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Original Article

Congenital Anomalies of Urinary Tract in Kosovo Population Diagnosed by Renal Scintigraphy

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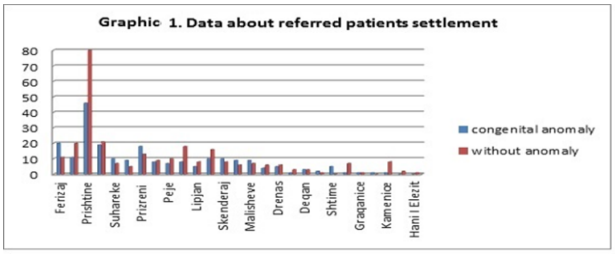
ABSTRACT

Congenital kidney and urinary tract abnormalities are considered among common congenital anomalies in people, resulting in loss of renal function and progression to the kidney disease terminal stage. The aim of this study was to determinate the frequency of the urinary tract congenital anomalies among Kosovo people and the variability in Glomerular filtration rate (GFR) using renal scintigraphy. In a prospective study, spanning a one-year period, September 2018 to September 2019, we examined a group of 509 patients referred for renal scintigraphy in the Department of Nuclear Medicine at the University Clinical Centre of Kosovo. Dynamic renal scintigraphy with 99mTc DTPA was performed in all referred patients, while the static scintigraphy with 99mTc DMSA only in patients with kidney congenital anomalies and lower urinary tract. Among 509 patients, 228 (44.8%) were found to have congenital urinary tract anomalies. The most frequent congenital anomaly was renal hypoplasia (71 cases) followed by ureter-pelvic junction stenosis (45 cases). The elevated urea and creatinine values were found in 18 (7.9%) patients with the congenital urinary tract anomalies. The decreased GFR determined using DTPA scintigraphy was found in 99 (43.42 %) patients, despite the fact urea and creatinine values in 81 patients were normal. Our study found that patients with congenital renal and urinary tract abnormalities are at high risk for compromised glomerular renal function, particularity in those with horseshoe-shaped kidney, renal hypoplasia, and unilateral renal agenesis.

GRAPHICAL ABSTRACT



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Introduction

According to the available literature, congenital urinary tract anomalies are among the most frequent types of congenital malformations [1]. Kidney and urinary tract malformations represent 20% of all birth defects, appearing in 3-7 cases out of 1000 live births [1]. The congenital anomalies of the kidneys and/or lower urinary tract (CAKUT) comprise the most common causes of renal failure in children and account for nearly 25% of renal end-stage disease in adults [2-4]. According to the referenced data of Hattori *et al.*, approximately 39.8% of end-stage renal disease cases in patients younger than 20 years old in Japan are due to CAKUT [5]. The prevalence of CAKUT ranges from 4.2 per 10,000 births in Taiwan to 4.0 per 1000 births in Russia and some Asian and European countries [6, 7]. CAKUTs comprise a wide range of renal system structural and functional malformation that occur at the kidney level (e.g., hypoplasia and dysplasia), collecting system (e.g., hydronephrosis and megaureter), bladder (e.g., ureterocele and vesicoureteral reflux), or urethra (e.g., posterior urethra valves) [8]. In most of the reported data, CAKUT were more frequent in males than in females with a ratio of 1.44-6.4:1.13 [9-11]. One of the most severe congenital renal anomalies that had been recognized since the 18th century was complete absence of both kidneys, reported for the first time from Dr. Edith Potter in 1946 [12]. According to the refereed data, including Bin Zhang *et al.*, hydronephrosis was the most frequent congenital urinary tract anomaly, found in 0.78% of cases, followed by ureterovesical junction obstruction in 0.19%, renal dysplasia in 0.17%, renal cysts 0.15%, duplex kidney 0.14%, solitary kidney 0.12%, ureterocele 0.09%, fused kidney 0.06%, renal hypoplasia 0.05%, ectopic kidney 0.03%, and polycystic kidney 0.02% [13-16]. These abnormalities can result in the recurrent urinary tract infections or retention, which may damage the kidneys or other structures [16]. Murugapoopathy V. and Gupta I. consider that by understanding the causes of CAKUT and low nephron number, we can begin to identify preventive treatments and establish clinical guidelines for how these patients should be followed [17]. The causes of these urinary abnormalities are complex and usually include combination of genetic and environmental factors [18]. With the advent of modern genetic testing, over 50 genes have been implicated in nonsyndromic or syndromic forms of CAKUT, the most common ones being due to HNF1B and PAX2 genes mutation [18]. Several environmental risk factors have been recognized so far, including maternal diabetes [19] and intrauterine exposure to ACE-inhibitors [20]. Therefore, the early detection and optimal management are essential for favourable outcomes [20].

The goal of this study was to diagnose congenital anomalies of the urinary tract (CAKUT), their type, frequency, and impact on glomerular filtration rate using renal scintigraphy.

Martials and methods

The study was prospective, conducted during the period September 2018 - September 2019. The study included 509 patients referred for renal scintigraphy in the Department of Nuclear Medicine at the University Clinical Centre of Kosovo (UCCK). All patients referred for renal scintigraphy were recommended by nephrologists, urologists, and paediatricians, and less frequently by family physicians and physicians of other profiles. Most patients are referred with ready-made diagnoses confirmed by other methods, in most cases, by ultrasonography examination and in special cases, by intravenous urography, Magnetic resonance imaging (MRI), computed tomography (CT), and conventional abdominal roentgen imaging (X-ray abdominal test). The necessary conditions for inclusion in the study were pre-existing tests of urea and creatinine.

Renal dynamic scintigraphy

After clinical examination, dynamic renal scintigraphy was performed in all patients. Dynamic renal scintigraphy was performed according to the Gate GFR (DTPA) protocol for 20 minutes. 99mTcDTPA (diethylene triamine penta-acetic acid) was provided by the Radioisotope Centre Polatom. The radioactive chemical purity was >95%. Recording of the

dynamic kidney function images began from the moment of injection of 99mTcDTPA via intravenous route with a dose of activity 1-4 mCi (37-148 MBq) depending on the patient's age and body weight. With patients in the supine position, images were acquired posteriorly at 3 sec/frame for 20 frames and 20sec/frame for 57 frames. The dose of injected activity was calculated automatically by estimating the activity dose in the full syringe before injection and the remaining dose in the empty syringe after injection. The scintigraphic images were acquired using SIEMENS (ECAM) dual probe SPECT gamma camera. In cases presented with non-elimination of urine during dynamic scintigraphy, in the 15th minute of the study, we administered Furosemide intravenously to distinguish functional from organic obstructions.

Data processing and GFR-Gates calculation

Data processing was performed by determining the functional regions on each kidney separately and the background activity around the two kidneys. For the analysis of renal function, dynamic images recorded in the third minute (frame 27) of the study were selected.

After processing the data, results were obtained which presented the separate function of each kidney in their common function, data on glomerular filtration rate, tubular function, glomerular filtration fraction, and half-elimination time of radioactive urine. The GFR gates of the both kidneys present the sum of GFR right and left kidney, and were calculated automatically with the Gates equation is as follows.

$$GFR\ (mL/min) = \{[(L\text{-}LB)/e^{-\mu\chi L} + (R\text{-}RR)/e^{-\mu\chi R}]/\ (Pre - Post)\} \times 100 \times 9.81270 - 6.82519$$

[pre, pre-count; post: post-count; L, left kidney counts; LB left kidney background counts; R, right kidney counts; RB, right kidney background counts; χL, left kidney depth; χR, right kidney depth; μ, attenuation coefficient of 99mTc in soft tissue (0.153/cm); e, constant].

Renal static scintigraphy

A DMSA renal scan is a diagnostic exam that allows better evaluation of the renal cortex, shape, size, and position of the kidneys and detects scarring caused by frequent infections. Renal static scintigraphy was performed via intravenous administration of 99mTc DMSA (2,3 dimercaptosuccinic acid), with activity dose of 1-4 mCi, depending on the patient's age and body weight. Images were taken 3 hours after the dose administration. The images were taken in the supine position of patients, with both detectors placed simultaneously in the anterior and posterior position of the abdomen.

Test of blood urea and creatinine

Urea and creatinine tests were brought a priory by patients as they were a necessary condition for performing kidney scintigraphy. The analyses were performed in the Clinical Biochemistry laboratory at University Clinical Centre of Kosovo as well as the biochemical laboratories in the hospital centres and family medicine centres from where the patients were referred. The normal reference values of urea in biochemical laboratories in adults were (2.1-8.5 mmol/L) while in children were (2.5-7.8 mmol/L). Normal reference values of creatinine in biochemical laboratories in male adults were (65.4-119.3 mmol/L) while in female adults (52.2-91.9 mmol/L). In children, the normal reference values are determined by age. Thus, at age 0-14 days the reference values were (28-81 mmol/l), at age 15 days -2 years (9-32 mmol/L), 2-5 years (18-38 mmol/L), 5- 12 years (27-52 mmol/L), 12-15 years (40-72 mmol/l) 15-19 years (55-95 mmol/L) in males and (43-74 mmol/L) in females.

Ethical statement

All procedures performed in the study were in accordance with the ethical standards of the Ethic Committee of University Clinical Centre of Kosovo No. 248/21.02.2018 and we confirm with high competency that studies have been performed according to the 1964 Declaration of Helsinki.

Statistical analysis

Statistical data were analysed using IBM SPSS Version 25 (IBM Corp., Armonk, N.Y). Patient characteristics data were summarized using descriptive statistics. Sub-group analyses were performed, separating the patient population into single or multiple drain cohorts. Fisher's exact testing was used to assess categorical variables. A paired sample Student's t- test was implemented to examine the outcome data between two groups. The statistical significance was defined as a value $p<0.05$.

Results and Discussion

The study included 509 patients, 236 males and 273 females referred for renal scintigraphy. The mean age of all patients included in the study was 38.2±23.4 years and was approximately the same in both sexes. During the study, we found 228 patients with congenital anomalies of the urinary tract, which constitutes for 44.8% of all patients examined. The other group of 281 patients (55.2%) was diagnosed with other urinary tract diseases (Table 1). The mean age of patients with congenital anomalies of the urinary tract was 21.1 years and was significantly younger compared with the mean age of the other group 53.09 years ($p <0.00001$). Based on these data, males with urinary tract abnormalities were significantly younger (16.6 years) than females (23.2 years) with urinary tract abnormalities $P<0.05$.

Congenital urinary tract abnormalities are found in almost all age groups. In the age group of 0 to 12 months were observed in 58 cases, in children aged 1 to 5 years were in 30 cases, in the age group of 6 to 10 years were in 29 cases, in the age group of 11 -20 years old were in 31 cases, and in the age group older than 20 years old were in 80 cases (Table 2).

We have observed that 58 patients with congenital anomalies of the urinary tract were born in the period 1 September 2018- 30 September 2019. According to data reported by the Kosovo Agency of Statistics, between 1 September 2018 until 30th September 2019, there were registered 23897 live births. As such, the CAKUT incidence within the population of Kosovo was 0.24% or 2.4 cases of congenital urinary tract abnormalities in 1,000 live births (Table 3).

Most of patients with congenital urinary tract abnormalities were been referred from Pristine, the capital town of Kosovo (20.7%), while the rest of patients with congenital urinary tract abnormalities were referred from all other centres of Kosovo (Figure 1).

Table 1: Data about number and average age of patients included in the study

Patients	Male			Female			Total			P-Value
	N	%	Average age	N	%	Average age	N	%	Average age	
Without anomaly	120	50.85	54.3±13.82 SD=18.25	161	59	53.25±13.55 SD=17.24	281	55.2	53.09±13.71 SD=17.67	>0.05
With congenital anomaly	116	49.15	16.66±17.56 SD=21.63	112	41	23.17±19.22 SD=22.44	228	44.8	21.1±18.56 SD=22.23	<0.05
Total	236	46.37	36.29±25.33 SD=27.41	273	53. 63	41.17±21.53 SD=24.44	509	100	38.25±23.4 SD=25.94	>0.05
P-value			<0.0001			<0,05			<0.0001	

Table 2: Data about the finding of congenital urinary tract abnormalities in certain age groups

Age group	Male		Female		Total	
	N	%	N	%	N	%
0-12 months	35	15.35	23	10.09	58	25.44
1-5 years old	20	8.78	10	4.38	30	13.16
6-10 years old	16	7	13	5.7	29	12.7
11-20 years old	11	4.82	20	8.78	31	13.6
>20 years old	34	14.91	46	20.17	80	35.09
Total	116	50.88	112	49.12	228	100

Table 3: Statistical data about live births with congenital urinary tract anomalies

Calendric years	Months	Number of Live births	Live with congenital anomalies of urinary Tract	
			N	%
2018	September	1950	5	0.25
	October	1990	3	0.15
	November	1692	4	0.23
	December	1625	4	0.24
2019	January	1896	4	0.21
	February	1528	6	0.39
	March	1777	1	0.05
	April	1655	0	0
	May	1961	6	0.3
	June	1907	7	0.36
	July	2126	6	0.28
	August	1884	7	0.37
	September	1906	5	0.26
Total		23897	58	0.24

Congenital anomalies of the urinary tract in males seemingly occur at a slightly higher rate, 116 cases (50.87%), compared with females, 112 cases (49.13%). The most common anomaly encountered in both sexes was renal hypoplasia with 71 cases (31.14%), followed by ureteropelvic junction obstruction with 45 cases (19.73%). The most common congenital anomaly in males was renal hypoplasia (29 cases), followed by ureteropelvic junction stenosis (24 cases). In females, the most common congenital anomaly was also renal hypoplasia (42 cases) followed by ureteropelvic junction stenosis (21 cases). The occurrence of congenital anomalies of the urinary tract was almost similar in both sexes, except renal hypoplasia, unilateral renal agenesis, and congenital megaureter. It has been observed that renal hypoplasia is encountered for 19.15% more often in females compared to males and presents a noticeable difference in the occurrence of this anomaly between the two sexes, $p < 0.05$.

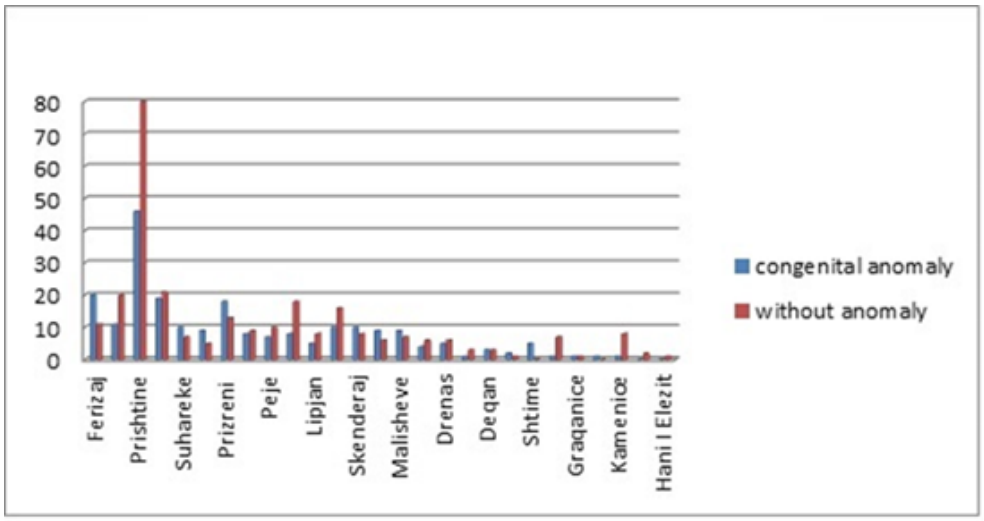

Figure 1: Data about referred patients' settlement

Table 4: The frequency of congenital urinary-tract anomaly

Urinary tract anomaly	Male					Female				Total		
	Left	Right	L+R	Total	%	Left	Right	L+R	Total	%	N	%
Ectopic kidney	4	5		9	7.75	5	6		11	9.82	20	8.77
Horseshoe kidney								2	2	0.87	2	0.87
Hydronephrosis	10	7	6	23	20.05	7	6	5	18	16.07	41	18.8
Renal agenesis	12	3		15	12.93	6	2		8	7.14	23	10.08
Renal hypoplasia	8	21		29	25	23	19		42	37.5	71	31.14
UP junction Stenosis	10	7	7	24	20.68	11	7	3	21	18.75	45	19.73
Megaureter	2	3	2	7	6.03		1	1	2	1.78	9	3.94
Polycystic kidney	1	1	2	4	3.44		1	2	3	2.67	7	3.07
Vesical-ureteral reflux		1	1	2	1.72			3	3	2.67	5	2.19
Dysplastic kidney						1	1		2	1.78	2	0.87
Ureter duplex		1		1	0.86						1	0.43
Pelvis duplex	1	1		2	1.72						2	0.87
Total	48	50	18	116	50.87	53	43	16	112	49.13	228	100.0

It is observed that unilateral renal agenesis is about 30% more common in males, while the congenital megaureter is about 55.54% more common in males than in females ($p < 0.05$). Congenital anomalies in the left urinary tract were encountered in 101 cases (44.3%), while in the right urinary tract were encountered in 93 cases (40.79%). Bilateral congenital anomalies were encountered in 34 cases (14.9%) (Table 4). In the group of patients with other diseases of the urinary tract, referred to as those without urinary tract abnormalities, the largest number of referred patients was diagnosed with renal failure 37.01%. In relatively high percentages, patients with nephrolithiasis (13.8%), urinary tract infections (9.96%), hydronephrosis (8.18%), as well as renal hypofunction and type 2 diabetes with 7.47% of cases were also referred. In a smaller percentage were referred patients with arterial high blood pressure (4.98%), patients with pyelonephritis (3.2%), cystic kidney disease (2.13%), and chronic nephritis 1.42% (Table 5).

The mean concentration of creatinine (72.02±32.29 mmol/L), and urea (5.15±3.25 mmol) in the blood of the all patients with congenital urinary tract anomalies as is presented in Table 6, were in the range of normal values. In the group of patients younger than 14 years old, the mean concentration of creatinine was in the range of normal values (49.05±23.22 mmol/L), while in adults older than 14 years the mean concentration of urea was 95±27.32 mmol/L). The mean GFR value in patients with congenital urinary tract abnormalities (85.16±24.14 ml/min) was slightly lower compared with the mean minimum optimal values (86.24 ±5.03).

In patients with congenital renal hypoplasia, were found 2 cases with the elevated value of urea and 8 cases with elevated value of creatinine. The decreased of GFR values were found in 41 patients with congenital renal hypoplasia (Table 7). Based on statistical criteria, the mean value of GFR in the group of patients with renal hypoplasia, unilateral renal agenesis, renal ectopy and horseshoe kidney is significantly lower, as compared with the mean minimum optimal value of GFR ($p < 0.05$). As it is presented in Table 7, the elevated values of urea were

obtained only in 4 patients (2 patients with renal hypoplasia,1 patient with hydronephrosis and 1 patient with ectopic kidney. The high values of creatinine were obtained in 15 patients (8 patients with renal hypoplasia, 3 patients with unilateral renal agenesis, 2 patients with ectopic kidney, 1 patient with polycystic kidney, and 1 with hydronephrosis).

Table 5: Data of patients with other renal disease

Kidney disease	M		F		Total	
	N	%	N	%	N	%
Non-functional kidney	3	1.07	1	0.35	4	1.42
Hypo functional kidney	11	3.91	10	3.56	21	7.47
Kidney failure	46	16.37	58	20.64	104	37.01
Urinary tract infection	12	4.27	16	5.69	28	9.96
Nephrolithiasis	18	6.41	21	7.47	39	13.88
Hydronephrosis	11	3.91	15	5.34	26	8.18
Cystic kidney	2	0.71	4	1.42	6	2.13
DBM T2	5	1.78	16	5.69	21	7.47
Pyelonephritis	3	1.07	6	2.13	9	3.2
Chronic nephritis	2	0.71	2	0.71	4	1.42
HTA	6	2.13	8	2.85	14	4.98
Nephrotic syndrome	0	0	1	0.35	1	0.35
Glomerulonephritis	0	0	1	0.35	1	0.35
Diabetic nephropathy	1	0.35	2	0.71	3	1.07
Total	120	42.7	161	57.3	281	100

Table 6: Value of urea, creatinine, and GFR in patients with CAKUT

Age group	Mean value of urea	Mean value of creatinine	Mean value of GFR
< 14 years	4.05±2.75	49.05±23.22	100.25±20.12
>14 years	6.75±2.79	95.05±25.37	70.12±32.26
Total	5.15±3.25	72.05±32.29	85.16±24.14

Table 7: Data about mean values of urea, creatinine, and GFR in congenital urinary tract anomaly

Congenital Urinary tract anomalies	N	Urea (mmol/L)	Creatinine (mmol/L)	GFR (mmol/L)	Min GFR (mmol/L)	GFR P-value
Ectopic kidney	20	3.67	56.36	66.39	86.42	<0.005
Horseshoe kidney	2	6.5	92.65	68.45	76.5	<0.05
Hydronephrosis	41	4.52	52.61	105.97	89	>0.05
Renal agenesis	23	5.37	81.16	67.4	83.48	<0.05
Renal hypoplasia	71	6.48	97.21	70.82	82.52	<0.005
UP junction Stenosis	45	5.46	57.68	103.34	88.77	>0.05
Megaureter	9	2.77	34.86	93.39	90	>0.05
Polycystic kidney	7	7.61	130.15	71.06	78.5	>0.05
VUR	5	3.48	60.7	90.1	90	>0.05
Dysplastic kidney	2	5.35	68.9	90.1	90	>0.5
Ureter duplex	1	3.1	53	112.4	90	>0.05
Pelvic duplex	2	3.2	50.7	117.45	90	>0.05
Total	228	5.15±3.25	72.02±32.29	85.16±24.14	86.24±5.03	<0.05

The reduced GFR values were obtained in 99 patients (43.42%) including 4 patients with increased values of urea and 15 patients with increased values of creatinine. The reduced

values of GFR (DTPA) mostly were found in patients with renal hypoplasia (41 patients) followed by patients with unilateral renal agenesis (16 cases) and renal ectopy (13 cases).

In this study, we found that 44.8% of research subjects in the Department of Nuclear Medicine were diagnosed with urinary tract anomalies. Diagnosis of congenital abnormalities of the kidneys and lower urinary tract is made mainly using ultrasound examination of the abdomen. In cases with unclear diagnosis, CT, MRI, and intravenous urography were used as complementary imaging methods. The importance of ultra-sonographic examination in the CAKUT diagnosis is very high, given the non-invasiveness, easy access to the examination and the cheapest cost of examination. The limitations of ultrasonography are the inability to determine glomerular renal function and the difficulties in correctly diagnosing renal ectopy and unilateral renal agenesis. As a complimentary imaging method and the main method for determining kidney function was used kidney scintigraphy which as a diagnostic material uses radiopharmaceuticals in low doses of activity, which in a way make this method potentially dangerous to health due to ionizing radiation.

The mean age of patients diagnosed with congenital anomalies was significantly younger compared with the mean age of the other group of patients, without congenital urinary tract anomalies ($p < 0.00001$). In almost all of the reported studies, the urinary tract abnormalities in males were more common than in females and the ratio ranged from 1.4: 1 to 2.13: 1 (9), 4.26: 1 (10) and 6.4: 1 (8). However, in our study, we observed that the frequency of congenital urinary tract anomalies in males and females was almost equal, with a reported ratio of 1.03:1. The mean age of males with urinary tract anomalies was significantly younger than mean age of females of the same group ($p<0.05$).

The fact of a younger average age in men with congenital abnormalities of kidney and urinary tract, may be either coincidental or as result of earlier health problems in males and the earlier visits to the doctor. As most studies point out, the frequency of various forms of congenital anomalies of the urinary tract varies from country to country. However, in most cases, the most common anomaly is congenital hydro nephrosis (31.79 %) followed by polycystic kidney disease, unilateral renal agenesis, renal ectopy, and renal duplication (6, 11, 12). One other study conducted in Taiwan, reported that the most common malformations of the genitourinary system were polycystic kidney disease (10.63%), UPJ obstruction (10.22%), cryptorchidism (9.81%), and renal hypoplasia (9.73%) (7). Lisa Nowel *et al.* in their study found that prevalence of renal anomalies in infants younger than 2 months at the time with urinary tract infection was < 5% (14). VUR has been reported in up to 33% of all children diagnosed with a UTI (15). Kanellopoulos *et al.* in their study found that 24% of infants less than 1 month and 21% of infants 1–12 months of age had VUR after a first UTI. Furthermore, in that study they found that 8% of infants less than 1 month and 9% of infants 1-12 months had other structural abnormalities, such as hydronephrosis and posterior valves (16). Our data show that the most common anomaly of the urinary tract is renal hypoplasia, found in 31% of cases, followed by ureterovesical junction stenosis (19.73%), congenital hydronephrosis (18.8%), unilateral renal agenesis (10.08%), renal ectopy (8.77%), congenital mega ureter (3.94%), polycystic kidney (3.07%) etc. Our study showed almost the same rankings of congenital urinary tract abnormalities in both males and females. However, we observed that renal hypoplasia occurs approximately 19.5% more often in females than in males ($p <0.05$). Furthermore, we observed that unilateral renal agenesis (about 30%) and congenital megaureter (about 55.54%) are significantly more frequent in males than females ($p <0.05$). While, Melo *et al.* (4) and Radhakrishna *et al.* (8) in their studies found that the majority of patients with urinary tract abnormalities had bilateral disease (54-65%) with more frequent occurrence on the left side (22%-30%), in our study, we found that urinary bilateral tract abnormalities are recorded in

Table 8: Alteration of renal parameters in patients with urinary tract anomaly

Congenital urinary tract anomalies	N	Urea value		Creatinine value		GFR value		
		high	normal	high	normal	low	high	normal
Ectopic kidney	20	1	19	2	18	13	0	7
Horseshoe kidney	2	0	2	0	2	2	0	0
Hydronephrosis	41	1	40	1	40	9	2	30
Renal agenesis	23	0	23	3	20	16	0	7
Renal hypoplasia	71	2	69	8	63	41	0	30
UP junction Stenosis	45	0	45	0	45	8	0	37
Megaureter	9	0	9	0	9	4	0	5
Polycystic kidney	7	0	7	1	6	3	0	4
VUR	5	0	5	0	5	2	0	3
Dysplastic kidney	2	0	2	0	2	1	0	1
Ureter duplex	1	0	1	0	1	0	0	1
Pelvic duplex	2	0	2	0	2	0	0	2
Total	228	4	224	15	213	99	2	127

14.9% of cases, with a slightly more pronounced frequency of about 3.6% on the left side. Based on statistical data on the number of live births in Kosovo for 2018 and 2019, it appears that congenital urinary tract abnormalities have a frequency of 0.24% or 2.4 cases of congenital urinary tract abnormalities in 1,000 live births in Kosovo during the one-year period from September 1, 2018 to October 1, 2019 [21].

Studies have shown that in cases of renal and urinary tract abnormalities there is initially a temporary increase in GFR. However, after a few years, there is a decrease in glomerular function and gradual loss of renal function [22]. Thus, we have considered that the evaluation of biomarkers such as creatinine and urea in blood serum may be important in the early detection of impaired renal glomerular function. Our results have shown that high concentrations of urea and creatinine were recorded in only 4 cases of urea, and 15 cases of creatinine respectively, representing only 6.57% of cases with congenital abnormalities of the kidneys and urinary tract. Our results reported a decrease in GFR in 99 patients representing 43.42% of cases and which are results similar to the results reported by Veerbhadra Radhakrishnan *et al.* [23] who report reduced GFR in 50% of children with solitary kidney function.

According to the obtained data, it is evident that both cases with high urea values (100% of cases) and 8 cases with elevated creatinine values (53.33% of cases) were registered in the group of patients with renal hypoplasia. Low GFR values were encountered in 41 cases with renal hypoplasia accounting for 41.41% of all cases with reduced GFR [23].

We have reported interesting findings in patients with unilateral renal agenesis. While high creatinine values were recorded in only 3 cases (13.4%), low GFR values were recorded in 16 cases, accounting for about 69.56% of cases with unilateral renal agenesis. Even in patients with renal ectopy, high creatinine values were encountered in only 2 patients (10%), while low GFR values were encountered in 13 patients (65% of cases). We observed that despite the high number of patients with ureteropelvic stenosis and renal hydronephrosis, urea and creatinine values were mostly normal in all these patients, while low GFR values were recorded in only 8 cases with ureteropelvic junction stenosis (17.77% of cases), respectively, 7 cases of congenital hydro nephrosis (17.9% of cases). Decreased GFR values were further recorded in 2 patients with horseshoe kidney (100% of cases), in 4 patients with megaureter 44.44% of cases), in 3 patients with polycystic kidney disease (75% of cases), and in 2 patients with VUR (66.66% of cases).

As can be seen from the results of the present study, urea and creatinine values were normal in most cases and are normal even in 84 cases (84.84%) when GFR values were found to decrease. We consider that these normal values of creatinine and urea in cases with reduced GFR are due to activation of the functional glomerular reserve of the kidney in the early stages of renal disease. Based on our results, it was observed that GFR reduction was a significantly more

sensitive parameter in determining renal impairment compared with the elevated creatinine and urea values, $p < 0.05$.

Conclusion

For congenital anomalies of the kidneys and urinary tract in Kosovo are presented in almost all of their possible variations, but with a significantly more frequent occurrence of renal hypoplasia and ureteropelvic junction stenosis. Patients with congenital urinary tract abnormalities, in particular patients with horseshoe kidney, renal hypoplasia, and unilateral renal agenesis are at high risk of experiencing impaired glomerular function. According to our examinations, determining the GFR value through dynamic scintigraphy has resulted in a more sensitive method for the early detection of impaired renal function than determining the concentration of urea and creatinine in the blood.

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Authors' contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

Conflict of Interest

The author declared that they have no conflict of interest.

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