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ORIGINAL PAPER

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Frequency of Urinary Tract Infection When Diagnosing Vesico Urethral Reflux in Children in Tuzla Canton

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ABSTRACT

Background: Vesicoureteral reflux (VUR) represents the return of urine from the bladder into the ureter and the renal canal system. Reflux can occur only on one or both kidneys. VUR most often occurs due to an incompetent ureterovesical junction, which consequently leads to hydronephrosis and dysfunction of the lower parts of the urinary system. **Objective:** The aim of the study was to determine the frequency of urinary infection when diagnosing vesicourethral reflux in children in the Tuzla Canton, in the five-year period from 01.01.2016 to 01.01.2021. **Methods:** Through a retrospective study, we analyzed data from 256 children with vesicourethral reflux (VUR), examined in the Nephrology Outpatient Clinic, Clinic for Children's Diseases, University Clinical Center Tuzla, in the period from 01.01.2016 to 01.01.2021, from early neonatal to 15 years of age. The age and gender of children, the most common symptoms of urinary tract infections during the detection of VUR, and the degree of VUR were analyzed. **Results:** From 256 children with VUR, 54% were male and 46% female. The highest prevalence of VUR was in the age group 0–2 years, and the lowest in the age of children > 15 years. There was no statistically significant difference between the groups of our respondents in relation to age groups, nor in relation to the gender of the children. Statistically significantly more children were without nonspecific symptoms and with asymptomatic bacteriuria in the group without UTI symptoms in children with VUR compared to the group with UTI symptoms in children with VUR. Pathological urine culture between the groups was without a statistically significant difference. **Conclusion:** Although

urinary tract infection in children is common, the possibility of permanent consequences should always be kept in mind if VUR is not diagnosed and treated in time.

Keywords: vesicourethral reflux, children, urinary tract infection.

1. BACKGROUND

Vesicoureteral reflux (VUR) represents the return of urine from the bladder into the ureter and the renal canal system. Reflux can occur only on one or both kidneys. VUR most often occurs due to an incompetent ureterovesical junction, which consequently leads to hydronephrosis and dysfunction of the lower parts of the urinary system (1). It is the most common anomaly of the urinary system in childhood. In asymptomatic children, the frequency of VUR is unknown, in general it is around 1% in the general population. Smaller children are more susceptible to reflux due to the relatively shorter submucosal section of the ureter. In children with a urinary tract infection (UTI), the frequency of VUR ranges from 29 to 50% (2).

Urine that returns to the kidney is due to bacteria, which often contains the source of repeated kidney infections, and even the return of urine to the kidneys due to water pressure or retention of urine can damage the delicate structures and epithelium of the kidney canal and calyx system. VUR acts insidiously, mostly without direct clinical symptoms. It is revealed through the consequence, a urinary infection. The clinical picture varies from almost asymptomatic UTI to severe pyelonephritis. Along with infec-

tions of the respiratory system, UTIs, to which girls are particularly susceptible, are among the most common childhood infections. Considering the high frequency of urinary system anomalies in UTI, especially at a younger age, each infection should be given adequate attention, especially the younger the child (1-3). The likelihood of damage to the renal parenchyma after UTI depends on bacterial virulence factors, the presence of reflux, characteristics of the uroepithelium for bacterial adhesion, anatomical characteristics of the affected kidney, and the host's inflammatory response. During infection, certain bacteria, especially those with P-fimbriae, can reach the ascending route into the ureter and further into the renal pelvis and calyx (4). If children repeatedly find bacteria in their urine in significant numbers, and without specific signs of infection, it is possible that VUR is present in the background. In the clinical picture of children with VUR, in addition to UTI, we often find asymptomatic bacteriuria, sometimes with only lumbar pain when urinating or retention of urine in the bladder (4-5). In infants, the symptoms are mostly non-specific, the younger the child and the symptoms are more varied, and VUR can manifest itself together with lack of progress in body weight, elevated body temperature, cyanosis, along with convulsions, jaundice, diarrhea, vomiting (5, 6). VUR is the most common cause of febrile UTI in infancy and early childhood, during which it is diagnosed in 40% of cases. Often, even intrauterine during ultrasound examinations of the fetus, the dilation of the renal tubules (prenatal hydronephrosis) can be detected before the newborn's UTI has occurred (6). In most cases, reflux is discovered during the workup of a UTI. Laboratory findings of blood and urine (C Reactive Protein, blood count, urea, creatinine, urine, culture of urine) help us in the diagnosis, which indicate inflammation and kidney function. These are the first objective tests that should be done when VUR and the resulting UTI are suspected. The diagnosis of VUR is established by X-ray or ultrasound imaging of the ureter during urination, with prior application of a contrast medium into the bladder (5-7). The gold standard and the most important test used to diagnose VUR and determine its degree is micturition cystoureterography (MCUG). MCUG is performed when the child recovers from the infection. After curing the first or second UTI, especially in infants, it is necessary to perform tests aimed at proving or ruling out the existence of VUR, determining the degree and setting a strategy for further treatment and procedures (7). In acute cystitis, bacterial endotoxins can paralyze and weaken the ureteral musculature, so a higher degree of VUR can be falsely presented. A significant disadvantage of MCUG is the exposure of the child to radiation, especially radiation to the gonads, and the knowledge that one negative finding does not rule out the existence of VUR (7).

2. OBJECTIVE

The aim of the study was to determine the frequency of urinary infection when diagnosing vesicourethral reflux in children in the Tuzla Canton, in the five-year

period from 01.01.2016 to 01.01.2021.

3. MATERIAL AND METHODS

Through a retrospective study, we analyzed data from 5,221 children who were examined in the Nephrology Outpatient Clinic, Clinic for Children's Diseases, UKC Tuzla, in the period from 01.01.2016 to 01.01.2021, of different ages, from early neonatal age to 15 years of age. The age and gender of children with VUR, the most common symptoms and the presence of urinary infections during the detection of VUR, and the degree of VUR were analyzed. Data processing was performed using standard statistical methods, statistical program SPSS Windows.

4. RESULTS

During the previous 5 years, a total of 5,221 children were examined, 53.6% were male and 46.4% female. Out of the total number of children examined in the Nephrology Outpatient Clinic, the Children's Clinic, the most children, 3001 (57.5%), were diagnosed with pyeloectasia. In second place were children with UTI, 1706 (32.8%). A total of 256 (4.9%) children were diagnosed with VUR, 104 (1.9%) had neurogenic bladder, while 154 (2.9%) were referred and examined for other reasons. Children presented to the Nephrology Outpatient Clinic due to various pathological conditions, shown in Table 1.

VUR can be diagnosed in children at different ages. Our research included 256 children diagnosed with VUR, of which 139 (54%) were male and 117 (46%) were female. The highest prevalence of VUR was in the age group 0-2 years (35%), and the lowest in the group of children > 15 years (3%). There were more male subjects in all age groups, although in the 3-6 years old group and the > 15 years old group, the prevalence of VUR was almost equal in boys and girls (39:38; 4:3). There was no statistically significant difference between the groups of our respondents in relation to age groups, nor in relation to the gender of the children. Table 2 shows the frequency of children's age, according to different age groups, when VUR was diagnosed in relation to the children's gender.

The most common symptoms and the presence of UTI during the detection of VUR in children are shown in Table 3. In the group of children with symptoms of UTI with VUR, 100 (86.2%) children had an elevated temperature, 70 (60%) elevated CRP and leukocytes, while 105 (90.5%) had pathological findings in the urine, and 90 (77.6%) had a positive urine culture. In the group of children without symptoms of UTI with VUR, 130 (92.8%) children had an elevated temperature, 98 (70%) elevated CRP and

The most common pathological conditions diagnosed of children examined in the Nephrology Outpatient Clinic, in the previous 5 years

Pyeloectasia	3001 (57,5%)
Urinary tract infection	1706 (32,8%)
Vesicourethral reflux	256 (4,9%)
Neurogenic bladder	104 (1,9%)
Other reasons	154 (2,9%)
Total	5221 (100%)

Age of children with VUR	Male (n;%)	Female (n;%)	Total (n;%)	Chi-kvadrat test	p
0-2 years	50 (36%)	40 (34%)	90 (35%)	1,3	0,24
3-6 years	39 (28%)	38 (33%)	77 (30%)	1,7	0,19
7-10 years	34 (24,4%)	27 (23%)	61 (24%)	1,27	0,26
11-14 years	12 (8,6%)	9 (7,7%)	21 (8%)	1,4	0,17
>15 years	4 (3%)	3 (2,3%)	7 (3%)	1,5	0,16
Total	139 (54%)	117 (46%)	256 (100%)	2,1	0,32

Table 2. Children with VUR in relation to age and gender

Specific and non-specific symptoms of UTI	Presence of UTI symptoms in children with VUR (Yes) n=116 (45,3%)	Absence of UTI symptoms in children with VUR (No) n=140 (54,7%)	Chi-kvadrat test	p
Increased body temperature	100 (86,2%)	130 (92,8%)	1,3	0,24
Increased CRP i Leukocyte	70 (60%)	98 (70%)	1,7	0,19
Pathological urine	105 (90,5%)	127 (90,7%)	1,8	0,26
Positive urine culture	90 (77,6%)	129 (92,1%)	3,4	0,17
Non-specific symptoms: failure to gain weight, cyanosis, convulsions, jaundice, diarrhoea, vomiting	14 (12%)	133 (95%)	1,5	0,04
Asymptomatic bacteriuria	16 (10,4%)	120 (85,7%)	2,6	0,02
Pathological ultrasound findings of the urinary system	104 (89,6%)	128 (91,4%)	3,2	0,4

Table 3. The most common symptoms and presence of UTI during the detection of VUR in children

Degrees of VUR in children	Male n=139; (54%)	Female n=117; (46%)	Chi-kvadrat test	p
VUR I (n;%)	28 (20%)	20 (17%)	1,27	0,26
VUR II (n;%)	40 (28,7%)	32 (27,3%)	1,32	0,32
VUR III (n;%)	39 (28%)	28 (24%)	1,34	0,12
VUR IV (n;%)	20 (14,3%)	20 (17%)	1,42	0,17
VUR V (n;%)	12 (9%)	17 (14,7%)	1,5	0,23

Table 4. Children with different degrees of VUR in relation to gender

leukocytes, while 127 (90.7%) had pathological urine findings, and 129 (92.1%) had a positive urine culture. No statistically significant difference was found between the mentioned groups. Statistically significantly more children were without nonspecific symptoms (lack of progress in body weight, cyanosis, convulsions, jaundice, diarrhea, vomiting) and with asymptomatic bacteriuria in the group without UTI symptoms in children with VUR compared to the group with UTI symptoms in children with VUR. In the group of children with symptoms of UTI with VUR, 104 (89.6%) children had a pathological urine culture, while 128 (91.4%) were in the group of children without symptoms of UTI with VUR, without a statistically significant difference.

Our respondents had different degrees of VUR. The representation of respondents according to different degrees of VUR in relation to gender is shown in Table 4.

In our subjects, second-degree VUR was most often diagnosed in males (28.7%), while fifth-degree VUR was diagnosed in 12 male and 17 female. No statistically significant difference was found in the presence of VUR of different degrees between male and female.

5. DISCUSSION

Vesicoureteral reflux is a significant medical problem from prenatal to adulthood. It has no specific symptoms, it is often diagnosed early in life during regular ultrasound examinations during pregnancy, or later with acute or recurrent urinary tract infections. Undi-

agnosed and untreated reflux leads to the formation of kidney scars and a decrease in kidney function, which can progress to chronic kidney disease (2, 3).

During the previous 5 years, a total of 5,221 children were examined in the Nephrology Outpatient Clinic of the Children's Hospital, JZU UKC Tuzla, of which 53.6% were male, while 46.4 were female. From the total number of children examined in the Nephrology Clinic, Clinic for Children's Diseases. A total of 256 (4.9%) children were diagnosed with vesicoureteral reflux. Our research included 256 children diagnosed with VUR, of which 139 (54%) were male and 117 (46%) were female. The highest prevalence of VUR was in the age group 0–2 years (35%), and the lowest in the group of children > 15 years (3%). According to similar research (7, 8) by English and American authors, the most common is the period of early infancy, but the period of a small preschool child, when VUR is diagnosed. This can be explained by more frequent urinary infections in that period of life, but also by more frequent screening examinations. The widespread use of pre- and postnatal ultrasound led to the discovery of a large number of children with asymptomatic hydronephrosis (9,10). Most hydronephrosis is detected in the 18th-20th week of gestation and the frequency of fetal hydronephrosis is about 2% if the diameter of the drip >5 mm is used as a criterion. The frequency of clinically significant hydronephrosis is thought to be around 1:600 newborns. Despite numerous researches, it is still not fully known or defined how pronounced the dilatation in cm or mm must be, to represent a real obstruction and to require operative treatment. If children with transient and physiological hydronephrosis are excluded, stenosis of the pyeloureteric neck and VUR remain the most common causes of clinically significant dilatation of the renal duct system (2, 10).

In all age groups of our respondents, there were more male respondents, although in the 3-6 years old group and in the > 15 years old group, the prevalence of VUR

was almost equal in boys and girls (39:38; 4:3). Several different studies have confirmed that the frequency of VUR is higher in girls than in boys (9, 11). According to data from the literature, VUR ranges from 3:1 to 5:1 in girls compared to boys (10, 11). Apart from perhaps the small sample of our subjects, there is no other explanation for the more frequent VUR in our girls compared to boys.

VUR is diagnosed in the largest number of children due to the occurrence of a urinary infection, which is present in over 85% of patients. Although it is also discovered during the examination of the cause of antenatal hydronephrosis or during the examination of hypertension, renal insufficiency and unclear proteinuria. In the group of children with symptoms of urinary infection with VUR, 100 (86.2%) children had an elevated temperature, 70 (60%) had elevated CRP and leukocytes, while 105 (90.5%) had pathological findings in the urine, and 90 (77.6%) had a positive urine culture. In the group of children without symptoms of urinary infection with VUR, 130 (92.8%) children had an elevated temperature, 98 (70%) had elevated CRP and leukocytes, while 127 (90.7%) had pathological urine findings, and 129 (92.1%) had a positive urine culture. No statistically significant difference was recorded between the mentioned groups. Statistically significantly more children were without nonspecific symptoms (lack of progress in body weight, cyanosis, convulsions, jaundice, diarrhea, vomiting) and with asymptomatic bacteriuria in the group without UTI symptoms in children with VUR compared to the group with UTI symptoms in children with VUR. In the group of children with symptoms of urinary infection with VUR, 104 (89.6%) children had a pathological urine culture finding, while 128 (91.4%) were in the group of children without symptoms of urinary infection with VUR, without a statistically significant difference. Other authors also pointed out in their research that during the early years of the life of subjects with VUR there were also more male subjects than female subjects (10-12).

In our subjects, second-degree VUR was most often diagnosed in males (28.7%), while fifth-degree VUR was diagnosed in 12 male and 17 female. No statistically significant difference was found in the presence of VUR of different degrees between male and female. In a similar study, 231 children with VUR were diagnosed, of which 39 children had VUR of the first degree, 62 of the second, 51 of the third, 49 of the fourth and 30 of the fifth degree (16). It is known that subjects with a high degree of VUR (degrees IV and V) are 4–6 times more prone to developing renal scars than those with lower degrees of reflux (I–III), and 8–10 times more than those without VUR (9, 10,8).

6. CONCLUSION

Vesicoureteral reflux interferes with normal urodynamics, allows the transfer of bacteria from the lower parts of the urinary system to the upper, is the most important cause of febrile urinary tract infections in infancy and can lead to scarring of the parenchyma. If it is not diagnosed and treated in time, VUR can leave

permanent morphological and functional changes in children's kidneys. VUR has a tendency to disappear spontaneously with increasing age, on the one hand due to the extension of the intravesical segment of the ureter, and on the other hand, due to the maturation of urinary control. The prognosis of grade III and IV VUR, regardless of whether the reflux is unilateral or bilateral, depends on the degree of kidney damage. Although urinary tract infection in children is common, the possibility of permanent consequences should always be kept in mind if VUR is not diagnosed and treated in time.

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