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Autosomal Dominant Polycystic Kidney Disease: Epidemiological, Clinical Aspects and Predictive Factors of Poor Renal Prognosis (About 300 Cases)

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Abstract

Introduction: Autosomal dominant polycystic kidney disease (ADPKD) is a common, multisystemic, and progressive hereditary disease. It accounts for 6 to 8% of incident cases of end-stage chronic renal disease (ESRD) in developed countries. The aim of this study is to describe the predictive factors for the development of end-stage chronic kidney disease (CKD) in the course of this disease. **Material and Methods:** This is a retrospective, descriptive, and analytical study including 300 cases of ADPKD collected at the Nephrology Department of Ibn-Sina Hospital in Rabat over a period of 30 years (1993 to 2023). Included in the study are all patients with ADPKD meeting the ultrasound diagnostic criteria. The analysis focused on demographic, clinical, paraclinical, evolutionary data, as well as prognostic factors associated with renal function deterioration. **Results:** The mean age of patients at diagnosis is 51.53 +/− 17 years [16 - 93] with a male predominance. The median serum creatinine at diagnosis is 15.5 mg/l [10 - 34]. 21% of patients had ESRD (eGFR < 15 ml/min) at admission and 35.66% progressed to ESRD after a median follow-up of 16 months. The most common circumstances of discovery are renal failure (40%) and low back pain (30.3%). High blood pressure (HBP) is noted in 46.7%. Urinary manifestations are urolithiasis (14%), gross hematuria (14.7%), urinary infection (10.3%) and positive proteinuria > 300 mg/24h (21%). The most common cystic complication is hemorrhage (12.3%). 21.3% of patients had hepatorenal polycystic disease. In adjusted analysis, the predictive risk factors for the occurrence of ESRD were smoking ($p = 0.019$), anemia ($p < 0.001$), and polycystic liver disease ($p < 0.001$). Positive proteinuria remains of borderline interpretation (OR = 0.999; $p = 0.022$). **Conclusion:** ADPKD can progress insidiously to ESRD. Identification and early treatment of predictive factors for poor renal prognosis could contribute

to a better outcome for this disease.

Keywords

ADPKD, ESRD, Factors of Poor Renal Prognosis, Renal and Extra-Renal Manifestations

1. Introduction

Autosomal Dominant Polycystic Kidney Disease (ADPKD) is the most common inherited renal disease worldwide. It has been identified in all racial and ethnic groups [1]. Its prevalence is estimated between 1/400 and 1/1000 births [2] [3]. It is transmitted in an autosomal dominant manner. It is characterized by the insidious and progressive development of countless renal cysts affecting any segment of the renal tubules, leading to compression and progressive fibrosis of the non-cystic renal parenchyma. It is an evolving multisystemic disease, with manifestations appearing during the 3rd and 4th decades of life [4] [5]. It can affect the kidneys, liver, pancreas, heart, spleen, colon, and intracerebral arteries. ADPKD is the consequence of a mutation in the PKD1 and PKD2 genes encoding polycystin-1 (PC-1) and polycystin-2 (PC-2) respectively. About 5% of patients have a de novo mutation. Mutations in PKD1 lead to a more severe disease due to earlier cyst development than PKD2 mutations [6]. Its diagnosis is easy and based on ultrasound. It is the genetic disease most likely to lead to ESRD worldwide. It can cause a more rapid decline in the glomerular filtration rate (GFR) than other kidney diseases [7]: on average 5.9 ml/min/year leading to ESRD after the age of 55 in half of the patients [8]. It is therefore responsible for approximately 6% to 8% of incident ESRD cases in developed countries [9] and represents 8% to 10% of patients found in hemodialysis units [10]. The rate of decline in renal function to the stage of ESRD differs from one individual to another. Several modifiable (clinical and biological) and non-modifiable (genetic) risk factors have been identified to explain the progression of the disease to end-stage.

We conducted a retrospective study at the Nephrology Department of Ibn-Sina Hospital in Rabat from 1993 to 2023, including 300 patients with ADPKD.

Objective of Our Work

- To describe the epidemiological, clinical, and paraclinical profile of patients.
- To identify renal (blood pressure, creatinine, creatinine clearance, macroscopic hematuria, 24-hour proteinuria) and extra-renal manifestations of ADPKD in our patients.
- To determine the predictive factors for progression to ESRD.

2. Material and Methods

2.1. Definitions

Chronic kidney disease (CKD) is defined by a GFR less than 60 ml/min/1.73m^2

and ESRD by a GFR less than 15 ml/min/1.73m^2 (KDIGO 2012 classification) (appendix 1). The estimated glomerular filtration rate (eGFR) is calculated using the Modification of Diet in Renal Disease (MDRD) equation [11]. Anemia is defined in our study as a hemoglobin level <12 g/dl in men and <11 g/dl in women.

2.2. Study Type

This is a retrospective, monocentric, descriptive, and analytical study of 300 patients with ADPKD, collected within the Nephrology-Dialysis-Renal Transplantation Department of Ibn-Sina University Hospital in Rabat over a 30-year period, from 1993 to 2023.

2.3. Inclusion and Exclusion Criteria

Included in our study are all patients meeting the ultrasound criteria for the positive diagnosis of ADPKD, namely at least 3 renal cysts (unilateral or bilateral) before the age of 39, at least 2 cysts in each kidney between 40 and 59 years old, and more than 4 cysts in each kidney after the age of 60; and followed within our institution for at least sixteen months. Patients lost to follow-up and those with follow-up of less than sixteen months were excluded from our study, to study the progression of kidney function as it is a chronic disease with progressive evolution.

2.4. Methodology

Clinical and biological data are collected from medical records and reported on a pre-established form (appendix 2). This form is completed for each selected file. Data were entered into Microsoft Excel 2010 and analyzed using IBM SPSS Statistics 25 software. Quantitative variables were presented as means ± standard deviations, medians with interquartile ranges, or proportions, as appropriate. Continuous variables were compared using the Student's t-test or the Mann-Whitney U test. Qualitative variables were expressed as percentages and compared using the chi-square test or Fisher's exact test. A p-value less than 0.05 was considered statistically significant. The data distribution was verified by the Shapiro-Wilk test. The student's t-test is used if the data meets normality, and if normality is not met, the Mann-Whitney test is used.

Variables were further analyzed by univariate and multivariate logistic regression analysis.

The parameters studied and analyzed in all our patients are as follows:

- Demographic data (age, sex);
- Family history (family history of ADPKD);
- Circumstances of discovery (HBP, RF, lower back pain, macroscopic hematuria, urinary tract infection, urinary stones, family screening, incidental discovery by imaging);
- Clinical data (HBP, RF, lower back pain, macroscopic hematuria, urinary tract infection, urinary stones, hepatic cystic disease, extra-renal involvement of ADPKD);

- Biological data (creatinine, 24-hour proteinuria, hemoglobin);
- Ultrasound data (kidney size, number of cysts in each kidney and their location);
- Evolutionary profile of renal function;
- Prognostic factors associated with deterioration of renal function.

To determine the main predictive factors for ESRD and those influencing the progression of chronic kidney disease, we divided our patients into 2 groups at the time of diagnosis. Patients with ESRD with a glomerular filtration rate (GFR) < 15 ml/min (group A) and chronic patients with a GFR > 15 ml/min (group B). Patients admitted initially with ESRD are managed by extra-renal clearance techniques. We then focused on group B, which we divided into 2 groups: Group C comprising patients who progressed to ESRD (GFR < 15 ml/min) and Group D comprising patients who maintained a GFR > 15 ml/min during follow-up.

We specify that the admission time is the time of diagnosis for all patients.

3. Results

We studied the records of 300 patients with ADPKD over a period of 30 years. The average age of our patients at the time of diagnosis of the disease is 51.53 +/− 17 years with age extremes between 16 and 93 years. We noted a slight male predominance (168 men (56%) versus 132 women (44%)) with a M/F sex ratio of 1.27. The most common circumstances of discovery are RF (40%) and low back pain (30.3%). The disease is more rarely discovered during macroscopic hematuria, renal lithiasis, urinary infection, during family screening or incidentally by renal ultrasound. A family history of ADPKD was present in 99 patients (33%). HBP is present in 140 cases (46.7%) and anemia in 48 cases (16%) with an average hemoglobin level of 8 g/dl. 38 patients or 12.7% of cases are smokers. The urinary manifestations found were urolithiasis in 42 cases (14%), macroscopic hematuria in 44 cases (14.7%) and urinary infection in 31 cases (10.3%). 24-hour proteinuria was positive in 63 cases (21%) with an average rate of 800 mg/day and extremes of 100 and 1500 mg/day. A cystic complication was observed in 47 patients. This involves intracystic hemorrhage in 37 cases (12.3%), cyst infection in 9 cases (3%) and cyst rupture in one patient (0.3%). 64 patients or 21.3% of cases have hepatorenal polycystic disease. The other extra-renal manifestations observed were valvular heart disease in 3 cases (1%), left ventricular hypertrophy in 9 cases (3%), ischemic stroke in 6 cases (2%) and hemorrhagic in 3. cases (1%), inguinal and umbilical hernia in 7 cases each (2.3%). The median serum creatinine at the time of diagnosis is 15.5 mg/l [10; 34] (see **Table 1**).

Among our 140 hypertensive patients, 97 were on monotherapy with ACE inhibitors alone and 43 were on combination therapy with both ACE inhibitors and calcium channel blockers (CCB). ACE inhibitors alone reduced the mean systolic blood pressure from 150 mm Hg to 126 mm Hg and the mean diastolic blood pressure from 90 mm Hg to 72 mm Hg. For patients on combination therapy, their mean systolic blood pressure decreased from 170 mm Hg to 135

mm Hg, and the mean diastolic blood pressure from 94 mm Hg to an average of 75 mm Hg.

Table 1. Epidemiological and clinical characteristics of patients included in the study.

Characteristics	Results (N = 300)
Mean age at diagnosis (years)	51.53 +/− 17 ans
Median serum creatinine at diagnosis	15.5 mg/l
Sex ratio (M/F)	1.27
Family history	99 (33%)
HBP	140 (46.7%)
Anemia	48 (16%)
Smoking	38 (12.7%)
Urolithiasis	42 (14%)
Gross hematuria	44 (14.7%)
Urinary infection	31 (10.3%)
Polycystic Liver disease	64 (21.3%)
Intracystic hemorrhage	37 (12.3%)
Cyst infection	9 (3%)
Cyst rupture	1 (0.3%)
Valvular diseases	3 (1%)
Left ventricular hypertrophy	9 (3%)
Ischemic stroke	6 (2%)
Hemorrhagic stroke	3 (1%)
Inguinal hernia	7 (2.3%)
Umbilicale hernia	7 (2.3%)

N = Number of patients.

Upon admission, 63 patients (21%), 39 men (62%) and 24 women (38%) already had ESRD with a GFR < 15 ml/min, 129 patients (43%) had a GFR between 15 and 60 ml/min, and 108 patients (36%) had a GFR > 60 ml/min.

After a median follow-up of 16 months, 89 out of 108 patients with a GFR > 60 ml/min upon admission maintained stable renal function, and 19 patients experienced renal function decline: 13 had a GFR between 15 and 60 ml/min, and 6 progressed to ESRD. For the 129 patients with a GFR between 15 and 60 ml/min: 6 improved their renal function (GFR > 60 ml/min), 85 maintained stable renal function (GFR between 15 and 60 ml/min), and 38 progressed to end-stage disease (see Table 2).

Table 2. The evolving profile of eGFR in our patients after an average follow-up of 16 months.

eGFR at admission (N: number of patients)	eGFR after a median follow-up of 16 months (N: number of patients)
N = 108: eGFR > 60 ml/min	**N = 89:** eGFR > 60 ml/min
	N = 13: 15 ml/min < eGFR < 60 ml/min
	N = 6: eGFR < 15 ml/min
N = 129: 15 ml/min < eGFR < 60 ml/min	**N = 6:**eGFR > 60 ml/min
	N = 85: 15 ml/min < eGFR < 60 ml/min
N = 63: eGFR < 15 ml/min	**N = 38:** eGFR < 15 ml/min

Figure 1 illustrates the evolution of creatinine clearance in our 300 patients included in the study between the time of diagnosis and the end of follow-up.

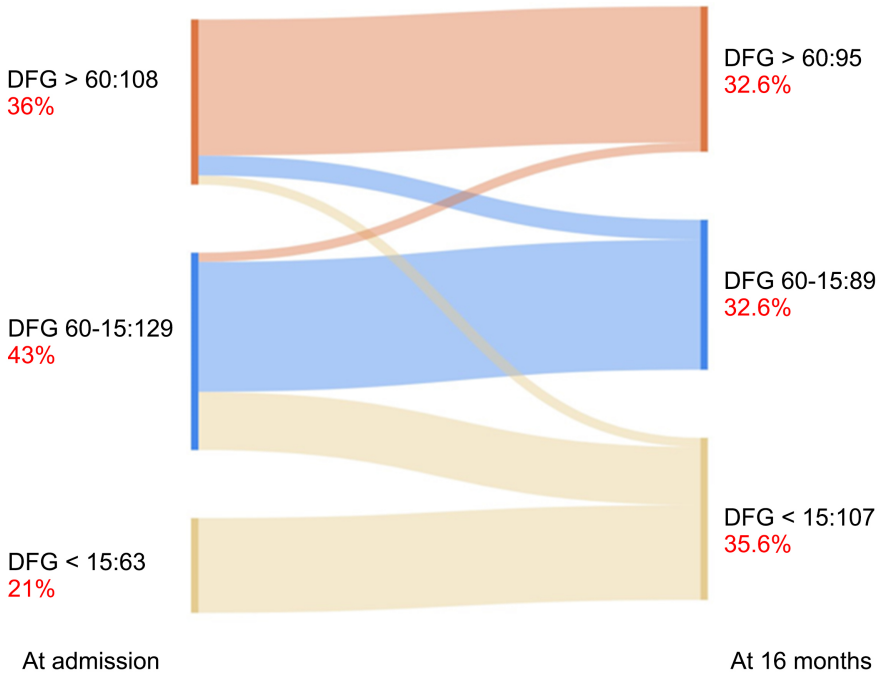

Figure 1. The evolving profile of eGFR of the 300 patients included in the study between the time of diagnosis and the end of follow-up.

At admission:

- 108 patients (36%) had a GFR > 60 ml/min;
- 129 patients (43%) had a GFR between 15 and 60 ml/min;
- 63 patients (21%) had ESKD and had a GFR < 15 ml/min.

Thus, at the end of the follow-up period:

- 95 (31.68%) out of our 300 patients have a GFR > 60 ml/min;

- 98 (32.66%) have a GFR between 15 and 60 ml/min;
- 107 patients (35.66%) progressed to end-stage disease with a GFR < 15 ml/min.

This evolution demonstrates the deterioration of renal function in our patients throughout the follow-up period.

It is imperative to identify biomarkers and predictive factors for worsening renal function to prevent or at least slow down the progression of autosomal dominant polycystic kidney disease to end-stage disease.

When comparing groups A and B, patients with ESKD (GFR < 15) at the time of diagnosis have a family history of ADPKD (p = 0.025), hepatic cystic disease (p = 0.009), and more HBP (P = 0.002). For a history of macroscopic hematuria, cystic infection, urinary stones, and smoking, there is no significant difference between the 2 groups. There is also no sex predominance between the 2 groups (Table 3).

Table 3. Factors significantly associated with ESRD upon admission.

	ESKD (eGFR < 15) (N = 63)	(eGFR ≥ 15) (N = 237)	P value
Mean age at diagnosis (years)	53.06 +/− 15.6	51.12 +/− 17.3	0.42
Sex			0.288
Male	39	129	
Female	24	108	
HBP	33	75	**0.002**
Family history	28	71	**0.025**
Smoking	9	29	0.664
Gross hematuria	9	32	0.872
Cyst infection	4	5	0.081
Urolithiasis	3	16	0.565
Polycystic liver disease	21	43	**0.009**

N = number of patients.

After a median follow-up of 16 months, the comparison between groups C and D reveals that patients who progressed to ESRD are significantly younger (46.2 +/− 16 vs 52.24 +/− 17.5 (p = 0.029)) and more anemic (p =< 0.001). They also experienced macroscopic hematuria during follow-up (p = 0.001) and had an umbilical hernia (p = 0.034). Smoking, 24-hour proteinuria, HBP during follow-up, cystic infection, urinary tract infection, and intracystic hemorrhage are not significantly associated with renal function deterioration during follow-up (Table 4).

Table 4. Factors significantly associated with the occurrence of ESRD after an average of 16 months of progression.

	ESKD (eGFR < 15) (N= 44)	(eGFR > 15) (N=193)	P value
Mean age at diagnosis (years)	46.2 +/− 16	52.24 +/− 17.5	**0.029**
Sex			0.508
Male	26	103	
Female	18	90	
HBP	21	70	0.397
Smoking	9	20	0.076
Anemia	14	12	**<0.001**
Gross hematuria	13	17	**0.001**
Cyst infection	2	3	0.234
Urinary infection	7	16	0.155
Intracystic hemorrhage	3	14	0.919
Hemorrhagic stroke	1	1	0.337
Ischemic stroke	0	4	0.753
Umbilical Hernia	2	0	**0.034**
Inguinal hernia	2	3	0.233

N = Number of patients.

In univariate analysis, the factors associated with worsening renal function are young age (p = 0.039), anemia (p < 0.001), macroscopic hematuria (p < 0.001), and the presence of hepatic cystic disease (Table 5).

Table 5. Factors correlated with progression to ESRD in simple logistic regression < 0.2.

Variables	OR	IC 95%	P value
Age	1.021	[1.001; 1.042]	**0.039**
Smoking	2.224	[0.935; 5.291]	0.071
Anemia	7.039	[2.97; 16.67]	**<0.001**
Gross hematuria	4.34	[1.9; 9.8]	**<0.001**
Urinary infection	2.13	[0.184; 1.243]	0.130
Polycystic Liver disease	3.51	[1.6; 7.4]	**0.001**
positive proteinuria	1	[0.999; 1]	0.096

In adjusted analysis, the predictive risk factors for the occurrence of ESKD are smoking (p = 0.019), anemia (p < 0.001), hepatic cystic disease (p < 0.001), and proteinuria (p = 0.022) (Table 6).

Table 6. Factors correlated with progression to ESRD in multiple logistic regression.

Variables	OR ajusté	IC 95%	P value
Age	1.023	[0.953; 1.001]	0.064
Smoking	3.37	[0.107; 0.817]	**0.019**
Anemia	6.7	[0.055; 0.403]	**<0.001**
Gross hematuria	1.667	[0.221; 1.63]	0.316
Urinary infection	1.5	[0.205; 2.184]	0.5
Polycystic Liver disease	5	[0.085; 0.467]	**<0.001**
positive proteinuria	0.999	[1.00; 1.001]	**0.022**

4. Discussion

PKRAD is a hereditary and progressive kidney disease with clinical manifestations appearing in the 3rd and 4th decades of life [5] [7]. The age of onset of renal dysfunction in this pathology varies. The decline in renal function begins after the fourth decade of life [12], and by age 65, 45% - 70% of patients reach the stage of end-stage renal disease (ESRD) [13].

In our study, 21% of our patients were already in ESRD at the time of diagnosis, compared to 23% in a Tunisian study [14] and 31.5% in a study conducted in Senegal [15].

After a median duration of 16 months, 35.66% of our patients progressed to ESRD, compared to 54.6% and 45.8% after median durations of 25 [14] and 110 months [13] respectively.

Given the highly variable progression of PKRAD among individuals, it is essential to predict which patients will rapidly progress to renal insufficiency, in order to assess the benefit-risk ratio of any intervention and consider the early implementation of long-term renal protection measures. Thus, prognostic biomarkers need to be identified to predict future renal function decline. Clinical, biological, genetic, epigenetic, radiological, and environmental factors have been studied in various studies, including ours.

As previously mentioned, PKRAD is caused by mutations in the PKD1 and PKD2 genes. The presence of one or more family members who reached ESRD before the age of 55 suggests a PKD1 genotype, while satisfactory renal function until age 70 suggests a PKD2 genotype [16]. The PKD1 mutation is considered a risk factor for worsening renal function in PKRAD [12]. Unfortunately, our patients did not undergo genetic studies, which is a significant limitation of this study.

However, a family history of PKRAD can also be used as a diagnostic tool for the disease [17]. It is present in 33% of our patients and in 43.7% in a Tunisian study [14]. This family history is significantly reported among our patients who were immediately admitted to ESRD (p = 0.025). According to a 2016 Italian study, renal impairment is more severe in subjects with a family history of ESRD occurring before age 55 [18].

The average age of our patients at the time of diagnosis is 51.53 +/− 17 years. It is 37 years in an Iranian study [19] and 43.1 ± 14.1 in a South Korean study [13]. We examined the effect of age on the deterioration of renal function. The average age of our patients in ESRD at admission is 53.06 +/− 15.6 years, and that of patients who progressed to ESRD during follow-up is 46.2 +/− 16 years. In our study, younger age is significantly associated with renal function deterioration in univariate analysis (p = 0.039) only. According to Panizo *et al.*, younger age is an independent predictive factor influencing the progression of renal insufficiency in multivariate analysis [20]. According to Hajji *et al.*, age > 40 years is a risk factor for progression to ESRD in multivariate analysis [21]. According to Park *et al.*, age at diagnosis after 30 years (P = 0.007) is a predictive factor for ESRD in multivariate analysis [13].

The influence of sex on PKRAD is reported by several authors. Male sex is associated with the early onset of hypertension (HTN) and a faster and more severe progression of renal function to end-stage renal [22]-[25]. In the Cox multivariate regression analysis of the Orskov *et al.* study, male sex is associated with a significant reduction in survival and an increased risk of death that can reach 34% after the onset of ESRD [26]. Gretz *et al.* reported that women progress to ESRD on average six years later than men [27]. In our series, we note a slight male predominance (168 men (56%) vs. 132 women (44%)), aligning with literature data [13] [14] with a male-to-female sex ratio of 1.27, but without a significant sex difference in terms of diagnosis (p = 0.288) or progression to ESRD (p = 0.508). This result is nonetheless supported by other studies that do not consider male sex a risk factor for worsening renal function in PKRAD [28] [29].

We focused on the impact of cardiovascular risk factors in PKRAD, especially since about half of the patients in our series are hypertensive (46.7%). HTN is a serious complication of PKRAD that can lead to both an increased incidence of cardiovascular complications and a faster progression of renal insufficiency [30], especially if it occurs early [12] [21]. It is a significant independent risk factor for progression to ESRD in multivariate analysis [20] [25] [31], its control has a limited beneficial influence on the rate of progression in patients with advanced renal disease with significant renal insufficiency [31] [32] and reduces mortality [33]. In our study, patients in ESRD at admission are significantly more hypertensive (p = 0.002), but this HTN is not considered a predictive factor for ESRD in either univariate or multivariate analysis. The second well-known cardiovascular risk factor is smoking. 12.7% of our patients are smokers. Smoking is a predictive factor for ESRD occurrence (p = 0.019) in our study in multivariate

analysis. It has been associated with rapid progression of renal function in a prospective observational study [34]. Smoking increases the risk of ESRD in men with chronic kidney disease in a dose-dependent manner [27].

Anemia is rare in PKRAD [35] compared to other nephropathies, with higher hemoglobin levels in ESRD [36]. The production of erythropoietin by the cyst wall and parenchymal cells explains this fact [35] [37]. In our study, anemia is present in 48 out of 300 patients, with an average hemoglobin level of 8 g/dl (6 - 10 g/dl). It is significantly associated with poor renal prognosis in multivariate analysis ($p < 0.001$). Few studies have focused on anemia in PKRAD. A study conducted in Japan in 2019 found that anemia is a poor renal prognostic factor in PKRAD [38].

In our study, 24-hour proteinuria is a factor in progression to ESRD in adjusted analysis ($p = 0.022$). It is positive in 63 patients (21%) with an average level of 800 mg/day, ranging from 400 to 1500 mg/day. Some studies have confirmed the role of proteinuria in the progression of chronic renal failure in PKRAD [20]. According to the MDRD (Modification of Diet in Renal Disease) study, higher levels of proteinuria are associated with a more marked decline in glomerular filtration rate (GFR) [39]. In another study of 270 adults with PKRAD, the 48 patients (18%) with proteinuria (300 mg/day) had more impaired renal function, higher blood pressure, larger kidney volume, and more aggressive renal disease progression ($P < 0.05$) [40].

After an average follow-up of 16 months, the patients in our cohort who progressed to ESRD (group C) experienced at least one episode of macroscopic hematuria ($p = 0.001$). We do not know the exact age of onset of hematuria in our patients, but studies show that early (before age 30) [41] [42] and recurrent [22] macroscopic hematuria is a predictive factor for PKRAD progression [21], affecting renal survival.

We also analyzed the relationship between urinary tract infections (UTIs) and renal insufficiency progression. UTI occurred in 31 of our patients, or 10.3%. It was not associated with worsening renal function and was not considered a predictive factor for ESRD. Contrary to our results, several small studies have linked UTIs in PKRAD patients to faster renal function decline. This is also confirmed by a Saudi study published in 2006 [32]. According to an uncontrolled study, antibiotic prophylaxis in recurrent UTIs significantly reduces UTI incidence and limits renal function loss [41].

A relationship between kidney size and renal function is established [43]. Total kidney volume is associated with rapid disease progression [21]. According to Dalgaard *et al.*, the median interval between palpable kidneys and ESRD is less than five years [44]. Unfortunately, total kidney volume was not calculated in our patients, which is a limitation of our study.

Cyst infection is found in 3% of cases in our study and is not associated with poor renal prognosis. However, it is in the Park *et al.* study in multivariate analysis ($P = 0.005$), which found it in 9.7% of their patients [13].

We also examined the extra-renal manifestations of PKRAD. Liver cysts are the most common extrarenal manifestation of autosomal dominant polycystic kidney disease (ADPKD) and are often discovered incidentally, being clinically insignificant in most cases. They are present in over 90% of ADPKD patients over 35 years old [45] [46]. In our study, hepatic polycystic disease emerged as a predictive factor for renal function deterioration in both univariate and multivariate analyses ($p = 0.001$). A 2008 study comparing clinical characteristics of patients with isolated hepatic polycystic disease and those with both hepatic and renal polycystic disease concluded that the clinical course of isolated hepatic polycystic disease, despite a higher number of cysts, is relatively benign compared to the hepatorenal form [47]. Factors significantly associated with the development and severity of hepatic cysts in ADPKD patients, according to a Korean study, include advanced age, female sex, and larger kidney volume [48].

The presence of an umbilical hernia was significantly associated with renal function deterioration in our study, though this was not confirmed in multivariate analysis and has not been reported in the literature.

Renal stones, cyst rupture, intracystic hemorrhage, and intracranial aneurysm rupture were not identified as predictive factors for end-stage renal disease (ESRD) in our study or the literature.

5. Conclusions

In conclusion, ADPKD can insidiously progress to ESRD, which marks the severity of the disease. In our study, smoking, anemia and hepatic polycystic disease were predictive risk factors for the onset of ESRD in multivariate analysis. However, the interpretation of 24-hour proteinuria remains limited regarding its role as a predictive factor for progression to ESRD.

Identifying these risk factors and predicting the individual progression of ADPKD could aid in implementing approved treatments, such as vasopressin V2 receptor antagonists (Tolvaptan), which are not currently used in our patients, thus slowing the progression of the disease.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Abbreviations

Autosomal Dominant Polycystic Kidney Disease = ADPKD
End-stage chronic renal disease = ESRD
Chronic Kidney Disease = CKD
Chronic Renal Failure= CRF
Renal failure = RF
High blood pressure = HBP
Glomerular Filtration Rate = GFR
Estimated Glomerular Filtration Rate = eGFR
Angiotensin-Converting Enzyme Inhibitor = ACE inhibitor
Inhibitor Calcium Channel Blocker = CCB
Polycystin-1 = PC-1
Polycystin-2 = PC-2
Intracranial Aneurysm = ICA

Appendix 1

The estimated glomerular filtration rate (eGFR) is calculated using a Modification of diet in renal disease (MDRD) equation.

Chronic kidney failure (CKD) is defined by an eGFR less than 60 ml/min/1.73m^2 (KDIGO 2012 classification).

Stages of chronic kidney disease	Definitions	GFR (ml/min/1.73m^2)
1	No renal failure*	≥90
2	Mild renal failure	60 - 89
3	Moderate renal insufficiency	30 - 59
4	Severe kidney failure	15 - 29
5	End stage renal failure	<15

GFR: glomerular filtration rate. *Renal damage manifested by histological and/or biological and/or morphological abnormalities.

Appendix 2: Reference Sheet

Epidemiological profile

Name

Phone number:

Age:

Sex: M ☐ F ☐

Family History:

Family history of ADPKD: yes ☐ no ☐

Personal history:

Circumstances of discovery:

HBP yes ☐ no ☐

Renal failure yes ☐ no ☐

Lower back or abdominal pain yes ☐ no ☐

Gross hematuria yes ☐ no ☐

Urinary Infection yes ☐ no ☐

Urolithiasis yes ☐ no ☐

Family screening yes ☐ no ☐

Chance discovery by imaging yes ☐ no ☐

Median age at diagnosis

Serum creatinine at diagnosis:

Mean eGFR at diagnosis:

eGFR group at diagnosis: >60 ml/min ☐ 15 - 60 ml/min ☐ <15 ml/min ☐

Kidney damage and complications:

Intracystic hemorrhage yes ☐ no ☐

Cyst rupture yes ☐ no ☐

Cyst infection	yes ☐	no ☐
Urolithiasis	yes ☐	no ☐
Gross hematuria	yes ☐	no ☐
Lower back or abdominal pain	yes ☐	no ☐
Fever	yes ☐	no ☐

Extra –rénal damage

Liver damage: liver cysts + hepatomegaly (polycystic liver disease), liver fibrosis, pulmonary arterial hypertension.

Other cystic lesions: spleen, pancreas, arachnoid, seminal vesicle, ovaries.

Cardiac involvement: valvular heart disease, pericarditis, aortic aneurysm, mitral valve prolapse, left ventricular hypertrophy.

Brain damage: Ischemic vascular accident, transient ischemic attack, subarachnoid hemorrhage, rupture of intracranial aneurysms.

Digestive damage: constipation, abdominal or lower back pain, abdominal bloating, polyps, diverticulosis, esophagitis, gastroesophageal reflux, inguinal or umbilical hernia.

Others (carpal tunnel syndrome, sensory-motor neuropathy of all 4 limbs, male infertility, etc.).

Radiological data:

☐ Renal and extrarenal ultrasound manifestations: Size of the kidneys, location, number of cysts:

☐ Abdominal, brain or other scan:

Evolutionary profile of hypertension:

Blood pressure at the start of follow-up:

Blood pressure at the end of follow-up:

Therapeutic class:

Evolution:

Lost

Duration of follow-up:

Evolution: ESRD/Worsening renal function during follow-up/Stable renal insufficiency/Normal renal function

- Serum creatinine at 6 months
- Serum creatinine at 12 months
- Serum creatinine at 18 months
- Serum creatinine at 24 months
- End of follow-up serum creatinine
- eGFR end of follow-up
- -eGFR group end of follow-up: >60 ml/min 15 - 60 ml/min

>60 ml/min ☐ 15 - 60 ml/min ☐ <15 ml/min ☐

Factors for progression towards ESRD:

Age

Sex (male)

HBP

Macroscopic hematuria
Urinary Infection
Cyst Infection
Intracystic hemorrhage
24-hour proteinuria (>300 mg/day) Rate if positive:
Anemiahemoglobin level
Smoking