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Case Report

# The Early Diagnosis of Autosomal Dominant Polycystic Kidneys and Possible Prevention of the Development of Chronic Renal Failure: an Educational Article and Expert Opinion

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## Abstract

**Background:** Adult polycystic kidney disease is an important cause of chronic renal failure, but it is associated with a very variable clinical course and progression to chronic renal failure. Diagnosis is made by ultrasound, and genetic study is not generally required. Management aims at delaying the onset of chronic renal failure or retarding its progression, and it includes antihypertensive medications, dietary protein restriction, and early treatment of urinary tract infections. The aim of this paper is to report an Iraqi patient who was diagnosed early before the onset of renal failure, and to describe the current evidenced based possible treatments.

**Patients and methods:** At about the age of thirty years, a female who was having recurrent urinary tract infection was studied as her uncle has recently diagnosed as having chronic renal failure caused by adult polycystic kidney disease. Her uncle developed progressive symptomatic uremia at about the age of 52 years, and he had progressive hearing impairment over few years. The case of her uncle was reported as an extremely rare association of adult polycystic kidney disease with hearing impairment. Her aunt died from chronic renal failure.

**Results:** The patient was not hypertensive and had normal echocardiography. Renal function tests were normal (Serum creatinine was 0.6 mg/dL and blood urea was 19 mg/dL). Renal ultrasound confirmed the diagnosis of adult polycystic kidney disease.

**Conclusion:** The current evidence-based expert opinion suggest the long-term use simvastatin plus octreotide-long-acting release monthly injection in patients with adult polycystic kidney disease to slow the growth of cysts and the deterioration in renal function. The use of tolvaptan can also be considered, but it is associated increased adverse effects such as thirst, polyuria, and hepatic injury.

**Keywords:** adult polycystic kidney disease; early diagnosis; evidence-based therapies; expert opinion

## Introduction

Adult polycystic kidney disease is an important cause of chronic renal failure, but it is associated with a very variable clinical course and progression to chronic renal failure. Diagnosis is made by ultrasound, and genetic study is not generally required. Management aims at delaying the onset of chronic renal failure or retarding its progression, and it includes antihypertensive medications, dietary protein restriction, and early treatment of urinary tract infections [1, 2, 3, 4]. Stephen Báthory (Figure-1A),

**Figure-1A:** Stephen Báthory (September 27, 1533-12 December 12, 1586), King of Poland and Grand Duke of Lithuania (1576-1586)

a Polish king was the first known person to have adult polycystic kidney disease. After dying at about the age of 53 years, and while extracting his internal organs for the preservation of his body as a mummy, Jan Zygolith, the surgeon who was assisting by Dr. Buccella, described the king's cystic kidneys as large like bull's kidneys and having an uneven and bumpy surface. During that that time, death of the king was not attributed to a renal disease. However, in 1933, Franciszek Walter (Figure-1B),

**Figure-1B:** Professor Franciszek Ksawery Walter (1885-1950)

a professor from Krakow Medical School, organized a meeting attended by doctors and historians to discuss the of King's autopsy abnormalities. It was concluded that the king died from uremia caused by polycystic kidneys disease. In 1793, Matthew Baillie (Figure-1C)

**Figure-1C:** Matthew Baillie (October 27, 1761-September 23, 1823), a British physician and pathologist

emphasized that the vesicular cysts in kidneys in this disorder were different from hydatid cysts, and named the condition "False hydatids of kidney". In 1888, Félix Lejars (Figure-1D)

**Figure-1D:** Félix Lejars from Paris

from Paris emphasized that the cysts in this condition were present on both sides and named the condition "Polycystic kidney".

In 1983, Szabó and colleagues emphasized that diagnostic ultrasound has been used since early 1970s for the early diagnosis of polycystic kidney disease and has been increasingly considered as a reliable diagnostic tool [2].

The aim of this paper is to report an Iraqi patient who was diagnosed early before the onset of renal failure, and to describe the current evidenced based possible treatments.

## Patients and methods

At about the age of thirty years, a female who was having recurrent urinary tract infection was studied as her uncle has recently diagnosed as having chronic renal failure caused by adult polycystic kidney disease.

Her uncle developed progressive symptomatic uremia at about the age of 52 years, and he had progressive hearing impairment over few years. The case of her uncle was reported as an extremely rare association of adult polycystic kidney disease with hearing impairment. Her aunt died from chronic renal failure.

## Results

The patient was not hypertensive and had normal echocardiography. Renal function tests were normal (Serum creatinine was 0.6 mg/dL and blood urea was 19 mg/dL). Renal ultrasound (Figure-2)

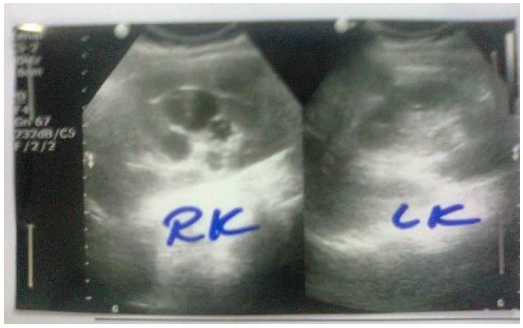


**Figure-2**: Renal ultrasound confirming the diagnosis of adult polycystic kidney disease

performed on the 6th of January 2024, showed that both kidneys were normal in size, and had normal texture and normal cortical thickness. There was no renal mass or stone. The pelvi-calyceal systems were not dilated. However, there were several cysts on both kidneys; the largest one was 3 centimeter in diameter. Thus, the ultrasound confirmed the diagnosis of adult polycystic kidney disease.

## Discussion

Management aims at delaying the onset of chronic renal failure or retarding its progression, and it includes antihypertensive medications, dietary protein restriction, and early treatment of urinary tract infections. In 1996, Maschio from Italy reported a three-year placebo-controlled study which included 583 patients with renal insufficiency resulting from a variety of diseases, and included 64 patients with adult polycystic kidney disease. Three hundred patients were treated with an angiotensin-converting-enzyme inhibitor, benazepril, while 283 patients were treated with placebo. After three years, thirty-one patients who received benazepril experienced doubling of the base-line serum creatine level or required for dialysis, while fifty-seven patients who received placebo experienced doubling of the base-line serum creatine level or required for dialysis ($P<0.001$). **However,** the study found that although benazepril had a protective effect against the progression of renal insufficiency in several kidney diseases, it was not effective polycystic kidney disease [5].

In 2001, van Dijk et al from the Netherland emphasized that experimental animal studies showed that Hydroxymethylglutaryl-CoA (HMG-CoA) reductase inhibitors, the statins can retard the progression of chronic renal insufficiency. They reported a clinical study which included ten patients adult polycystic kidney disease who had normal cholesterol level whom were treated in random order for one month with simvastatin 40 mg a day or placebo.

Simvastatin treatment was associated with marked increase in glomerular filtration rate and, effective renal plasma flow (P<0.05). Treatment was also associated with a marked decrease in cholesterol level (P<0.001). van Dijk et al suggested that simvastatin treatment can improve renal function in patients with adult polycystic kidney disease by improving renal plasma flow, possibly through improving endothelial function [6].

In 2005, Piero Regiment from Italy and his research group suggested that the renal cysts in adult polycystic kidney disease are filled with fluid secreted mostly by the tubular epithelium lining the cysts through secondary chloride transport. They thought that the fluid filling can possibly be inhibited by somatostatin resulting in shrinkage of the cysts. They reported a six-month cross-over, placebo-controlled study which included patients with mild-to-moderate renal insufficiency caused by autosomal-dominant adult polycystic kidney disease. Twelve patients were treated with octreotide-long-acting release (A long-acting somatostatin) 40 mg intramuscularly four weeklies. The increase in renal volume was markedly lower in patients treated with somatostatin than in 2010, Marie C Hogan from the United States and her research group reported a one- in patients who received placebo. Regiment from and his research group reported that the use of somatostatin for six months was well tolerated and safe, and can slow the expansion of renal volume in adult polycystic kidney disease. Therefore, somatostatin treatment can inhibit growth of smallest cysts [7].

In 2010, Anna Caroli from Italy and her research group reported a post hoc analysis of the study of Piero Regiment from Italy and her research group reported that octreotide treatment also reduced liver volumes in the patients with adult polycystic kidney disease [8].

Also, year placebo-controlled study which included 42 patients with autosomal dominant polycystic kidney and liver disease (34 patients had polycystic kidneys and 8 had polycystic liver disease). Twenty-eight patients were treated with octreotide-long-acting release depot (A long-acting somatostatin analogue) up to 40 mg every four weeks (+/-5 days), and fourteen patients received placebo. Octreotide treatment was associated with reduction in liver volume, while liver volume almost remained unchanged in the patients who received placebo (P=0.048). Octreotide treatment prevented the increase kidney volume, while the patients who received placebo experienced an increase in kidney volume (P=0.045). Changes in GFR were similar in both groups. Octreotide was found to be well-tolerated and was considered to have acceptable side effects [9].

In 2011, Maria V Izabal from the United States and her research group emphasized the preliminary evidence from experimental studies suggesting that tolvaptan (A V (2)-specific vasopressin receptor antagonists) can retard disease progression in polycystic kidneys animal models. They reported a study which included twenty patients with adult polycystic kidney disease which showed that tolvaptan treatment can markedly decrease total kidney volume and renal cyst volume especially of larger cysts when the renal function is maintained. The effect of tolvaptan was attributed to inhibition of V (2)-driven adenosine cyclic 3, 5-monophosphate generation and to the aquaretic effect (Promotion of the excretion of water without electrolytes) [10].

Also in 2011, Higashinari et al from Japan showed that although the long-term use of tolvaptan can retard growth of cysts in adult polycystic kidney disease, it was associated with high incidence of side effects. In 2012, Torres et al from the United States and their collaborators reported a placebo-controlled study which included 1445 patient's adult polycystic kidney disease, and showed that a three-year tolvaptan treatment retarded the increase in total renal volume and slowed the loss of renal function, but tolvaptan was associated with a higher discontinuation rate than placebo because of the occurrence of adverse side effects [12].

In 2013, Caroli et al from Italy and their collaborators reported a three-year placebo-controlled study which included 75 patients with adult polycystic kidney disease. 38 were treated with two 20 mg intramuscular injections of octreotide-long-acting release, and 37 patients received placebo. At one year, MRI studies showed that octreotide-long-acting release treatment was associated with much less increase in total kidney volume. It was possible to study thirty-five patients treated with octreotide-long-acting release, and thirty-five patients who received placebo with MRI at three years. Octreotide-long-acting release treatment was again associated with less increase in total kidney volume Thirty-seven patients treated with octreotide-long-acting release, and thirty-two patients received placebo experienced at least one adverse effect (p=0·16). Patients with serious adverse effects were similarly distributed in the treated patients and in the patient's received placebo. Nevertheless, four patients treated with octreotide-long-acting release experienced acute cholecystitis or cholelithiasis [13].

In 2019, Norberto Perico from Italy and his research group reported a study which included 100 patient's adult polycystic kidney disease who had glomerular filtration rate between 15 to 40 ml/min/1.73 square meter. Fifty-one patients were treated with two intramuscular injections of 20 mg octreotide-long-acting release every four weeks for 3 years, forty-nine patients received placebo. The study showed that octreotide-long-acting release treatment can slow growth of cysts and kidneys and slow the progression to end-stage renal disease. Of 63 patients with chronic kidney disease stage 4, three of the patients treated with octreotide-long-acting release, and eight of the patient's received placebo developed end-stage renal disease (P = 0.036). Three of the patients who received placebo experienced a serious renal cyst rupture/infection and one patient developed a serious urinary tract infection/obstruction. However, only one patient of the patients treated with octreotide-long-acting release experienced a serious infection of renal cyst [14].

In 2023, Lu et al from China reported a meta-analytic study which included 13 placebo-controlled studies which included 3575 patients with adult polycystic kidney disease. The study showed that tolvaptan treatment was associated with slowing of the deterioration in renal function, slowing the increase in total kidney volume, and reduction of complications including renal pain, urinary tract infections, hematuria, and hypertension. However, tolvaptan increased adverse effects such as thirst, polyuria, and hepatic injury [15].

## Conclusion

The current evidence-based expert opinion suggests the long-term use simvastatin plus octreotide-long-acting release monthly injection in patients with adult polycystic kidney disease to slow the growth of cysts and the deterioration in renal function. The use of tolvaptan can also be considered, but it is associated increased adverse effects such as thirst, polyuria, and hepatic injury.

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**Conflict of interest:** None.

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