



## Ukrainian Journal of Nephrology and Dialysis

Scientific and Practical, Medical Journal

### Founders:

- State Institution «Institute of Nephrology NAMS of Ukraine»
- National Kidney Foundation of Ukraine

ISSN 2304-0238;

eISSN 2616-7352

Journal homepage: <https://ukrjnd.com.ua>

Nephrology School

Olayinka Rasheed Ibrahim<sup>1</sup>, Michael Abel Alao<sup>2</sup>

doi: 10.31450/ukrjnd.1(69).2021.08

### Pediatric chronic kidney disease: Manifestations and evaluation

<sup>1</sup>Federal Medical Centre, Katsina, Nigeria,

<sup>2</sup>University College Hospital, Ibadan, Nigeria

#### Citation:

Ibrahim OR, Alao MA. Pediatric chronic kidney disease: Manifestations and evaluation. Ukr J Nephrol Dial. 2021;1(69):54-60. doi: 10.31450/ukrjnd.1(69).2021.08.

#### Article history:

Received January 09, 2021

Received in revised form

January 29, 2021

Accepted February 01, 2021

**Abstract.** *Chronic kidney disease (CKD) is unique in children due to varying etiology, manifestation, and impact. Whereas it is far a lesser burden compared with adult CKD, childhood CKD has a psychosocial impact on caregivers, impair growth, quality of life, and ultimately associated with increased mortality. We summarize the manifestation, diagnosis, and evaluation of a child with CKD, whose early detection, and appropriate management will improve their outcome. Thus, we hope this will be valuable to the general medical practitioners, and pediatricians in the care of children with CKD.*

**Keywords:** *child, chronic kidney disease, manifestations, evaluation.*

**Conflict of interest statement.** The authors declare no competing interest.

© Ibrahim O.R., Alao M.A., 2021.

Correspondence should be addressed to Olayinka Rasheed Ibrahim: [ibroplus@gmail.com](mailto:ibroplus@gmail.com)



© Ібрагім О.Р., Алао М.А., 2021

УДК 616.61-036.12-053.2-07

Олаїнка Рашид Ібрагім<sup>1</sup>, Майкл Абель Алао<sup>2</sup>

## Хронічна хвороба нирок у дітей: маніфестація та діагностика

<sup>1</sup>Федеральний медичний центр, Катсіна, Нігерія,

<sup>2</sup>Університетська лікарня, Ібадан, Нігерія

**Резюме.** Хронічна хвороба нирок (ХХН) у дітей є унікальною з точки зору етіології, клінічних проявів та впливу. Незважаючи на значно менший тягар порівняно з ХХН у дорослих, ХХН у дитячому віці має психосоціальний вплив на опікунів, погіршує зростання, якість життя і, зрештою, пов'язана зі збільшенням смертності. У цій роботі ми підсумовуємо клінічні прояви та діагностичну оцінку дитини з ХХН, раннє виявлення та відповідне лікування якої може поліпшити наслідки. Ми сподіваємось, що наша робота буде цінною для лікарів загальної практики, нефрологів та педіатрів у догляді за дітьми з ХХН.

**Ключові слова:** дитина, хронічна хвороба нирок, клінічні прояви, діагностика.

**Introduction.** Chronic Kidney Disease (CKD), a unification term proposed by National Kidney Foundation-Kidney Disease Outcomes Quality Initiative almost two decades (2002), and referred to an abnormality in the kidney functions or structure that lasted three months or more with implication for health [1, 2]. The Kidney Disease: Improving Global Outcomes (KDIGO) updated the CKD definition and classification in 2012 with the modification and stratification into categories rather than stages, and incorporation of albuminuria (proteinuria in children), besides the glomerular filtration rate (GFR). The guideline also subdivided the third category into 3a and 3b in furtherance to data that suggested differences concerning risks and outcomes [3].

Globally, CKD is a public health challenge with an enormous burden among adults compared with children [4, 5]. However, the impact on the relatively fewer children compared with adults is huge. The CKD in children is associated with increased mortality of 30-150 times compared with their peers [6]. Besides, CKD in children affects their growth, overall quality of life, and could be a form of psychosocial stress on the family [7, 8, 9]. Also, the etiology and manifestation of CKD differ compared with adults, necessitating a unique approach in their evaluation and management [5]. Thus, in this paper, we described CKD in children with a focus on the various forms of manifestations, diagnosis, and evaluation. We hope this will be valuable to the general practitioners, and pediatricians in the care of children with CKD.

**Epidemiology.** The data on childhood CKD is still sparse compared with the data in the adult population. Notwithstanding, current data suggested an increase in the global incidence and prevalence of childhood CKD

[10]. Besides, recent efforts from the United States of America (USA), European countries, and parts of Asia have yielded significant improvement in the Epidemiology of Pediatric CKD. United States Renal Data System (USRDS) annual data on end-stage kidney disease in children, and adolescents (0 to 21) years showed an incidence of 12.9 per million population (PMP) with a prevalence of 98.7 PMP [11]. Italkid Project showed the incidence of 12.1 per million of the age-related population (MARP) and a point prevalence of 74.7 per MARP [12]. The incidence in Europe ranges from 7.7 to 12.1 per MARP with a prevalence as high as 74 per MARP [10]. Data from Asian countries showed a lesser incidence of CKD in children. In Japan, the incidence of end-stage kidney disease (ESKD) was 4.0 per MARP [13]. There is no available national registry from Africa on the burden of pediatric CKD, but data from hospitals based mostly from tertiary health facilities showed an incidence of 1 to 3 per MARP [14, 15]. The lower prevalence in Africa may be the tip of the iceberg because of scarce data with the few from the tertiary health facility and will not reflect the entire population, especially where there is limited access to health care [16]. The data on CKD in children also showed a higher proportion in males than females because of the higher incidence of urinary tract malformation in the male population.

**Etiology.** The etiology of pediatric CKD differs from adults and varies with age, gender, race, and geographical location. The causes of childhood CKD include congenital anomalies of the kidney and urinary tract (CAKUT) in the younger age group and the predominance of glomerular diseases in the older age group in the high-income countries [5]. In contrast, infection-related causes and nephrotic syndrome predominate are the leading causes of childhood CKD in Africa and most low-income countries (Table 1) [14, 15].

Olayinka Rasheed Ibrahim  
ibroplus@gmail.com

Table 1

## Etiology of chronic kidney disease in children

Italy [12]	NAPRTCS [41]		Japan [13]		South Africa [15]		Nigeria [14]	
	n (%)	Renal diseases	n (%)	Renal diseases	n (%)	Renal diseases	n (%)	Renal diseases
Hypodysplasia	689 (57.5)	CAKUT	3361 (48)	CAKUT	215 (39.8)	Nephrotic syndrome	46 (36.5)	CGN
Neurogenic bladder	44 (3.7)	GN	993 (14)	Hereditary nephropathy	70 (12.9)	GN	20 (15.9)	NS
CGN	31 (2.6)	HUS	141 (2)	FSGS	66 (12.2)	Renal hypoplasia with obstructive uropathy	15 (11.9)	CAKUT
FSGS	21 (1.8)	Hereditary nephropathy	717 (10)	Cystic Kidney disease	52 (9.6)	Renal hypoplasia with recurrent UTI	8 (6.3)	Malignancy
Congenital nephrotic syndrome	13 (1.1)	Cystic Kidney Disease	368 (5)	GN	35 (5.9)	Congenital anomalies	4 (3.3)	
Membranous nephropathy	3 (0.3)	Ischemic renal failure	158 (2)	HUS	9 (1.7)	Others	23 (18.3)	
SLE	13 (1.1)	Miscell	1,485 (21)	Ischemic renal failure	9 (1.7)	HUS	8 (6.3)	
HUS	43 (3.6)	Unknown	182 (3)	Miscellaneous	47 (8.7)	SLE	2 (1.5)	
Polycystic kidney disease	60 (5.0)			Unknown	18 (3.3)			
Nephronophthisis	41 (3.4)			Missing	22 (4.2)			
Alport's syndrome	18 (1.5)							
Cystinosis	22 (1.8)							
Hereditary nephropathies	45 (3.8)							
Cortical necrosis (perinatal)	49 (4.1)							
Medications	14 (1.2)							
Idiopathic interstitial nephritis	24 (2.0)							
Wilms' tumor	4 (0.3)							
Miscellaneous non-hereditary diseases	23 (1.9)							
Unknown	40 (3.3)							

CGN – chronic glomerulonephritis; FSGS- Focal segmental glomerulosclerosis; SLE- systemic lupus erythematosus; HUS- haemolytic uraemic syndrome; GN- glomerulonephritis; NS- nephrotic syndrome; CAKUT- congenital anomalies of kidney and urinary tract; NAPRTCS- North American Pediatric Renal Trials and Collaborative Studies.

The lesser frequency of CAKUT from Africa may be because of the absence of regular screening programs and slower progress of CKD. Thus, the CAKUT may be missed until later in life or when there are superimposed complications or infections.

**Diagnosis of Pediatric CKD.** The diagnostic criteria and categories for CKD in children aged two years and above are the same as that of adults (Table 2).

Table 2

Glomerular filtration rate of classification of CKD

GFR category	Interpretation	GFR (ml/min/1.73 m <sup>2</sup> )
G1	Normal or high	90
G2	Mildly decreased	60 to 89
G3a	Mildly to moderately decreased	45 to 59
G3b	Moderately to severely decreased	30 to 44
G4	Severely decreased	15 to 29
G5	Kidney failure	< 15

However, there is less emphasis on the albuminuria criteria for which a protein creatinine criterion may be used in place [3]. Besides for children less than two years, age-specific glomerular value is necessary for interpreting decline in the GFR. The age-specific is because the GFR is low at birth and increased to the adults' value about the age of two years [17]. However, a major limitation is the absence of a GFR nomogram with few studies from high-income countries and thus, possessing a challenge for the diagnosis and staging of CKD based on the GFR category in children less than two years. Whereas measurement of GFR using reliable biomarkers such as iohexol appears better, this is often not visible in the clinical scenario, hence the use of validated bedside equations that rely on the endogenous biomarkers [18]. The commonly use bedside endogenous biomarkers include serum creatinine and cystatin C. Either serum creatinine or cystatin C may be used alone, although there are indications that equations that combined both biomarkers for estimating GFR performed better [18].

**Manifestation of pediatric CKD.** Although the early stages may not show any clinical features and remain silent, the clinical presentations of pediatric CKD vary based on the age and underlying causes. A child with congenital anomalies of the kidney and urinary tract (CAKUT) may present with poor growth, recurrent urinary tract infections, poor urinary streams, or recurrent abdominal distention depending on the degree of urinary involvement and obstruction [19]. Those with severe mechanical obstruction may present with severe bilateral hydronephrosis in utero or at birth, or history of oligohydramnios during pregnancy [20]. An infant with congenital nephrotic syndrome may present with generalized body swelling, normal birth weight, and a large placental. Infants with renal tubular disorders present with poor weight gains and acidosis [21].

Older children with less severe obstruction may be asymptomatic and may be an incidental finding or present with urinary tract infection (UTI) [19]. Older children with CKD may present with recurrent body swelling, reduced urinary output, and hypertension (though uncommon) in a clinical condition such as nephrotic syndrome [22]. The other forms of manifestation include an incidental abdominal mass in the early stage of Wilms's tumor. Other symptoms include non-specific gastrointestinal symptoms such as vomiting [23].

When complications set in at the advanced category of the disease (CKD), features are predominantly those of complications from kidney failure. The complications include anemia because of multifactorial factors including iron deficiency, reduced erythropoietin, and anorexia induced micronutrient deficiency [24].

Growth impairment is another manifestation of Pediatric CKD, which occurs even in the early stages of the disease. The height for age falls below the 5th percentile because of elevated hepcidin, insulin resistance, and impair insulin growth factor (IGF) [25]. The growth may fall as early as the first year of life and poor growth remains a way of presentation of congenital CKD in infants because of electrolyte imbalance, reduce intake, recurrent infections, and hospitalization. Growth impairment remains a major effect of CKD in older children and children may require growth hormone therapy to ensure optimal growth [26].

Impair calcium and phosphate because of abnormal metabolism due to reducing 1,25 dihydroxycholecalciferol and secondary hyperthyroidism causing bone changes are common in the late stage of pediatric CKD [27]. A common manifestation in the advanced stage of CKD is renal osteodystrophy. Renal osteodystrophy is characterized by the high and low turnover of skeletal

lesions on the background of secondary hyperthyroidism with phosphate retention and hypocalcemia [27].

Progression of CKD will lead to metabolic acidosis because of loss of filtered bicarbonate, decrease synthesis of ammonia, and loss of titratable acid [28]. Chronic acidosis will also blunt the action of growth hormone and thus contribute to growth failure.

Elevated blood pressure is more consequence rather than a common cause of CKD in children compared with adults. Thus, quite many pediatrics CKD will present with blood pressure above the 95th percentile for age and sex. The control of blood pressure remains important, and may require multiple drugs to achieve controls [28].

**Evaluation.** The evaluation of CKD in children revolves around the confirmation, determination of the etiology or underlying predisposition, and categorization of CKD [3]. Thus, the evaluation should include a detailed history, examinations, and investigations.

The history of pregnancy especially oligohydramnios is important in children with CAKUT, including prenatal ultrasound scans which may detect hydronephrosis early [20]. Also, a history of poor urinary streams may point toward posterior urethral valve [20]. History of poor weight gains may point towards renal tubular disorders such as renal tubular acidosis [21]. The family history is also important, especially hereditary kidney disease such as polycystic kidney disease and monogenic kidney diseases such as Alport syndrome [29]. History of polydipsia and nocturia in a child with tubulointerstitial disorders.

Examination findings may show stunting, pallor, anasarca (nephrotic syndrome), hypertension, edema, abdominal mass (nephroblastoma) [23].

Investigations for pediatric CKD include the estimation of GFR and occasionally, an absolute measurement of GFR may be indicated [18]. The GFR may be estimated from the formula and widely used is the Schwartz formula, which is available for both serum creatinine and cystatin C [18]. Ioxehol and other exogenous biomarkers may be used for actual measurement of GFR where indicated. The estimated GFR should also assess the progression of CKD in children and it helps in planning actions such as pre-emptive transplant that is advocated in the advanced category of CKD in children [30].

Urinalysis is also important, especially in the community screening for CKD in children. The presence of persistent proteinuria and albuminuria indicate CKD [30]. Whereas the collection of 24 hours urinary may be difficult, urinary albumin/protein creatinine may confirm and classify CKD in children [3]. Where a 24hour urine is not workable, early morning urine is preferred as it minimizes the likelihood of impact of orthostatic proteinuria [31]. The Protein-creatinine ratio is preferred in children and is also useful in following up patients with nephrotic syndrome. The urinalysis may also show hematuria and may the only features in children with chronic glomerulonephritis [23].

A urine microscope may show casts and crystals and maybe a clue towards the underlying cause of CKD [32]. And urine culture remains an important tool in the CAKUT that may present with recurrent UTI.

The other investigations include an imaging study that provides information on kidney status and functionality. Ultrasound remains a simple and inexpensive tool that can evaluate the kidney in CKD [33]. It gives information on the sizes of the kidney, the anatomy of the kidney, including the pelvic-caliceal system. This should be carried out by an experienced sonologist to ensure appropriate, and normal interpretation.

Other imaging studies that are valuable in children with CKD will depend on the probable underlying cause and include the micturating cystourethrogram in a posterior urethral valve or lower urinary tract disorders and reflux disorders [34, 35]. The dimercaptosuccinic acid scan can be to assess the kidney functions in acute pyelonephritis and renal scars [36]. The computed tomography scan with contrast to outline the urinary tract system and Magnetic resonance imaging are valuable in the evaluation of renal cystic lesions and tumors, where they will give details information on the structural involvements [37].

Renal biopsy remains a critical component in the evaluation of kidney diseases where it gives information on the histologic type of kidney diseases and is important in the planning of treatment and prognosis [38].

The genetic studies are also important, as many etiologies of renal disease have some genetic involvement [29]. An example is a mutation in the nephrin coding gene for congenital nephrotic syndrome.

Electrolytes including the serum calcium, phosphate, and Parathyroid hormone (PTH) levels should be tested [39]. The serum calcium, phosphate, and PTH should be critical for metabolic management of the patient because of the risk for renal osteodystrophy. The serum bicarbonate should also be monitored and patients may require bicarbonate for severe acidosis, especially those on kidney replacement therapy [40].

**Conclusions.** Chronic kidney disease in children differs from adults with a varying etiology and a high impact on them. The manifestation of childhood CKD also varies based on the age and underlying cause. Evaluations should be tailored and based on the history, examination findings, and most likely cause.

**Conflict of interest.** None to be declared.

**Authors' contributions and participation.** *ORI* and *MAA*: conceptualized the work, did literature search, draft, revised and approved the final manuscript. Both authors approved the final version of the manuscript.

**Funding source.** The research was self-funding.

## References:

1. K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: evaluation, classification and stratification. *Am J Kidney Dis.* 2002; 39(2 (Suppl 1)):S1–266. Available from: <https://jhu.pure.elsevier.com/en/publications/kdoqi-clinical-practice-guidelines-for-chronic-kidney-disease-eva-3>.
2. *Vassalotti JA, Piraino B, Szczech LA.* A decade after the KDOQI CKD guidelines: Impact on the national kidney foundation. *Am J Kidney Dis.* 2012;60(5):689–91. doi: 10.1053/ajkd.2012.08.013.
3. *Milik A, Hryniewicz E.* KDIGO 2012 Clinical Practise Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int Suppl.* 2013;3(1):1–150. Available from: <https://linkinghub.elsevier.com/retrieve/pii/S1474667016423049>.
4. *Bikbov B, Purcell CA, Levey AS, Smith M, Abdoli A, Abebe M, et al.* Global, regional, and national burden of chronic kidney disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet.* 2020;395(10225):709–33. doi: 10.1016/S0140-6736(20)30045-3.
5. *Becherucci F, Roperto RM, Materassi M, Romagnani P.* Chronic kidney disease in children. *Clin Kidney J.* 2016;9(4):583–91. doi: 10.1093/cjk/sfw047.
6. *McDonald SP, Craig JC.* Long-Term Survival of Children with End-Stage Renal Disease. *N Engl J Med.* 2004;350(26):2654–62. doi: 10.1056/NEJMoa031643.
7. *Dotis J, Pavlaki A, Printza N, Stabouli S, Antoniou S, Gkogka C, et al.* Quality of life in children with chronic kidney disease. *Pediatr Nephrol.* 2016 Dec 27;31(12):2309–16. doi: 10.1007/s00467-016-3457-7.
8. *Medway M, Tong A, Craig JC, Kim S, Mackie F, McTaggart S, et al.* Parental Perspectives on the Financial Impact of Caring for a Child With CKD. *Am J Kidney Dis.* 2015 Mar;65(3):384–93. doi: <https://doi.org/10.1053/j.ajkd.2014.07.019>.
9. *Bignall ONR, Goldstein SL.* Childhood CKD affects the entire family. *Am J Kidney Dis.* 2015;65(3):367–8. doi: 10.1053/j.ajkd.2014.11.013.
10. *Harambat J, van Stralen KJ, Kim JJ, Tizard EJ.* Epidemiology of chronic kidney disease in children. *Pediatr Nephrol.* 2012 Mar 29;27(3):363–73. doi: 10.1007/s00467-011-1939-1.
11. US Renal Data System 2019 Annual Data Report: Epidemiology of Kidney Disease in the United States: Executive summary [Internet source]. 2019. Available from: <https://www.usrds.org/annual-data-report/>
12. *Ardissino G, Dacco V, Testa S, Bonaudo R, Claris-Appiani A, Taioli E, et al.* Epidemiology of Chronic Renal Failure in Children: Data From the ItalKid Project. *Pediatrics.* 2003 Apr 1;111(4):e382–7. doi: 10.1542/peds.111.4.e382.
13. *Hattori S, Yosioka K, Honda M, Ito H.* The 1998 report of the Japanese National Registry data on pediatric end-stage renal disease patients. *Pediatr Nephrol.* 2002 Jun 8;17(6):456–61. doi: 10.1007/s00467-002-0848-8.
14. *Asinobi AO, Ademola AD, Ogunkunle OO, Mott SA.* Paediatric end-stage renal disease in a tertiary hospital in South West Nigeria. *BMC Nephrol.* 2014;15(1):1–9. doi: 10.1186/1471-2369-15-25.
15. *Bhimma R, Adhikari M, Asharam K, Connolly C.* The spectrum of chronic kidney disease (stages 2-5) in KwaZulu-Natal, South Africa. *Pediatr Nephrol.* 2008;23(10):1841–6. doi: 10.1007/s00467-008-0871-5.
16. *Dauids MR, Eastwood JB, Selwood NH, Arogundade FA, Ashuntantang G, Benghanem Gharbi M, et al.* A renal registry for Africa: first steps. *Clin Kidney J.* 2016 Feb;9(1):162–7. doi: 10.1093/cjk/sfv122.
17. *Heilbron DC, Holliday MA, Al-Dahwi A, Kogan BA.* Expressing glomerular filtration rate in children. *Pediatr Nephrol.* 1991;5(1):5–11. doi: 10.1007/BF00852829.
18. *Pottel H.* Measuring and estimating glomerular filtration rate in children. *Pediatr Nephrol.* 2017 Feb 26;32(2):249–63. doi: 10.1007/s00467-016-3373-x.
19. *Nogueira PCK, Paz I de P.* Signs and symptoms of developmental abnormalities of the genitourinary tract. *J Pediatr (Rio J).* 2016 May;92(3):57–63. doi: 10.1016/j.jped.2016.01.006.
20. *Kumar BH, Krishnamurthy S, Chandrasekaran V, Jindal B, Ananthkrishnan R.* Clinical Spectrum of Congenital Anomalies of Kidney and Urinary Tract in Children. *Indian Pediatr.* 2019 Jul 29;56(7):566–70. Available from: <https://www.indianpediatrics.net/july2019/july-566-570.htm>.
21. *Soleimani M, Rastegar A.* Pathophysiology of Renal Tubular Acidosis: Core Curriculum 2016. *Am J Kidney Dis.* 2016 Sep;68(3):488–98. doi: 10.1053/j.ajkd.2016.03.422.
22. *Viswanath D.* Nephrotic Syndrome in Children. Kailasam S, editor. *J Indian Acad Oral Med Radiol.* 2013;25:18–23. doi: 10.5005/jp-journals-10011-1333.
23. *Quigley R.* Chronic Kidney Disease: Highlights for the General Pediatrician. *Int J Pediatr.* 2012;2012:1–5. doi: 10.1155/2012/943904.

24. *Atkinson MA, Furth SL.* Anemia in children with chronic kidney disease. *Nat Rev Nephrol.* 2011 Nov 6;7(11):635–41. doi: 10.1038/nrneph.2011.115.
25. *Salas P, Pinto V, Rodriguez J, Zambrano MJ, Mericq V.* Growth Retardation in Children with Kidney Disease. *Int J Endocrinol.* 2013;2013: Article ID 970946. doi: 10.1155/2013/970946.
26. *Stonebrook E, Mahan JD.* Treatment of Growth Retardation in a Child with CKD. *Clin J Am Soc Nephrol.* 2019 Nov 7;14(11):1658–60. doi: 10.2215/CJN.03960319.
27. *Hanudel MR, Salusky IB.* Treatment of Pediatric Chronic Kidney Disease–Mineral and Bone Disorder. *Curr Osteoporos Rep.* 2017 Jun 28;15(3):198–206. doi: 10.1007/s11914-017-0365-0.
28. *Harambat J, Kunzmann K, Azukaitis K, Bayazit AK, Canpolat N, Doyon A, et al.* Metabolic acidosis is common and associates with disease progression in children with chronic kidney disease. *Kidney Int.* 2017 Dec;92(6):1507–14. doi: 10.1016/j.kint.2017.05.006.
29. *Vivante A, Hildebrandt F.* Exploring the genetic basis of early-onset chronic kidney disease. *Nat Rev Nephrol.* 2016 Mar 11;12(3):133–46. doi: 10.1038/nrneph.2015.205.
30. *Amaral S, Sayed BA, Kutner N, Patzer RE.* Preemptive kidney transplantation is associated with survival benefits among pediatric patients with end-stage renal disease. *Kidney Int.* 2016 Nov;90(5):1100–8. doi: 10.1016/j.kint.2016.07.028.
31. *Leung AKC, Wong AHC, Barg SSN.* Proteinuria in children: Evaluation and differential diagnosis. *Am Fam Physician.* 2017;95(4):248–54. Available from: <https://pubmed.ncbi.nlm.nih.gov/28290633/>.
32. *Perazella MA.* The Urine Sediment as a Biomarker of Kidney Disease. *Am J Kidney Dis.* 2015 Nov;66(5):748–55. doi: 10.1053/j.ajkd.2015.02.342.
33. *O'Neill WC.* Renal Relevant Radiology: Use of Ultrasound in Kidney Disease and Nephrology Procedures. *Clin J Am Soc Nephrol.* 2014 Feb 7;9(2):373–81. doi: 10.2215/CJN.03170313.
34. *Lee LC, Lorenzo AJ, Koyle MA.* The role of voiding cystourethrography in the investigation of children with urinary tract infections. *Can Urol Assoc J.* 2016 Jun 16;10(5–6):210. doi: 10.5489/cuaj.3610.
35. *Gomes N, Miller M, Lawrence M.* Micturating Cystourethrogram Findings in Children with Urinary Tract Infections: A Five Year Review. *SM J Clin Med.* 2016;2(2):1017. Available from: <https://smjournals.com/clinical-medicine/full-text/smjcm-v2-1017.php>.
36. *Vidal E, Miorin E, Zucchetta P, Benetti E, Longo G, Meneghesso D, et al.* Usefulness of 99mTc-dimer-captosuccinic acid renal scan in the diagnosis and follow-up of acute tubulointerstitial nephritis in children. *Clin Kidney J.* 2017;10(5):655–60. doi: 10.1093/ckj/sfx041.
37. *Hiorns MP.* Imaging of the urinary tract: The role of CT and MRI. *Pediatr Nephrol.* 2011;26(1):59–68. doi: 10.1007/s00467-010-1645-4.
38. *Dhaun N, Bellamy CO, Cattran DC, Kluth DC.* Utility of renal biopsy in the clinical management of renal disease. *Kidney Int.* 2014;85(5):1039–48. doi: 10.1038/ki.2013.512.
39. *Dhondup T, Qian Q.* Electrolyte and Acid-Base Disorders in Chronic Kidney Disease and End-Stage Kidney Failure. *Blood Purif.* 2017;43(1–3):179–88. doi: 10.1159/000452725.
40. *Dhondup T, Qian Q.* Acid-Base and Electrolyte Disorders in Patients with and without Chronic Kidney Disease: An Update. *Kidney Dis.* 2017;3(4):136–48. . doi: 10.1159/000479968.
41. The EMMES Corporation, Rockville M. North American Pediatric Renal Transplant Cooperative Study (NAPRTCS) 2008 Annual report. 2008. Available from: [https://www.naprtcs.org/system/files/2008\\_Annual\\_CKD\\_Report.pdf](https://www.naprtcs.org/system/files/2008_Annual_CKD_Report.pdf).