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# Clinical Presentation and Outcomes of Autosomal Dominant Polycystic Kidney Disease in the Elderly

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**Abstract** The patient characteristics and outcomes associated with autosomal dominant polycystic kidney disease (ADPKD) have not been characterized in elderly population. The purpose of theis study was to delineate clinical presentation and outcome of ADPKD in elderly patients. We performed a retrospective study. Thirty four elderly patients were diagnosed with ADPKD between 1975 and 2005. The diagnosis of ADPKD was made using family history and ultrasound. There were 21 (61.7%) males and 13 (38.3%) females. The mean age at the time of diagnosis of ADPKD was 69.74 ± 3.36 years (range, 65-79 years). The earliest clinical features were renal failure in 67.6%, back pain in 38.2%, and hypertension in 17.6%. Most common form of presentation was hypertension in 70.6%. Kidneys were palpable in 26.5%, and liver was palpable in 32.4%. Left ventricular hypertrophy confirmed by trans-thoracic echocardiography was found in 5(1.5%) patients. Three (0.8%) patients had colonic diverticula and two (0.6%) had neurological manifestation. Twenty six 26 patients (76.5%) patients had end stage renal disease and 30 patients (88.23 %) patients had anemia. Median follow-up period for all patients was 17.9 months (range, 1-120 months). Two (0.6%) patients developed renal carcinoma while five patients (14.7%) died within six years following diagnosis Anemia was the strongest and an independent predictor of poor renal outcome. ($p<0.03$). The diagnosis of ADPKD in elderly patients was made late in most cases, with patients already at end stage renal disease. Anemia is risk factor of poor renal prognosis. Eearly diagnosis and efforts at prevention of the disease progression and complications are most essential.

***Keywords:*** *Autosomal Dominant Polycystic Kidney Disease, elderly, renal function, outcome*

## 1. Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is a common hereditary disorder, affecting 1 in 400 to 1 in 1000 people and is the single most common cause of end-stage renal disease (ESRD) after diabetes mellitus and hypertension in the United States [1,2]. In Tunisia, ADPKD is an important cause of renal failure, accounting for 6.9% patients who receive hemodialysis [3], but there is a lack of data on the prevalence of ADPKD in Africa . Although previously considered to be an adult disease, it has become clear that systemic manifestations can occur in childhood, with a diagnosis possible as early as in utero [4,5].

The trait theoretically has a 100% penetrance and 96% of affected persons will manifest the disease clinically by age of 90 years [6]. Unfortunately, in developing countriesy the diagnosis of ADPKD is often was made in late [7]. The objective of our study was to characterize clinical presentations and outcomes of ADPKD in elderly patients.

## 2. Patients and Methods

### 2.1. Patients

Medical records of all patients diagnosed to have ADPKD and who were over 65 years old from January 1975 to December 2005, were reviewed retrospectively. The diagnosis of ADPKD was made by ultrasound using Ravine diagnostic criteria [8].

Medical records were evaluated for initial presenting complaints, co-morbids conditions, family history of ADPKD, palpable mass on abdominal examination, cardiac abnormalities and use of anti-hypertensive drugs. Laboratory parameters included complete blood count, serum sodium and potassium levels, blood urea nitrogen, serum creatinine, blood glucose levels, lipid profile, urinalysis, micro-albuminuria and urine culture. Estimated glomerular filtration rate (eGFR) was calculated using the Cockroft and Gault formula [9]. Records of presence of hepatic cyst, splenic cyst, pancreatic cyst, diverticulosis and nephrolithiasis using ultrasound scan were also sought for. Dependency on dialysis, renal transplant and death were the final outcomes in this study.

### 2.2. Statistical Analysis

The Statistical package SPSS 10.5 was used for data analysis. The results are expressed as mean ±SD and percentages. Frequencies were compared using two-tailed Fisher's exact test. Comparisons between groups were made using Chisquare test for qualitative parameters and

non paired student's t test for continuous variable. Test. Multiple regression analysis to determine strength of relation and predictors of outcomes was performed. Kaplan Meier patient survival was performed. Statistical significance was set at $p < 0.05$.

## 3. Results

A total of 34 patients fulfilled inclusion criteria for the study, of ADPKD and over 65 years old. There were 21 (61.7%) males and 13 (38.3%) females. The mean age at the time of diagnosis of ADPKD was 69. ± 3.3 years (range, 65-79 years).

Parental consanguinity was found in 38.2% and 17.6% had an affected parent. The clinical features were uremic features in 67.6%, back pain in 38.2%, hypertension in 17.6%, microscopic hematuria in 14.7% and urinary infection in 11.8% (Table 1 and Table 2).

**Table 1. Earliest clinical features in elderly patients with ADPKD.**

| Clinical features | Number of patients [N = 34] | % |
|---|---|---|
| Chronic renal failure | 23 | 67.6 |
| Flank pain | 13 | 38.2 |
| Hypertension | 6 | 17.6 |
| Gross hematuria | 5 | 14.7 |
| Urinary infection | 4 | 11.8 |
| Renal colic | 3 | 8.8 |

**Table 2. Physical signs at presentation in elderly patients with ADPKD.**

| Signs | Number of patients [N = 34] | % |
|---|---|---|
| Hypertension | 24 | 70.6 |
| Palpable kidneys | 9 | 26.5 |
| Palpable liver | 3 | 8.8 |
| Cardiac murmur | 6 | 17.6 |
| Hernia | 7 | 20.8 |
| Intestinal manifestation | 9 | 26.5 |
| Neurological manifestation | 2 | 5.9 |

The most common presentation was hypertension in 70.6%. Kidneys and liver were palpable in 26.5%, and 32.4% of patients respectively, while 17.6% of patients had heart murmurs and 20.6% of patients had inguinal hernia. Left ventricular hypertrophy determined by trans-thoracic echocardiography was found in 5 (%) patients. Three (%) patients had colonic diverticula and 2 (%) had neurological manifestation.

The laboratory parameters are summarized in Table 3. Proteinuria (0.3 – 2.8 g/24 hours) was present in 14 (41%) patients. Gross haematuria was present in 5 (14.7%) patients. Urine culture was positive in 14 (41%) patients with 8 (%) having *E. coli* and 2 (%) each *Klebsiella* and *Pseudomonas aeuroginosa species*. Twenty six (76.5%) patients had end stage renal disease and 30 patients (88.23 %) had anemia.

**Table 3. Laboratory parameters in elderly patients with ADPKD.**

| Laboratory Parameters | Mean ±standard deviation |
|---|---|
| Estimated Glomerular Filtration Rate (e-GFR) [ml/min/1.73m2] | 14.8±??? |
| Hemoglobin[g/dl] | 8.7 ±2.4 |
| Serum uric acid [µmol/L] | 438.3 ±182.5 |
| Serum potassium [mmol/L] | 4.9 ±1 |
| Serum calcium [mmol/L] | 1.87 ±0.4 |
| Serum phosphorus [mmol/L] | 2.22 ±0.8 |

**Table 4: Gender comparisons in elderly ADPKD patients**

| Signs | Men | Women | P-value |
|---|---|---|---|
| Liver cysts | 28.5% | 38.5% | 0.07 |
| ESRD | 28.6% | 18.2% | 0.4 |

All patients had ultrasound examination of the abdomen from ~~on~~ which the diagnosis of ADPKD were made. Eleven (32.4%) had concomitant cysts in the liver.

Median follow-up period for all patients was 17.9 months (range, 1-120 months). Twenty six (76.5%) patients were dialysis dependent at the end of study and two patients developed renal carcinoma. A total 4 (11.7%) were lost to follow-up. Five (14.7%) patients died within six years following diagnosis (Figure 1). Chi-square analysis revealed that presence of cysts in the liver ($p = 0.03$) and anemia ($p = 0.03$) were associated with poor renal prognosis and ESRD. However, with Logistic regression analysis only anemia was found to be independent risk factor associated with a poor renal prognosis ($p = 0.03$). There was no significant association between gender, age at presentation, urinary tract infection and the presence of hypertension.

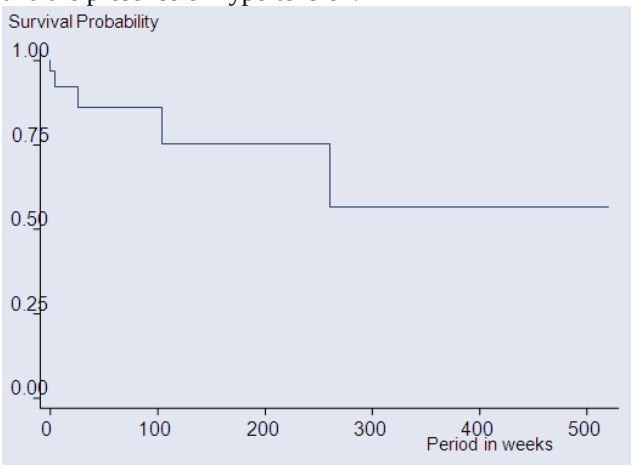


**Figure 1.** Kaplan-Meier survival curve for all ADPKD patients.

## 4. Discussion

ADPKD is the most common form of polycystic kidney disease and genetically heterogeneous, being caused by a mutation in the PKD1 gene in ~ 85 % of cases and by a mutation in the PKD2 in ~15% of cases (10). ADPKD disease arises as a spontaneous mutation in approximately 5% of cases. *PKD2* is a milder form of the disease, with a mean age of ESRD approximately 20 years later than PKD1 (11). However, in about one fourth of newly diagnosed cases, patients report no history of the disease, indicating that many familial cases go undetected [11]. An ADPKD diagnosis is usually made by renal imaging, and ultrasound is most frequently used. Ultrasound criteria for diagnosis have been published, based on ultrasound examinations with known ADPKD type 1 and type 2 compared to the ultrasound frequency of cysts in a normal unaffected population [7]. Thus, the number of cysts correlated with patient age helps make the diagnosis.

In the literature reports on clinical manifestations of ADPKD in patients older than 50 years are scanty. And in one such study [12] the diagnosis of ADPKD was made in 56 % of at-risk subjects versus 17.6 % in our study. At presentation, only one patient with the disease was asymptomatic and normotensive and denied any previous

symptoms suggestive of the disease in our study. The main clinical manifestations of ADPKD in this cohort [12] were comparable to our study: hypertension (69%), a history of back and abdominal pain (47%), symptoms consistent with UTI (41%), hematuria (31%), but less frequency of end-stage renal failure (47%). Liver cysts were found in 44% of patients. No statistically significant differences in the frequency of any manifestations of ADPKD between men and women like our study. Most patients developed symptoms after the age of 40 years. Notably, 31% of the older patients with ADPKD had normal serum creatinine levels. Thus, older subjects with kidney cysts who are at risk to have inherited the gene for ADPKD should be considered to have the disease even in the presence of well-preserved kidney function. This observation may play an important role in assessing the prognosis of older subjects at risk who have bilateral renal cysts and in genetic counseling of their relatives.

As patients with ADPKD have an increased renal mass, erythropoietin levels are increased, making anemia unusual even when ESRD is present [13], however, the mean hemoglobin in our series was 8.75 ± 2.41 g/dl. The main explanation of this anemia that majority of patients in our cohort diagnosed with advanced renal insufficiency. Massive proteinuria is a rare finding [14], and none of our patients had proteinuria in the nephrotic range. The reason of proteinuria in ADPKD is still unclear; however possible explanation would be damage to capillary endothelium and glomerulosclerosis due to hypertension [15]. Hematuria is usually due to rupture of a cyst into the pelvis of the kidney [16]. Approximately 68% of patients had hematuria on urinalysis and 17.9% had gross hematuria.

The rate of progression of ADPKD to ESRD is highly variable, with age at onset of ESRD ranging from childhood to old age. The present study demonstrated that anemia in elderly ADPKD patients is associated with a significantly faster decline in renal function. This study did not find the others classic factors of progression of renal disease such as the younger age at diagnosis, male gender, hypertension, increased left ventricular mass, hepatic cysts in women, three or more pregnancies, gross hematuria, urinary tract infections in men and renal size expressed as renal volume [17,18,19].

## 5. Conclusion

The diagnosis of ADPKD in these elderly patients was mostly late with majority already in end stage renal disease. Anemia was common and found to be an independent predictor of poor outcomes. Early diagnosis and prevention of disease progression and complications are most essential.

## Conflict of Interest

None.

## Disclosure

None.

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