

Diagnostic approach and monitoring of chronic kidney disease in the primary care pediatric population

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Abstract

Chronic kidney disease (CKD) has severe consequences on the quality and expectancy of life and is considered a major health problem worldwide. This is, especially relevant in pediatric patients, as they have unique characteristics and a mortality rate 30 times higher (in advanced stages) than healthy people. This review aims to define the minimum components for the diagnostic approach and monitoring of CKD in the pediatric population from primary health care to promote comprehensive care and adequate risk management. For this purpose, we performed a systematic review of the literature with a panel of experts. Based on the evidence, to optimize the definition, diagnosis, and timely treatment of CKD in the pediatric population, we formulated 21 recommendations. These were approved by the research team and peer-reviewed by clinical experts. They will facilitate the definition of the diagnostic approach for CKD in the pediatric population in primary health-care settings, allowing for timely treatment intervention, comprehensive care, and monitoring of this disease.

Keywords: Chronic renal insufficiency. Primary Health Care. Pediatrics. Kidney Diseases.

Abordaje diagnóstico y seguimiento de la enfermedad renal crónica en la población pediátrica desde la atención primaria en salud

Resumen

La enfermedad renal crónica (ERC) tiene graves consecuencias en la calidad y la esperanza de vida, y se considera un importante problema de salud a nivel mundial. Esto es especialmente relevante en pacientes pediátricos, ya que presenta características únicas y una tasa de mortalidad en etapas avanzadas que es 30 veces mayor que en personas sanas. El objetivo de esta revisión fue definir los componentes mínimos para el abordaje diagnóstico y para el seguimiento de la ERC en la población pediátrica desde la atención primaria en salud, con el fin de promover la atención integral y una adecuada gestión del riesgo. Para esto, se realizó una revisión sistemática de la literatura con panel de discusión de expertos. Basándonos en la evidencia, y con el objetivo de optimizar la definición, diagnóstico y tratamiento oportuno de la ERC en

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la población pediátrica, se formularon 21 recomendaciones. Estas fueron aprobadas por el equipo desarrollador y los pares expertos clínicos evaluadores, y permitirán definir de manera oportuna el abordaje diagnóstico de la ERC en la población pediátrica desde la atención primaria en salud, facilitando la intervención temprana, una atención integral y el seguimiento de esta patología.

Palabras clave: Insuficiencia Renal Crónica. Atención Primaria de Salud. Pediatría. Enfermedades Renales.

Introduction

Chronic kidney disease (CKD) has significant consequences on the quality of life of those who suffer from it¹. This aspect has a greater impact on the pediatric population, as in this population, the mortality rate in end-stage renal disease is 30 times higher than in healthy patients². Kidney disease in pediatrics is associated with a 4 times higher risk of kidney failure compared to adults³. In particular, CKD in pediatrics can have medium and long-term effects, such as growth suppression, bone disease, delayed sexual development, chronic anemia, and anorexia. However, available therapeutic interventions can prevent these complications and decrease the rate of disease progression^{4,5}. Late diagnosis leads to consequences such as increased morbidity and mortality. Similarly, late referral to specialized care is associated with more severe clinical manifestations, the need for emergency dialysis with temporary vascular access, and hinders the selection of the renal replacement therapy (RRT) modality and prevents adequate preparation for it⁶. The prevalence of CKD has increased, and this is partly evident due to the higher number of patients using RRT². In Colombia, according to data from the High-cost Account for the 2021 period (from July 1, 2020, to June 30, 2021), the indicator was 213 cases per million in people between 0 and 19 years old and 86 new cases per million. Of the latter, 9.87% were classified as end-stage⁷, which raises questions about the timeliness of diagnosis and treatment of this condition in the Colombian health system. This article seeks to establish the minimum contents for a correct diagnostic approach, follow-up, and referral of patients with kidney disease in pediatrics from primary health care.

Methods

Type and design of the research

A systematic literature review (SLR) with an expert discussion panel.

SLR

The SLR was carried out to identify the minimum components for the diagnostic approach and follow-up of CKD in the pediatric population from primary health care. For this, the following guiding questions were generated for the search:

- What are the minimum strategies and interventions for the diagnosis of CKD in the pediatric population and its adequate follow-up?
- What are the indications and conditions for referral to pediatric nephrology and RRT initiation in pediatric CKD patients?

Eligibility criteria

Studies published between 2006 and 2022, written in English or Spanish, with designs such as topic reviews, observational studies (cross-sectional, case-control, and cohort), SLRs, meta-analyses, clinical practice guidelines, management protocols, and gray literature were included in the study.

Information sources and study selection: The electronic databases PubMed, Cochrane Database of Systematic Reviews, Embase-Medline, Ovid, Lilacs – Virtual Health Library, and Web of Science were used. A manual search was conducted using the snowball technique for related articles based on the title and abstract. The keywords listed in table 1 were used for literature searches and to formulate the search strategy (Supplementary Data 1 and 2).

For the selection of studies, two evaluators (KJSA and LJHP) independently examined the titles and abstracts of the articles for possible inclusion and subsequently independently determined study eligibility using a standardized inclusion form in Rayyan.

Data extraction

This process was carried out using a standardized form, which recorded details of patients, methodology, results, and interventions. The quality of evidence was

Table 1. Search terms DeCS and MeSH used

Category	DeCS terms	MeSH terms	Free terms
Population	Children, infant, adolescent, teenager, adolescence.	Child, pediatrics, infant, newborn, adolescents, adolescence, teenagers.	
	Chronic kidney disease, chronic renal disease, end-stage kidney disease, ESRD, end-stage renal disease.	Chronic kidney disease, end-stage renal disease, end-stage renal failure, Chronic renal failure, ESRD.	
Intervention/Results	Diagnosis, screening.	Diagnosis, clinical decision making, screening.	Detection, GFR estimation
	Patient care management, disease management, evidence-based practice, evidence-based health care, primary health care, the standard of care, clinical practice patterns, prevention, and control.	Disease management, patient care management, primary health care, evidence-based practice, evidence-based management, evidence-based healthcare, standard of care, clinical practice patterns	Follow-up
	Renal replacement therapy, renal dialysis, peritoneal dialysis, hemodialysis transplantation, waiting list, consultation and referral	Renal replacement therapy, renal dialysis, peritoneal dialysis, hemodialysis, renal transplantation, kidney transplantation, waiting list, referral and consultation, referral	Initiation, Pediatric nephrology, Patient referral, criteria
Excluded terms	Acute, pregnancy, genetic, quality of life, liver disease		

DeCS: descritores em ciências da saúde; MeSH: medical subject headings.

assessed according to each type of research design or publication (Supplementary Data 3).

Expert panel and elaboration of recommendations

Two virtual meetings were held with the group of experts delegated by the Colombian Association of Pediatric Nephrology (ACONEPE, for its Spanish acronym), in which the results of the search, data extraction, and quality were presented. With the available evidence, the recommendations were structured together with a group of experts who considered the applicability of each recommendation and its adaptation to the Colombian context. The final document was subjected to external peer review.

Results

Seven hundred and seventy-six articles were identified, and 48 were included in the recommendations. The PRISMA diagram with the SLR results is shown in figure. 1.

Recommendations

Question 1

What are the minimum strategies and interventions for the diagnosis of CKD in the pediatric population and its adequate follow-up?

Screening

RECOMMENDATION 1

– Universal screening for kidney disease in children is not recommended; it should be reserved for those populations with risk factors^{4,8,9}.

RECOMMENDATION 2

– It is recommended to evaluate renal function in at-risk populations^{8,10}. Low birth weight (2500 g or less) and/or prematurity, diabetes, hypertension, heart disease, congenital and urinary tract malformations, multisystemic diseases with potential kidney involvement and compromise, family history of end-stage renal

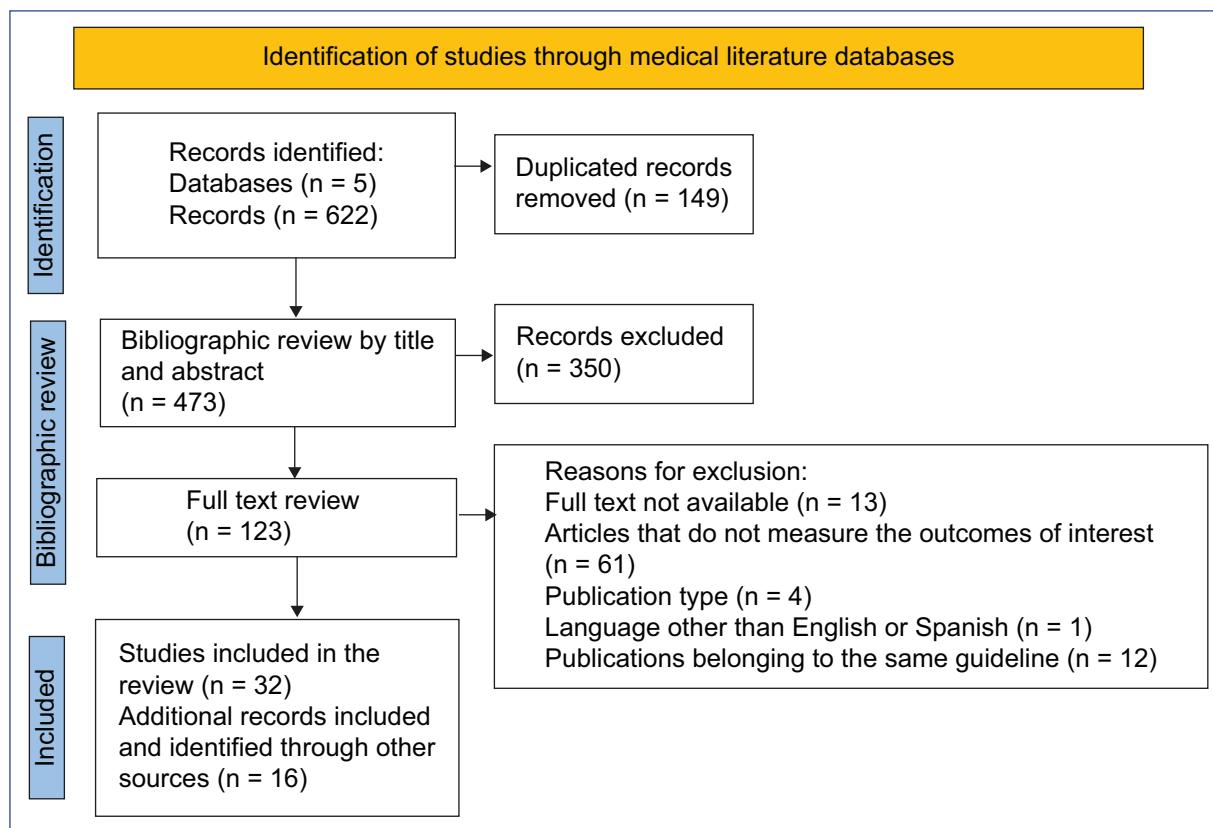


Figure 1. PRISMA diagram with the results of the systematic literature review.

disease (G5), congenital or acquired solitary kidney, history of acute kidney injury of any degree of severity, consumption of nephrotoxic medications (chemotherapeutic agents, lithium, nonsteroidal anti-inflammatory drugs, and calcineurin inhibitors, among others), obesity, and incidental detection of hematuria or proteinuria

Diagnosis

RECOMMENDATION 3

- For diagnosis, it is recommended to perform a complete medical history and anamnesis, including prenatal, perinatal, and childhood history; pathological, family, and pharmacological history; and characterization of current signs and symptoms^{11,12}.

RECOMMENDATION 4

- It is recommended that children with risk factors or signs or symptoms of kidney disease undergo

proteinuria assessment with dipstick or quantitative methods^{10,12}.

RECOMMENDATION 5

- The diagnostic approach can be done as follows in the population with risk factors. (Fig. 2).

RECOMMENDATION 6

- To evaluate renal function in children, measuring serum creatinine and estimating the glomerular filtration rate (GFR) using a predictive formula that includes a height term¹⁰⁻¹⁴ is recommended.

RECOMMENDATION 7

- When available, it is recommended that the measurement of serum creatinine concentration in children and adolescents be performed using a method based on an enzymatic assay due to its better sensitivity. The Jaffe measurement method is recommended in

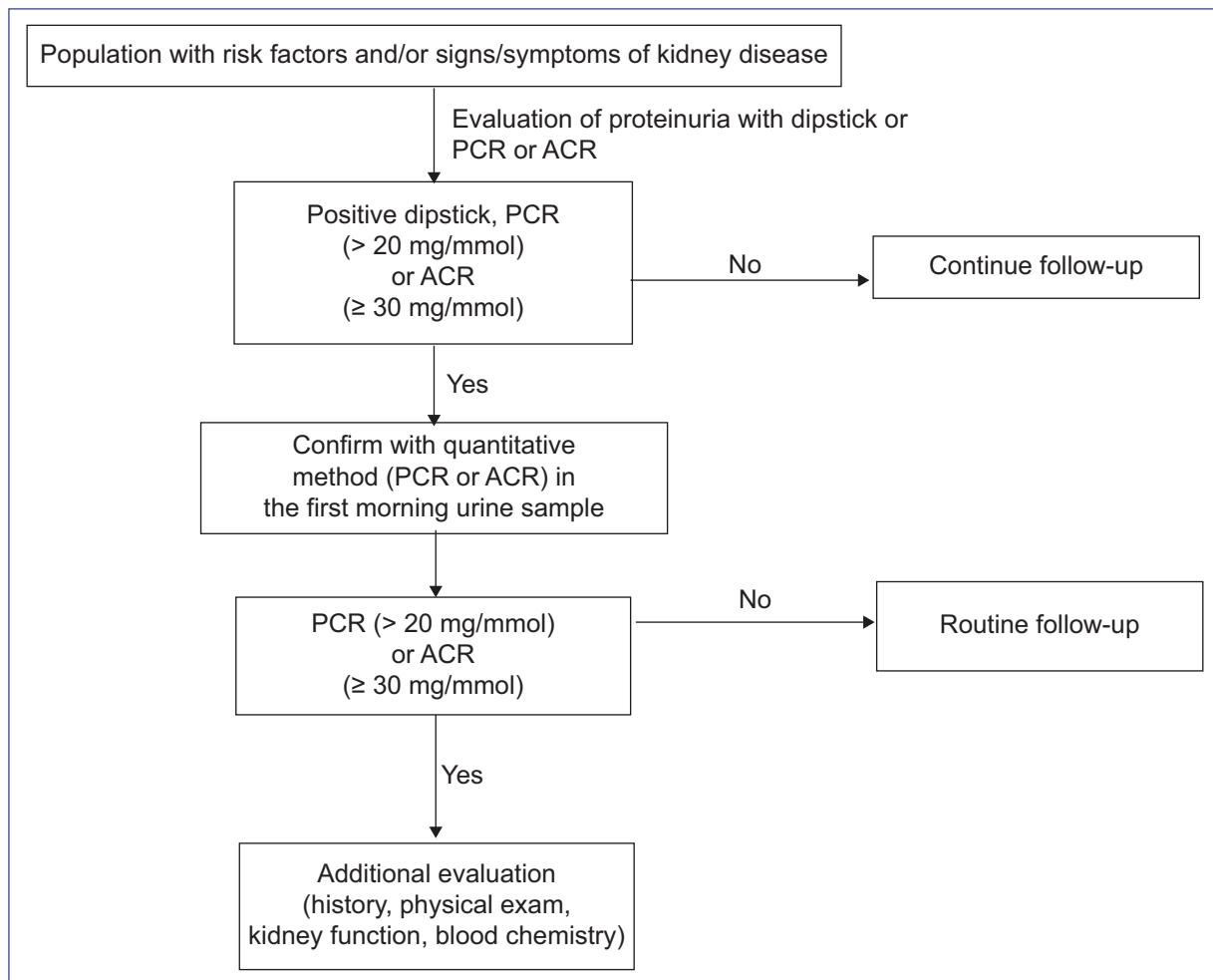


Figure 2. Algorithm for the diagnostic approach in the population with risk factors for chronic kidney disease. PCR: urine Protein to creatinine ratio; ACR: urine albumin to creatinine ratio.

clinical contexts where enzymatic assay is not available¹⁵⁻¹⁷.

RECOMMENDATION 8

- In case of its future availability in the country, the use of Cystatin C for the evaluation of renal function should be reserved for patients with conditions in which serum creatinine measurement is not useful (for example, alterations in muscle mass, nutritional alterations, diseases that generate muscle wasting, spina bifida, anorexia nervosa, and liver cirrhosis)^{12,17-20}.
- Cystatin C is a non-glycosylated protein produced in all nucleated cells at a relatively constant rate. The glomerulus freely filters, it has no active secretion by the tubules and is almost completely reabsorbed in the proximal tubules¹⁷. Its concentration is high at birth and progressively decreases over the next 12-18 months when it

stabilizes similar to adult levels²⁰, which some authors suggest may reflect the physiological maturation of the glomerulus²¹. This biomarker does not depend on muscle mass, dietary protein intake, age, gender, height, or body composition, which is an advantage over creatinine^{8,18,20}. However, conditions such as hyperthyroidism, high-dose corticosteroid therapy, levothyroxine treatment, and C-reactive protein levels can increase^{17,18,20}. It is considered a more accurate and sensitive biomarker for early decreases in renal function^{17,18}.

RECOMMENDATION 9

- If Cystatin C becomes available in the country in the future, it is recommended to be used to calculate GFR using an equation based on this marker instead of using only the serum level for the interpretation of renal function^{12,20}.

Estimation formulas

RECOMMENDATION 10

- Adult GFR estimation formulas (MDRD, CKD-EPI, Cockcroft-Gault) are not recommended in the pediatric population²⁰⁻²⁵.

RECOMMENDATION 11

- The “Modified Schwartz” equation is recommended for estimating GFR in the pediatric population due to its better accuracy^{12,14,24,26,27}.

$$GFR = 0.413 * \left(\frac{\text{Height}}{\text{CrS}} \right)$$

Where height is reported in centimeters and CrS in mg/dL

- Note: This equation should be used when creatinine has been measured using enzymatic methods.
- Since the Schwartz 2009 equation was established in children with GFR below 75 mL/min/1.73 m², all values above this should be reported as >75 mL/min/1.73 m²²⁸.

RECOMMENDATION 12

- In the pediatric population, when creatinine measurement using enzymatic methods is not available and has been performed using the Jaffe method, it is recommended to estimate GFR using the classic Schwartz equation^{16,17,20}.

$$GFR = k * \left(\frac{\text{height}}{\text{CrS}} \right)$$

Where height is reported in centimeters and CrS in mg/dL and where k = 0.33 in preterm infants in the 1st year of life, k = 0.45 in term infants in the 1st year of life, k = 0.55 in children and adolescent females, and k = 0.7 in adolescent males¹⁷.

RECOMMENDATION 13

- It is recommended that for the calculation of GFR based on Cystatin C, the following formula should be used, provided that the biomarker is available in the country and its use is fully indicated^{12,20,29}.

$$GFR = 70.69 \times (\text{cystatin C})^{-0.931}$$

Classification

RECOMMENDATION 14

- It is recommended that the classification and staging of CKD in children older than 2 years be based on cause, albuminuria, and GFR (Tables 2 and 3)¹².

RECOMMENDATION 15

- The classification and staging of CKD in children younger than 2 years can be done based on GFR as normal, moderately reduced, or severely reduced, according to the normal value of GFR for age and standard deviations (Table 2)^{12,20}.

Follow-up

RECOMMENDATION 16

- It is recommended that the risk of progression and CKD staging determine the follow-up frequency. In addition, it should be individualized according to the etiology, comorbidities, and the presence of complications^{10,12,30}.

RECOMMENDATION 17

- In general, it is recommended that the minimum frequency of follow-up for Stages 1 and 2 be 1-2 times/year; for stages 3 and 4, it should be at least 3-4 times/year; and for stage 5, more than 4 times/year¹⁰⁻¹².

Question 2

What are the indications and conditions for referral to pediatric nephrology and RRT initiation in pediatric CKD patients?

RECOMMENDATION 18

- It is recommended to seek early referral (at least 3 months before requiring the initiation of RRT) to a pediatric nephrologist consultation, as the late referral is associated with the requirement for emergency dialysis, the lower opportunity for anticipated or “pre-emptive” kidney transplantation, and a higher probability of progression and morbidity^{3,31,32}.

Table 2. Classification of CKD by GFR in children under 2 years and over 2 years

Classification of CKD in children under 2 years	GFR	
Normal GFR	GFR \leq 1 SD below the mean	
Moderately reduced GFR	GFR > 1 to < 2 SD below the mean	
Severely reduced GFR	GFR > 2 SD below the mean	
GFR category in children over 2 years	GFR (mL/min/1.73 m ²)	Term
G1	≥ 90	Normal or high
G2	60-89	Slightly decreased
G3a	45-59	Slightly to moderately decreased
G3b	30-44	Moderately to severely decreased
G4	15-29	Severely decreased
G5	< 15	Kidney failure

Taken from KDIGO 2012¹² and Zaritsky and Warady, 2014¹³. CKD: chronic kidney disease; GFR: glomerular filtration rate.

Table 3. Categories of Albuminuria in CKD

Category	Albumin excretion rate (AER)	Albuminuria/creatinine in urine ratio (ACR)		Terms
	(mg/24 h)	(mg/mmol)	(mg/g)	
A1	< 30	< 3	< 30	Normal to slightly increased
A2	30-300	3-30	30-300	Moderately increased
A3	> 300	> 30	> 300	Severely increased

Taken from KDIGO 2012¹¹. CKD: chronic kidney disease.

RECOMMENDATION 19

- It is recommended to refer children who meet any of the following criteria to pediatric nephrology^{4,10-12}: GFR < 60 mL/min/1.73 m² (CKD stage 3). Structural, anatomical, or functional renal alteration. Arterial hypertension. Systemic diseases with a high probability of renal involvement or compromise. Obstructive uropathy. Albumin-to-creatinine ratio > 30 mg/g.

the following are present^{2,17,34-38}: signs and symptoms of fluid overload. Metabolic acidosis and failure to thrive, neurological complications associated with uremia, electrolyte abnormalities (hyperkalemia, hyperphosphatemia, hypercalcemia), refractory hypertension, or conditions that warrant it according to the pediatric nephrologist's assessment.

Conclusion

This document aims to define the minimum components for the diagnostic approach and follow-up of CKD in the pediatric population from primary health care, to ensure comprehensive care and adequate risk management. It establishes the criteria for referral to specialized consultation and the initiation of RRT in pediatric patients with CKD. It proposes health risk management strategies in the pediatric population with CKD for their correct application by primary health care professionals.

RECOMMENDATION 20

- It is recommended that in patients with a GFR < 30 mL/min/1.73 m², an educational intervention be carried out with the family and/or caregivers about RRT and its modalities^{4,11,33}.

RECOMMENDATION 21

- It is recommended to initiate RRT when the GFR is < 15 mL/min/1.73 m² or when complications such as

Conflicts of interest

The authors declare no conflicts of interest.

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Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author has this document.

Supplementary material

Supplementary data are available at DOI: 10.24875/BMHIM.23000174. These data are provided by the corresponding author and published online for the benefit of the reader. The contents of supplementary data are the sole responsibility of the authors.

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