Urinary Tract Dilations in Prenatal and Postnatal Life

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Study protocol

Brief Title

Urinary Tract Dilations in Prenatal and Postnatal Life

Director of study and central contact person

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Main sponsor

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Workplaces collaborating on the project

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Solvers

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Scientific goals of the study

1. Multidisciplinary survey on awareness, state of diagnosis and management of patients with dilatation of the urinary tract.
2. The primary goal is the prediction of severe postnatal course and surgical intervention in fetuses with dilatation of the urinary tract according to the UTD classification from 2014.
3. The secondary goal is the creation of a model proposal for prenatal and postnatal care of a patient with dilatation of the urinary tract.

Duration of the study

Study start: january 2023

Study completion: juny 2026

Introduction

Currently, in Slovakia, we do not have a multidisciplinary standard of health care for patients with dilatation of the urinary tract. Prenatal diagnosis of anomalies of the urinary tract includes the entire spectrum of anomalies, genetic diseases or anatomical deviations, which have a non-uniform classification and different terminology in a wide range of literature. Therefore, prenatal diagnosis of these anomalies, as well as dilatation diseases of the urinary tract, in different centers is different, often subjective and outdated. However, some findings on the urinary tract, even with regard to the sex of the fetus, require great attention, defining the degree of severity and precisely targeted management, the task of which is to prevent serious complications in postnatal life. Dilative diseases of the urinary tract may not be clinically obvious after birth, but in the long term, if they are not detected, serious and irreversible kidney damage may occur. The goals of this study are therefore 1. to confuse the current situation in the multidisciplinary medical sector regarding the issue of dilations of the urinary tract; 2. in the conducted study to identify fetuses with such a degree of dilation of the urinary tract (according to the UTD classification from 2014) that requires stricter management in the prenatal and postnatal period and which are at high risk of surgical intervention postnatally and 3. subsequently create a model of health care for multidisciplinary cooperation for a patient with dilation of the urinary tract.

Focus of the study

The probands will be fetuses with dilation of the urinary tract examined by ultrasound prenatally in centers of prenatal ultrasound diagnostics (SonoClinic, Emporia) and, in indicated cases, also children with persistent severe findings of dilation of the urinary tract examined by a pediatric nephrologist in the pediatric nephrology clinic (NefroSa). The study will also include a multidisciplinary survey of awareness regarding the issue of urinary tract dilatation diseases. Specialists from the fields of pediatrics, neonatology, pediatric nephrology, pediatric nephrology, gynecology, ultrasound in gynecology and obstetrics, or radiology will be approached by filling in a short questionnaire, in which we will find out information about the methods used for prenatal and postnatal diagnosis of dilatations of the urinary tract, the method of classification of these anomalies and their subsequent solution.

Review of the literature

Dilative diseases of the urinary tract are the most frequent findings during prenatal ultrasound examination of the fetus. We detect them in approximately 1-2% of fetuses examined during pregnancy (Nguyen 2014). Although in 50-70% of cases they are a physiological or transient finding, they can be a sign of a wide spectrum of anomalies of the urinary tract. These include uteropelvic junction obstruction (10-30%), vesicoureteral reflux (10-40%), ureterovesical junction obstruction (5-15%), multicystic renal dysplasia (2-5%) and posterior urethral valve (1-5%). Less frequent causes are ectopic ureter and the presence of a ureterocele in a double outlet system, polycystic kidney disease. Prenatal identification of the above-mentioned urinary tract anomalies is extremely important in order to prevent the development of possible complications (urinary tract infection, kidney stones, kidney failure) and to enable the creation of adequate, precisely targeted postnatal management of the detected anomaly (Nguyen 2010).

In common clinical practice, for many years, there was a lack of correlation between prenatal and postnatal ultrasound findings of urinary tract dilatation diseases with inconsistency in the description and classification of the degree of severity, which ultimately affected the clinical assessment and treatment planning (Mileto 2018). For this reason, the Urinary Tract Dilation Classification System (UTD Classification System) was created in 2014 in the city of Lithicum in the United States. It was compiled by representatives of eight major scientific societies: the American College of Radiology (ACR), the American Institute of Ultrasound in Medicine (AIUM), the American Society of Pediatric Nephrology (ASPN), the Society for Fetal Urology (SFU), the Society for Maternal-Fetal Medicine (SMFM), the Society for Pediatric Urology (SPU), the Society for Pediatric Radiology (SPR), and the Society of Radiologists in Ultrasounds (SRU), (Nguyen 2014, Mileto 2018). Their meeting had a two goals: to propose a unified description of urinary tract dilatation diseases prenatally and postnatally and to create a standardized framework for prenatal evaluation of isolated urinary tract dilatation based on USG findings, which can be applied in the postnatal period (Nguyen 2014, Mileto 2018).

Several aspects were taken into account when developing the common consensus: 1. The classification system was not created as a definitive final system for the evaluation of prenatal dilations of the urinary tract. It is expected that the created system will be validated and possibly modified by clinical experience and studies. 2. The classification system is based on an analysis of the currently available literature, which is inconsistent and relatively limited. 3.

The classification system is designed to evaluate isolated urinary tract dilation and cannot be applied to other urinary tract anomalies such as solitary, ectopic, multicystic dysplastic kidney (MCDK) or cystic kidney disease. Also, this scoring system cannot be used in patients who have undergone urinary tract surgery (Nguyen, 2014).

The UTD classification system has 6 recommendations (Nguyen, 2014):

Recommendation 1 – Terminology:

The consensus of the authors does not recommend using non-specific terms (hydronephrosis, pyelectasis, pelviectasis, uronephrosis, etc.) when describing a dilation anomaly, but using the term "urinary tract dilation - UTD" and subsequently characterizing the degree of severity of the dilation using specific ultrasound findings proposed in the UTD classification .

Recommendation 2 – consultation and communication of results:

Consensus recommends consultation of prenatal findings of dilation of the urinary tract with a doctor who will deal with the findings postnatally. The report should contain a description of the anomaly according to the specified classification and also representative US images of the given anomaly. If the findings are serious and likely to require surgical intervention, it is advisable to contact a specialist before delivery (urologist, nephrologist).

Recommendation 3 - classification system:

The UTD classification system includes the assessment of these parameters, (table 1).

Table 1. USG examined parameters included in the UTD classification system (Nguyen 2014)

Table 2 US parameters included in the Urinary Tract Dilation Classification System.

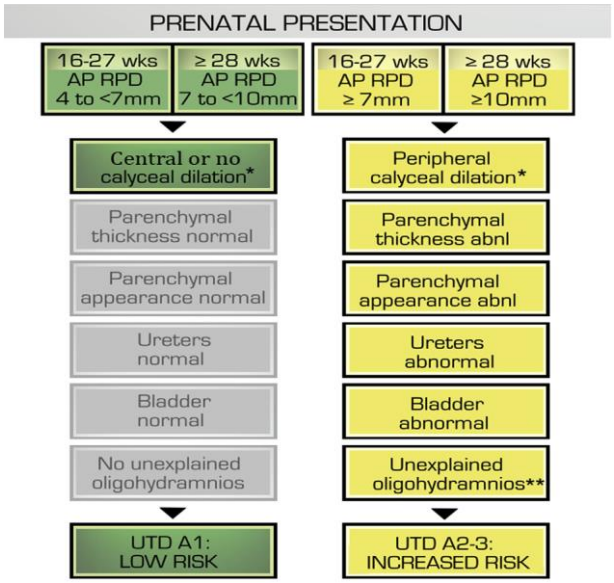
US parameters		Measurement/findings	Note
Anterior-Posterior Renal Pelvic Diameter (APRPD)		(mm)	Measured on transverse image at the maximal diameter of intrarenal pelvis
Calyceal dilation	Central (major calyces)	Yes/No	
	Peripheral (minor calyces)	Yes/No	
Parenchymal thickness		Normal/Abnormal	Subjective assessment
Parenchymal appearance		Normal/Abnormal	Evaluate echogenicity, corticomedullary differentiation, and for cortical cysts
Ureter		Normal/Abnormal	Dilation of ureter is considered abnormal; however, transient visualization of the ureter is considered normal postnatally
Bladder		Normal/Abnormal	Evaluate wall thickness, for the presence of ureterocele, and for a dilated posterior urethra

A normal finding on the kidneys prenatally and postnatally is considered if the APD of the pelvis is less than 4 mm until the 28th week, less than 7 mm from the 28th week until the due date and less than 10 mm postnatally. A normal kidney does not have dilatation of the calyces,

the thickness and echogenicity of the parenchyma is normal, the ureter is not visible and the bladder has a normal image. Oligohydramnios is not present.

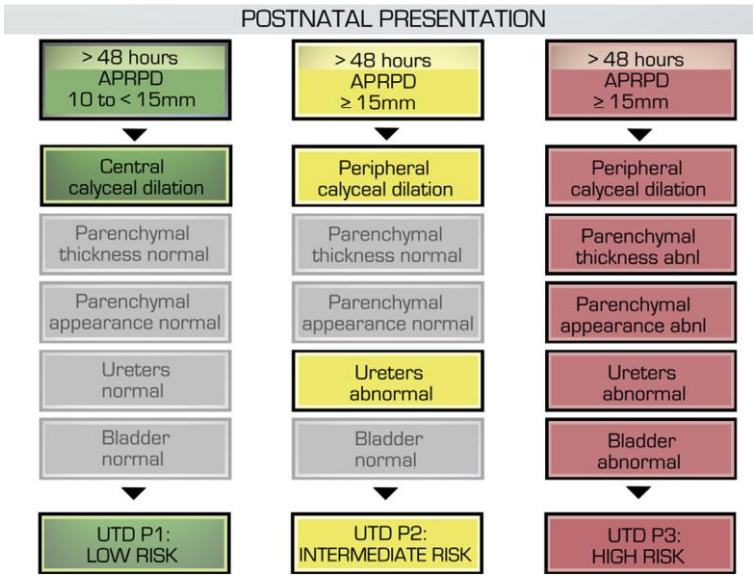
If dilation of the urinary tract is diagnosed prenatally, the finding is classified as low-risk UTD A1 or high-risk UTD A2-3 (table 2).

Table 2. Prenatal findings and risk stratification (Nguyen 2014).



If dilatation of the urinary tract is detected or persists postnatally, the risk group P1-P3 is determined based on the USG examination of the newborn, which is carried out at least 48 hours after birth (Table 3).

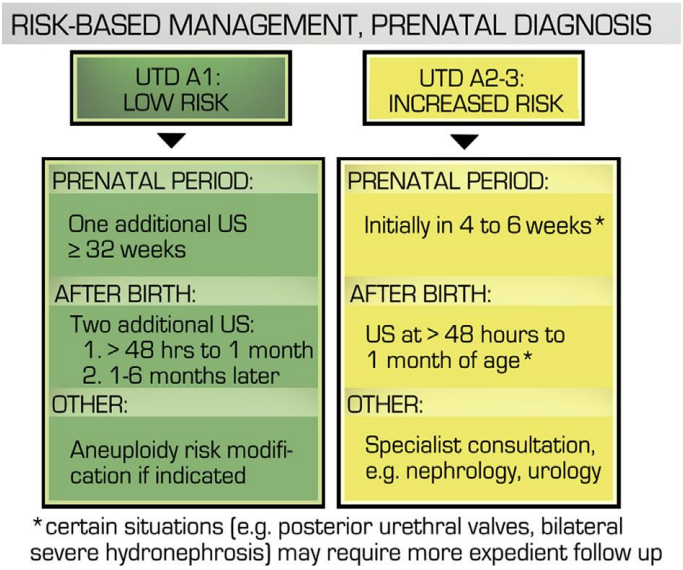
Table 3. Postnatal findings and risk stratification (Nguyen 2014).



Recommendation 4 – proposed management scheme:

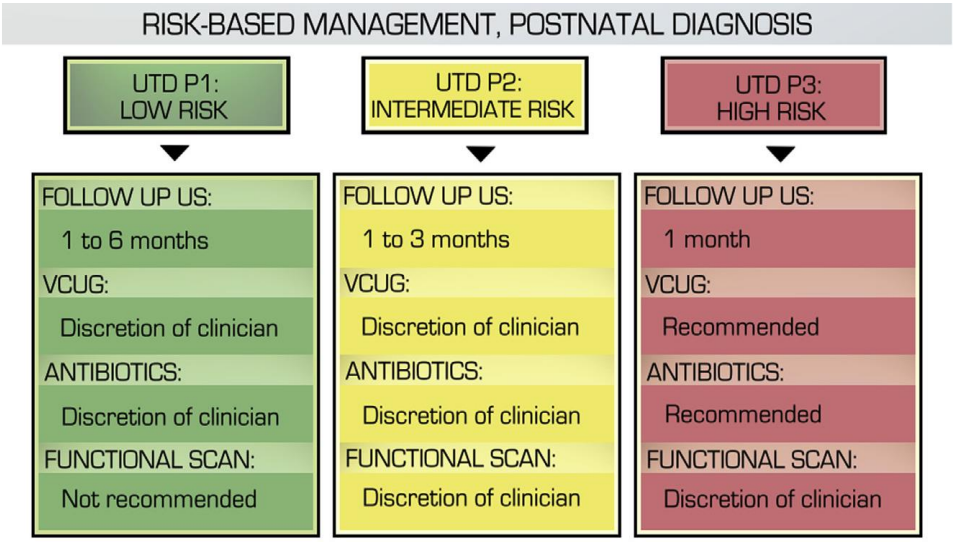
Based on prenatal and postnatal USG findings, management is suggested in the care of a patient with urinary tract dilation. If during the US examination in the third trimester (32th week and more) an adjustment of the finding to the norm is detected (pelvis without dilatation, no changes in the kidney tissue), no further control is necessary. If the dilation persists in the third trimester, the following procedure is determined according to the degree of severity of UTD A1 or UTD A2-3 (table 4).

Table 4. Management of a fetus with dilatation of the urinary tract (Nguyen 2014).



When dilation of the urinary tract is found postnatally, the management is adapted and adjusted individually according to the workplace. It depends on the degree of severity P1-P3 (table 5).

Table 5. Management of a child with urinary tract dilatation (Nguyen 2014).



The choice to utilize prophylactic antibiotics or recommend voiding cystourethrogram will depend on the suspected underlying pathology

Recommendation 5 – UTD classification modifiers:

Deteriorating prenatal or postnatal ultrasound findings are associated with an increased risk of the presence of urogenital pathology. There is no clear evidence of gender predominance in relation to dilative diseases with the exception of the posterior urethral valve in men. There is also no study where the prevalence of unilateral or bilateral urinary tract pathology is different. If the occurrence is bilateral, the degree of risk is indicated according to the side with the more difficult finding of dilatation.

Recommendation 6 – reporting:

If dilation of the urinary tract is diagnosed, the consensus panel recommends a description of the pathology in seven imaging parameters (Table 1). Subsequently, it is necessary to classify the anomaly according to the degree of severity (A1-A3, P1-P3) and propose a solution scheme. It would be ideal if representative images of the detected anomaly were also available in the report.

The UTD classification system combines 3 broad categories of sonographic findings – the degree of dilation of the urinary tract, the quality of the parenchyma and the presence of associated anomalies of the urinary tract. It simplifies and combines specific aspects of existing evaluation systems into a single, unique system, as a result of which the conversion of other systems to the new one is uncomplicated. For example SFU grade 1 and 2 (Society for Fetal Urology Grading System) is equivalent to UTD P1, SFU grade 3 to UTD P2 and

grade 4 to UTD P4. Its main goal is to create a correlation between prenatal and postnatal findings of dilatation of the urinary tract, predict the postnatal course and then create an optimal scheme for solving this anomaly postnatally. The task of other studies that incorporated the new classification into the evaluation of urinary tract dilations was to create correlations between it and the postnatal consequences of urinary tract dilatations, such as the need for surgical intervention, abnormal renal function, or urinary infections (Braga 2018).

Despite the obvious advantages, the UTD classification is generally not often used in clinical practice. It is most commonly used by pediatric radiologists. Only 19% of pediatric urologists use this system compared to 70% of those who use the SFU scoring system despite UTD showing higher reliability (Gray, 2022). Also, a literature review between 2017 and 2019 confirmed that only 6% of studies use the UTD classification system, while 37% use the SFU grading system and 33% use the APRPD system. Interestingly, approximately 20% of studies do not use any scoring system when describing urinary tract dilations in children (Suson, 2020). While the authors, members of pediatric radiology, created a computer application as a training aid for teaching the UTD classification system, which can be shared and used at any time (Maizels, 2017).

There are several reasons for the less-than-expected use of the UTD classification system. Complexity described by some departments, lack of information between departments, as the system was created for multidisciplinary cooperation, incompleteness (classification is always based on the presence of intrarenal dilation, does not take into account isolated dilatations of the ureter or other anomalies of the urinary tract, which is gradually being modified), impossibility to predict some dilatational anomalies of the urinary tract, such as vesicoureteral reflux, as well as national or international standards that have not yet been developed in many countries (Nguyen 2022).

The UTD classification system proposes a unified evaluation system for prenatal and postnatal dilative diseases of the urinary tract. A review of available studies and literature showed that the system can predict the clinical consequences of the disease and has better inter- and intraobserver reliability compared to other systems. The goal is to increase awareness of this system among specialties and create standardized management plans for the patient with dilated urinary tract disease (Green 2022, Nguyen 2022).

Methodology of study

Multidisciplinary survey on awareness

The study will also include a multidisciplinary survey of awareness regarding the issue of urinary tract dilation diseases. Specialists from the fields of pediatrics, neonatology, pediatric nephrology, pediatric nephrology, gynecology, ultrasound in gynecology and obstetrics, or radiology will be approached by filling in a short questionnaire created via docs.google.com, in which we will find out information about the methods used for prenatal and postnatal diagnosis of dilations urinary tract, the method of classifying these anomalies and their subsequent solution.

Questionnaire for gynecologists, prenatal sonographers:

1. Do you encounter dilation of the urinary tract in fetuses in your practice?

a) Yes, often.

b) Sporadic.

c) Rarely, almost never.

2. In case of US finding of dilation of the urinary tract in the second or third trimester:

a) I will only describe the given anomaly descriptively.

b) I will classify the anomaly in the classification system.

3. When describing the anomaly, do you use terms such as "pyelectasis, pelviectasis, hydronephrosis"?

a) Yes.

b) No.

4. If you use a classification in the evaluation of dilations of the urinary tract, which one?

a) SFU classification system (Society for Fetal Urology Grading system).

b) UTD (Urinary Tract Dilation) classification system.

c) I don't use any.

5. If dilatation of the urinary tract is found in the third trimester, do you recommend a pregnant woman to be checked by a pediatric nephrologist after birth?

a) Yes.

b) No.

c) I will instruct her to mention the finding as part of the newborn USG screening.

6. Are you informed about the postnatal finding in a child with prenatally diagnosed dilation of the urinary tract?

a) Yes, I will ask the pregnant woman to inform me about the child's examinations.

b) Yes, I work with a pediatric nephrologist who sends me the findings.

c) No, it is not in my interest.

7. Do you think that the system of care for a patient (fetus, child) with dilatation of the urinary tract is sufficient in our country?

a) After the prenatal diagnosis of dilation of the urinary tract, I do not deal with the management of the fetus and the child.

b) It is not sufficient, there are no standards in prenatal care for a fetus with dilation of the urinary tract.

c) The current management system for excretory system anomalies and dilatations is sufficient.

8. Have you encountered or do you use the prenatal UTD classification system (2014) when evaluating dilations of the urinary tract?

a) Yes.

b) No.

9. Do you think that the UTD classification system is optimal for prenatal and postnatal management of a patient with urinary tract dilatation?

a) Yes, it is usable in practice in risk stratification in fetuses with UTD.

b) No, it is too complex and does not cover all dilative diseases of the urinary tract.

c) I can't comment on that.

10. What are the normal values of renal pelvis width (APRPD) in the second, third trimester and postnatally?

a) 4-7 mm, 7-10 mm, over 10 mm

b) Up to 4 mm, 4-7 mm, 10 mm

c) 4-5 mm, 7-8 mm, 10 mm

<u>Questionnaire for pediatricians, neonatologists, pediatric urologists and nephrologists, radiologists:</u>

1. In your practice, do you encounter a patient with dilation of the urinary tract?

a) Yes, often.

b) Sporadic.

c) Rarely, almost never.

2. In case of US finding of dilation of the urinary tract in a child:

a) I will only describe the given anomaly descriptively.

b) I will classify the anomaly in the classification system.

3. When describing the anomaly, do you use terms such as "pyelectasis, pelviectasis, hydronephrosis"?

a) Yes.

b) No.

4. If you use a classification system when evaluating urinary tract dilations, which one?

a) SFU classification system (Society for Fetal Urology Grading system).

b) UTD (Urinary Tract Dilation) classification system.

b) I don't use any.

5. When examining a child with dilatation of the urinary tract, are you interested in prenatal findings?

a) Yes, I am interested in the finding and its severity in the prenatal period.

b) It is not useful information for me

c) Sometimes I ask the patient about it, or she reports it to me herself.

6. Have you encountered or are you using the postnatal UTD classification system (2014) when evaluating dilations of the urinary tract?

a) Yes.

b) No.

7. Do you think that the UTD classification system is suitable for the prenatal and postnatal management of a patient with urinary tract dilation?

d) Yes, it is applicable in practice in risk stratification in a patient with UTD.

e) No, it is too complex and does not cover all dilative diseases of the urinary tract.

f) I can't comment on that.

8. Do you think that the system of care for a patient (fetus, child) with dilatation of the urinary tract is sufficient in our country?

a) It is not sufficient, the standards in prenatal and postnatal care of a patient with dilation of the urinary tract are insufficient.

b) The current management system for excretory system anomalies and dilatations is sufficient.

9. Would we welcome greater cooperation between specialists (gynecologist, neonatologist, pediatrician, pediatric urologist, pediatric nephrologist) in the diagnosis and treatment of a patient (fetus, child) with dilation of the urinary tract?

a) Yes, it is necessary.

b) No, as it is now, it is sufficient.

c) I can't judge it.

Study

Inclusion criteria of cases in the study:

1. Singleton pregnant women whose fetuses were diagnosed with dilation of the urinary tract as an isolated US finding before the 28th week of pregnancy. Dilation of the urinary tract was categorized according to the 2014 UTD classification system.
2. Fetal patients with subsequent US control in the third trimester after the 28th week of pregnancy.
3. Newborns and children with prenatally diagnosed UTD, which, depending on the severity, required a postnatal examination by a pediatric nephrologist within a month after birth and then in his follow-up up to 6 months after birth.

Exclusion criteria:

Multiple pregnancies, UTD diagnosed only in the third trimester, associated anomalies of other organs, aneuploidy, newborns and children monitored by someone other than a selected pediatric nephrologist, patients who were lost from follow-up (did not come for recommended control, etc.).

Study population:

Approximately 4,000 morphological ultrasound examinations of fetuses are performed annually at the SonoClinic and Emporia workplaces. Approximately 60-80 cases of dilation of the urinary tract are detected annually. In 80% of them there is a complete adjustment before delivery, the remaining approximately 20% have persistent dilation of the urinary tract with varying degrees of severity (UTD A1 – low risk, UTD 2-3 – high risk). According to the recommendations of the UTD classification, these fetuses are subsequently recommended for postnatal examination by a pediatric nephrologist. The estimated number of cases with dilation of the urinary tract for analysis postnatally will be 180 to 230.

Demographics:

Age, parity, occurrence of urinary tract anomalies in the child's father and siblings, sex of the fetus, method of conception.

Study design:

The study is designed as a prospective observational study with ongoing data collection and subsequent analysis. It is divided into four parts:

First part – ultrasound examination of the fetus in the second trimester of pregnancy:

Morphological examination of the fetus performed by gynecologists in medical centers with permission to practice Ultrasound in gynecology and obstetrics (prenatal diagnosis centers), SonoClinic and Emporia. Ultrasound examinations are performed on GE Healthcare ultrasound devices, Voluson E8, E10, E22 Expert. Morphological examination is performed primarily between the 18th and 24th week of pregnancy, in rare cases, when an anomaly of the urinary tract is detected later, the patient should be examined no later than the 28th week of pregnancy.

The second part – classification of diagnosed dilation of the urinary tract:

According to the 2014 UTD classification, the detected dilation of the urinary tract is described using 7 examined ultrasound parameters (AP - width of the renal pelvis in its intrarenal part, echogenicity and thickness of the parenchyma, dilatation of the calyces, ureters, bladder and amount of amniotic fluid, table 1). The laterality is determined and the detected finding (UTD A1 or UTD A2-3, tab. 2) is assigned a corresponding risk - for UTD A1 low risk, for UTD A2-3 high risk. The pregnant women with afected fetus is then instructed, informed and recommended for an ultrasound control in the third trimester by a selected specialist (solvers of the study).

Third part - ultrasound control in the third trimester:

The selected specialist (sonographer, soler) is the fetus examined by ultrasound in the third trimester after the 28th week, optimally after the 32nd week of pregnancy. The urinary tract of the fetus is examined again according to the recommendation of the UTD classification system, all 7 parameters and the amount of amniotic fluid are assessed again. Re-classification or re-evaluation of the finding and carried out risk stratification according to the severity of the finding. Fetuses with normal findings are not recommended for further follow-up, fetuses with UTD A1 are recommended for a postnatal control by a pediatric nephrologist within a month after birth. Fetuses with a high risk of persistence or progression of the finding, i.e. UTD A2-3, are recommended for ultrasound control in 4-6 weeks, and then according to the findings, prenatal consultation with a pediatric nephrologist is recommended, with whom postnatal management will be discussed and postnatal controls will be optimized. The aim of

the evaluation of findings will be to predict the risk of postnatal surgical intervention in the child in the case of serious prenatal findings.

The fourth part of the study – management of a child with UTD by a pediatric nephrologist:

According to the stratification of the risk of UTD pathology of the urinary tract in the child, an examination by a specialist is established, where the initial examination is carried out within a month of the child's age (individually according to the findings). Subsequently, the ultrasound finding on the urinary system is reevaluated according to the UTD classification to UTD P1-P3 (table 3) with the assignment of the corresponding risk (low, intermediate, high, table 4 and 5) and the child is adequately managed according to the recommendations and condition (conservative management, VCUG, cystoscopy, surgical procedure, antibiotic prophylaxis and the like). The child is followed in the study until the age of 6 months.
All case findings are recorded on prepared media (USB), archived (external hard disks) and described according to the recommendations of the 2014 UTD classification system.

The obtained results will be subjected to statistical analysis. A multidisciplinary management plan for a patient with urinary tract dilatation will be created. All results and conclusions will be subsequently published.

Literature

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