THE PARTICULARS OF THE HEREDITARY RENAL POLYCYSTOSIS WITH CHILDREN

(information from science literature and own observation)

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The article deals with features of polycystic kidney disease according to literature data and results of own clinical observations. Diagnostics of the disease is difficult and includes genetic consultation and complex examination of main clinical and instrumental indexes. The main in treatment is adequate renoprotective therapy, hemodialysis with further organ transplantation.

Key words: children, polycystic kidney disease, diagnostics, treatment.

Introduction. Annually for each 1000 viviparous children there are from 25 to 65 children with deviation from norm, hard, incompatible with life diseases – 50–70 %. Urine system defects make one third of all inborn defects of development. In genesis of cystic kidney diseases of children the leading role belongs to gene mutation (autosomal-recessive and autosomal-dominant renal polycystosis) and chromosomal aberrations (Down syndrome and Edwards syndrome and others) [6, 8, 9]. More than 100 genetic syndromes are marked with renal polycystosis [2]. In some cases renal polycystosis appears as a result of direct teratogenic influence on fetus (multicystosic dysplasia, sponge kidney) [1].

Polycystic renal disease – hereditary nephropathy connected with genes mutation that define the structure of renal canals in their embryo development that is characterized by cyst-formation in renal parenchyma, the increase of which causes sclerosis of renal material and chronic renal failure [2].

The actuality of problem is called forth by such complications as arterial hypertension and renal failure, that in most cases shows progress of disease [1, 6, 8, 10]. According to the information given by some authors [2] 22–35 % of ill people with chronic renal failure have diagnosis as hereditary and inborn renal diseases, and according to other authors [5] the main cause of chronic renal failure – 88 % – it is children with inborn kidney anomaly.

Polycystic kidney disease happens in two main types. These types differ by the principle of heredity, clinical evidence and morphologic picture. According to International recommendations there appear autosomal-dominant, autosomal-recessive and less precise polycystic kidney disease [1–8]. Recently autosomal dominant type has been called “adult type”. It is connected with the fact that clinical illness display: hematuria, hypertension, and chronic renal failure- happen mostly after 30 years of life. However modern methods of ultrasonography have shown ADPKD with children of first years of life and even in antenatal period that makes the term “adult type” of renal polycystosis doubtful.

There exist several genetic variants of ADPKD [2, 4, 5, 8].
- type 1, that appears at 80–85 % of ill people and is connected with mutation in genes PKD-1 located on sort arm of chromosome16 (16 p 13.3);
- type 2, that appears in 15 % of diseases connected with mutation in gene PKD-2 located on long arm of chromosome 4 (4q21–23);
- type 3, rare variant mutation in genes is not identified (7a chromosome).

Molecular genetic research has shown that gene ARPKD – PKD-1s situated on short arm of chromosome 6.

ADPKD is widely spread genetic disease, it happens in one case for 400–1000 children [2–4, 6, 7]. ARPKD happens in population more seldom than ADPKD, one
case for 6000–40000 newborn [1–7, 12]. Possibility of ADPKD heredity in case of one-parent disease is 50 %, if both – 100 %. ARPKD is inherited from parents-carriers of pathological gene and is realized with probability of 25 %, if gene-carrier is only one parent then probability of ill-child birth is very low – less than 1 % [3, 4].

Pathogenesis of renal polycystosis is caused by abnormal connection of straight and winding canals in the period of antenatal development, as the result of which the outflow of primary urine from proximal canal is disturbed and then cyst formation happens. The important reasons of cyst formation are: cell proliferation that brings to canal obstruction; tension of inner canal pressure and stretch of canals; excessive liquid collection; hereditary excessive stretch of basal membrane of canals and their dilation [2, 5].

Clinical picture. There are two clinical variants of ADPKD – neonatal and adult. Neonatal makes 25 %, is shown early, adult type makes 75 %, is seen clinically at teenage, juvenile and adult age being slower and more favourable [3].

The disease with children may be without symptoms and can be seen during kidney ultrasonography. First signs of renal polycystosis can be accidental discovery of swelling from one or two sides of stomach. The doctor is addressed mainly because of stomachache or pain in waist line, this pain is intensified during physical exercises and outdoor games. The reason of the pain can be prolapse of heavy cystic kidneys or signs of pyelonephritis or disturbance in urine outflow. Rather typical is discovery of microhematuria, proteinuria, leukocyturia, crystalluria. The disease can result in chronic recurring pyuria that can be marked at an early age. Special attention should be paid to the signs of groundless anemia. With age there appears a tendency to hypertension that can bear latent character with children [2]. Hypertension is more characteristic for adults; it has stable character and often is the first sign of disease. Polyuria and polydipsia are characteristic symptoms for all types of renal polycystosis and they are caused by the disturbance of canal renal function. Urine has low density, isohyposthenuria is also typical. Decrease of concentration of renal function appears with more than half of the children [2]. There is information that increase of cyst sizes which happens after 7–15 years of life correlates with abdominal pain syndrome character, arterial hypertension and changes in urine [2]. One third of ill people with ADPKD may have liver cysts, in 10 % they are in pancreases, in 5 % they are in spleen, aneurism of brain arteries is also possible [2–5, 7]. According to literary information in half of the cases ADPKD has latent character and is completed by chronic renal failure [1, 5, 12]. The researchers declare that the verification of ADPKD is done by revelation of minimum two cysts in one or both kidneys which have continuous growth in diameter [1, 5, 12]. However within long period the only sign of ADPKD may be only decrease of concentration renal function [1, 12].

There exist four clinical variants of ARPKD: prenatal, neonatal, infant, and juvenile [3, 4, 7]. Recently it has been considered that per cent of survival of the given variant of disease is rather low, but the information within last years shows that in 50 % of cases patients can live up to 10 years. With prenatal ARPKD more than 90 % of canals have cysts and non-viable (during pregnancy there appears oligohydramnios, children are born with Potter syndrome, i.e. sunken chin, epicanic hypertelorism, microgasthia, anomaly of extremities, also lung hypoplasia, spontaneous pneumothorax at birth oliguria). Neonatal type is characterized by the disease of 60–90 % of canals, at birth newborn has huge stomach due to deformed changed kidneys with cysts, kidneys can occupy all abdominal cavity, in the given case renal failure appears within first months of life [1, 5, 12]. Often patients with ARPKD have symptoms of inborn fibrosis of liver that is followed by portal hypertension; liver disease can play the leading role in clinical disease picture [2, 5, 10]. Infant and juvenile types progress slower, but is followed by anemia, hypertension. At juvenile type the length of life can last up to 30 years.

Diagnosis of polycystic kidney disease is based on clinical and instrumental criteria. Unfavourable family history should be taken into consideration. Ultrasonography of parenchymatous organs under renal polycystic kidney disease is highly informative algorithm of examination of patients with given pathology. This method allows to make dynamic examination of patients. Prenatal diagnostics at 20th–24th weeks of
pregnancy is auxiliary under ARPKD; ultrasonography shows increased kidneys, bad
differentiation of corticomedullar layer, also it shows hepatomegaly and expanded in-
der liver flows [4–7, 11, 12]. In difficult diagnostic cases of ARPKD during third
trimester of pregnancy magnetic resonance therapy [6] after which the question about
necessity of abortion is considered.
The particulars of ultrasonic picture of polycystosis with children and teenagers
under ARPKD are minimal. Ultrasonography shows only considerably increased kid-
ney size with smooth surface [5, 11, 12]. Microcysts with size 1,4 mm in diameter
(diameter is not more than 1 cm) are found under microscope, cysts are small and
numerous, situated on all the length from cerebral layer to cortical [5], their quantity
increases with time passed, crустate and cerebral layers are vaguely differentiated.
Kidneys affection is as a rule bilateral, unilateral polycystosis happens rarely. At that
kidney sizes are higher than age indexes from 50 to 75 %. However existence of normal
or reduced sizes of kidneys with children do not exclude polycystosis as with the rise
of chronic renal failure, kidney size can become gradually smaller [4, 5].

Compared to ADPKD cysts are rarely found in liver and other organs. The chang-
es in liver with ARPKD patients make the picture of fibrous changes of different
degree [2, 5, 9]. It is accompanied with significant heterogeneous rise of parenchyma’s
ehcogenicity of organ, with infiltration of vessels walls of portal system, induration
and enlargement of glisson’s capsule. Ultrasonic signs of portal hypertension are reg-
istered, i.e. growth of portal vein diameter and reduction of blood flow speed in portal
vein, significant growth of spleen size, rise of diameter of spleen vein.

Ultrasonography of the ADPKD of patientsshow that kidneys are of big sizes,
grown weight (can be up to 1,5 kg of each and even more). Cysts seen under capsules
contours of the kidneys are uneven and tuberous, cysts are big (with diameter more
than 5 cm and more) [5]. There is dependence between size of cyst and age, between
cysts there are parts of parenchyma with normal differentiation. Localization of big
cysts in porta renis and renal sinus causes significant hemodynamic disturbances. In
86 % of cases pyelonephritis appears in kidneys with polycystosis.

X-ray methods of investigation are very important in diagnosing of polycystic
renal disease and primarily excretory (infusion) urography. Computer and magnetic-
resonance tomography is used to diagnose cysts. But X-ray methods of investigation
of kidneys are seldom used for children. To study functional state of kidneys they
define creatinine content, urea in blood serum, also they make Zimnitskii’s test, dy-
namic kidney scintigraphy and kidney scanning, clearance test. Molecular genetic
examination proves the diagnosis of renal polycystosis [1, 2, 5, 6].

Treatment. Treatment of polycystosis is a complex task for clinicists as specific
treatment doesn’t exist, it is characteristic to use syndromic therapy, as hypotensive
medicine APT inhibitors. Pyelonephritis that follows must be treated with antibiotics
that penetrate easily through cysts. In case of rise of chronic renal failure hemodi-
alysis with following transplantation is advised [2, 4–6].

Below the cases of own clinical observation can be found.

Clinical case № 1. Ilya, born in 1990 was under observation at Infant neurological division
of Mariupol hospital № 3 in April 2006, at the age of 15 years complaining for headaches,
vomiting due to headache. He has been ill for about a year.

Life history of illness. Till one year there happened febrile convulsions, in 1999 closed
cranioencephalal injury, brain concussion. Family illness history is unfavourable. Mother, aunts
and uncles from mother’s side have renal polycystosis. Grandfather from mother’s side had
macrogematuria, right kidney was operated, diagnosis is renal polycystosis, died at 52 years.

At the hospital the child was examined. Objective status is in norm. Laboratory results are
normal. Rheoencephalography showed hypotension of cerebral vessels in the area of inner carotic
arteries, dystonia of cerebral vessels in vertebrae basilar area. Functional test shows normaliza-
tion of vessels tonus. Blood pressure is 110/60 mm Hg. Syndrome of nonmalignant inner cra-
nial hypertension is diagnosed.

Taking into consideration family illness history, kidney ultrasonography was made of
20.04.2006 (15 years): kidneys are in typical place, sizes enlarged, right kidney 136 × 75 mm, left
140 × 67 mm, contours are even, clear, parenchyma 15 mm and 21 mm correspondingly, heterogeneous, there are numerous liquid formations from 6 to 24 mm. Calyceal system is not indurated and enlarged. Conclusion: echosigns of renal polycystosis. Ultrasonography of liver, pancreatic and spleen are normal. On 24.10.2006 in Donetsk hospital named after Kalinin rhenography was made. Rhenography showed that secretory and excretory renal functions are satisfactory.

He was an out-patient of nephrologist. Biochemical blood and urine analysis (creatinine, urea, proteinogram, electrolytes) were in norm. Ultrasonography of kidneys in 2013, 2015 showed the growth of cyst sizes in both kidneys in renal sinus, in parenchyma, liquid formation from 6–7 mm to 25 in the right kidney, from 10 to 35 in the left kidney are defined in parenchyma. Numerous punctate line hyperechogenic inclusions from 2–3 to 5–6 mm are also defined (echosigns of urolithiasis disease). From 2014 (24 years of age) the patient has been suffering from blood pressure – 145/100, 160/100 mm Hg. Laboratory tests show normal results.

Elder brother Sergey, born in 1987, got hospital treatment in an Infant neurological division of Mariupol hospital № 3 in October 2001 (14 years) with vegetation dysfunction of pubertal period syndrome with migraine-like paroxysms. Ultrasonography of kidneys was made for the first time at the hospital. Both kidneys are situated normally, contour is even, clear, they are not enlarged and parenchyma differentiation is not affected. In parenchyma to right and in the medium third there are liquid formations in Calyceal system area of 17 mm and 11 mm, in parenchyma to the left, in medium third there is liquid formation up to 19 mm, in Calyceal area there are liquid formations sized 4 mm and 6 mm. Conclusion: echosigns of polycystic kidney disease. Ultrasonography of liver, pancreases, spleen is in the norm. Laboratory tests are also in norm. He was nephrologists' out-patient from 2010 (23 years of age), he suffers from blood pressure (hypertension), chronic pyelonephritis of latent character, chronic renal failure - 0.

Children’s mother Larisa, born in 1964, being 14 years old, was treated from acute pyelonephritis. Ultrasonography of kidneys was made: kidneys are enlarged; contours are uneven, not clear. Right kidney is 186×98 mm, left kidney – 178 × 73, right kidney parenchyma is heterogeneous, there are numerous liquid formations with size 3–8 mm, in Calyceal system area their sizes are 20, 23, 26 mm, left kidney’s parenchyma is fully substituted for liquid formations in Calyceal system area, their sizes are 10, 17, 24 mm. Calyceal system area is indurated, enlarged from both sizes, echopositive structures 2–6 mm with acoustic shadowing are defined. Conclusion: echosigns of polycystic kidney disease, urolithiasis disease, pyelonephritis. In 2003 the control ultrasonography shows cysts in liver: liver isn’t enlarged, contour is even, structure is heterogeneous, there is a group of liquid formations with maximal size up to 15 mm in both lobes. Conclusion: echosigns of cysts in liver. In 2003 she was examined and treated in Donetsk hospital named after Kalinin. Diagnosis: Polycystic degeneration of kidneys, liver, chronic pyelonephritis, exacerbation, chronic renal failure, symptomatic hypertension, angiopathy of the retina (VOD, VOS-0,3), duodenal ulcer, moderate disease, with existence of ulcer 0,6 × 0,5 cm, bulb deformation, erosive gastroduodenitis. From 2006 – chronic renal failure – II.

In May 2014 – ischemic stroke in the left middle-cerebral artery with right-side hemiparesis.

Clinical case № 2. Anton, born in 1998 (16 years old) was treated in pediatrics №1 of Mariupol Territorial Medical Association “Children and Women Health” 08.12.2014 with complaints on general weakness, headache, periodical rise of blood pressure to 140/100 mm Hg, periodical pains in stomach, occasional edema of the eyelids in the morning.

Life history of illness. All the above-mentioned complaints exist for 1,5–2 years, hypotensive medicine was taken. At the 7 years of age renal polycystosis was found in Donetsk Regional Child Clinical Association, after that time the patient hasn’t been observed.

Family illness history is unfavourable. Mother (35 years old) has polycystic degeneration of kidneys, secondary chronic pyelonephritis, in recession, chronic renal failure – 1, arterial hypertension of II degree, urolithiasis disease. For the first time kidney polycystosis was diagnosed during pregnancy at the age of 19, when the clinical picture of acute pyelonephritis and arterial hypertension was firstly noted. Since 2003 (at the age of 24 years) mother has stable rise of blood pressure, rise of urea, creatinine, reduction of glomerular filtration rate (GFR). She was observed in Donetsk hospital named after Kalinin.

Ultrasonography of kidneys of 2015: Kidneys are not enlarged in size; contours are wavy, uneven, not clear. In parenchyma and renal sinuses there are numerous cysts with maximal size in the right 32 mm in the upper polus, in the left polus up to 41 mm in the middle segment. Both kidneys are visualized as numerous cysts, in septum between those there are a lot of hyperechoic formations that give acoustic shadow 6–7 mm. Conclusion: Echosigns of polycystic kidney disease, urolithiasis disease. Mother’s brother (child’s uncle) died at the age of 30 years old; he suffered from polycystosis of the single kidney, chronic renal disease. Grandmother,
from mother's line died, she also suffered from polycystic kidney disease, chronic renal disease. Cousin, daughter of mother's brother, a teenager, suffers from polycystic kidney disease.

Objectively: General state is satisfactory. Body type is normal, satisfactory nourishment. Skin and mucous seen are clear, of normal coloring. No edema, inner organs without peculiarities. Blood pressure is 135/80 mm Hg.


Ultrasonography of kidneys of 11.12.2014: Kidneys are not enlarged, contours are even, clear, right kidney 116 × 52, left kidney 113 × 61, parenchyma 19 mm and 17 mm correspondingly. Parenchyma is heterogeneous due to liquid formations on all its length with sizes from 9 mm to 23 mm in the right kidney, from 7 mm to 18 mm in the left kidney, differentiation of parenchyma is kept. Conclusions: Echosigns of polycystic kidney disease. Ultrasonography of pancreas, spleen is without peculiarities. Clinical diagnosis: chronic renal disease of the 1 degree. Polycystic kidney disease. Chronic renal failure – 0. Treatment received: lespephlan, smart-omega, enap. Recommended: to continue treatment of lespephlan in turn with nephropatin, smart-omega Q10 and essentiale. The child should be under regular nephrologist care, hypertension is registered, blood pressure is 140/100 – 160/100 mm Hg, from January 2015 creatinine rose to 114–137 mkmol/l.

Next hospitalization on 04.05.2015–12.05.2015.Creatinine blood test of 30.04.2015 – 137 mkmol/l, GFR – 84 ml/min. Chronic renal failure – 1.

From 08.12.2014 to 17.12.2014 in pediatrics № 1 of Mariupol Territorial Association “Health of Mother and Child” a cousin, daughter of mother’s brother Valentine, born in 2000 (14 years old) was investigated. Complaints: headaches, hypertension up to 140/100 mm Hg, periodical stomachaches. All the above-mentioned complaints exist within a year.

Early life history is without peculiarities. Family life history is unfavourable due to renal polycystosis (see above).

Objective conclusion: Child’s state is satisfactory. Body type is normal, satisfactory nourishment. Skin and mucous seen are clear, of normal colouring. No puffiness, inner organs without peculiarities. Blood pressure is 120/60 mm Hg.


Ultrasonography of kidneys of 10.12.2014: Kidneys are enlarged, contours are uneven, clear, right kidney 139 × 56, left kidney 128 × 62, parenchyma 21 mm and 19 mm correspondingly. Parenchyma is indurated; heterogeneous due to liquid formations on all its length with sizes from 5 mm to 30 mm in the right kidney, differentiation of parenchyma is kept. In the projection of Calyceal area there are concrements 3–7 mm that give acoustic shadow. Conclusions: Echosigns of polycystic kidney disease. Urolithiasis disease. Ultrasonography of liver, pancreas, spleen is without peculiarities. Neurologist examination: Vegetative dysfunction syndrome. Clinical diagnosis: Chronic renal disease. Polycystic kidney disease, chronic renal failure – 0. Vegetative dysfunction syndrome. Treatment received: Mg – B 6, glycine, urostone, enap under the control of blood pressure.

Clinical case № 3. Child Vyacheslav’s (born in 2003) parents showed him to the city infant nephrologist in the city of Mariupol when he was 5 years old because of changes in kidneys ultrasonography.

Family history of illness. Boy’s father suffers from renal polycystosis, his grandmother from father’s side died from kidneys disease.
Boy’s kidney ultrasonography at 5 years old, 9 years old, 12 years old was done. Kidneys ultrasonography of 16.11.2012: Right kidney is $89 \times 35$ mm, left kidney is $96 \times 38$ mm, they are insignificantly enlarged, contours are even, parenchyma is differentiated, there are numerous liquid formations from 3 mm to 14 mm in both kidneys. Partial doubling of left kidney is visualized. Conclusions: Echosigns of renal polycystosis, partial doubling of left kidney.

The child is observed for 7 years. No complaints. General state is normal. Objective status is without peculiarities. Blood and urine tests don’t show any deviations from the norm. Ziminitskii’s test, GFR within age norm. The enlargement of cyst sizes in kidneys is not found in next ultrasonography.

His younger brother Artyom, born in 2012 (3 years old) and his sister Albina, born in 2015 (1 year old) were also examined. No complaints. Objective status is without peculiarities. Laboratory tests are within age norms.

Artyom was made ultrasonography of kidneys when he was 3 months old, 1 year old, 2 years old. Kidneys ultrasonography: Kidneys’ sizes correspond to age. Contours of kidneys are even. Parenchyma is differentiated, with liquid formations in it. At the age of 3 months (24.12.2012) the liquid formations in parenchyma of both kidneys were from 3 to 10 mm. At the age of 1 year (18.10.2013) the liquid formations in the parenchyma of left kidney were from 3 to 10 mm in diameter, in the right kidney they were 10–21 mm. At the age of 2 years (14.04.2015) liquid formation in kidneys parenchyma were from 3 to 15 mm in diameter, in the right kidney in the low polus there were liquid formations with sizes 25 mm, 37 mm. Conclusions: Echosigns of polycystic kidney disease. In dynamic enlargement of cysts is defined mainly in the right kidney.

Ultrasonography of kidneys was done to the girl Albina at the age of 20 days and 1 year. Kidneys are not enlarged, contour is even, parenchyma is differentiated. In parenchyma of both kidneys there are numerous liquid formations from 4 to 8 mm. Conclusions: Echosigns of polycystic kidney disease.

Medical genetic investigation in the family wasn’t done. Children need further observation in order to find out arterial hypertension, infections of urinary tract, the beginning of chronic renal failure development and other aftereffects of renal polycystosis. It is necessary to do medical genetic investigation to find out the type of heredity and probability of possible character of the disease.

Conclusions. 1. Thus, children’s and teenagers’ may differ by its clinical picture. Proteinuria, micro-, macrogammaturia, recurring pyuria, crystalluria, polyuria, lagging in physical development, hypertension, ungrounded anemia, stable hypostenuria must be reason for investigation in specialized hospital division. 2. The main methods of diagnostics are ultrasonography of urinary system, studying of family history of illness, molecular-genetic investigation as well as gene carrier so his near relatives. 3. Polycystosis treatment is a hard task for clinicists because there is no specific treatment, only syndromological treatment is used. In case of chronic renal failure rise hemodialysis and the following transplantation is recommended.

References

ОСОБЕННОСТИ ТЕЧЕНИЯ СЕМЕЙНОГО ПОЛИКИСТОЗА ПОЧЕК У ДЕТЕЙ
(данные литературы и собственного наблюдения)
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Проанализированы особенности течения поликистоза почек у детей по данным литературы и результатам собственных клинических наблюдений. Диагностика заболевания сложна, предусматривает медико-генетическое консультирование, а также комплексное обследование с применением клинико-лабораторных и инструментальных методов. Основной в лечении является адекватная ренопротективная терапия, показано проведение гемодиализа с последующей трансплантацией почек.

Ключевые слова: дети, поликистоз почек, диагностика, лечение.

ОСОБЕННОСТИ ПЕРЕБИГУ СІМЕЙНОГО ПОЛИКИСТОЗУ НИРОК У ДІТЕЙ
(дані літератури та власного спостереження)
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Висвітлені особливості перебігу полікістозу нирок за даними літератури та власних клінічних спостережень. Діагностика складна, передбачає медико-генетичне консультування, а також комплексне дослідження основних клініко-лабораторних та інструментальних показників. Основною в лікуванні захворювання є адекватна ренопротективна терапія, показаній гемодіаліз з подальшою трансплантацією нирок.

Ключові слова: діти, полікістоз нирок, діагностика, лікування.