SUMMARY

Introduction: Autosomal dominant polycystic kidney disease (ADPKD) is the most frequent inherited renal disorder with an incidence of 1:500-1:1000. It is characterized by progressive development of renal cysts leading to deterioration of renal function and chronic renal failure in adults. Other common renal complications are hypertension, proteinuria, macrohaematuria and urinary tract infections. Extrarenal complications include the cardiovascular system, gastrointestinal system and connective tissue abnormalities – most common are cardiac valve abnormalities, cerebral berry aneurysms and hepatic, pancreatic or spleen cysts, and herniae of the anterior abdominal wall. ADPKD is caused by mutation in one of two known genes – PKD1 (85% of patients) or PKD2 (14%). A proposed third gene PKD3 (about 1%) has not yet been localised. Many studies in adults have shown that patients with mutations in the PKD2 gene have a better prognosis than PKD1 patients. The mean age at end stage renal disease (ESRD) or death was 53 yrs in PKD1 and 69 yrs in PKD2, the mean age at ESRD in PKD1 was 54 yrs, in PKD2 74 yrs and the patients with PKD1 mutations had a four times higher prevalence of arterial hypertension. The cyst number and the volume of the cysts are higher in PKD1 than in PKD2 patients. Several studies have proved that symptoms of ADPKD such as renal cysts, hypertension or proteinuria may be observed also in childhood.

Objective of the study: In children with ADPKD, genotype-phenotype correlation has never been investigated - there is no study on possible differences in the manifestation of ADPKD in children with known PKD1 and PKD2 mutations. The aim of this study was to compare phenotypes between children with mutations in PKD1 and PKD2 genes.

Patients and methods: 50 PKD1 and 10 PKD2 children were investigated. Their mean age was similar (8.6±5.4 and 8.9±5.6 yrs). Renal ultrasound, office blood pressure (BP), ambulatory BP, creatinine clearance and proteinuria were retrospectively analysed.

Results: PKD1 children had in comparison to PKD2 children significantly higher total number of renal cysts (13.3±12.5 vs. 3.0±2.1, p=0.004), larger kidneys (right/left kidney length 0.89±1.22 vs. 0.17±1.03 SDS, p=0.045 and 1.19±1.42 vs. 0.12±1.09 SDS, p=0.014, successively) and higher ambulatory daytime and nighttime systolic BP (daytime/nighttime BP index 0.93±0.10 vs. 0.86±0.05, p=0.021 and 0.94±0.07 vs. 0.89±0.04, p=0.037, successively). There were no significant differences in office BP, creatinine clearance or proteinuria between both groups. Prenatal renal cysts (14%), hypertension defined by ambulatory BP (27%) and enlarged kidneys (32%) were observed only in PKD1 children.

Conclusions: This is the first study on genotype-phenotype correlation in children with ADPKD. It showed significant differences between patients with mutations in the PKD1 gene and PKD2 gene in an early stage of ADPKD. Children with PKD1 mutations have a higher number of renal cysts and larger cysts than children with PKD2 mutations. Moreover, children with PKD1 mutations more often have enlarged kidneys and bilateral renal cysts. Furthermore, they have higher systolic ambulatory blood pressure and are more often hypertensive than children with PKD2 mutations. Prenatally detected renal cysts and enlarged kidneys are highly specific for PKD1 children.