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Investigation of Demographic and Clinical Data of Patients with Autosomal Dominant Polycystic Kidney Disease

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Abstract

Background: Autosomal dominant polycystic kidney disease (ADPKD) is an important etiological factor causing chronic kidney disease (CKD), cardiovascular diseases and hypertension (HT). The purpose of the present study is to investigate the clinical information and demographic characteristics of autosomal dominant polycystic kidney disease patients who received treatment at our hospital for the last five years. **Material and Method:** Among 21400 people who sought care at Siirt State Hospital Urology and Nephrology Outpatient Clinics between January 2015 and January 2020 for various reasons, a total of 36 patients experiencing autosomal dominant polycystic kidney disease were included in the present research. Retrospective patient file access was used to gather demographic information and laboratory data. **Results:** The study included 36 patients in all, 25 (69.4%) male and 11 (30.6%) female. The patient's average age was 50.8 ± 19.0. The average age at diagnosis was 43.4 ± 17.2. Family history was positive in 29 (80.5%) of the patients. There were hypertension in 27 (75.0%) patients, coronary artery disease in five (13.9%) patients, diabetes mellitus in five (13.9%) patients, left ventricular hypertrophy in 18 (50%) patients, proteinuria in 11 (30.6%) patients, and six (16.7%) patients had macroscopic hematuria. Liver cysts were found in 23 (63.9%) of the patients and nephrolithiasis in eight (22.2%). **Discussion:** Hypertension is the most common finding when clinical and demographic data of autosomal dominant polycystic kidney disease are examined. Providing blood pressure control reduces the risk of death due to left ventricular hypertrophy and slows down the rate at which chronic kidney disease progresses. The rate was found to be 80.5% for patients with a positive family history. It may be possible to diagnose and treat people with autosomal dominant polycystic kidney disease earlier by screening their family members.

Keywords

Hypertension, Autosomal Dominant Kidney Disease, Demographic Information, Chronic Kidney Disease

1. Introduction

The most prevalent hereditary kidney disease is autosomal dominant polycystic kidney disease (ADPKD) [1]. Polycystic kidney disease 1 (PKD 1) gene mutation on chromosome 16 is responsible for 85% of the disease, which has an autosomal dominant inheritance pattern, and PKD 2 gene mutation on chromosome 4 is responsible for 15% [2]. It is distinguished by increasing kidney cyst development that results in end-stage renal disease (ESRD) [3]. In addition to kidney cysts, cysts can be seen in the liver, pancreatic cysts and other tissues. Early hypertension (HT) and heart valve disorders are abnormalities that can be seen at different rates of the disease [4]. Patients of all ages may apply. However, clinical findings are more noticeable after the age of 30 [5]. It is responsible for approximately 5 to 10 percent of all cases of end-stage renal disease (ESRD) across racial/ethnic groups worldwide [6]. Patients with ADPKD are 1.6 to 3.2 times more likely to die compared to the general population, and deaths associated with cardiovascular diseases are the most common cause of mortality [7]. Earlier disease onset and high blood pressure in ADPKD patients are associated with cardiovascular mortality and progression to renal failure [8] [9].

Since no definitive treatment for ADPKD exists, the current approaches to treatment focus on nonspecific treatments for the slow progression of chronic kidney disease [10] [11]. HT is the most important factor determined in the progression of ADPKD [12]. It has been reported that there is a relationship between high serum uric acid levels and early-onset HT in ADPKD patients [13], large renal volume and increased risk of ESRD [14].

ADPKD is predicted to affect more than ten million people worldwide and therefore constitutes a major public health burden. A significant number of individuals who are mildly or moderately affected by autosomal dominant kidney disease remain undiagnosed [2].

Our study that made to draw attention to ADPKD and contribute to the data on ADPKD in Türkiye, it is made with a limited number of participants, in a small city. The purpose of the present study is to investigate the clinical and demographic data regarding ADPKD patients treated in our hospital for the last 5 years.

2. Material and Method

36 patients with ADPKD were selected retrospectively for the study among 21,400 people who sought care at Siirt State Hospital Urology and Nephrology Clinics between January 2015 and January 2020 for various reasons, and demo-

graphic and laboratory data were retrospectively obtained from patient files. Patients between the ages of 18 and 70 were included in the study. Exclusion criteria from the study: 1) Having a current or past history of malignancy, 2) Having liver cirrhosis, 3) Having an infectious disease, and 4) Having advanced stage heart failure (Stages 3 - 4 according to the New York Heart Association Functional Class).

In this study, the development rates of complications such as HT, CKD, CAD, nephrolithiasis, hematuria, other organ cysts, and intracranial aneurysms were evaluated in patients with ADPKD. For this study, ethics committee decision no **2020/09.02** was taken from the Non-Invasive Clinical Research Ethics Committee of the Rectorate of the Republic of Türkiye Siirt University. This research was conducted by the World Medical Association Declaration of Helsinki.

The CKD-EPI "Chronic Kidney Disease Epidemiology Collaboration" formula was used to determine the patient's glomerular filtration rate (GFR). Patients who had a protein-to-creatinine ratio of more than 150 mg/gr were considered to have proteinuria.

Statistical Analysis

For the definition of continuous variables, descriptive statistics were employed. The mean ± standard deviation is given for normally distributed parameters. The median (minimum-maximum) is given for non-normally distributed parameters. The Shapiro-Wilks test was used to test the normality of continuous variables.

When comparing two dependent groups that are not normally distributed, the Wilcoxon Signed Rank Test was performed.

The level of statistical significance was established at 0.05. The MedCalc Statistical Software Program, version 12.7.7 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2013), was used to conduct the analyses.

3. Results

The study included 36 patients in all: 25 (69.4%) male and 11 (30.6%) female. The patient's average age was 50.8 ± 19.0. The mean age of the patients was 50.8 ± 19.0. The average time since diagnosis was 6 years. Family history was positive for ADPKD in 24 (66.7%) of the patients. When accompanying diseases were examined, 27 (75.0%) patients had HT and 5 (13.9%) patients had coronary artery disease (CAD). Liver cysts accompanying renal cysts were found in 23 (63.9%) of the patients. Nephrolithiasis was detected in 8 (22.2%) patients. While 7 (19.4%) patients entered the routine hemodialysis program due to CKD, 3 (8.3%) patients had kidney transplantation. Nine of the patients had (25%) (angiotensin receptor blocker) ARB, 8 (22.2%) angiotensin-converting enzyme inhibitor (ACE-I), 4 (11.1%) ARB + Calcium channel blocker, 2 (5.6%) ARB + Beta Blocker, 3 (8.3%) While ACE-I + Calcium channel blocker, 1 (2.8%) ACE-I + Beta blocker, 9 (25.0%) patients did not use antihypertensive medication (**Table 1**).

Table 1. Demographic and clinical characteristics of ADPKD patients.

	n = 36
Age (year)	50.8 ± 19.0
Age range (year)	19 - 82
Diagnosis age (year)	43.4 ± 17.2
Sex	
Male	25 (69.4%)
Female	11 (30.6%)
Diagnosis length (year)	6 (1 - 20)
Family history	29 (80.5%)
Accompanying disease	
HT	27 (75.0%)
CKD	21 (58.3)
Liver Cyst	23 (63.9%)
Intracranial aneurysm	1 (%2.8)
Valve disease	6 (16.7%)
CAH	5 (13.9%)
LVH	18 (50%)
DM	5 (13.9%)
Nephrolithiasis	8 (22.2%)
Macroscopic hematuria	6 (16.7%)
Proteinuria	11 (30.6%)
CKD length (year)	6 (3 - 15)
Hemodialysis	7 (19.4%)
Renal transplantation	3 (8.3%)
Antihypertensive medication used	
ARB	9 (25%)
ACE-I	8 (22.2%)
ARB + Calcium channel blocker	4 (11.1%)
ARB + Beta blocker	2 (5.6%)
ACE-I + Calcium Channel blocker	3 (8.3%)
ACE-I + Beta blocker	1 (2.8%)
None	9 (25.0%)

Eight (22.2%) of the patients were found to have Stage 1 CKD, 6 (16.7%) Stage 2 CKD, 6 (16.7%) patients with Stage 3A CKD, while 16 (44.4%) patients had Stage 3B - 5 CKD. At the end of the five-year follow-up, it was observed that the number of patients in CKD Stages 1 - 2 decreased and the number of patients in Stages 3, 4, and 5 increased (Table 2).

Proteinuria was detected in 11 (30.6%) of the patients. Patients who had a spot urine protein to creatinine ratio of more than 150 mg/gr were considered to have proteinuria. Patients who had proteinuria experienced a significantly higher annual loss of GFR when compared to patients who did not have proteinuria ($p < 0.001$).

Laboratory information for the patients is shown in Table 3. Creatinine values have increased statistically significantly since 2015 according to Wilcoxon Signed

Table 2. Frequency distribution of ADPKD patients according to CKD stages.

N (%)	Current	2015
Stage 1	8 (22.2)	14 (38.9)
Stage 2	6 (16.7)	11 (30.6)
Stage 3A	6 (16.7)	0
Stage 3B	4 (11.1)	6 (16.7)
Stage 4	5 (13.9)	3 (8.3)
Stage 5	7 (19.4)	2 (5.6)

Table 3. Laboratory parameters.

	Average ± std. dev.	Med (min-max)
Urea	61.1 ± 36.3	46 (24 - 149)
Creatinine (current)	2.5 ± 2.6	1.5 (0.7 - 11.5)
Creatinine (2015)	1.4 ± 1	1 (0.6 - 4.8)
Sodium	139.3 ± 3.5	140 (127 - 144)
Potassium	4.3 ± 0.5	4.2 (3.6 - 5.4)
Calcium	9.2 ± 0.4	9.2 (8.5 - 10.1)
Albumin	3.8 ± 1	3.5 (2.5 - 6.8)
Phosphorus	4.2 ± 0.4	4.2 (3.4 - 4.7)
Uric acid	6.5 ± 1.8	6.7 (2.3 - 9.6)
Chlorine	104.6 ± 5.7	104.5 (88 - 115)
Proteinuria	445.7 ± 933.5	204 (40 - 5225)
Urea density	1009.2 ± 3.9	1009 (1003 - 1012)
Hb	13.4 ± 2	13.8 (8.6 - 16.5)
Ferritin	157.1 ± 193.1	77.6 (6.6 - 675)
PTH	213.7 ± 241.6	128.5 (29.4 - 1240)
Vitamin D	15.1 ± 8.3	12.5 (5.4 - 42.6)
GFR (current)	54.3 ± 39.3	46.6 (3.9 - 129.3)
GFR (2015)	76.6 ± 40.2	79.1 (12 - 142.4)
PH	7.4 ± 0.04	7.4 (7.3 - 7.5)
Bicarbonate	26.5 ± 5	25.1 (19 - 48)
CO_2	43 ± 6.8	42.3 (24 - 54)

Rank test results ($p < 0.001$). GFR values have decreased statistically significantly since 2015 according to Wilcoxon Signed Rank test results ($p < 0.001$). It was observed that there was no anemia or iron deficiency. While the median hemoglobin value was 13.8 (8.6 - 16.5), the median ferritin value was 77.6 (6.6 - 675). Median serum sodium 140 (127 - 144), potassium 4.2 (3.6 - 5.4), phosphorus 4.2 (3.4 - 4.7), calcium 9.2 (8.5 - 10.1), albumin 3.5 (2.5 - 6.8) and chlorine 104.5 (88 - 115) were found. The median value of parathyroid hormone (PTH) was found to be 128.5 (29.4 - 1240) and the median value of vitamin D was 12.5 (5.4 - 42.6) (**Table 3**).

4. Discussion

The most prevalent hereditary kidney disease is autosomal dominant polycystic kidney disease (ADPKD) [1]. Patients might apply at any age. However, clinical findings are more noticeable after the age of 30 [5]. The mean age at diagnosis was 42 (13 - 70) for our patients. Our rate of patients under the age of 35 was 27.8%. 40% of these patients had chronic kidney disease. In a study, the rate of patients diagnosed under the age of 35 was reported to be 33% [15].

Family history was positive in 80.5% of the patients. According to Yıldız *et al.*'s study, 83% of participants had a family history [16].

The most prevalent ADPKD symptom is hypertension, which also plays a significant role in the development of cardiovascular morbidity and mortality as well as the progression of renal disease. In ADPKD, damage to target organs develops at an early stage. The increase in total renal volume causes the development of hypertension by causing renal ischemia and activating the Renin Angiotensin Aldosterone system. HT significantly affects both renal failure and the development of cardiovascular and cerebrovascular events that determine mortality [8]. A high rate of HT is detected in ADPKD before even kidney failure develops [16] [17]. The most common clinical finding among our patients was HT. We detected HT in 75% of the patients. Similar to our study, HT Kazancioğlu *et al.* [18] found 72.6% and Taylor *et al.* [19] found 71% in their studies. About 50% of people with ADPKD with normal kidney function between the ages of 20 and 34 have HT [20]. In our study, the GFR values of all patients without HT were within normal limits.

Patients with ADPKD are 1.6 to 3.2 times more likely to die compared to the general population, and the most frequent cause of mortality is cardiovascular disease [4]. In a study conducted in China, CAD was detected in 21% of ADPKD patients [21]. In our study, the rate of coronary artery disease was found to be 16.7%. Chapman *et al.* [10] detected LVH in 48% of ADPKD patients with hypertension. This rate was found to be 50% in our study.

The presence of proteinuria is an independent risk factor for the development of kidney failure in ADPKD. Mild to moderate proteinuria is observed in ADPKD in patients with advanced renal failure. Proteinuria and microalbuminuria are linked to higher blood pressure along with more extensive cystic involvement in

patients with ADPKD [22]. In Chapman *et al.*'s study [23], the proteinuria rate was found to be 27%. Proteinuria was found in 30.6% of our patient population.

Heart valve abnormalities are common in ADPKD patients [24]. Hossack *et al.* reported the rate of mitral valve prolapse in patient groups as 25% [24]. Mitral valve prolapse was found in 16.7% of our patient group.

It is estimated that the prevalence of hepatic cysts in ADPKD patients reaches up to 80%. Hepatic cysts arise from the bile duct epithelium. The number and size of cysts increase with age [25]. In our study, the rate of liver cysts was 63.9%.

The prevalence of urinary tract stones in ADPKD patients is higher than in the general population. Urinary system stones accelerate the onset of renal failure [26]. The incidence of stones was 27% in the study of Kazancioglu *et al.* [18] and 23.7% in the study of Kaygısız *et al.* [27]. The incidence of stones in our patient group is similar to previous studies and is 22.2%.

In 13% - 23% of patients with ADPKD, the first presentation symptom is macroscopic hematuria [28]. In our study, the rate of patients with a history of macroscopic hematuria was found to be 16.7%.

For ADPKD patients, the risk of intracranial aneurysm is five times higher compared to the normal population. Since the risk of rupture is low in patients, routine screening is not recommended. While the rate of intracranial aneurysm was found 3.2% in a meta-analysis [29], similarly, this rate was 2.8% in our study.

For individuals with ADPKD, the glomerular filtration rate (GFR) follows a curvilinear pattern with accelerated decline later in life [30]. In our investigation, the five-year follow-up period revealed statistically significant increases in creatinine values ($p < 0.001$). The five-year follow-up period also revealed a statistically significant decrease in GFR values ($p < 0.001$). Especially in hypertensive patients, GFR loss was found to be statistically significantly higher than in non-hypertensive patients ($p < 0.001$). This result is consistent with the literature [31]. Therefore, providing blood pressure regulation in ADPKD may slow down the development of end-stage renal failure.

One of the limitations of this study is the small number of patients. The reason for this is that it is a single-center study. Another limitation is the lack of genetic analysis of the patients.

5. Conclusion

ADPKD patients are at high risk for ESRD and cardiovascular disease. Since there is no specific treatment for ADPKD, the current treatment approach is focused on nonspecific treatments such as blood pressure regulation and diet for slow progression of chronic kidney disease. Screening of family members of patients is important for early diagnosis and early initiation of treatment.

Conflicts of Interest

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

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