Pristop k obravnavi in zdravljenju otrok s kroničo boleznijo ledvic

Management and treatment of children with chronic kidney disease

Avtor / Author

Ustanova / Institute

Mirjam Močnik[1], Nataša Marčun Varda[1,2]

[1] Univerzitetni klinični center Maribor, Klinika za pediatrijo, Maribor, Slovenija; [2] Univerza v Mariboru, Medicinska fakulteta, Maribor, Slovenija

[1] University Medical Centre Maribor, University Division of Paediatrics, Slovenia; [2] University of Maribor, Faculty of Medicine, Maribor, Slovenia

Ključne besede:
kronična ledvična bolezen, otrok, obravnava, preventiva

Key words:
chronic kidney disease, child, management, prevention

Članek prispel / Received
22. 5. 2025
Članek sprejet / Accepted
27. 5. 2025

Naslov za dopisovanje / Correspondence
asist. dr. Mirjam Močnik, dr. med.
mirjam.mocnik@ukc-mb.si
+386 40 323 726

Izvleček

Kronična ledvična bolezen (KLB) je definirana kot motnja ledvične funkcije ali strukture, ki je prisotna več kot tri mesece, in ima pomemben vpliv na zdravje s tveganjem za postopno izgubo ledvične funkcije. Pred kratkim so bila objavljena nova priporočila o obravnavi bolnikov s KLB. Osnovna obravnava otrok s KLB vključuje spodbujanje zdravega življenjskega sloga, preprečevanje napredovanja KLB, zdravljenje zapletov KLB ter pripravo bolnika in njegove družine na nadomestno ledvično zdravljenje, ko je potrebno. Vzdrževanje zdravega življenjskega sloga vključuje natančno spremljanje ledvične funkcije in morebitnih zapletov, spremljanje rasti, prehrane, nevrološkega razvoja in krvnega tlaka. V okviru preprečevanja napredovanja KLB

Abstract

Chronic kidney disease (CKD) is defined as a disorder of kidney function or structure that is present for more than 3 months and has a significant impact on health with the risk of progressive loss of kidney function. New recommendations for the management of patients with CKD have recently been published. The basic management of children with CKD includes promoting a healthy lifestyle, preventing the progression of CKD, treating associated complications, and preparing the patient and their family for renal replacement therapy if needed. Maintaining a healthy lifestyle includes close monitoring of kidney function and potential complications, monitoring growth, nutrition, neurological development, and blood pressure. In the context

https://doi.org/10.18690/actabiomed.283, CC BY 4.0

je pomembno zdravljenje osnovne bolezni, če je mogoče, ter preprečevanje nadaljnje akutne poškodbe ledvic. Dobro urejen krvni tlak in kontrola proteinurije dokazano upočasnjujeta napredovanje ledvične bolezni pri otrocih in sta zato življenjskega pomena. KLB pomembno vpliva na kakovost življenja otroka in njegove družine. Celostna obravnava otroka vključuje obravnavo v multidisciplinarnem timu, ki deluje proaktivno.

of preventing the progression of CKD, it is important to treat the underlying disease, if possible, and prevent further acute kidney injury. Well-controlled blood pressure as well as proteinuria have been shown to slow the progression of kidney disease in children, and are therefore vital. CKD significantly affects the quality of life of a child and his family. Comprehensive treatment of a child includes treatment by a multidisciplinary team that works proactively.

INTRODUCTION

Chronic kidney disease (CKD) in children is a long-term condition characterized by increased risk of gradual loss of kidney function over time. The Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group has recently updated the definition, which describes an abnormality of kidney structure or function, present for a minimum of 3 months, with implications for health (1). To define CKD, one or more markers of kidney damage should be present: albuminuria (albumin-to-creatinine ratio ≥ 30 mg/g or ≥ 3 mg/mmol), urine sediment abnormalities, persistent haematuria, electrolyte and other abnormalities due to tubular disorders, abnormalities determined by histology, structural abnormalities detected by imaging, or a history of kidney transplantation. Decreased glomerular filtration rate (GFR) < 60 ml/min/1.73 m2 without other markers of kidney damage is also defined as CKD (1). The classification system is based on cause, GFR (G1–G5), and albuminuria category (A1–A3). Both categorical classifications are presented in Table 1, summarized from the recent published guidelines (1). It is important to note that healthy children and adolescents should have excellent kidney function; therefore, even an estimated GFR of only stage G2 indicates decreased kidney function and poses a threat to overall health across the lifespan (1).

While CKD is more commonly associated with adults, it significantly affects the paediatric population. Epidemiological studies of all-stage CDK in children

Table 1: Glomerular filtration rate and albuminuria categories in defining chronic kidney disease according 2024 Kidney Disease: Improving Global Outcomes guidelines (1); GFR – glomerular filtration rate; CKD – chronic kidney disease.

GFR (ml/min/1.73 m²) categories in CKD		
G1	≥ 90	Normal or high
G2	60 – 89	Mildly decreased
G3a	45 – 59	Mildly to moderately decreased
G3b	30 – 44	Moderately to severely decreased
G4	15 – 29	Severely decreased
G5	< 15	Kidney failure
Albuminuria categories in CKD		
A1	< 30 mg/24 h or < 3 mg/mmol or < 30 mg/g	Normal to mildly increased
A2	30 – 300 mg/24 h or 3 – 30 mg/mmol or 30 – 300 mg/g	Moderately increased
A3	> 300 mg/24 h or > 30 mg/mmol or > 300 mg/g	Severely increased

Table 2: Aetiology of chronic kidney disease in children, categorized by congenital and acquired causes.

Aetiology type	Aetiology group of causes	Examples
Congenital	Congenital anomalies of the kidney and urinary tract; known more commonly as abbreviation CAKUT	Kidney aplasia/hypoplasia/dysplasia, vesicoureteral reflux, reflux nephropathy, obstructive uropathy anomalies (e.g. posterior urethral valves)
	Hereditary nephropathies	Polycystic kidney disease, Alport syndrome, nephronophthisis, congenital nephrotic syndrome
	Metabolic causes	Cystinosis, primary hyperoxaluria, methylmalonic acidemia
	Syndromic causes	Bardet-Biedl, Joubert, Branchio-oto-renal, Townes-Brocks syndrome
Acquired	Glomerular diseases	Focal segmental glomerulosclerosis, membranoproliferative glomerulonephritis, postinfectious nephropathy, IgA nephropathy
	Acquired obstructive reflux nephropathy	Urolithiasis, iatrogenic causes
	Haemolytic uremic syndrome	Most commonly due infestation with shiga toxin producing E. coli (STEC) and complement dysregulation; some hereditary causes also possible
	Interstitial nephritis	Infections, medications, autoimmune diseases (lupus nephritis)
	Infections	Recurrent pyelonephritis, tuberculosis
	Neoplasms	Wilms tumour most common; may also cause obstruction
	Drug-induced nephrotoxicity	Non-steroidal anti-inflammatory drugs, chemotherapy agents, calcineurin inhibitors, antibiotics (most commonly aminoglycosides), radiation nephritis

are lacking; however, some studies indicate that the prevalence of all-stage CKD among children may be as high as 1% (2,3). Furthermore, CKD in children presents numerous challenges in terms of its diagnosis, treatment, and long-term management. Several unique aspects have also been defined by KDIGO: growth, nutrition, weight/body-surface-area-based drug dosing, neurocognitive development, education support, transition to adult care, and holistic approach to care for the whole family unit (1). The impact of CKD on a child's physical, emotional, and cognitive development underscores the need for a multidisciplinary approach to care. Early intervention with prevention and individualized treatment plans can significantly improve quality of life and long-term outcomes of affected children.

AETIOLOGY

The aetiology of CKD in children varies by age. It includes congenital CKD, more likely diagnosed in infancy, and acquired causes, seen more commonly in later childhood and adolescence. Currently, an increasing number of patients are diagnosed antenatally (4). Congenital disorders are responsible for about two-thirds of all cases in the developed world, while acquired causes predominate in countries in development (5). A comprehensive list of congenital and acquired causes of paediatric CKD is presented in Table 2, with examples provided (5,6). Several diagnostic tools are used to establish the diagnosis, mainly imaging (ultrasound, magnetic resonance), specific laboratory markers, genetic testing, and kidney biopsy (7). In recent years, new management protocols for children with different kidney diseases potentially progressing to CKD have also been published, facilitating treatment of children in accordance with the latest guidelines (8,9).

DIAGNOSIS

After the aetiological determination, the stage of CDK is established based on GFR and albuminuria. In the case of the latter, first morning urine sample is preferred initially with protein/creatinine or albumin/creatinine ratio determination (1). Still, the key to determining the stage of CKD is the measurement or evaluation of GFR, critical also for monitoring

the progression of the disease. Estimating GFR using serum creatinine is the simplest tool, but in children it is not always informative due to changing muscle mass and growth. Nevertheless, serum creatinine measurement is inexpensive and a component of routine biochemical blood tests. Creatinine-based estimated GFR is therefore most widely used to obtain information on kidney function (10). Creatinine-based evaluation should include expected range of values for the age of the patient; also, estimated GFR should be determined with validated equations in children (1). Cystatin C has become an interesting alternative kidney biomarker, and recently, GFR estimation using equations with cystatin C has been gaining more attention (10). The most reliable method is GFR measurement, and for children, it is preferable to avoid use of ionizing agents. This method usually requires an intravenous injection of an exogenous filtration marker, such as iohexol, the use of which is becoming increasingly common, as well as several blood samples to determine the concentration-time decay curve, meaning that the method is burdensome and less appropriate in children (10). This and other studies are focused on simplifying the procedure with the same accuracy to provide a clinically useful method for GFR measurement (11). According to our research, this could be achieved by using only a 2- or 3-point sampling protocol (12).

In children under 2 years of age, the cut-offs from Table 1 do not apply, because they normally have a GFR lower than 60 ml/min/1.73 m2. Instead, the GFR is estimated and defined as mild kidney function impairment when it is decreased to more than one standard deviation from normal, moderate when decreased by two standard deviations, and severe when decreased by three standard deviations (13).

MANAGEMENT APPROACH BY STAGE OF CKD

Management of a child with CKD depends on its stage; however, some key components of management are incorporated in all-stage kidney disease: routine health maintenance with cardiovascular risk stratification, prevention or slowing the progression of kidney disease, preventing and treating the complications of CKD and preparation for kidney replacement therapy, if needed (1). Children with stages G1 and G2 are usually asymptomatic and are therefore harder to identify. They should be closely monitored due to hazard of kidney function deterioration (1,7). Children, who progress to stages G3a and G3b frequently begin to display CKD-associated complications – disorders of fluid and electrolyte balance, anaemia, hypertension, dyslipidaemia, endocrine abnormalities, growth impairment, mineral and bone disorder, and decreased clearance of substances (14). Patients who progress further to stage G4 should start preparations for kidney replacement therapy (1). Albuminuria and GFR should be assessed at least annually in children with CKD and further evaluated when a change in eGFR is >20% or when albumin/creatinine ratio is doubled (1).

ROUTINE HEALTH MAINTENANCE AND TREATMENT OF CKD-RELATED COMPLICATIONS

Critically, since CKD can affect child growth and development, meticulous attention should be paid to interventions aimed at growth and nutrition. Outpatient clinic and hospital visits should include height and weight measurements along with head circumference monitoring in children under 3 years of age. With the progression of paediatric CKD, appetite and nutritional intake decrease, resulting in malnutrition due to poor appetite, decreased intestinal absorption of nutrients, and metabolic acidosis associated with CDK, which affects overall health status. This condition is referred to as fragility phenotype in children with CKD (15). On the other hand, obesity is a risk factor for CKD, since it has the potential to accelerate deterioration of already existing CKD or cause CKD development through the interplay among obesity, insulin resistance, and renal hemodynamics (16). Therefore, it is recommended that children with CKD aim to maintain normal weight. When children do not meet the criteria for normal weight, a nutritional assessment should be carried

out. The initial prescribed energy intake for children with CKD is similar to that for healthy children of the same age. With advancing disease, recommended dietary intake is increased, preferably by oral route or by different feeding tubes, as necessary (1,17). Supplementation should be considered if the child's initial intake does not meet their estimated energy needs and they are not gaining weight or growing at the expected rate. Furthermore, protein restriction is not advised due to the risk of growth impairment and should be higher in patients on peritoneal dialysis due to dialytic protein loss (1,17). Adequate vitamin and mineral intake is equally essential (1).

Routine health maintenance also includes other aspects of general well-being, with special consideration given to cardiovascular risk factors (e.g., sedentary lifestyle, blood pressure, dyslipidaemia, under-/over-weight). Children with CKD should be physically active every day and are advised to maintain a healthy weight (1). Office blood pressure (BP) measurement should be performed at each healthcare visit. Strict BP control is essential to slow the progression of the kidney disease (18). In children with CKD, 24-hour mean arterial pressure by ambulatory BP monitoring should be lowered to ≤50th percentile for age, sex, and height (1,18). Patients with CKD and elevated BP should have echocardiogram as these patients are at risk for left ventricular hypertrophy, associated with adverse cardiovascular disease (19).

Laboratory testing is used to monitor kidney function and detect associated CKD complications; the frequency of assessment is based on the severity of kidney dysfunction. Commonly used tests include serum creatinine, urea, electrolytes with calcium and phosphorus, cystatin C, bicarbonate, alkaline phosphatase, albumin, haemoglobin, indices of iron status (ferritin, iron), fasting lipid profile, 25-hydroxyvitamin D, parathyroid hormone, urinalysis and urinary protein/creatinine ratio. With unexpected results or specific CKD aetiology,

Table 3: Complications of chronic kidney disease in children with their management and treatment (20).

Complication	Management and treatment
Nutrition disorders	Monitoring of anthropometric measurements, optimization of caloric intake, restriction of protein (rarely in children), phosphate, potassium, sodium and renal solutes in the diet according to needs, consideration of dietary supplements for appropriate weight gain, consideration of gastrostomy
Growth impairment	Ensure adequate nutrition, treat acidosis and sodium deficiency, consider growth hormone therapy, prevent/treat mineral bone disease
Chronic kidney disease-mineral and bone disorder	Ensure maintenance of adequate levels of calcium, phosphate, calcium and phosphate product, and parathyroid hormone; if plasma 25-OH vitamin D levels are low, supplement vitamin D3 (cholecalciferol 400–800 U/day); correct metabolic acidosis with sodium bicarbonate; consider vitamin D analogues (calcitriol) if calcium levels are low and parathyroid hormone levels exceed recommended levels; if plasma phosphate levels are high, restrict dietary phosphate, phosphate binders if needed
Neurodevelopmental delay, lower quality of life	Promoting school engagement, preventive counselling for parents and patients
Anaemia	Parenteral erythropoietin once to twice a week or darbepoetin once a week or every two weeks; iron supplementation orally 6 mg/kg/day two to three times a day, intravenously once a week at a maintenance dose of 2 mg/kg to a maximum of 100 mg; supplementation 7 mg/kg to a maximum of 200 mg in case of iron deficiency
Hypertension and cardiovascular disease	Drug therapy (mainly renin-aldosterone-angiotensin system blockers) to achieve normal blood pressure for age; limitation of calcium-containing phosphate binders and daily calcium intake to 2500 mg
Hyperlipidaemia	Lipid-lowering medications
Metabolic acidosis	Adding bicarbonate solutions
Hyponatremia	Adding salt, unless it is dilutional hyponatremia
Hyperkaliemia	Dietary potassium restriction, potassium exchange resins
Proteinuria	Renin-aldosterone-angiotensin system blockers, some calcium channel blockers, and beta-blockers
Hyperphosphatemia	Dietary phosphate restriction, phosphate binders

additional testing is required. Table 3 presents a summary of CKD complications and treatments (20). Targeted and early treatment of the specific aetiology of disease can slow or prevent progression to higher stages of CKD or even end-stage renal disease, optimizing the prognosis of renal outcome (7).

PREVENTION AND SLOWING THE PROGRESSION OF KIDNEY DISEASE

Some paediatric studies have confirmed that the time course of CKD development and progression can be variable and influenced by a number of potentially modifiable and non-modifiable risk factors (21,22). Reported interventions to slow CKD progression include BP control, reducing protein excretion, correcting anaemia, and maintaining normal 25-hydroxyvitamin levels (23,24). Avoiding acute episodes of kidney hypoperfusion and nephrotoxic drugs is of equal importance. Newer medications, such as SGLT2 (sodium-glucose transporter 2) inhibitors, are not yet approved for the treatment of CKD in children, though they have been shown to slow its progression in adult patients with both diabetic and non-diabetic CKD. Because they improve renal hemodynamic adaptation and provide additional beneficial effects on general complications of CKD, SGLT2 inhibitors are potential drugs for the treatment of CKD and glomerular diseases, including those in children (25).

Chronic kidney disease is a unique and challenging disease in childhood, the complications of which affect not only the child but also the person the child will grow up to be. Looking to the future of paediatric nephrology patients, we are aware that the leading cause of morbidity and mortality is cardiovascular risk. The common denominator is atherosclerosis, which is accelerated in these patients. Several newer functional (pulse wave velocity) and imaging techniques (intima media thickness, ultrasound elastography) and biochemical markers (salusins, adropine, kidney-injury molecule 1, inflammatory markers, miRNA ...) are being researched to facilitate accurate assessment of cardiovascular risk in children with CKD and timely intervention (26–29).

NOVEL THERAPIES FOR CKD IN ADULTS AND CHILDREN

A range of novel therapies for CKD are emerging, primarily in the adult population, with promising potential for application in paediatric care. We emphasize the critical role of basic, translational, and clinical research in advancing this field, along with the need to better define combination therapies that target multiple disease pathways.

In addition to SGLT2 inhibitors, finerenone – a non-steroidal mineralocorticoid receptor antagonist with anti-inflammatory and anti-fibrotic properties – is gaining traction. It has demonstrated cardio-renal benefits in adults with type 2 diabetes mellitus (30). Ongoing studies are currently exploring its use in children with CKD and proteinuria (31). For paediatric patients with obesity, growing evidence suggests the possible therapeutic role of glucagon-like peptide-1 receptor (GLP-1R) agonists (32).

Inherited kidney diseases are a significant cause of CKD in children, posing a lifelong burden. Exciting progress is being made in treatment strategies, particularly in the realm of genetic therapies, which are rapidly advancing. Gene therapy is being investigated in animal models for conditions such as Alport syndrome, Dent disease, Fabry disease, primary hyperoxaluria, and cystinosis, with some studies progressing to preclinical stages, e.g. in both autosomal dominant and recessive polycystic kidney diseases (33).

Other therapeutic agents under investigation include microRNAs for Alport syndrome, PCSK9 inhibitors and sparsentan for congenital nephrotic syndrome, and calcineurin inhibitors and vaptans for polycystic kidney diseases. For tubulopathies, drugs such as indomethacin, acetazolamide, spironolactone, cyclooxygenase inhibitors, and hydrochlorothiazide are being explored. In Fabry disease, lucerastat, pegunigalsidase-alfa, and adeno-associated virus vectors are under study. Treatments for primary hyperoxaluria include RNA interference-based therapies such as Lumasiran and Nedosiran, as well as stiripentol, while cysteamine bitartrate continues to be evaluated and used for cystinosis (34, 34).

More recently, the therapeutic landscape has seen a surge in agents targeting complement system inhibition. Promising data have emerged for agents such as eculizumab, ravulizumab, crovalimab, avacopan, danicopan, iptacopan, pegcetacoplan, and narsoplimab. These therapies have shown effectiveness in reducing proteinuria and stabilizing kidney function in various complement-mediated kidney disorders. Given their high efficacy and target specificity, these drugs hold the potential to significantly improve outcomes in affected children (35).

Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin II receptor blockers (ARBs), already established in the management of hypertension, proteinuria, and CKD progression, continue to be investigated in paediatric populations. Current research is focused on evaluating whether combined ACEI and ARB therapy offers additive benefits and improved clinical outcomes (36).

Recent advancements in paediatric renal replacement therapy (RRT) have led to the development of specialized devices tailored for neonates and infants, addressing the limitations of adapting adult-sized equipment for small patients, and offering precise fluid management and improved safety profiles. These technologies have demonstrated effectiveness in managing acute kidney injury and fluid overload in critically ill newborns, expanding the therapeutic options available for this vulnerable population (37). Finally, novel palliative interventions for children with advanced CKD involve life participation and care plan development, allowing for holistic and family-centred management (38).

CONCLUSIONS

In summary, treating children with CKD involves promoting a healthy lifestyle, slowing disease progression, managing complications, and preparing for potential renal replacement therapy. This requires regular monitoring, addressing underlying causes, preventing further kidney damage, and ensuring proper nutrition, blood pressure, and proteinuria control. Care should be multidisciplinary and family-centred, starting early to support the child's overall well-being and quality of life.

REFERENCES

1. Stevens PE, Ahmed SB, Carrero JJ, Foster B, Francis A, Hall RK, et al. KDIGO 2024 Clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int. 2024;105:S117-314.
2. Harambat J, Madden I, Hogan J. Épidémiologie de la maladie rénale chronique chez l'enfant. Néphrologie Thérapeutique. 2021;17:476-84.
3. Harada R, Hamasaki Y, Okuda Y, Hamada R, Ishikura K. Epidemiology of pediatric chronic kidney disease/kidney failure: learning from registries and cohort studies. Pediatr Nephrol. 2022;37:1215-29.
4. Costigan CS, Rosenblum ND. Antenatally diagnosed kidney anomalies. Pediatr Clin North Am. 2022;69:1131-47.
5. Harambat J, Van Stralen KJ, Kim JJ, Tizard EJ. Epidemiology of chronic kidney disease in children. Pediatr Nephrol. 2012;27:363-73.
6. Warady BA, Chadha V. Chronic kidney disease in children: the global perspective. Pediatr Nephrol. 2007;22:1999-2009.
7. Romagnani P, Remuzzi G, Glassock R, Levin A, Jager KJ, Tonelli M, et al. Chronic kidney disease. Nat Rev Dis Primer. 2017;3:17088.
8. Savige J, Lipska-Zietkiewicz BS, Watson E, Hertz JM, Deltas C, Mari F, et al. Guidelines for genetic testing and management of Alport syndrome. Clin J Am Soc Nephrol. 2022;17:143-54.
9. Vivarelli M, Samuel S, Coppo R, Barratt J, Bonilla-Felix M, Haffner D, et al. IPNA clinical practice recommendations for the diagnosis and management of children with IgA nephropathy and IgA vasculitis nephritis. Pediatr Nephrol. 2025;40:533-69.
10. Pottel H, Schwartz GJ. Measuring and estimating the GFR in children: state of the art in 2025. Pediatr Nephrol. 2025;[epub ahead of print].
11. Swinkels DW, Hendriks JCM, Nauta J, De Jong MCJW. Glomerular filtration rate by single-injection inulin clearance: definition of a workable protocol for children. Ann Clin Biochem Int J Lab Med. 2000;37:60-6.
12. Golob Jančič S, Klavž J, Filipič M, Močnik M, Marčun Varda N. Comparison of different eGFR formulas to measured glomerular filtration rate using iohexol in children and adolescents with mild chronic kidney disease. Eur J Pediatr. 2024;184:107.
13. Schwartz GJ, Furth SL. Glomerular filtration rate measurement and estimation in chronic kidney disease. Pediatr Nephrol. 2007;22:1839-48.
14. Obrador GT, Pereira BJG. Systemic complications of chronic kidney disease: pinpointing clinical manifestations and best management. Postgrad Med. 2002;111:115-22.
15. 15. Sgambat K, Matheson MB, Hooper SR, Warady B, Furth S, Moudgil A. Prevalence and outcomes of fragility: a frailty-inflammation phenotype in children with chronic kidney disease. Pediatr Nephrol. 2019;34:2563-9.
16. Barlabà A, Grella C, Tammaro M, Petrone D, Guarino S, Miraglia Del Giudice E, et al. Kidney function evaluation in children and adolescents with obesity: a not-negligible need. Eur J Pediatr. 2024;183:3655-64.
17. Shaw V, Polderman N, Renken-Terhaerdt J, Paglialonga F, Oosterveld M, Tuokkola J, et al. Energy and protein requirements for children with CKD stages 2–5 and on dialysis – clinical practice recommendations from the Pediatric Renal Nutrition Taskforce. Pediatr Nephrol. 2020;35:519-31.
18. Flynn JT, Urbina EM, Brady TM, Baker-Smith C, Daniels SR, Hayman LL, et al. Ambulatory blood pressure monitoring in children and adolescents: 2022 update: a scientific statement from the American Heart Association. Hypertension. 2022;79:e114-e24.
19. Mitsnefes M, Flynn J, Cohn S, Samuels J, Blydt-Hansen T, Saland J, et al. Masked hypertension associates with left ventricular

hypertrophy in children with CKD. J Am Soc Nephrol. 2010;21:137-44.
20. Marčun Varda N. Ledvično zdravje in preventiva kronične ledvične bolezni pri otrocih. In: Marčun Varda N, ed. IV. pediatrična nefrološka šola: Preventiva in zdravljenje kronične ledvične bolezni: zbornik predavanj. Maribor: Univerzitetni klinični center Maribor;2022.p. 49-59.
21. ESCAPE Trial Group; Wühl E, Trivelli A, Picca S, Litwin M, Peco-Antic A, Zurowska A, et al. Strict blood-pressure control and progression of renal failure in children. N Engl J Med. 2009;361:1639-50.
22. Fathallah-Shaykh SA. Proteinuria and progression of pediatric chronic kidney disease: lessons from recent clinical studies. Pediatr Nephrol. 2017;32:743-51.
23. Warady BA, Abraham AG, Schwartz GJ, Wong CS, Muñoz A, Betoko A, et al. Predictors of rapid progression of glomerular and nonglomerular kidney disease in children and adolescents: The Chronic Kidney Disease in Children (CKiD) Cohort. Am J Kidney Dis. 2015;65:878-88.
24. Fathallah-Shaykh SA, Flynn JT, Pierce CB, Abraham AG, Blydt-Hansen TD, Massengill SF, et al. Progression of pediatric CKD of nonglomerular origin in the CKiD Cohort. Clin J Am Soc Nephrol. 2015;10:571-7.
25. Cirillo L, Ravaglia F, Errichiello C, Anders HJ, Romagnani P, Becherucci F. Expectations in children with glomerular diseases from SGLT2 inhibitors. Pediatr Nephrol. 2022;37:2997-3008.
26. Savant JD, Betoko A, Meyers KEC, Mitsnefes M, Flynn JT, Townsend RR, et al. Vascular stiffness in children with chronic kidney disease. Hypertension. 2017;69:863-9.
27. Ayoob RM, Mahan JD. Pediatric CKD-MBD: existing and emerging treatment approaches. Pediatr Nephrol. 2022;37:2599-614.
28. Daiber A, Steven S, Weber A, Shuvaev VV, Muzykantov VR, Laher I, et al. Targeting vascular (endothelial) dysfunction. Br J Pharmacol. 2017;174:1591-619.
29. Močnik M, Marčun Varda N. Cardiovascular risk factors in children with obesity, preventive diagnostics and possible interventions. Metabolites. 2021;11:551.
30. Romagnani P, Agarwal R, Chan JCN, Levin A, Kalyesubula R, Karam S, et al. Chronic kidney disease. Nat Rev Dis Primers. 2025;11:8.
31. Schaefer F, Montini G, Kang HG, Walle JV, Zaritsky J, Schreuder MF, et al. Investigating the use of finerenone in children with chronic kidney disease and proteinuria: design of the FIONA and open-label extension studies. Trials. 2024;25:203.
32. Larkins NG, Craig JC. Hypertension and cardiovascular risk among children with chronic kidney disease. Curr Hypertens Rep. 2024;26:389-98.
33. Wang G, Liao M, Tan DJ, Chen X, Chao R, Zhu Y, et al. Advances in diagnosis and treatment of inherited kidney diseases in children. Kidney Dis (Basel). 2024;10:558-72.
34. Dejban P, Lieske JC. New therapeutics for primary hyperoxaluria type 1. Curr Opin Nephrol Hypertens. 2022;31:344-50.
35. Antonucci L, Thurman JM, Vivarelli M. Complement inhibitors in pediatric kidney diseases: new therapeutic opportunities. Pediatr Nephrol. 2024;39:1387-404.
36. Stotter BR, Ferguson MA. Should ACE inhibitors and ARBs be used in combination in children? Pediatr Nephrol. 2019;34:1521-32.
37. Parolin M, Ceschia G, Vidal E. New perspectives in pediatric dialysis technologies: the case for neonates and infants with acute kidney injury. Pediatr Nephrol. 2024;39:115-23.
38. House TR, Wightman A. Enabling flourishing: novel approaches in palliative medicine for children with advanced kidney disease. Curr Opin Nephrol Hypertens. 2023;32:41-8.