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Chronic Kidney Disease in Paediatries: An Overview of Complication and Pharmacology Management

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ABSTRACT:

Children's chronic kidney disease (CKD), which impairs growth, development, and general quality of life, is a rising health concern. It is divided into five stages according to eGFR and is typified by kidney injury or diminished function that lasts longer than three months. Inherited diseases, glomerulopathies, and congenital anomalies (CAKUT) are common causes. Clinical assessment, laboratory testing, imaging, and occasionally biopsy are all part of the diagnosis process. A multidisciplinary strategy involving nephrologists, paediatricians, and dietitians is necessary for management. Pharmacological treatments include ACE inhibitors, erythropoiesis-stimulating drugs, phosphate binders, and diuretics; non-pharmacological techniques concentrate on blood pressure management, diet, and psychosocial support. Dialysis or transplantation are examples of renal replacement treatment (RRT) required for ESRD. Roxadustat, SGLT2 inhibitors, and precision medicine advancements provide hope for reducing the course of the disease and enhancing results.

Keywords: *Chronic Kidney Disease, Pediatric CKD, Renal Replacement Therapy, Early Diagnosis, Multidisciplinary Management, SGLT2 inhibitors.*

Introduction

A child's growth, development, and general quality of life are all significantly impacted by chronic kidney disease (CKD), which has become a major health concern in children. Kidney damage or a decline in kidney function that lasts longer than three months is known as chronic kidney disease (CKD). A child's capacity to flourish in daily activities may be hampered by a number of issues that may arise as the illness worsens and affect both physical and mental health. Improving clinical outcomes, postponing the onset of end-stage renal disease (ESRD), and decreasing the progression of chronic kidney disease (CKD) all depend on early identification. Prompt intervention can help prevent further kidney damage and contribute to a better quality of life for affected children. Managing pediatric CKD requires a holistic, team-based approach. This involves collaboration among specialists, including nephrologists who specialize in kidney care, dietitians who offer essential nutritional guidance, and pediatricians who monitor the child's overall health and development. By working together, these healthcare providers can effectively address the challenges of CKD and deliver the best possible care to children living with this condition. Paediatric CKD management necessitates a comprehensive, team-based strategy. This calls for cooperation between experts, such as paediatricians who keep an eye on the child's general health and development, dietitians who provide crucial nutritional advice, and nephrologists who specialise in kidney care. Children with CKD can receive the best care possible if these healthcare professionals collaborate to successfully address the condition's problems . [1,2].

Classification of Disease and Epidemiology

Classification

The Kidney Disease: Improving Global Outcomes (KDIGO) guidelines classify CKD into five stages based on estimated glomerular filtration rate (eGFR):

Stage 1: eGFR ≥ 90 mL/min/1.73 m² (normal or increased function with kidney damage)

Stage 2: eGFR 60–89 mL/min/1.73 m² (mild dysfunction)

Stage 3: eGFR 30–59 mL/min/1.73 m² (moderate dysfunction)

Stage 4: eGFR 15–29 mL/min/1.73 m² (severe dysfunction)

Stage 5: eGFR < 15 mL/min/1.73 m² (end-stage renal disease) [3].

Epidemiology

Chronic kidney disease (CKD) in children is rarer than in adults, with an estimated prevalence of 18 cases per million children. The primary cause of CKD in children is congenital anomalies of the kidney and urinary tract (CAKUT), followed by glomerulopathies and inherited kidney diseases. The burden of the disease is particularly high in low- and middle-income countries, where late diagnosis and limited access to healthcare resources contribute to its increased With an estimated prevalence of 18 occurrences per million children, chronic kidney disease (CKD) in children is less common than in adults. Congenital kidney and urinary tract abnormalities (CAKUT) are the main cause of chronic kidney disease (CKD) in children. Glomerulopathies and hereditary kidney illnesses follow. Due to delayed diagnosis and restricted access to healthcare resources, the condition is more common in low- and middle-income nations, where its burden is especially significant [4].

Types of Pediatric CKD

Congenital CKD : refers to kidney disorders that are present from birth and are frequently brought on by structural abnormalities such renal hypoplasia, renal dysplasia, or congenital anomalies of the kidney and urinary tract (CAKUT).

Hereditary CKD includes hereditary disorders including Alport syndrome and polycystic kidney disease (PKD).

Acquired CKD happens as a result of autoimmune disorders such lupus nephritis, infections, or nephrotic syndrome**.** [5,6].

Clinical Evaluation

Symptoms:

Growth retardation,

anemia,

hypertension,

polyuria,

nocturia,

electrolyte imbalances.

Family history and genetic analysis (especially for hereditary kidney diseases).

Laboratory Investigations

- Serum creatinine and eGFR estimation
- Urinalysis (proteinuria, hematuria)
- Electrolyte levels (sodium, potassium, calcium, and phosphorus)
- Serum albumin and lipid profile
- Imaging and Biopsy
- Ultrasonography (USG): To detect structural anomalies.
- Renal biopsy: Indicated in suspected glomerular diseases [7,8].

Non-Pharmacological Treatment

Nutritional support is essential in CKD management, with protein intake controlled according to the disease stage. In advanced CKD, sodium and potassium intake should be restricted to prevent complications.

Blood pressure management involves regular monitoring and implementing lifestyle changes to help control hypertension.

Psychosocial support includes mental health evaluations to address the emotional challenges associated with the chronic nature of the disease [9,10] .

Pharmacological Treatment

Angiotensin-Converting Enzyme (ACE) inhibitors and Angiotensin Receptor Blockers (ARBs) help decrease proteinuria and slow the progression of CKD.

Erythropoiesis-Stimulating Agents (ESAs) treat CKD-related anemia by stimulating red blood cell production. Common types include epoetin alfa and darbepoetin alfa, requiring careful dosing and monitoring.

Phosphate binders lower serum phosphate, and vitamin D analogues regulate calcium and parathyroid hormone to manage mineral bone disorders in CKD.

Diuretics help manage fluid overload and hypertension by increasing urine output. They are commonly used in conditions like heart failure, CKD, and hypertension.

Growth hormone therapy is used in children with CKD-associated growth failure to promote growth and development. It helps stimulate growth factors and overcome the growth deficiencies caused by kidney disease [11,12].

RAAS Inhibitors (for hypertension and proteinuria):

- Enalapril (0.05–0.6 mg/kg/day, max 40 mg/day) inhibits angiotensin-converting enzyme (ACE), reducing angiotensin II levels, leading to vasodilation and decreased glomerular pressure, but can cause hyperkalemia, hypotension, and cough.
- Losartan (0.7 mg/kg/day, max 50 mg/day) blocks angiotensin II receptors (AT1), reducing vasoconstriction and proteinuria, but may lead to dizziness, hyperkalemia, and hypotension.

Antihypertensives (for blood pressure control):

- Amlodipine (0.1–0.6 mg/kg/day, max 10 mg/day) is a calcium channel blocker that relaxes vascular smooth muscles, lowering blood pressure, but can cause edema, flushing, and dizziness.
- Propranolol (0.5–4 mg/kg/day, max 640 mg/day) is a beta-blocker that reduces heart rate and cardiac output, but may cause bradycardia, fatigue, and bronchospasm.

Phosphate Binders (for hyperphosphatemia):

Calcium carbonate (30–75 mg/kg/day) binds dietary phosphate in the gut, preventing its absorption, but may cause hypercalcemia and constipation.

Sevelamer (100–400 mg/kg/day) binds phosphate without calcium, reducing serum phosphate levels, though it can cause nausea and diarrhea.

Vitamin D Analogues (for secondary hyperparathyroidism):

- Calcitriol (10–20 ng/kg/day) activates vitamin D receptors, increasing calcium absorption and suppressing PTH, but may cause hypercalcemia and hyperphosphatemia.
- Alfacalcidol (0.01–0.05 mcg/kg/day) has a similar mechanism and side effects to calcitriol.

Erythropoiesis-Stimulating Agents (ESAs) & Iron Therapy (for anemia):

- Epoetin alfa (50–100 units/kg 2-3 times/week) stimulates red blood cell production, treating anemia but may cause hypertension and thrombosis.
- Darbepoetin alfa (0.45 mcg/kg once weekly) has a longer half-life but similar side effects.
- Iron sucrose (IV) (1–3 mg/kg/dose) replenishes iron stores for hemoglobin synthesis but may cause hypotension and nausea.
- Ferrous sulfate (oral) (3–6 mg/kg/day) is used for iron deficiency anemia but may cause constipation and GI upset.

Sodium Bicarbonate (for metabolic acidosis):

- Sodium bicarbonate (1–2 mEq/kg/day) neutralizes acid to correct metabolic acidosis but may cause bloating and hypernatremia.

Diuretics (for fluid overload and hypertension):

- Furosemide (0.5–2 mg/kg/dose, max 6 mg/kg) inhibits the Na-K-2Cl transporter in the loop of Henle, causing diuresis, but can lead to hypokalemia and dehydration.
- Hydrochlorothiazide (0.5–1 mg/kg/day, max 50 mg/day) inhibits Na-Cl reabsorption in the distal tubule, promoting diuresis but may cause hyponatremia and hypokalemia.

Growth Hormone Therapy (for growth failure):

Recombinant human growth hormone (rhGH) (0.05 mg/kg/day) stimulates IGF-1 production, promoting growth but may cause hyperglycemia and intracranial hypertension.

Lipid-Lowering Agents (for cardiovascular risk reduction):

- Atorvastatin (10–20 mg/day) inhibits HMG-CoA reductase, reducing cholesterol synthesis, but may cause myopathy and liver dysfunction.

Immunosuppressants (for autoimmune-related CKD):

- Prednisolone (1–2 mg/kg/day) suppresses inflammation and immune response but may cause weight gain, immunosuppression, and Cushing's syndrome.
- Mycophenolate mofetil (600–1200 mg/m²/day) inhibits T- and B-cell proliferation, but can cause GI upset and bone marrow suppression.
- Tacrolimus (0.05–0.3 mg/kg/day) inhibits calcineurin, reducing T-cell activation, but may cause nephrotoxicity and hypertension [11,12].

Renal Replacement Therapy (RRT) in Pediatric Patients

When conservative treatment is insufficient for young patients with end-stage kidney disease (ESKD) or severe acute kidney injury (AKI), renal replacement therapy (RRT) is necessary. Hemodialysis (HD), peritoneal dialysis (PD), and kidney transplantation are the three primary forms of RRT in children. The child's age, weight, underlying medical condition, vascular access, and resource availability all influence the decision [13].

1. **Peritoneal Dialysis (PD)**

Indication:

PD is the preferred initial renal replacement therapy (RRT) for infants and younger children due to its ease of use and better hemodynamic stability.

Types:

Continuous Ambulatory Peritoneal Dialysis (CAPD): Requires manual fluid exchanges several times a day.

Automated Peritoneal Dialysis (APD): Uses a machine (cycler) to perform dialysis during nighttime.

Mechanism:

A catheter is inserted into the peritoneal cavity, allowing dialysis fluid (dialysate) to be introduced. The peritoneal membrane acts as a filter, enabling the removal of waste products and excess fluid, which are later drained out.

Advantages:

• Reduces cardiovascular stress since it avoids abrupt fluid changes;

• Can be done at home, improving the child's quality of life;

• Perfect for newborns and young children because it's easier to maintain.

Disadvantages:

- Risk of peritonitis (infection of the peritoneal cavity).
- Requires caregiver training for home-based dialysis.
- Less effective than hemodialysis (HD) in managing severe hyperkalemia or metabolic acidosis [14,15].

2. **Hemodialysis (HD)**

Indication:

HD is typically utilized in older children or when PD is unsuitable, particularly in cases of acute kidney injury (AKI) or severe metabolic imbalances.

Mechanism:

Blood is withdrawn through vascular access (AV fistula, graft, or catheter), filtered through a dialysis machine, and then returned to the body after the removal of waste products and excess fluid.

Advantages:

- More efficient at removing waste and excess fluid compared to PD.
- Suitable for acute renal failure and emergencies.
- Requires a shorter treatment duration (typically 3–4 hours per session, 3–4 times per week).

Disadvantages:

- Needs vascular access, which is challenging in small children.
- Causes hemodynamic instability, leading to potential issues like hypotension and electrolyte imbalances.
- Requires frequent hospital visits or specialized home dialysis facilities [16].

Continuous Arteriovenous Hemofiltration

Indication:

Critically sick patients who are unable to tolerate traditional haemodialysis because of haemodynamic instability are the main patients treated with CAVH. Acute kidney injury (AKI), severe fluid overload, sepsis with multi-organ failure, rhabdomyolysis, hepatorenal syndrome, and severe electrolyte abnormalities such metabolic acidosis and hyperkalaemia are among the circumstances for which it is recommended.

Convection is the method by which CAVH drives blood through a hemofilter utilising the patient's arterial blood pressure. After being extracted from an arterial catheter, blood is returned via a venous catheter after passing through a semi-permeable membrane that filters out water and other impurities. CAVH maintains electrolyte balance only through ultrafiltration and replacement fluids, as opposed to haemodialysis, which uses dialysate.

Advantages of CAVH:

- Hemodynamic Stability – Less impact on blood pressure compared to intermittent hemodialysis (IHD).
- Effective Fluid Removal – Helps in managing fluid overload in critically ill patients.
- Minimal Anticoagulation Requirement – Lower risk of clotting compared to Continuous Venovenous Hemofiltration (CVVH).
- Improved Toxin Clearance – Removes small and medium-sized solutes effectively.

Disadvantages of CAVH:

- Limited Efficiency , Slower clearance of solutes compared to CVVH or intermittent dialysis.
- Arterial Access Required , Higher risk of arterial complications like thrombosis, bleeding, and infection.
- Not Suitable for Hemodynamically Unstable Patients , Requires a certain level of arterial pressure, making it less effective in patients with severe hypotension.
- Risk of Electrolyte and Acid-Base Imbalance Continuous filtration can lead to imbalances if not closely monitored [17,18].

Kidney Transplantation

Indication:

For end-stage kidney disease (ESKD), kidney transplantation is the recommended and final treatment. When a suitable donor is available, kidney transplantation is a better option than long-term dialysis.

Types of Donors:

- Living donor (such as a parent, sibling, or close relative) – Generally provides the best long-term success rates.
- Deceased donor – Often involves extended waiting periods due to organ availability constraints.

Advantages:

- Provides better long-term survival rates and enhances overall quality of life.
- Eliminates the need for ongoing dialysis, reducing associated complications.
- Supports normal growth and development in pediatric patients.

Disadvantages:

- Necessitates lifelong immunosuppressive therapy, increasing the risk of infections and organ rejection.
- Potential for graft rejection and the possibility of transplant failure.
- Scarcity of appropriately sized organs for pediatric patients [19].

Feature	Peritoneal dialysis	Hemodialysis	Kidney transplantation
Indication	Infants , young children , home based theraphy	Older children, emergency cases	Long term treatment
Efficiency	Moderate	High	Best
Procedure	Dialysate instilled into peritoneum	Blood filtered through dailyzer	Kidney replacement

Frequency	Continous or nightly	3-4 times per week	One time surgery
Risks	Peritonitis, catheter infections	Hypotension , vascular access issues	Rejection , immunosupression side effects
Hospital visits	Minimal (home based)	Frequent (hospital based)	Only for follow ups

Complications and management :

Chronic kidney disease (CKD) in children affects multiple organ systems, leading to various complications that worsen as kidney function declines. Early identification and management of these complications are essential to improve long-term outcomes.

1. **Growth Retardation**

Children with CKD often experience poor growth due to nutritional deficiencies, metabolic acidosis, and hormonal imbalances, particularly affecting the growth hormone-insulin-like growth factor (GH-IGF) axis. Growth failure can result in short stature and delayed puberty, impacting overall development.

Management:

Adequate calorie and protein intake is essential to support growth. Metabolic acidosis should be corrected with oral sodium bicarbonate, and if growth failure persists, recombinant growth hormone (rGH) therapy may be initiated.

2. **Hypertension and Cardiovascular Disease**

Hypertension is common in pediatric CKD due to fluid retention, increased renin-angiotensin system activity, and endothelial dysfunction. It can lead to left ventricular hypertrophy (LVH), heart failure, and an increased risk of cardiovascular morbidity and mortality.

Management:

Blood pressure should be controlled using lifestyle modifications, including a low-sodium diet and weight management. Pharmacological treatment with ACE inhibitors or ARBs is recommended, along with regular blood pressure monitoring to prevent long-term complications.

3. **CKD-Mineral and Bone Disorder (CKD-MBD)**

CKD disrupts calcium and phosphate metabolism, leading to bone pain, growth deformities, fractures, and increased parathyroid hormone (PTH) levels (secondary hyperparathyroidism). These disturbances contribute to rickets and osteodystrophy in children.

Management:

Treatment includes phosphate binders (calcium-based or non-calcium-based), dietary phosphate restriction, and activated vitamin D (calcitriol) to suppress PTH secretion and prevent bone demineralization.

4. **Anemia**

Anemia in CKD results from erythropoietin (EPO) deficiency, which impairs red blood cell production. This leads to fatigue, pallor, delayed cognitive development, and reduced exercise tolerance.

Management:

Iron deficiency should be corrected with oral or intravenous iron supplementation, and recombinant erythropoietin (EPO) therapy is administered to maintain hemoglobin levels between 10–12 g/dL.

5. **Electrolyte and Acid-Base Imbalances**

As kidney function declines, there is an inability to regulate electrolyte levels, leading to hyperkalemia (high potassium), metabolic acidosis, and hypocalcemia. These imbalances can result in cardiac arrhythmias, muscle weakness, and bone demineralization.

Management:

Metabolic acidosis is corrected with oral sodium bicarbonate, hyperkalemia is managed through dietary potassium restriction and potassium binders, and calcium supplements are given for hypocalcemia.

6. **Neurocognitive Dysfunction**

Children with CKD may suffer from attention deficits, memory problems, and learning disabilities, which can affect academic performance and quality of life. The neurological impact is due to chronic inflammation, anemia, uremic toxins, and hypertension.

Management:

Early neurocognitive assessments should be conducted, and special educational support should be provided to help children with learning difficulties. In severe cases, cognitive rehabilitation programs may be beneficial.

7. **Malnutrition and Poor Appetite**

Poor appetite and malnutrition are common in CKD due to metabolic imbalances, nausea, and dietary restrictions. Malnutrition contributes to growth failure, immune dysfunction, and poor wound healing.

Management:

Nutritional counseling with pediatric dietitians ensures adequate calorie and protein intake. In severe cases, nasogastric or gastrostomy tube feeding may be required, and appetite stimulants can be considered when needed.

8. **Increased Infection Risk**

Children with CKD have a weakened immune system, making them more susceptible to urinary tract infections (UTIs), peritonitis (in peritoneal dialysis patients), and pneumonia. Immunosuppression following kidney transplantation also increases the risk of opportunistic infections.

Management:

Strict infection control practices, including hand hygiene and proper catheter care, are crucial. Prophylactic antibiotics may be used for recurrent infections, and routine vaccinations (pneumococcal, influenza, hepatitis B) are recommended.

9. **Psychosocial and Emotional Issues**

CKD in children can cause stress, anxiety, and depression, affecting mental well-being and social interactions. The chronic nature of the disease, dietary restrictions, and frequent hospital visits can impact emotional health.

Management:

Psychological counseling, family support, and peer interactions are essential to improve emotional well-being. In severe cases, antidepressants or anxiety medications may be prescribed under specialist guidance [20].

Lifestyle Modifications

Regular exercise improves cardiovascular health, boosts muscle strength, and enhances overall well-being. It helps manage weight, reduce blood pressure, and improve circulation. For CKD patients, physical activity supports kidney function and reduces complications.

Dietary adjustments in CKD include a low-sodium diet to manage blood pressure and fluid balance. Protein intake is controlled to reduce kidney strain, while adequate caloric consumption ensures proper nutrition. These adjustments help prevent complications and support overall health in CKD patients.

Adequate hydration is essential to prevent dehydration and maintain proper electrolyte balance. It helps support kidney function and regulate blood pressure. In CKD patients, fluid intake should be carefully monitored to avoid complications like fluid overload or dehydration [21].

Recent Advancements

Precision medicine in CKD involves using genetic testing to tailor treatments based on an individual's genetic profile. This approach helps optimize therapy, improving outcomes and minimizing adverse effects. By personalizing care, it can enhance disease management and slow CKD progression.

Novel biomarkers like cystatin C and urinary neutrophil gelatinase-associated lipocalin (NGAL) aid in the early detection of kidney dysfunction. These markers offer improved sensitivity and can identify kidney injury before changes in traditional markers like serum creatinine. Their use enhances early intervention and better management of CKD [22,23].

New Drug Therapies

SGLT2 inhibitors are showing promise in slowing CKD progression by reducing hyperglycemia and promoting natriuresis. They help lower blood pressure, reduce proteinuria, and protect kidney function. These benefits make SGLT2 inhibitors a key therapeutic option in managing CKD, particularly in diabetic patients.

Roxadustat is a hypoxia-inducible factor prolyl hydroxylase inhibitor used for managing CKD-related anemia. It stimulates erythropoiesis by increasing endogenous erythropoietin production and iron availability. Roxadustat offers an alternative to traditional erythropoiesis-stimulating agents, particularly for patients with iron deficiencies.

Advancements in Dialysis

Home-based peritoneal dialysis offers patients greater flexibility and independence in managing their treatment. It can improve quality of life by reducing the need for frequent clinic visits and allowing for personalized care. This approach also provides more consistent dialysis and better preservation of residual kidney function.

Kidney Transplantation

Paired kidney exchange programs allow incompatible donor-recipient pairs to swap kidneys, increasing the pool of compatible transplants. Advancements in immunosuppressive therapies help prevent organ rejection and improve long-term graft survival. Together, these innovations significantly enhance transplant success rates and patient outcomes [24,25].

Conclusion

Children's chronic kidney disease (CKD) is a dangerous illness that requires prompt diagnosis and appropriate treatment. It can lead to weak bones, high blood pressure, heart difficulties, and growth problems if left untreated. To control symptoms and halt its progression, treatment consists of medications, dietary adjustments, and lifestyle modifications. Dialysis or a kidney transplant are required in more severe situations. Results are getting better thanks to new medication therapies and improved dialysis techniques. Children live better lives when they receive regular checkups, emotional support, and good practices. Children with chronic kidney disease have a better future thanks to research and improved medical care.

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