# A Kindred of Aggregation of Polycystic Kidney Disease Cases: A Challenge to Medical Science

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## Abstract

The polycystic kidney disease (PKD) is a group of disorders characterized by the bilateral presence of a large number of fluid-filled cysts lined by tubular epithelium in the kidneys. Two major genes in autosomal dominant polycystic kidney disease- PKD1 (in 85 to 90% cases) and PKD2 (in 10 to 15% cases) have been identified. Diagnosis can be made by family history, clinical findings, Ultrasonography, Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) of abdomen. End stage renal disease, cardiovascular pathology and infections account for approximately 90% of deaths of those patients treated by haemodialysis or peritoneal dialysis and after renal transplantation.

**Key words:** polycystic kidney disease, autosomal dominant diseases, renal failure, renal transplant.

## Introduction

In polycystic kidney disease (PKD), both the kidneys have a large number of fluid-filled cysts in cortex and medulla of enlarged kidneys (as shown schematically in figure1) with characteristic of familial aggregation[1]. Surrounding normal kidney tissue gets attenuated resulting in renal failure with grossly enlarged kidneys[2]. Autosomal dominant PKD and autosomal recessive PKD are its two sub varieties. Decrease in urine concentration ability is an early manifestation with increased plasma vasopressin levels, which represent body's attempt to compensate for reduced concentrating capacity of the kidneys and could contribute to the development of renal cysts, hypertension and renal insufficiency [3]. Diagnosis of PKD can be done by family history, clinical findings, ultrasonography etc. Genetic linkage analysis, Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) studies are also helpful. End stage renal disease, cardiovascular pathology and infections account for approximately 90% of deaths of those patients treated by haemodialysis or peritoneal dialysis and after renal transplantation. Patient / family should be counselled well regarding hereditary pattern of the disease and their children having 50% chance of acquiring the disease. Adequate BP control might slow the progression of renal disease.

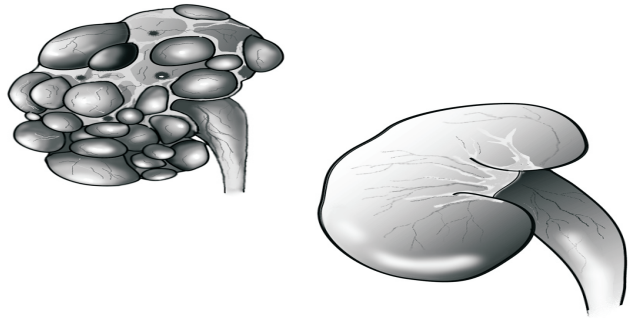

**Figure 1. Schematic presentation of PKD & Normal Kidneys**

## Case Report

A 28 year old male patient was investigated for recurrent symptoms of abdominal pains. His abdominal Ultrasonography revealed bilateral polycystic kidneys with cyst size measuring between 10-30 mms. Blood urea and serum creatinine levels and urine examination reports were within normal limits. As shown in flow chart, further detailed history revealed his father's death at the age of 52 due to kidney failure secondary to polycystic kidney disease. His elder brother of 34, is having polycystic kidney disease as revealed by ultrasonography with high blood pressure (156/100 mm of Hg, now put on treatment) and marginally raised blood urea (46.8

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mg%) and serum creatinine levels (1.9 mg%). Out of two sisters, one bed ridden sister expired at the age of 18 years by some congenital nervous system disease with respiratory illness and second sister of 32, is doing well with normal kidneys by ultrasonography. Even though his brother's son of 4 years now has normal kidneys by ultrasonography and blood urea and serum creatinine levels, with normal revealed pre senile death of two uncles at the age of around 45 to 50 years because of some kidney related elements (? PKD). His third uncle of around 52 and his cousin brothers of 20 to 30 years, although doing well now physically, we could not trace them for further investigations.

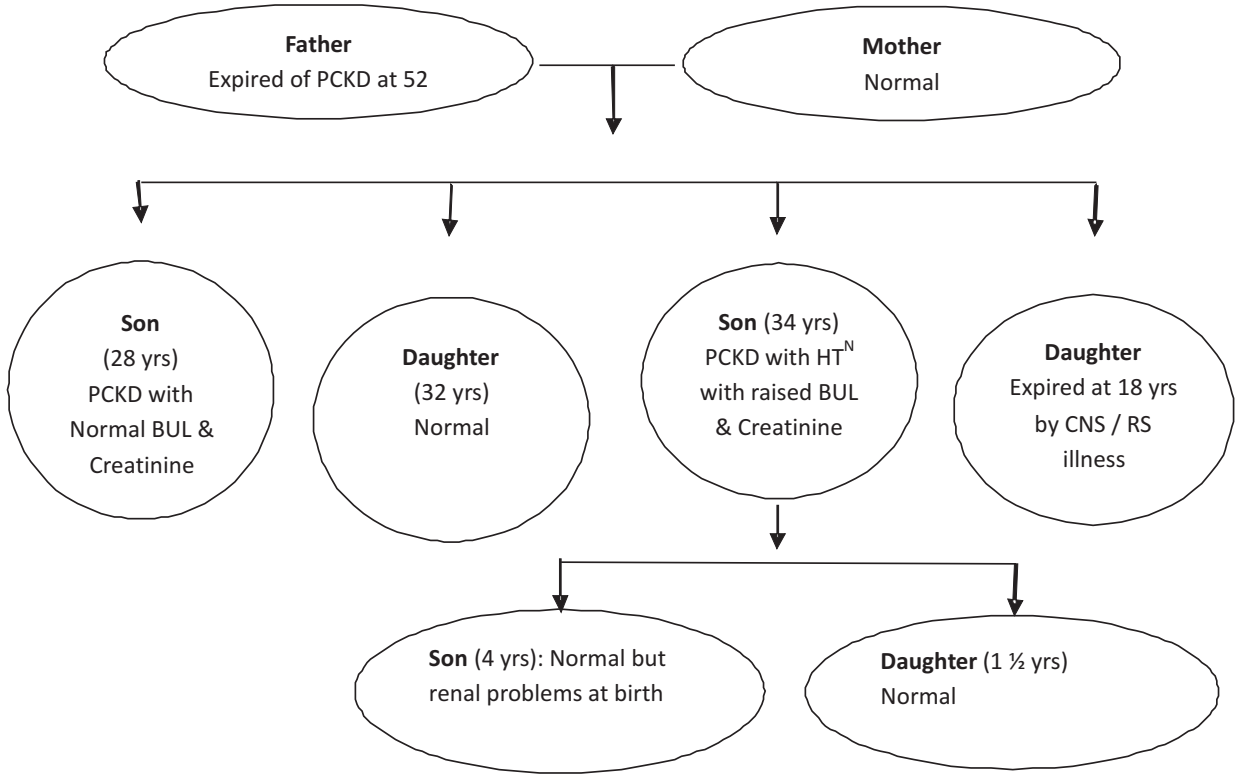


**Figure 1.Flow chart showing the familial aggregation of PKD cases**

developmental milestones and intellectual levels except delayed speech, his perinatal records showed intrauterine growth retardation with moderate oligohydramnios, delivered by caesarian section at 38 weeks of gestation and was treated in neonatal intensive care unit (NICU) after birth for anuria and septicaemia. Raised blood urea levels (76 mg %) with positive C-reactive protein test and ultrasonography changes of hyper echoic renal pyramids in both kidneys suggestive of medullary nephrocalcinosis was observed. After 10 days of treatment, blood urea and serum creatinine levels were within normal limits. Further familial history of uncles of the patient

**Discussion**

The polycystic kidney disease (PKD) is a

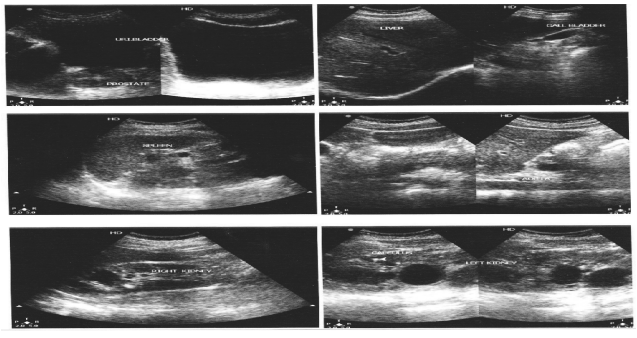

**Figure 2. USG films showing cystic lesions in the kidneys with normal liver, spleen and pancreas**.

group of disorders characterized by the bilateral presence of a large number of fluid-filled cysts in cortex and medulla of grossly enlarged kidneys with characteristic of familial aggregation [1]. Small cysts lined by tubular epithelium develop from infancy or childhood and enlarge slowly and irregularly. Surrounding normal kidney tissue gets attenuated resulting in renal failure with grossly enlarged kidneys [2].

There are two types of PKD - a) autosomal dominant PKD, and b) the less common autosomal recessive PKD. Autosomal dominant PKD is the most common inherited disorder of the kidneys in human [3]. It is the frequent genetic cause of renal failure in adults, accounting for 6-8% of patients on dialysis in US [3]. Adult PKD is a multicystic and progressive disorder characterized by formation and enlarged cysts in the kidney (as seen in figure 2) and other organs like liver, pancreas, spleen, etc. Clinical features usually begin in the third to fourth decade of life, but cyst may be detectable in the childhood and in- utero [3]. The Symptoms of autosomal recessive PKD begin in the earlier age of life, even in the womb [3, 4].

Two major genes in autosomal dominant polycystic kidney disease (PKD1 and PKD2) have been identified [5,6]. Approximately, 85 -90% of patients with adult polycystic kidney disease (ADPKD) have abnormality on the short arm of chromosome 16 (ADPKD type 1) / PKD1 (16p13.3). A second defect, termed ADPKD type 2 / PKD2 is responsible for 10 -15 % of ADPKD cases and is found on the long arm of chromosome 4 (4q21-q22). A third genotype may exist but no genome locus is assigned. PKD 1 and PKD2 are expressed in most organs and tissues of the human body. Decrease in urine concentration ability is an early manifestation of ADPKD. Plasma vasopressin levels are increased, which represent body's attempt to compensate for reduced concentrating capacity of the kidneys and could contribute to the development of renal cysts, hypertension and renal insufficiency [5]. A good phenotype-genotype correlation has not been well established for ADPKD-1 and ADPKD-2 [7].

Clinically it is manifested as a vague discomfort in loin / abdomen (due to increasing mass and renal tissue), acute loin pain or renal colic (due to haemorrhage into a cyst), hypertension, renal failure, haematurea (with no or little proteinurea), urinary tract infection or cyst infections[2]. About 30% of patients with PKD have hepatic cysts with rare disturbance of hepatic functions. Sometimes (and almost always in women) this causes massive and symptomatic hepatomegaly usually with renal enlargement. About 10% cases have subarachnoid haemorrhage due to Berry aneurysms of cerebral vessels in certain families (specific mutations), mitral / aortic regurgitation are frequent but rarely severe. Colonic diverticuli, abdominal wall hernias may occur.

Diagnosis of PKD can be done by family history, clinical findings, ultrasonography which demonstrates multiple cysts in 95% cases over the age of 20 years (as shown in figure 2), but may not detect small developing cysts in younger patients. Genetic linkage analysis, Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) studies can also be taken help for further studies.

Prognosis of ADPKD-1 is poor than ADPKD-2. End stage renal failure (ESRF) occurs in 50% of patients with ADPKD1 with mean age of 53 years and that for ADPKD - 2 patients it is 74 years. The genetic heterogeneity of ADPKD and the possible contribution of modifier genes, may explain the wide clinical variability in this disease, both within and between families [6,8]. Genetic classification of patients as PKD1 and PKD2 is of prognostic relevance as hypertension and urinary tract infection are four to two times respectively higher than with PKD2 [6]. Individuals with ADPKD may live normal life span without knowing that they have the disease. However, ADPKD typically causes progressive renal dysfunction resulting in grossly enlarged kidneys and kidney failure by $4^{th}$ to $6^{th}$ decade of life. There is inverse association between the size of polycystic kidneys and the level of glomerular filtration [9].

End stage renal disease cardiovascular pathology and infections account for approximately 90% of deaths of those patients treated by haemodialysis or peritoneal dialysis and after renal transplantation [10].

**Scope for further research**

Nothing has been yet found to alter the rate of progression of renal failure in polycystic kidney disease. Presently, symptomatic treatment in the form of blood pressure control, treatment of urinary tract infections and in severe cases, peritoneal dialysis, haemodialysis and renal transplantation are the only supportive, palliative care options developing and testing of new potential therapies for ADPKD will result in fewer people developing advanced kidney

disease and kidney failure. The research could be directed against- Immunotherapy / drug therapy which might restrain the hyperplasia of cystic lining cells, so that the genes for formation of cysts will no longer grow and cysts will regress in size and number.

The drug that decrease the secretion of fluid in the cyst and increase the permeability of cystic walls to make them smaller gradually and thereby prevent further renal parenchymal damage. The drug that targets kidney fibrosis would give patients additional years of life without dialysis. Identifying genetic markers for prognostic point of view, gene therapy and better strategies to maintain the function of transplanted kidneys might help to add life to years to the patients with PKD. Immunomodulators to develop resistance for bacterial / viral invasion of the cysts might play wonderful role in preventing renal failure and end stage renal disease.

**Patient / Family Counselling**

Patient / family should be counselled well regarding hereditary pattern of the disease and their children having 50% chance of acquiring the disease. Although different treatment modalities are being tested this disease has no cure. Only intervention that slow the progression of renal disease (ex. Adequate BP control) are of benefit. Prenatal diagnosis is available through DNA linkage studies. Patients should have regular BP checkups and urine screening for haematuria.

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