Received: December 21, 2025
Accepted: February 12, 2026

Acad Med J 2026;6(1):121-134
UDC: 616.61-073.916-053.1
DOI:
Case reports

THE ROLE OF NUCLEAR MEDICINE IMAGING IN OBJECTIVE EVALUATION OF CONGENITAL RENAL DISORDERS: CASE REPORT SERIES

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Abstract

Congenital anomalies of the kidneys and urinary tract (CAKUT) represent an alarming cause of chronic kidney disease among children. Management of these anomalies requires a palette of diagnostic methods, including imaging techniques like ultrasonography, cistouretrography, computed tomography and magnetic resonance imaging, which provide detailed information about the structural integrity of the kidneys and urinary tract. Nuclear medicine plays an important complementary role to these studies as it provides clinicians with irreplaceable data concerning the function and integrity of the kidneys and urinary tract. This case series highlights the contribution of nuclear medicine in the management of these anomalies. The aim was to address the gap created by the limited availability of pediatric case series that systematically document congenital renal anomalies using nuclear medicine methods. We present a series of five pediatric patients referred to the Institute of Pathophysiology and Nuclear Medicine in Skopje for nuclear medicine renal studies. In three of the cases static ^{99m}Tc DMSA scintigraphy was utilized to evaluate patient's cortical integrity, renal structure and position as well as differential renal function. In contrast, the other cases represent the role of ^{99m}Tc DTPA dynamic renal scintigraphy in the assessment of renal perfusion, drainage and response to diuretic stimulation. Across all cases, renal scintigraphy provided essential and objective metrics that later aided in clinician's management of the patients.

Keywords: ^{99m}Tc-DTPA, ^{99m}Tc-DMSA, congenital renal disorders

Introduction

Congenital anomalies of the kidneys and urinary tract (CAKUT) are developmental disorders with a prevalence of 4-60/10,000 births[1,2] and account for approximately 48% of the causes of chronic kidney disease in childhood[3]. The term CAKUT, introduced in 1998 by Ichikawa *et al*.[4], refers to a broad spectrum of congenital renal and urinary tract anomalies, including renal agenesis, multicystic dysplasia, abnormalities of kidney number, size, shape, or position, as well as vesicoureteral reflux (VUR) and obstructive lesions such as ureteropelvic junction obstruction, ureterovesical junction obstruction, and posterior urethral valves. Owing to this wide spectrum, clinical presentation ranges from mild phenotypes to severe conditions compromising renal function. CAKUT accounts for more than 50% of pediatric chronic kidney

disease cases[5]. Several types of anomalies can occur, with ureteropelvic junction obstruction as the most frequent cause of prenatal hydronephrosis in children, with an incidence of 1 in 1000-1500 newborns[6,7]. Horseshoe kidney is the most common congenital fusion anomaly of the urinary tract, with a prevalence of 1 in 400-600 individuals[8], as well as ectopic kidney, occurring approximately 1 in 900 individuals[9]. Primary VUR, which occurs in approximately 1-2% of the population[10], and congenital hydronephrosis very often is the main clinical presentation of the listed anomalies and is detected in 1-2% of all pregnancies[11]. In this clinical context, early diagnosis is essential to prevent permanent kidney damage and long-term complications[11]. The diagnostic assessment is primarily conducted using imaging techniques, particularly ultrasound - both 2D and endoluminal 3D[12] followed, when necessary, by more advanced investigations such as magnetic resonance imaging (MRI)[13]. Nuclear medicine also plays a fundamental role in the morphological and functional evaluation of these conditions, through techniques such as renal scintigraphy with Tc-99m DMSA[14] and Tc-99m DTPA[15]. The main difference between these two methods lies in the fact that DMSA scintigraphy provides a static assessment for evaluating cortical function and morphological presentation of the renal parenchyma, whereas DTPA scintigraphy offers a dynamic assessment for evaluating overall renal function and drainage[15]. The important characteristic of nuclear medicine methods is objectiveness in reporting and low interobserver variability in the reporting[15]. In Macedonia, there are few studies analyzing CAKUT patient cohorts and the diagnostic approach typically begins with ultrasonography, followed by second-line methods such as voiding cystourethrography, Tc-99m DMSA and DTPA scintigraphy, and, in selected cases, MR urography[16,17]. This article presents a case series study including five congenital pathologies evaluated and confirmed using nuclear medicine methods: case 1 - ureteropelvic junction obstruction and horseshoe kidney, case 2 - ectopic kidney, case 3 - vesicoureteral reflux and recidivant urinary tract infections, case 4 - congenital hydronephrosis due to posterior urethral valve, and case 5 - left ureteropelvic junction (UPJ) obstruction. The aim was to address the gap created by the limited availability of pediatric case series that systematically document congenital renal anomalies using nuclear medicine methods.

Case presentations

Case 1

A 4-year-old female child was referred to the Institute of Pathophysiology and Nuclear Medicine (IPNM) by the Pediatric Clinic in Skopje for a DMSA renal scan. The patient was referred with a history of a febrile episode and urinary laboratory findings of microglobulinuria and leukocyturia, but according to heteroamnestic data given by the parents, without previous urological symptoms. Ultrasonography (US) was performed and revealed the ectopic position of the left kidney and suspicion of a horseshoe kidney, and grade 3 hydronephrosis of the left kidney. Contrast CT urography with intravenous application of 370 mg I/mL of the contrast medium and Dose-Length Product (DLP) of 302 mGy/cm was performed, and the study revealed grade 3 hydronephrosis in the left kidney, accompanied by reduced cortical parenchyma. The cause of the hydronephrosis was suspected to be stenosis of the ureteropelvic junction, resulting from the crossing of the inferior mesenteric artery. A cystouretherography also revealed active and passive grade 1 vesicoureteral reflux on the left side. A static renal scan, with 88 MBq of 99mTc DMSA was obtained after 2 hours of intravenous administration. Planar static images were acquired in the anterior (AP), posterior (PA), right oblique (PRO), and left oblique (PLO) positions, with 300 kcounts/image with NephroCam (DDD) dedicated gamma camera for nephrological studies. The data were analyzed with Oasis software. Regions of interest (ROIs) were defined, and background activity was assessed to calculate differential relative renal function (DRF). The planar scans revealed normal position, shape, size, and

relatively homogenous uptake of the radiopharmaceutical in the renal parenchyma of the right kidney, while the left kidney was found to be in a horizontal position and fused with its lower pole with the right kidney, and with significantly lower activity, indicating lower uptake of the radiotracer in the renal cortex. DMSA scan confirmed *ren arcuatus*. The calculated DRF was 75% for the right kidney and 25% for the left kidney.

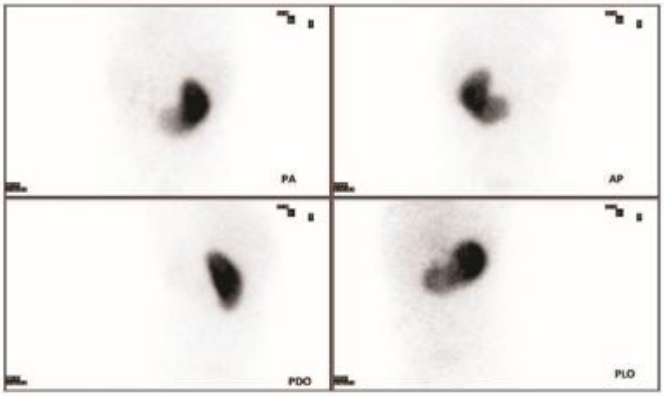


Fig. 1. a.

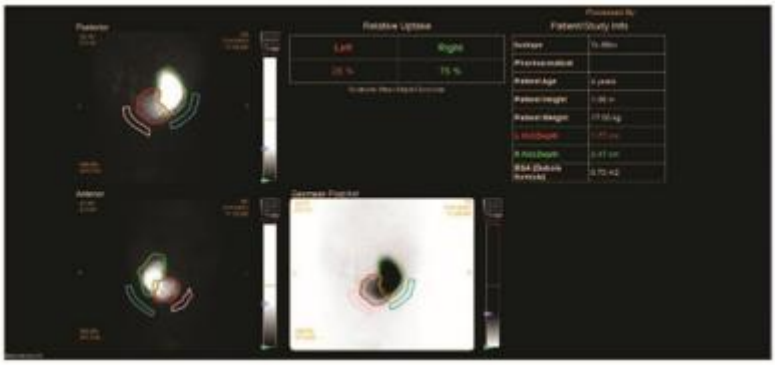


Fig. 1. b.

Fig. 1. a) Antero-posterior (AP), postero-anterior (PA), posterior right oblique (PDO) and posterior left oblique (PLO) positions of 99mTc-DMSA scan revealed left kidney in a horizontal position and fused with lower pole of the right kidney presented with normal position, scan findings for *ren arcuatus*; **b)** Relative uptake quantification (DRF) using geometric mean method with depth correction

Case 2

A 5-year-old female child was referred to the outpatient pediatric department due to cervical lymphadenopathy, which prompted US examination of the neck, but abdominal US was also performed and revealed an incidental finding of the absence of the left kidney in its usual anatomical position. This converged into the referral of the patient to our institution for a DMSA renal scan. Standard imaging protocol for planar DMSA scan was performed after 3 hours of intravenous application of 105 MBq of 99mTc-DMSA. Analysis of the planar scans revealed normal position, shape, and size of the right kidney, without parenchymal defects, while the left kidney was smaller in size with abnormal shape and ectopic position, lower than the right kidney. The DRF of 30% for the left kidney and 70% for the right kidney was calculated using the geometric mean method of DRF calculation, multiplying the counts from the anterior and posterior views, and then taking the square root.

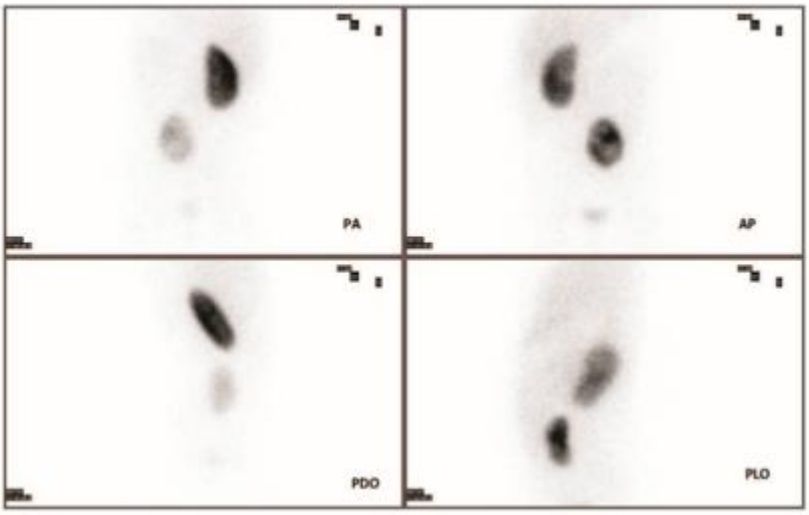


Fig. 2. a.

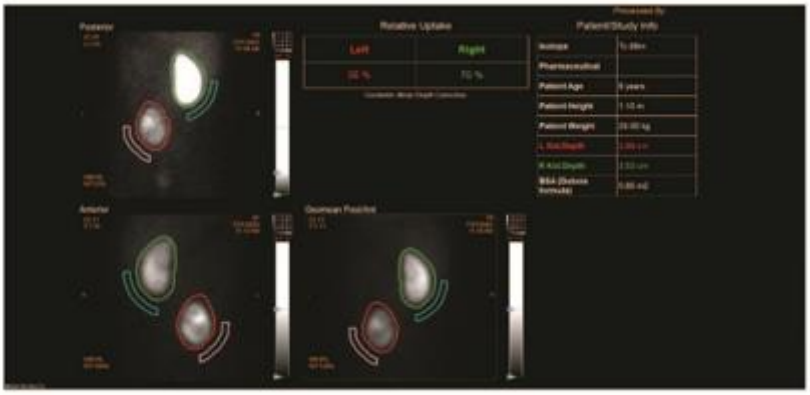


Fig. 2. b.

Fig. 2. a) PA, AP, PDO, PLO positions of the 99mTc-DMSA scan revealed a smaller and ectopic left kidney; **b)** Relative uptake revealed smaller, hypofunctional and distally located left kidney

Case 3

A 6-year-old male child had a history of a proximal urinary tract infection with *Klebsiella Pneumoniae,* approximately one month before the referral. Investigations during the acute phase of the infection revealed normal kidney function and normal urinary sediment findings. The infection prompted a US investigation, which revealed grade 2 hydronephrosis in the left kidney, and dilatation of both ureters due to vesicoureteral reflux (VUR) confirmed with a voiding cystourethrography. The study revealed grade 3/4 VUR on the right side, as well as VUR on the left side. Additional MRI urography confirmed the presence of grade 2 hydronephrosis of the left kidney with a reduction in size of both kidneys. A DMSA renal scan was performed according to standardized protocol, previously described with administration of 125 MBq ^{99m}Tc DMSA. On the planar scans, the right kidney showed photopenic defects in the upper and lower poles, while the left kidney had entirely reduced and inhomogeneous uptake of the radiotracer. Relative DRF was calculated with the geometric mean method to be 24% for the left kidney and 76% for the right kidney.

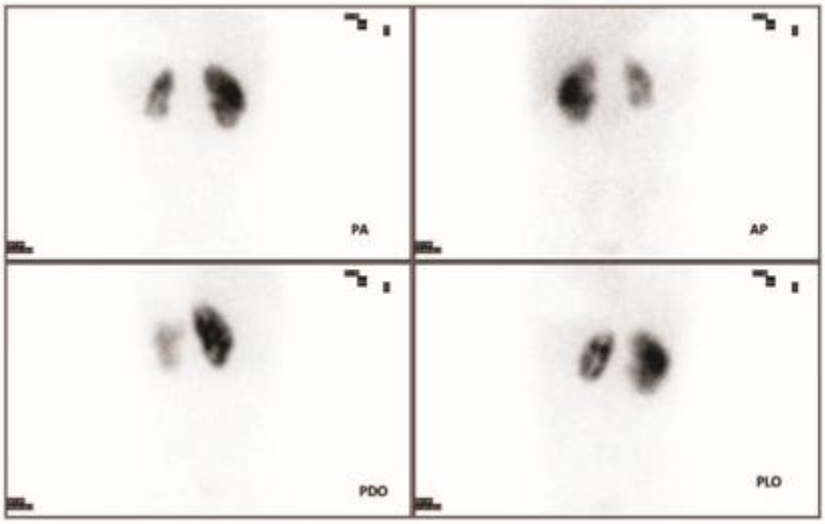


Fig. 3. a.

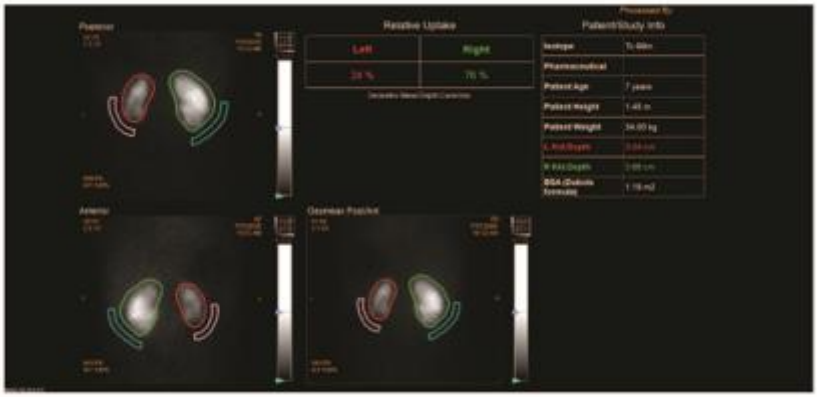


Fig. 3. b.

Fig. 3. a) AP, PA PDO, PLO positions of the 99mTc-DMSA scan visualizing a smaller left kidney, with entirely reduced uptake, thin parenchyma, and a defect in the lower pole, as well as defects in the lower and upper pole of the right kidney; **b)** Relative uptake confirmed smaller, hypofunctional left kidney and revealing chronic complications due to recurrent urinary tract infections.

Case 4

A 2-year-old male child diagnosed and surgically treated for a posterior urethral valve was referred to the IPNM for a DTPA dynamic renal study. A urinary tract US was performed, revealing bilateral grade 2/3 hydronephrosis and ureteral dilation measuring 11.7 mm. The patient was under antibiotic chemoprophylaxis at the time of the referral. A dynamic diuretic renal scintigraphy was performed after injection of 75 MBq 99m Tc DTPA. The imaging was according to standardized protocol with the vascular phase of the scintigraphy obtained by acquiring 2 s/frame for 60 seconds, followed by the sequential functional phase with 1 min/frame for an additional 20 minutes. ROIs were delineated around the kidneys, as well as semilunar ROIs along the lateral aspect of the kidneys for corresponding background activity. Evaluation of renal function was based on several parameters, including DRF, time to maximal activity in the kidneys (T-max), time to reduced activity to half of the Tmax (T1/2), and percentage of excreted tracer at 20 minutes from the maximal uptake. Subsequent to the baseline study, a diuretic study was conducted by intravenous administration of furosemide (F+20 protocol), with additional 1 min/frame for additional 15 minutes. After selecting the appropriate ROIs and background regions, the percentage of the excreted tracer was computed

to assess renal tracer excretion after diuretic administration. In the vascular phase, the scan revealed symmetrically reduced perfusion of both kidneys and on the sequential scans, the kidneys showed normal accumulation, but minimal spontaneous elimination of the radiotracer. The percentage of elimination of the tracer after furosemide-stimulated diuresis was 61% from the left kidney and 71% from the right kidney. The calculated DRF value of the left kidney was 45% and 55% for the right kidney. The DTPA scan showed the absence of urinary tract obstruction but revealed marked dilatation of the urinary tract.

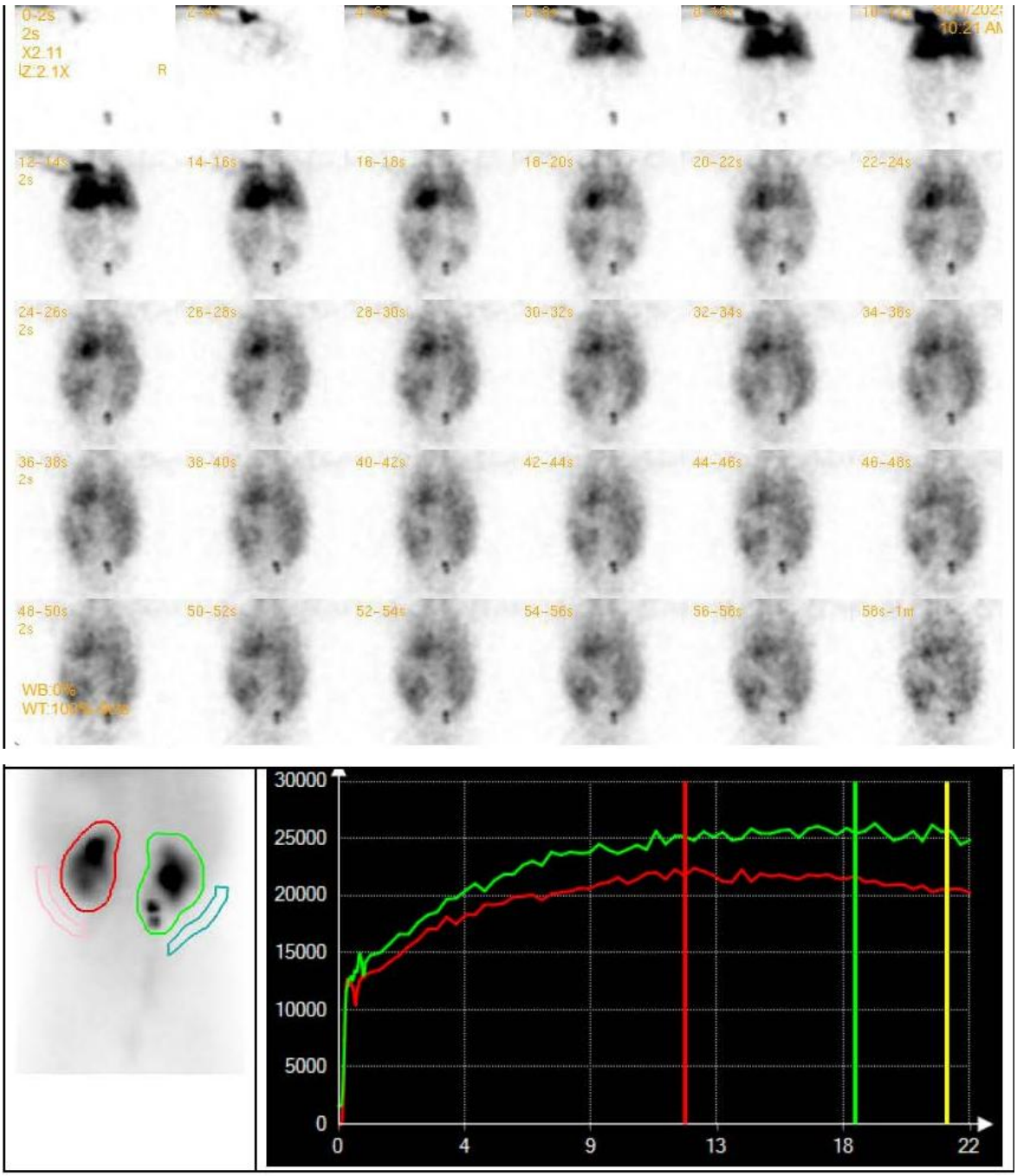
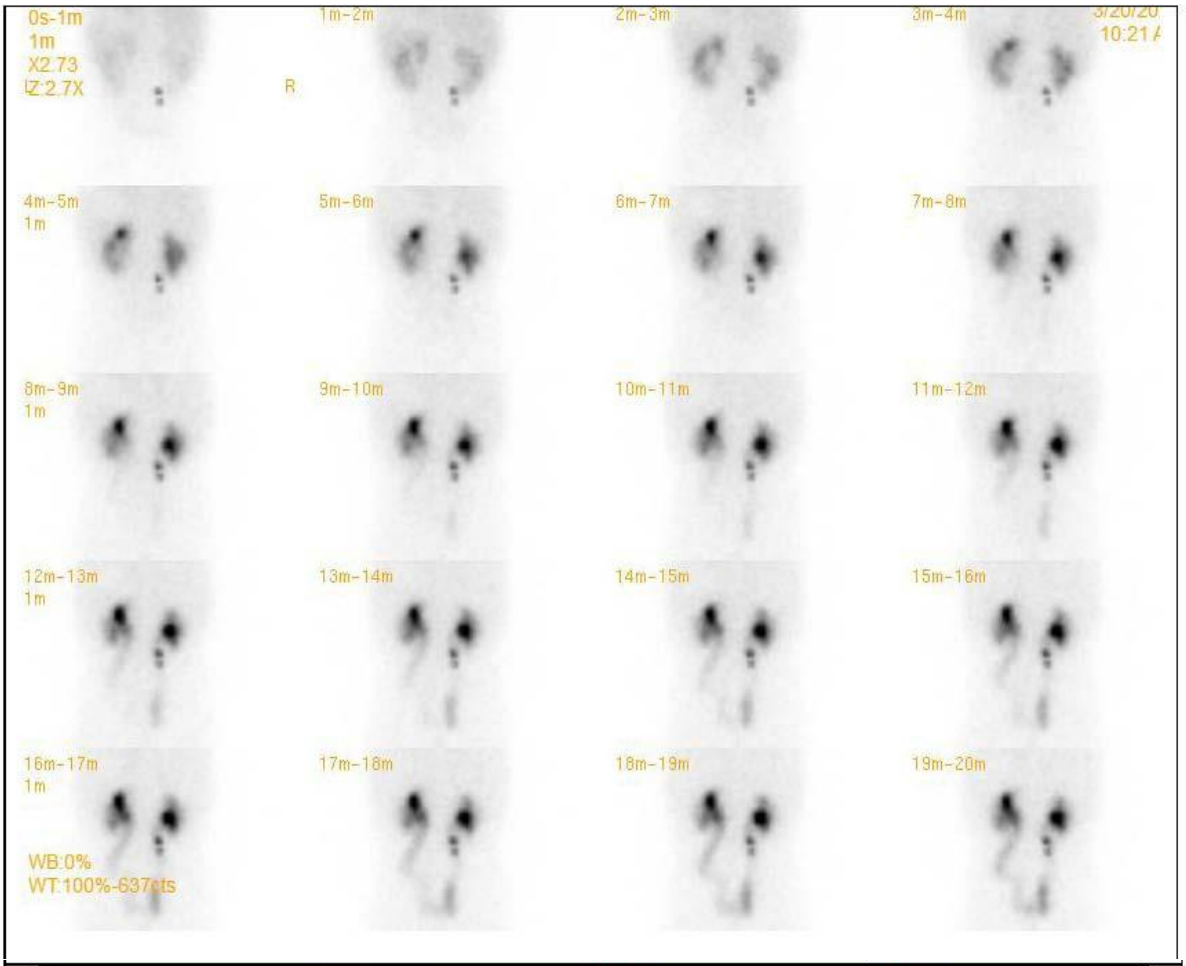


Fig. 4. Vascular phase of 99mTc-DTPA scan showing bilateral reduced perfusion of the kidneys and prolonged accumulation of the radiopharmaceutical



	at time	Left	Right
Relative Function		45 %	55 %
Kidney T-max		12.1 min	18.1 min
Kidney T-halfmax		0.0	0.0
% Excreted	21 min	8 %	2 %
Ratio/3min	20min	1.19	1.36

Fig. 5. Sequential scans showed elimination of the radiopharmaceutical from renal parenchyma, but retention in the renal pelvicalyceal system and along the tortuous and dilated ureters

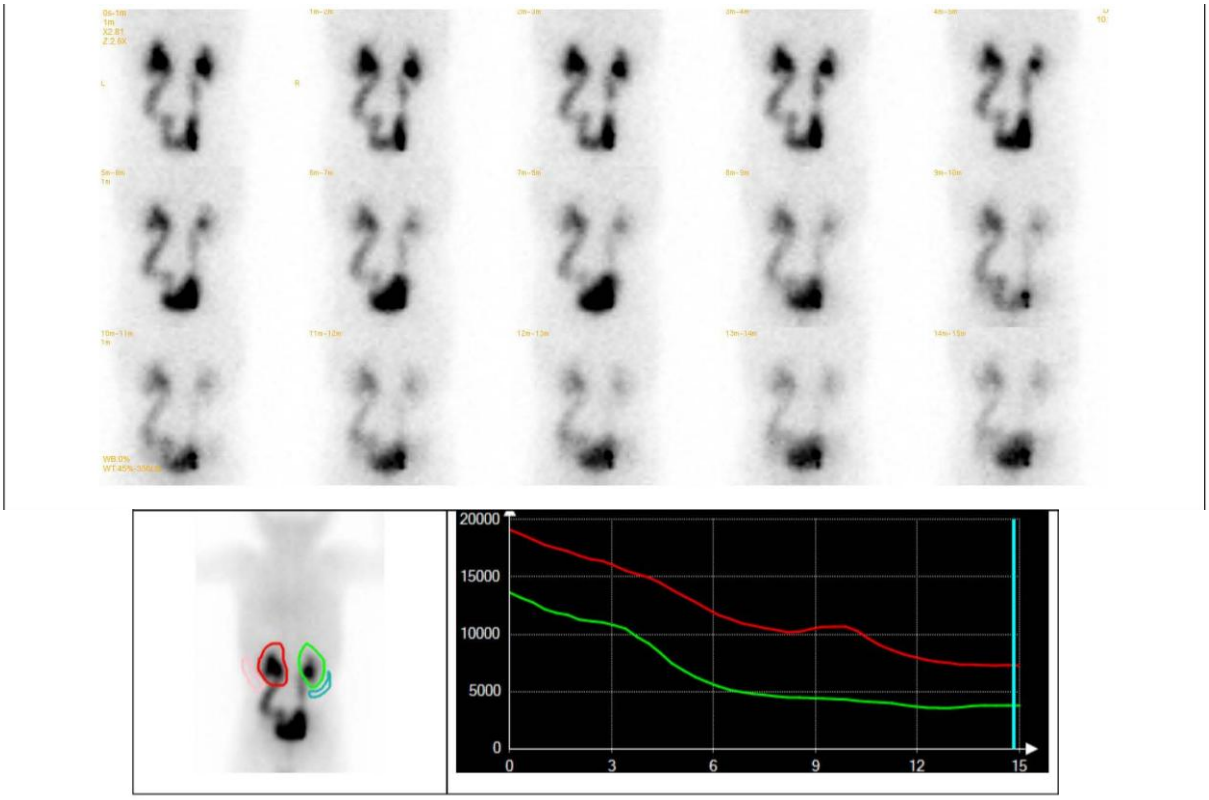


Fig. 6. Post-diuretic sequential scans during additional 15 minutes, and the generated radiorenogram curves showed further elimination; the scan did not reveal signs of urinary tract obstruction

Case 5

A 3-month-old male child was referred to our institution for a 99mTc- DTPA dynamic renal scan. The patient came in with previously obtained imaging studies, including US of the urinary tract and cystourethrography. The US had revealed grade 4 hydronephrosis of the left kidney with high suspicion of pelvo-ureteral junction stenosis. Cystourethrography had excluded VUR as an etiological cause of the hydronephrosis for this patient. A referral for a DTPA dynamic renal scan was made. The scintigraphy was performed after injection of 80 MBq of 99m Tc DTPA, according to standardized protocol with 2 min/frame for the first 60 seconds after intravenous administration of the radiopharmaceutical, followed by additional sequential 2 min/frame imaging for 20 minutes. The vascular phase revealed asymmetry, with reduced vascularization of the left kidney compared to the right kidney. On the sequential scans, the right kidney accumulated the tracer well and spontaneously eliminated it with slight residual accumulation in the cortical and pyelocaliceal system. The left kidney showed prolonged accumulation of the tracer with a Tmax of 5.1 minutes, with spontaneous elimination of the tracer from the parenchyma, but significant retention in the calices and pyelon. After intravenous injection of a diuretic, the left kidney eliminated 63% of the residual tracer. The DRF calculated was 56% for left kidney, and 44% for the right kidney.

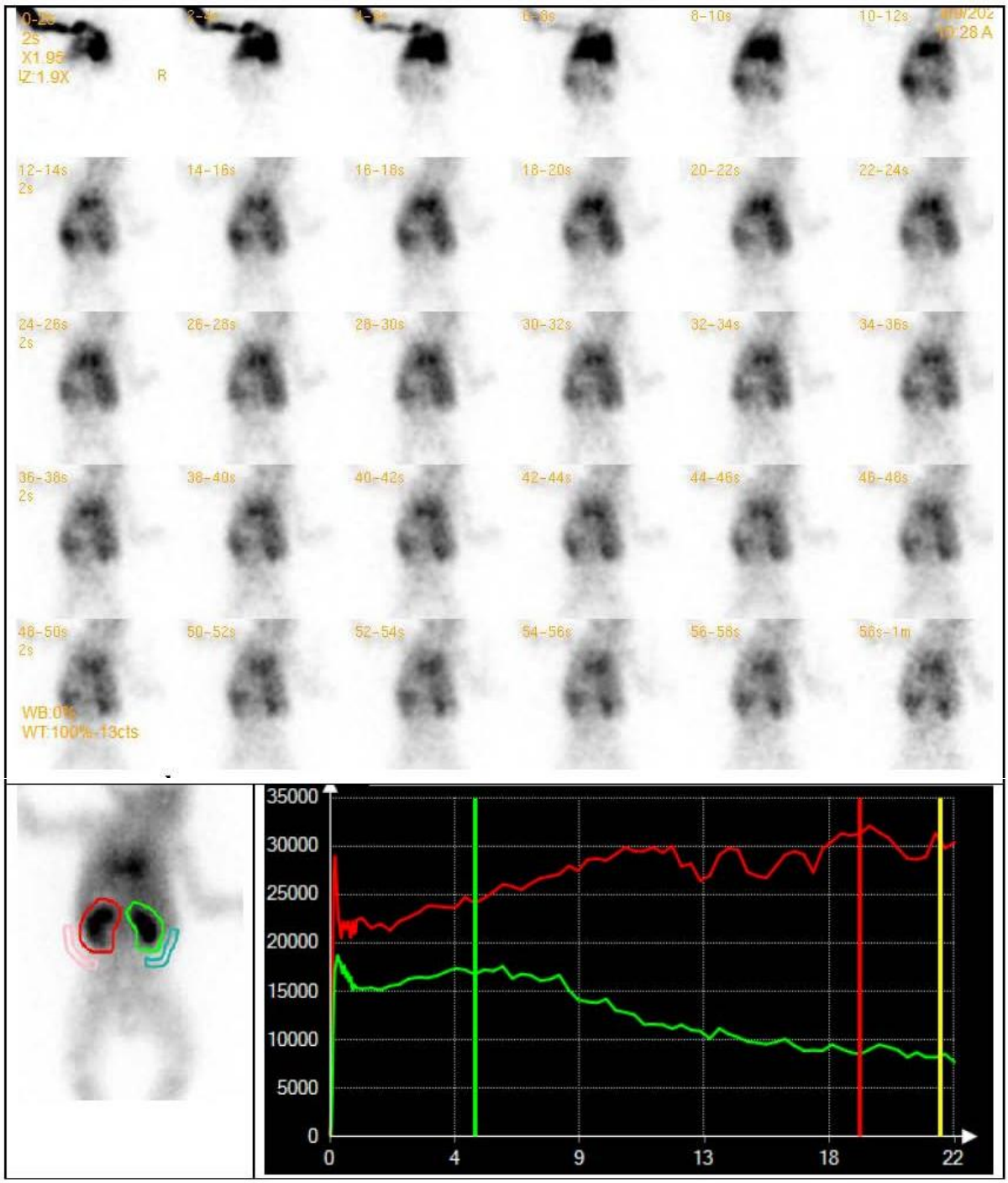
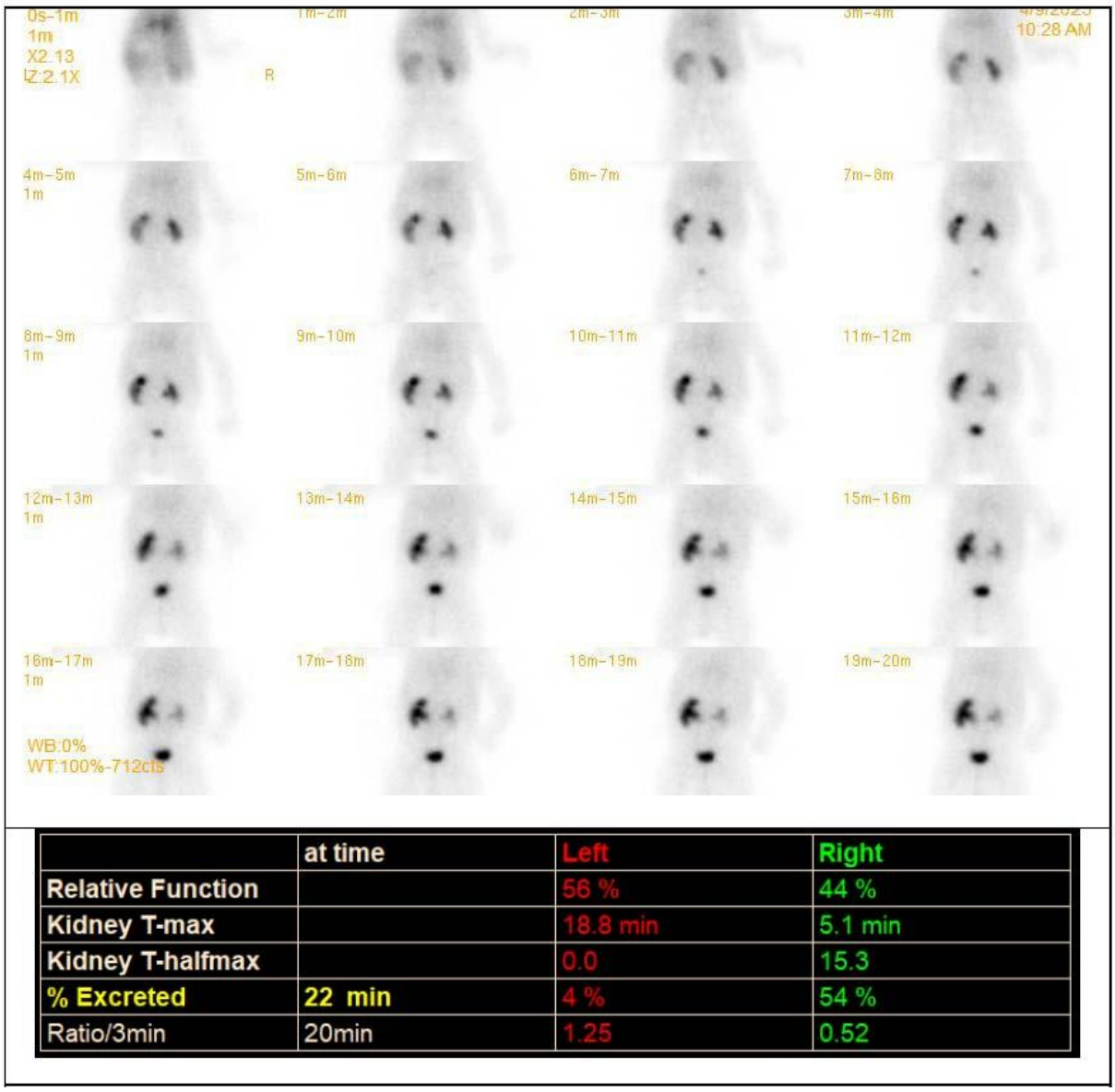


Fig. 7. Vascular phase of 99mTc-DTPA scan showing bilateral symmetric perfusion of the kidneys and prolonged accumulation of the radiopharmaceutical; left kidney without spontaneous elimination



	at time	Left	Right
Relative Function		56 %	44 %
Kidney T-max		18.8 min	5.1 min
Kidney T-halfmax		0.0	15.3
% Excreted	22 min	4 %	54 %
Ratio/3min	20min	1.25	0.52

Fig. 8. Sequential scans and radiorenogram curves revealed normal accumulation and elimination from the right kidney, but prolonged accumulation and elimination from the left kidney, with retention in the pyelon

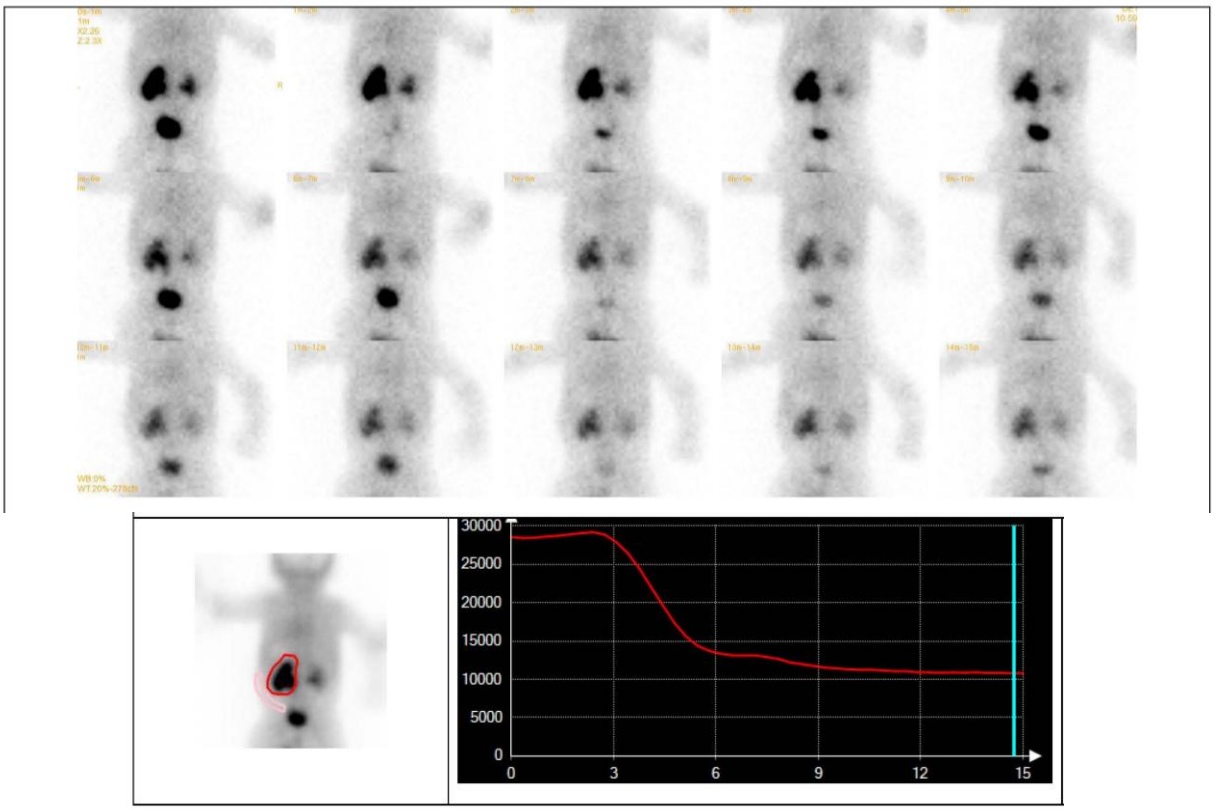


Fig. 9. Post-diuretic scans showed very good elimination after furosemide application from the left kidney, finding corresponding to hypomotilitated and dilated renal pyelo-ureteral system from the left kidney

Discussion

Since the introduction of routine fetal US screening in the 1990s, the antenatal detection of CAKUT has markedly increased, particularly in cases of urinary tract dilatation. The diagnostic workup of CAKUT typically begins with renal and bladder US as the first-line imaging modality[18]. Nuclear medicine complements this approach by providing functional assessment of the renal parenchyma, urinary tract anatomy, and drainage. These studies are minimally invasive, involve low radiation exposure, rarely require sedation, and offer high diagnostic accuracy[18]. Nuclear medicine renal imaging includes dynamic scintigraphy, static cortical scintigraphy, and both direct and indirect radionuclide cystography. In the presented first and second cases, the main contribution of the 99mTc-DMSA scan was in using objective and low-dose exposure methodology, confirming the anomaly in the position of the kidney, and an additional advantage was in the possibility of evaluating separate cortical kidney function, the semi-quantification possible only with nuclear medicine methods. Additional diagnostic information about developed chronic complications due to VUR and recurrent urinary tract infections was obtained in the third case. In this case, the renal scan revealed a hypofunctional left kidney with hypofixating defects and smaller defects in the right kidney. In the fourth and fifth cases, the DTPA diuretic study did not reveal obstruction, but dilatation and a reservoir phenomenon of the urinary tract. The evaluation of renal function and urinary tract anatomy relies on three categories of radiopharmaceuticals, classified by their mechanisms of uptake and elimination: glomerular filtration tracers (e.g. 99mTc-DTPA), which are filtered by the glomeruli and not retained in the parenchyma; tubular extraction tracers (e.g. 99mTc-MAG3), which are secreted by the tubules and also not retained; and cortical tracers (e.g. 99mTc-DMSA), which accumulate in the renal cortex[19]. The 99mTc-

DTPA scan is most frequently used because of availability and the possibility to easily and objectively evaluate kidney vascularization, glomerular filtration rate (GFR), cortical transit, transit of urine through the pyelocaliceal system, the ureter, and bladder. These include time of maximal uptake of the tracer in the cortex (Tmax), the percentage of excreted urine at a certain timeframe, separate kidney function, and the calculation of GFR. Parameters like these, along with images obtained at regular intervals throughout the study, are pivotal in the evaluation of obstructions and dilatations of the urinary tract. With UPJ obstruction being the most common CAKUT, it is clear why the dynamic renal scintigraphy plays an irreplaceable role in its management and other congenital urinary tract anomalies that cause dilatation or obstruction of the urinary tract, such as ureteral stenosis, ureter duplex, ureterocele, vesicoureteric junction obstruction, vesicoureteral reflux, posterior urethral valve, urethral stenosis, or atresia. After the initial scan, a diuretic scan can be performed, by which urinary tract obstruction can be differentiated from dilatation using the percentage of excreted tracer at the end of the diuretic study. In certain cases, both static and dynamic scans can be used to evaluate one single anomaly, such as vesicoureteral reflux which can cause urinary tract obstruction and dilatation that can be evaluated by dynamic scintigraphy, while cortical scarring resulting from recurrent urinary tract infections, caused by VUR can be diagnosed using static scintigraphy. Another tool that nuclear medicine has in its arsenal of diagnostic procedures and is used for diagnosis and management of VUR is the direct and indirect radionuclide cystourethrography, and the advantage is related to markedly lower radiation exposure associated with dynamic renal cystography, representing only 1-2% of the exposure from radiological voiding cystourethrography[20,21].

Conclusion

In conclusion, nuclear medicine imaging plays a pivotal role in the objective evaluation of congenital renal disorders, offering functional and anatomical insights that complement conventional radiological modalities. Techniques such as dynamic renal scintigraphy with diuretic renography, static cortical renal scintigraphy, direct and indirect radionuclide provide crucial information for diagnosis, treatment planning, and post-interventional follow-up, while minimizing radiation exposure and procedural invasiveness. These modalities are particularly valuable in pediatric populations, where early detection of functional impairment can guide timely interventions and improve long-term renal outcomes. Overall, nuclear medicine continues to be an indispensable tool in the comprehensive management of congenital anomalies of the kidney and urinary tract.

Conflict of interest statement. None declared.

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