Contribution of Neonatal Ultrasound Screening to Decrease Median Age at Diagnosis of Congenital Renal Anomalies

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Introduction: Considering the fact that approximately 10% of children are born with various, mild or severe anomalies of the urinary system, and most of them remain asymptomatic until the development of complications, early diagnosis plays a crucial role in the prognosis of these patients. In the era of ultrasonography, an early diagnosis means a diagnosis established during intrauterine life, but considering the multiple traps of prenatal diagnosis, neonatal screening of these malformations has a major importance.

Material and methods: We have performed a retrospective study of the cases with congenital malformations of the urinary system, admitted to the 2nd Pediatric Clinic of Tîrgu Mureş, between January 2003 and December 2008. Concidering that between 2006 and 2008 neonatal ultrasound screening has been performed for these malformations, the patients were divided into two groups based on the year of admission. Establishment of the median age of patients with renourinary malformations was considered an important factor as it was aimed at emphasizing the role of neonatal screening in the early diagnosis of these anomalies.

Results: The mean age of the patients at the time of diagnosis of congenital malformation of the urinary system in case of the 2003–2005 study group was 4.82 years. Using an ultrasound screening in the neonatal period, the mean age at the time of diagnosis of congenital malformations of the urinary system dropped to 50.9 months compared to 57.9 months calculated for the three years when this screening has not been performed.

Conclusion: In the absence of a neonatal ultrasound screening of congenital malformations of the urinary system, the diagnosis of these anomalies is established late, in most cases only at the time of occurrence of complications

Keywords: hypertension, ambulatory blood pressure monitoring, morning surge, pulse pressure, dipping

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Introduction

Renourinary malformations are borderline disorders between internal medicine and surgery. Their etiological factors are multiple and not yet sufficiently determined. They may be of genetic or teratogenic origin [1]. Recent studies of the human genome and genetic engineering experiments on mice have shown that congenital malformations of the urinary system have polygenic determination. This means that they are caused by concomitant defects of several genes [2,3].

Approximately 10% of all newborns display development anomalies of the urinary tract. Early diagnosis of these anomalies is possible only through implementation of screening programs, as the majority of these are asymptomatic until complications occur.

Considering the fact that renal malformations are the major cause of renal failure in children, early diagnosis plays an especially important role in the prognosis of these patients.

Globally the emphasis is placed on early detection of anomalies and their treatment using minimally invasive methods, which involves low costs for the society. Screening programs for urinary anomalies have been implemented in almost all countries of the European Union, in the USA and in Japan [4,5].

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The literature describes two stages of the urinary tract malformation screening: a prenatal screening by ultrasound examination performed between the 20th and 37th gestational weeks, and a neonatal screening by abdominal ultrasound examination between the age of 3 to 8 days [5,6,7].

In the absence of a national screening program, the diagnosis of renourinary malformations is mostly established at the time when the first urinary tract infections occur, or accidentally through paraclinical and imaging studies performed due to pathologies pertaining to other systems (digestive tract, internal or external genitalia, lymphatic system, etc.). As our country lacks this screening program, a larger percentage of cases are diagnosed late, sometimes over the age of 6 years.

The main objective of this study is to emphasize the necessity of implementation of a neonatal ultrasound screening program (completing the prenatal one) for the early diagnosis of renourinary congenital malformations.

Material and methods

We have performed a retrospective study of the cases with congenital malformations of the urinary system, admitted to the 2nd Pediatric Clinic of Tîrgu Mureş, between January 2003 and December 2008. We identified a total of 432 patients.

As in the interval between 2006 and 2008 neonatal ultrasound screening has been performed for the congenital

Table I. Mean age at time of diagnosis of patients with congenital malformation of the urinary tract according to the sex of the patients

Period: 2003–2005	Male	Female
Arithmetic mean	51.545	62.331
Standard deviation	57.751	52.436
Confidence interval (95%)	39.309–63.782	53.123– 71.539
Median	30	48
Minimum value	-1	-1
Maximum value	192	204
Mann-Whitney U test	p = 0.021	

Table II. Mean age at time of diagnosis of patients with congenital malformation of the urinary system according to studied periods

	2003–2005	2006–2008
Arithmetic mean	57.916	50.903
Standard deviation	54.800	55.120
Confidence interval (95%)	50.550– 65.283	43.528– 58.278
Median	42	36
Minimum value	-1	-1
Maximum value	204	204
Mann-Whitney U test	p = 0.026	

malformations of the urinary system, we considered useful grouping the patients into two groups based on the year of admission. Therefore we studied 215 patients between 2003 and 2005, and 217 patients admitted to the clinic between 2006 and 2008.

Establishment of the median age of patients with renourinary malformations was considered an important factor as it was aimed at emphasizing the role of neonatal screening in the early diagnosis of these anomalies.

For statistical data analysis Microsoft Excel and SPSS 15.0 software have been used. We also used comparative statistics and the λ^2 test. Comparisons for median pairs have been performed using a modified Mann-Whitney U test.

Results

In the period between January 2003 and December 2005, 215 patients with different congenital malformations of the urinary system have been admitted to the Pediatric Nephrology Compartment of Tîrgu Mureş.

All 215 patients considered for the study had significant malformations of the renourinary system. Patients with small grade hydronephrosis of uncertain etiology, those with neurogenic bladder, those with tubulopathies and those with normal anatomical variations of the renourinary system (bifidity of the renal pelvis, superior calyx syndrome, etc.) were not included in the study.

The distribution of patients by age groups at the time of diagnosis is presented in Figure 1. There were only 56 patients under 1 year, and only 14 of them were diagnosed in the neonatal period. In case of 10 patients the suspicion of renourinary malformation has been established by prenatal ultrasound screening.

The mean age of the patients at the time of diagnosis of congenital malformation of the urinary system in case of the 2003–2005 study group was 4.82 years.

Correlating the mean age at the time of diagnosis of patients with congenital malformation of the urinary tract with the sex of the patients we noted that in case of male patients this age was 51.54 months (i.e. approximately 4.3 years), and in case of female patients this was 62.33 months (i.e. 5.2 years) (Table I).

In the rural areas, the mean age at diagnosis was 58.62 months (i.e. 4.8 years), while in the urban areas, the mean age at diagnosis was 57.42 months (i.e. 4.7 years).

It is also apparent that in this interval without screening, most of the patients (84.19%) have been diagnosed by targeted imaging studies, performed upon occurrence of complications (usually urinary tract infection). There were 34 patients who have been diagnosed accidentally through ultrasound examinations requested due to pathologies of other systems (digestive tract, genitalia, etc.).

Correlating the mean age at the time of diagnosis of congenital malformations of the urinary system with the type of the malformation, we noted that renal cystic ill-

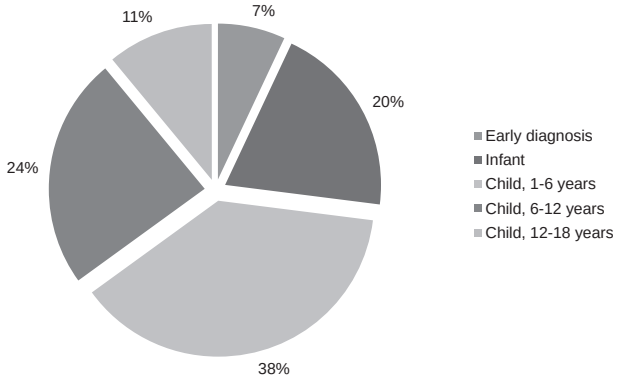

Fig. 1. Percent distribution of patients into age groups at the time of diagnosis of congenital malformation of the urinary system
(early diagnosis = prenatal and neonatal diagnosis)

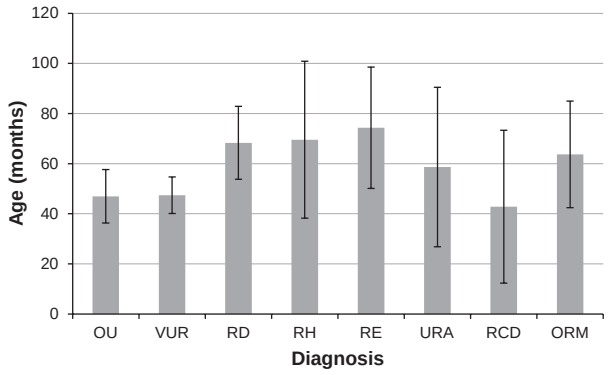

Fig. 2. Graphical representation of the main congenital malformations of the urinary system according to mean age (in months) at the time of diagnosis
OU = obstructive uropathy, VUR = vesicouretheral reflux, RD = renal duplication, RH = renal hypoplasia, RE = renal ectopia, URA = unilateral renal agenesis, RCD = renal cystic disease, ORM = other renal malformations

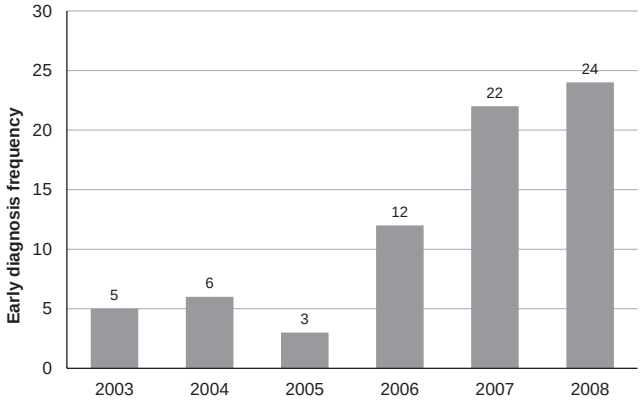

Fig. 3. Percent distribution of patients into age groups at the time of diagnosis of congenital malformation of the urinary system
(early diagnosis = prenatal and neonatal diagnosis)

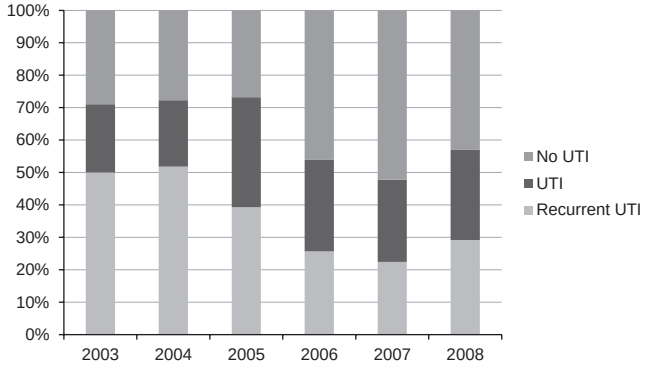

Fig. 4. Graphical representation of the percent of patients who developed UTI and recurrent UTI according to the studied periods

nesses were diagnosed the earliest, and these were followed by obstructive uropathies and vesicoureteral reflux disease (Figure 2).

In the interval between 2006 and 2008 neonatal ultrasound has been performed for screening of the congenital malformations of the urinary system on a group of 1108 newborns.

This group consisted of the following:

– newborns admitted to the 2nd Pediatrics Clinic of Tîrgu Mureș with different conditions (intercurrent respiratory or digestive infections, prolonged jaundice, digestive system pathologies). Newborns admitted with the diagnosis of urinary infection or renal failure, and those already diagnosed with congenital malformations of the renourinary system at other clinics, were not included in the group;
– newborns who underwent outpatient abdominal ultrasound examination at the 2nd Pediatrics Clinic of Tîrgu Mureș;
– newborns from the 1st Neonatology Clinic of Tîrgu Mureș, randomly selected, without an obvious pathology, who underwent screening for congenital malformations of the urinary system before being discharged from the maternity hospital.

Using this examination method, 76 cases of urinary system congenital malformations have been identified, and out of these, 45 had significant malformations. Patients with significant renourinary malformations have been admitted to our clinic for supplementary investigations and establishment of subsequent therapy.

Studying the cases of the Pediatric Nephrology Compartment of Tîrgu Mureș in the 2006–2008 interval, when neonatal ultrasound screening has been performed for congenital malformations of the urinary system, we found the following results: during this period a total of 217 patients with the diagnosis of congenital malformations of the urinary system have been admitted to the clinic.

Using an ultrasound screening in the neonatal period, the mean age at the time of diagnosis of congenital malformations of the urinary system dropped to 50.9 months (4.24 years) compared to 57.9 months (4.82 years) calculated for the three years when this screening has not been performed (Table II).

Between 2006 and 2008 more congenital malformations of the urinary system have been diagnosed at neonatal age compared to the period between 2003 and 2005 (Figure 3).

By early diagnosis of the congenital malformations of the urinary tract in a larger percentage of cases, the number of patients with complications decreased in general, and it showed a decrease especially in case of patients with episodes of UTI and recurrent UTI, which is the most frequent complication if these malformations.

Discussions

All authors note that early detection of reno-urinary tract malformations is essential for the subsequent evolution of the patient. Late detection, when complications have already occurred, generates elevated financial costs, as well as family drama that may possibly have been avoided [4,6,8].

By a simple abdominal ultrasound examination performed on the newborn by an experienced specialist, the chances of a early diagnosis of renourinary congenital malformations increase dramatically. Studies confirm that this ultrasound screening has to be used for all newborns, not only for those at risk [9,10,11].

Using renal ultrasound as a screening test in healthy infants, Steinhhardt et al. showed that 3.2% of them had a urinary tract anomaly, and half of these required surgery.

In the era of ultrasonography, an early diagnosis means a diagnosis established during intrauterine life, but considering the multiple traps of prenatal diagnosis, neonatal screening of these malformations has a major importance.

In most of the cases fetal ultrasound establishes only a probable diagnosis, and the exact diagnosis is established postnatally.

Some authors emphasize that up to 50% of newborns diagnosed with hydronephrosis during intrauterine life will not have hydronephrosis at the postnatal ultrasound examination [12,13]. Radet et al. demonstrated that out of 100 newborns diagnosed before birth with renourinary

malformation using ultrasound, in 71 cases postnatal ultrasound demonstrated a renourinary tract anomaly, and in 50% of the cases the prenatal diagnosis was confirmed [14]. Bhide et al. demonstrated that approximately 40% of the patients requiring surgery due to renourinary malformations did not have pathological signs on the prenatal ultrasound examinations [15]. Cacciari et al. underline the importance of neonatal ultrasound screening of renourinary malformation, demonstrating that almost 50% of the anomalies escape even the "most experienced eye" during prenatal ultrasound examinations [16].

In conclusion, in order to increase the chances of an early diagnosis of renourinary malformations, besides completing the antenatal screening and a neonatal screening.

As our study suggests, in the absence of neonatal screening the average age at diagnosis of congenital malformations of the urinary system was 4.82 years.

Mean age at diagnosis in case of females was a bit higher than in case of boys. The reason behind this seems to be the persistence of the concept that females need imaging investigation only after the second episode of urinary infection.

Although the obtained difference is not statistically significant, we would also like to note that mean age at diagnosis in the urban area is musch lesser than that of the rural areas. This might be explained by the fact that imaging studies and laboratory tests are much less available in the rural setting.

Unfortunately a lot of general practitioners and pediatricians from rural areas or small town hospitals choose to treat empirically the recurring urinary infections or other symptoms of the urinary system, thus delaying a great deal the time of diagnosis of the congenital malformation.

Conclusions

Considering the mean age of diagnosis to be 4.82 years in case of patients admitted to the Pediatric Nephrology Compartment of Tîrgu Mureș during the interval when no neonatal screening has been performed, we can conclude that in the absence of a well implemented screening program for these malformations, the diagnosis will be established late.

Abdominal ultrasound performed to screen for congenital malformations of the urinary system during the newborn period, has a significant role in the early diagnosis of the malformation.

Through application of this methods we managed to produce a 7 month mean decrease in the mean age at the time of diagnosis of urinary system congenital malformations, in case of the patients of the Pediatric Nephrology Compartment of Tîrgu Mureș. The aim is that in the coming years most of the cases should be diagnosed during infancy.

Large scale implementation of this screening would benefit on the long term patients, their families and the society. By implementation of a neonatal ultrasound screening (a relatively low cost examination), a significant decrease can be obtained in complications of the congenital malformations of the urinary system, which would require repeated hospitalization and medical treatment, involving much higher costs.

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