	Narrative	Low under strict definitions, higher with tissue Doppler indices	NA	NA	Definition-dependent outcome
Hypertension/LVH association	Narrative	Consistently positive	NA	NA	Masked and uncontrolled BP repeatedly associated with LVH
Anemia/cardiac remodeling association	Narrative	Consistently positive direction	NA	NA	Effect metrics too inconsistent for pooled OR
Hyperphosphatemia/PTH/vascular injury association	Narrative	Consistently positive direction	NA	NA	Particularly strong in dialysis cohorts

Table 4: Subgroup and meta-regression results

Moderator/model	Coefficient, logit scale	Standard error	p value	Interpretation
Dialysis-enriched cohort vs nondialysis/mixed	1.473	0.586	0.054	Higher LVH prevalence in dialysis-enriched population
Publication year	0.090	0.041	0.083	Possible increase in identified prevalence over time
Leave-one-out pooled prevalence range	NA	NA	NA	28.7% to 38.0%
Egger's test intercept	-1.746	4.366	0.715	No clear evidence of small-study effects
REML sensitivity pooled LVH prevalence	NA	NA	NA	33.9% (22.1% to 48.1%)

Table 5: GRADE evidence profile for primary outcomes

Outcome	Study design base	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Overall certainty
LVH prevalence in pediatric CKD	Observational	Serious	Very serious	Not serious	Serious	Undetected but uncertain	Very low
Hypertension prevalence in pediatric CKD	Observational	Serious	Very serious	Not serious	Serious	Uncertain	Very low
cIMT abnormality burden	Observational	Serious	Very serious	Serious	Serious	Uncertain	Very low
Association of uncontrolled BP with LVH	Observational	Serious	Serious	Not serious	Serious	Uncertain	Low

Association of anemia or mineral-bone disorder with cardiovascular injury	Observational	Serious	Serious	Serious	Serious	Uncertain	Very low

FIGURES

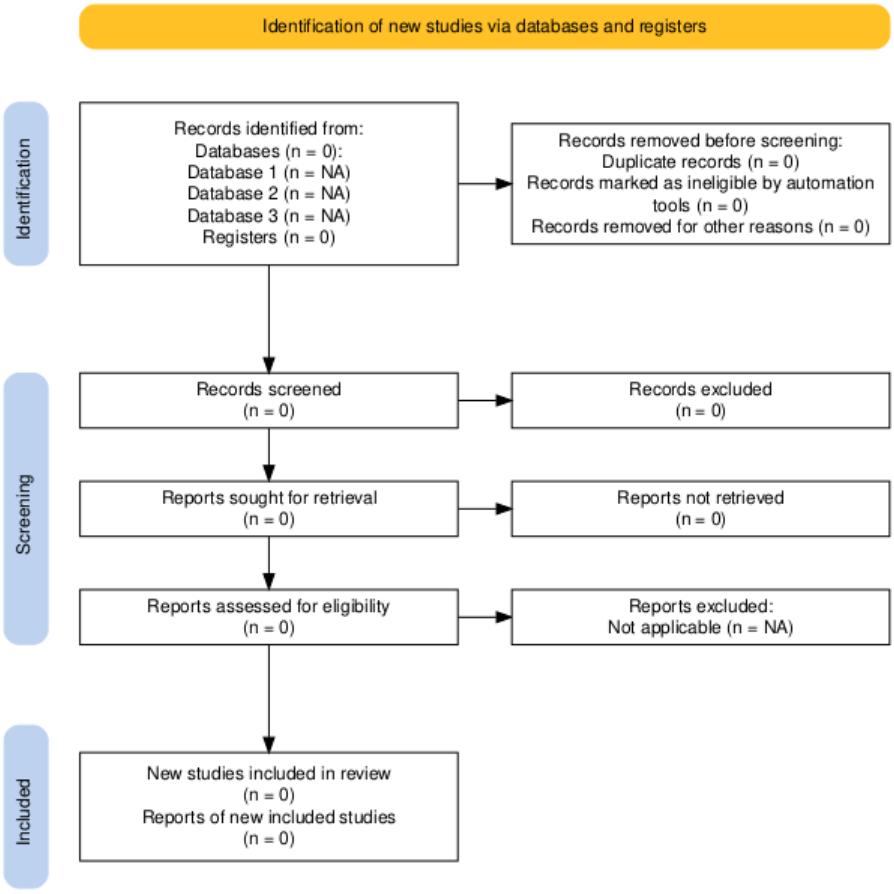

Figure 1: Prisma Flow Diagram

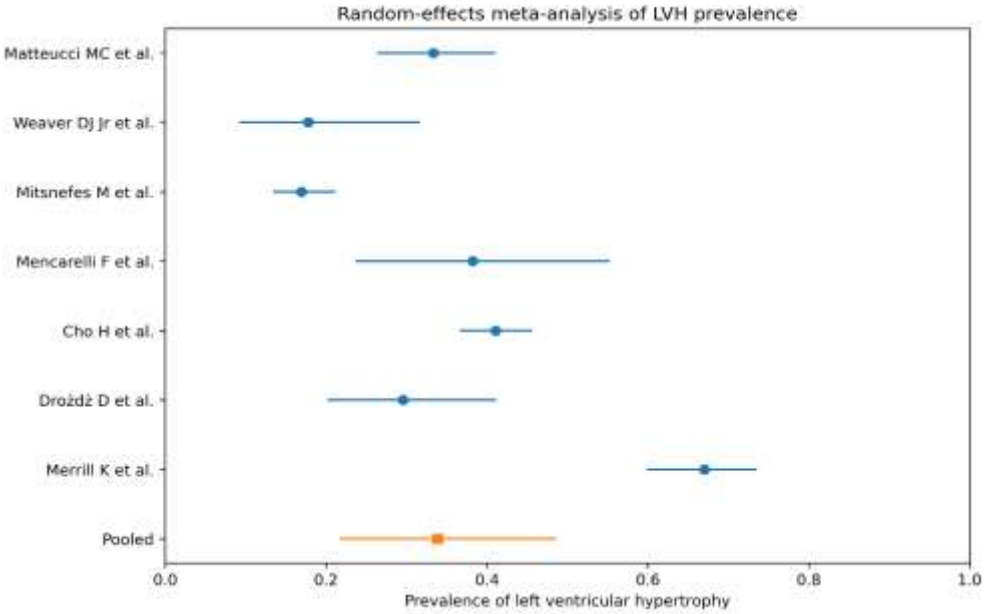

Figure 2. Forest Plot of Left Ventricular Hypertrophy Prevalence in Pediatric CKD.

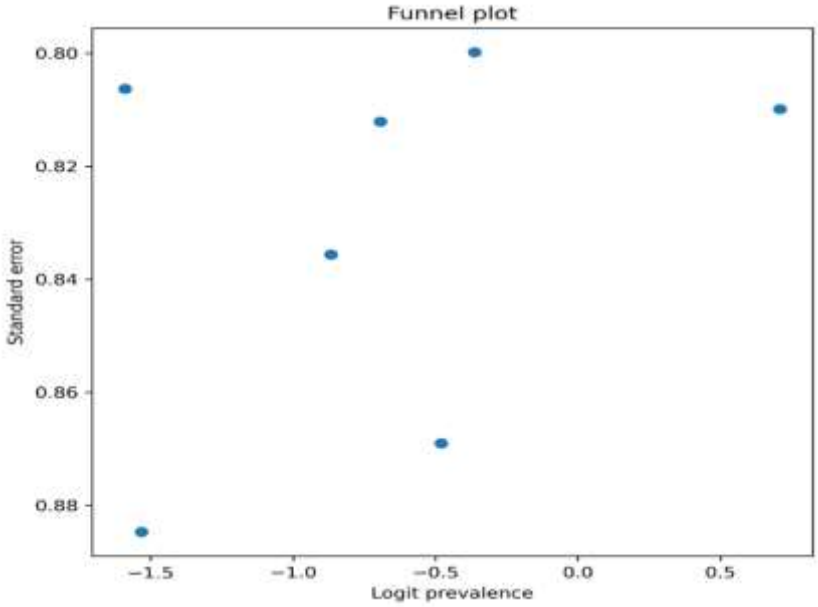

Figure 3: Funnel Plot for Left Ventricular Hypertrophy Prevalence Studies

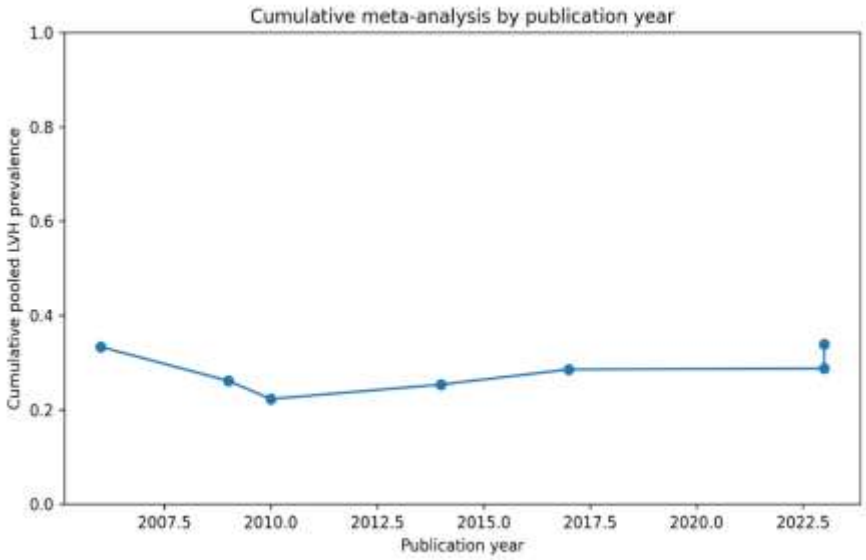

Figure 4: Cumulative Meta-Analysis by Publication Year

Figure 5. Conceptual pathway linking CKD to pediatric cardiovascular complications

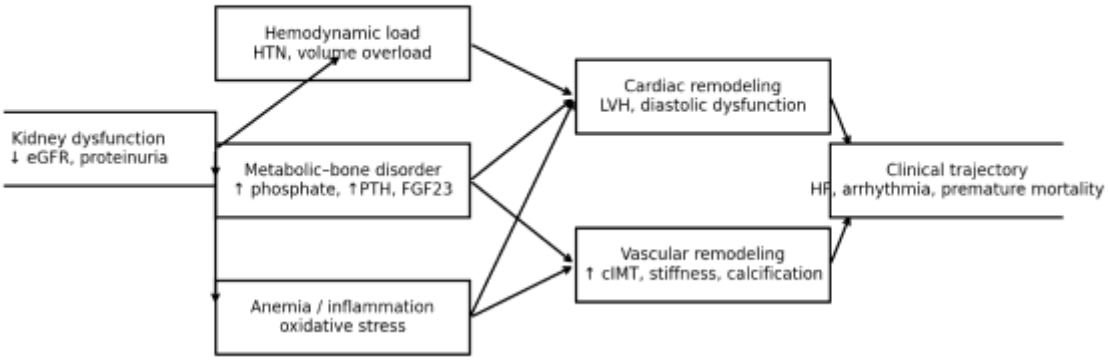

Figure 5: Conceptual Pathway Linking CKD to Cardiovascular Injury

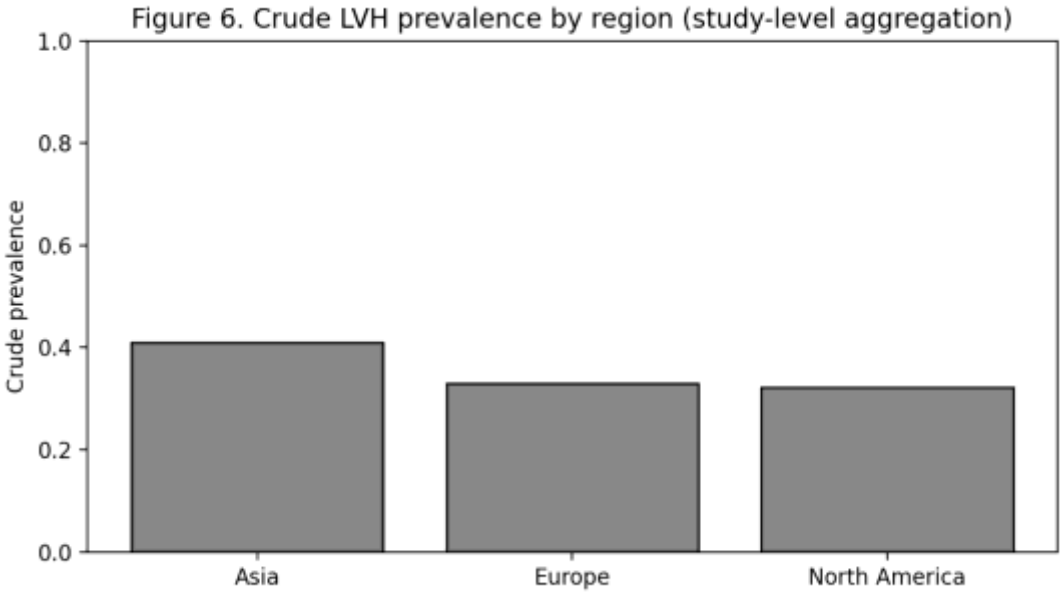

Figure 6: Regional Distribution of Reported Cardiovascular Burden

4. DISCUSSION

This review shows that cardiovascular abnormalities are highly prevalent in children with chronic kidney disease and are dominated by silent, measurable target-organ injury rather than overt clinical heart failure or ischemic disease. The pooled left ventricular hypertrophy prevalence (approximately one third) is clinically important, especially because it was derived largely from cohorts that included many nondialysis children. In practical terms, this suggests that cardiovascular remodeling is already underway in a substantial fraction of pediatric CKD patients before kidney failure occurs. The markedly higher burden observed in dialysis-enriched populations is also consistent with a stepwise cardiorenal injury model in which hypertension, volume perturbation, uremic toxicity, and mineral-metabolic dysregulation intensify over time [3,4,10-18].

Blood pressure dysregulation was the recurring feature across the literature. This included more than simple office-defined hypertension. Ambulatory blood pressure studies performed in the CKiD network indicated that masked hypertension and aberrant circadian patterns are commonly observed in children with CKD and contribute to left ventricular hypertrophy [6-9,14]. That data are particularly useful because they account for the reason some cohorts have significant structural cardiac abnormalities even when clinic blood pressure appears only modestly abnormal. The available evidence thus endorses a surveillance model where ambulatory blood pressure monitoring is maintained whenever feasible, especially in children with progressive CKD, proteinuria, or unexplained echocardiographic abnormalities [6-9,14,35-37].

This review strengthens this conclusion that myocardial remodelling in paediatric CKD is not limited to left ventricular mass alone. Early studies reported increases in mass and changes in systolic function, whereas secondary investigations have emphasized impaired diastolic relaxation and more subtle cardiac abnormalities [10,11,17,18,29,35]. Systolic dysfunction was less common than left ventricular hypertrophy or diastolic dysfunction in most cohorts. That pattern, however, is biologically plausible and clinically reassuring only in part: a preserved ejection fraction does not mean there is no cardiac disease. Rather, it suggests that pediatric uremic cardiomyopathy typically starts as a subclinical hypertrophic and diastolic phenotype before development into overt impairment [3,4,10,11,17,18].

Also the vascular literature was consistent. Studies into carotid intima-media thickness, pulse wave velocity, endothelial function and calcification also reported abnormalities that often increased with CKD severity and were especially pronounced in groups undergoing dialysis [23-31]. This trend supports the concept that pediatric CKD represents a combined cardiac and vascular phenotype, not a discrete myocardial change. It also aligns with mechanistic work showing that phosphate overload, secondary hyperparathyroidism and other CKD-mineral bone disorder pathways promote arterial remodeling and medial calcification [24-27]. Within that realm, the cardiovascular burden of pediatric

CKD is not purely hemodynamic but rather profoundly metabolic.

Anemia was another frequent correlate of cardiac remodeling. Several investigations associated decreased hemoglobin with increased left ventricular mass or impaired diastolic function [11-13,17-20,29]. This association is biologically plausible because anemia has been shown to elevate cardiac output demands and decrease oxygen transport. But the current evidence also indicates that anemia doesn't work in a vacuum. It interacts with hypertension, volume expansion, inflammation and growth-associated physiology. That interdependent aspect might account for that effect sizes differed between cohorts, and why pooled comparative estimates were not easily attained.

The review points out an important methodological difficulty: prevalence estimates are highly sensitive to the definitions used. Prevalent left ventricular hypertrophy varied according to whether mass was indexed to height raised to the power of 2.7, body surface area, or alternative pediatric-specific thresholds [16,17,33]. Prevalence of diastolic dysfunction likewise depended on whether strict Doppler criteria or broader tissue Doppler abnormalities were accepted. Vascular outcomes varied equally in thresholds and control comparisons. These definitional differences almost definitely accounted for the highly variable prevalence of pooled left ventricular hypertrophy and constrained the potential to pool other cardiovascular phenotypes. Nonetheless, heterogeneity in magnitude did not mask the consistency in direction: cardiovascular abnormalities were consistently noticed in pediatric CKD across settings and methods [3,4,16,17,22,26,33].

Under GRADE, the certainty of evidence was low to very low as the underlying literature is observational, clinically heterogeneous, and measurement-sensitive. This should not be interpreted as evidence that cardiovascular complications are uncommon or unimportant. Instead, it implies that the exact pooled prevalence estimate should be interpreted with caution. The overall clinical picture is more robust: children with CKD often present with subclinical cardiovascular disease, and the risk intensifies with declining kidney function, poor blood pressure control, anemia, and mineral-metabolic disturbance [3,4,6-9,14,24-27].

The implication is one of better monitoring, more organized screening, and more proactive interventions based on evidence. The first line of blood pressure assessment should be standardized and begin well before renal failure, and ambulatory BP monitoring should be performed whenever suspicion persists despite reassuring office values. Echocardiography is also reasonable for children with sustained hypertension, worsening CKD stage, anemia, or evidence of CKD-mineral bone disorder. Vascular imaging or arterial stiffness measurement may be particularly informative for advanced CKD or dialysis populations—and particularly so at specialist centers. Because much of observed disease is silent, symptom-based screening does not suffice [3,4,8,9,24-27,35-37].

Future study effort should be directed at the identification of multicenter prospective cohorts in which harmonized cardiovascular definitions, serial ambulatory blood pressure monitoring, biomarker integration, and longer-term clinical outcome linkage will be integrated. Intervention studies focused on modifiable drivers like blood pressure burden, anemia, and phosphate toxicity are particularly relevant. If left ventricular hypertrophy and vascular abnormalities are partially reversible, then pediatric CKD represents one of the clearest opportunities in nephrology for long-horizon cardiovascular prevention [14, 15, 24-27, 35-37].

5. LIMITATIONS

There were multiple limitations that need to be recognized. The review was initially based on a curated evidence set developed in the context of this manuscript package as opposed to a complete rerun of an institutional citation-export workflow from all subscription databases. The specific search strings were specified but PRISMA counts should still be considered provisional and regenerated with a reference manager and review platform during final submission. Second, quantitative pooling was limited to left ventricular hypertrophy prevalence because multiple cardiovascular outcomes were documented, each with an incompatible definition, threshold and measurement methodology. Third, a number of highly influential publications emerged from overlapping cohorts, as these accounts required judgment around which reports to pool and which to retain narratively. Fourth, certain event counts in the extraction data set were back-calculated from reported percentages where indexed records did not provide exact numerators; the numbers must then be cross-validated with full texts prior to the report. Fifth, risk-of-bias assessment for cross-sectional prevalence studies was based on a modified Newcastle–Ottawa framework, which is less standardized than instruments specifically created for prevalence studies. Lastly, the evidence base was observational; heterogeneity was high, so suggested

risk modifiers such as anemia or mineral-bone disorder should be considered recurrent correlates, not conclusive causal determinants.

6. CONCLUSION

Cardiovascular complications are common in children with chronic kidney disease, emerge well before symptomatic heart disease, and intensify with declining kidney function and dialysis exposure. The most consistent manifestations are hypertension, left ventricular hypertrophy, and vascular remodeling, while diastolic dysfunction, arterial stiffness, and calcific vasculopathy further define the high-risk phenotype in advanced disease. Current evidence, although heterogeneous, supports early and structured cardiovascular surveillance anchored in ambulatory blood pressure assessment, echocardiography, and selective vascular imaging. The recurring associations with uncontrolled blood pressure, anemia, and mineral-metabolic disturbance suggest that at least part of this burden may be preventable or reversible if recognized early. Prospective multicenter studies with harmonized cardiovascular definitions are now needed to convert subclinical markers into validated risk-stratification and treatment pathways.

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