

Demographic Analysis of Polycystic Kidney Disease Patients: A Single Center Experience

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Abstract

Background. Polycystic kidney disease is the most common genetic kidney disease, expressed autosomal dominantly. The incidence of this disease is 1/400-1/1000 and it's responsible for the 5-10% of all the end stage renal disease. In this study we retrospectively evaluated the demographic characteristics of polycystic kidney disease patients referred to our nephrology outpatient clinic between January 2003 and December 2006.

Methods. Demographic characteristics analyzed were gender, age, smoking and the existence of hypertension, hematuria, urinary system infection, renal calculi and renal replacement therapy, respectively. Hypertension was defined as a blood pressure measurement over 130/80 mmHg. The urinary system infection was diagnosed by urine culture and renal calculi by urinary system ultrasonography.

Results. We examined 136 patients (65 men, mean age: 47.31±16.34 years). Hypertension was the most common finding observed in our patient population. Only 42.85% of our patients' blood pressure was under effective control. Twenty two patients (16.17%) had urinary tract infection and 39 patients (28.67%) had renal calculi.

Conclusions. In conclusion, since penetrance of polycystic kidney disease is 100%, it should be investigated in suspected cases and among their family members. Careful follow up of these patients is mandatory because the disease can easily progress to renal failure.

Key words: End stage renal failure, polycystic kidney disease

Introduction

Polycystic kidney disease is the most common genetic kidney disease, expressed mainly as autosomal dominantly (1). The incidence of the disease is 1/400 - 1/1000 (2). In fact, the prevalence of Autosomal Dominant Polycystic Kidney Disease (ADPKD) is more common than Huntington disease, haemophilia, sickle cell disease, cystic fibrosis, myotonic dystrophy and Down syndrome combined (1, 3). The gene for PKD1 is localized to chromosome 16, and is associated with polycystin-1 protein, and it accounts for approximately 85% of patients with ADPKD. The gene for PKD2, found in chromosome 4, accounts for approximately

15% of ADPKD, and is associated with the polycystin-2 protein (1). These gene products such as polycystin 1 and 2, of PKD1 and PKD2 are plasma membrane proteins and components of a novel signalling pathway that regulates epithelial cell growth and differentiation (4). Further identification of these gene products, including progress in understanding of their functions and interrelationships, has been exciting developments in the field (5).

Polycystic kidney disease is characterized by the development of multiple cysts in the kidneys and other organs. Patients can present at any age, but more often come to clinical attention after age 30 (6). Although palpation of the abdomen occasionally suggests the presence of polycystic kidney disease, radiographic procedures are necessary for the definite diagnosis (3-6). Autosomal polycystic kidney disease may be clinically characterized by abdominal pain, hypertension, episodes of gross hematuria, polyuria, nephrolithiasis, urinary infections, headache, aortic and cerebral aneurysms, mitral valve prolapse, and polycystic liver disease (2, 3, 6).

It is a slowly progressive disease responsible for up 10% of end stage renal disease (ESRD) anywhere around the world (2, 6). According to United States Renal Data system: USRDS 2001 Annual Data Report, subsequent interstitial fibrosis developing in both kidneys, lead to renal failure in 50% of affected persons by the age of 60 years and accounting for 2.3% of end stage renal disease in the United States between 1997 and 2001 (7). It is the fourth most common cause of the ESRD. Patients who are diagnosed before age 30 have a worse renal survival. Male sex, PKD1 gene, episodes of hematuria, and the precocity and severity of hypertension play an important role in the progression of renal disease to ESRD (2, 6). The aim of this study was to retrospectively determine the presence of important prognostic characteristics of ADPKD patients followed by our nephrology clinic.

Patients and methods

Polycystic kidney disease patients referred to our nephrology outpatient clinic between January 2003 and December 2006 were included in the study. The demographic characteristics such as gender, age, smoking and clinical renal manifestations such as, hematuria, urinary system infection, renal calculi and renal replacement therapy, as well as

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cardiovascular manifestation such as hypertension were respectively recorded.

The blood pressure of the patients was measured three times on both arms after 10 min of rest in the sitting position with the manual manometer at the outpatient clinic by a single observer and hypertension was defined as a blood pressure over 130/80 mmHg.

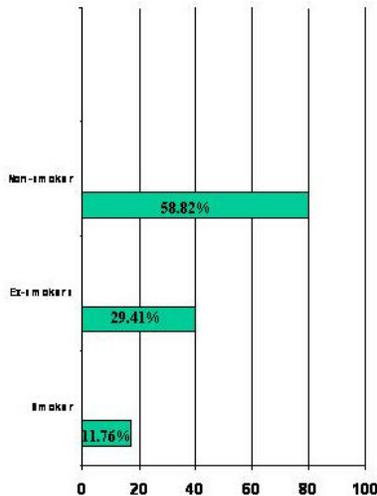
Urinary system infection was defined as infection confirmed by positive urinary culture only. The presence and absence of renal calculi was determined by an ultrasonographic examination.

The data was analyzed by SPSS and results are reported as the means ± SD and % variations in categorical variables.

Results

The diagnosis of ADPKD was confirmed a mean of 4.57±4.97 years ago. Sixteen patients (11.76%) were smokers, 40 patients (29.41%) ex-smokers and 80 patients (58.82%) were non-smokers (Figure 1).

Figure 1. Smoker/nonsmoker patients



Ninety-eight patients (72.05%) had hypertension among which only 42 patients' (42.85%) blood pressure (BP) was under control. Mean systolic BP, diastolic BP and arterial pressure were 111.33, 70.75 and 91.04 mmHg, respectively. Seventy-seven patients (56.61%) were taking antihypertensive drugs. The distributions of these drugs were; 12.98% diuretics (10 patients), 7.79% beta blockers (6 patients), 28.57% calcium channel blockers (22 patients), 42.85% renin-angiotensin system blockers (33 patients) and 10.38% alpha blockers (6 patients) (Table 1).

Table 1. Distribution of antihypertensive drugs

Antihypertensive drugs	Number of patients
Diuretics	10 (12.98%)
Beta blockers	6 (7.79%)
Calcium channel blockers	22 (28.57%)
Renin angiotensin system blockers	33 (42.85%)
Alpha blockers	6 (7.79%)

Forty-two patients (30.88%) were not using any hypertensive drugs.

Thirty-nine patients (28.67%) had macroscopic hematuria, 22 patients (16.17%) had urinary tract infection and 39 patients (28.67%) had renal calculi (Table 2).

Table 2. Clinical findings of the patients

Clinical findings	Number of patients
Hypertension	98 (72.05%)
Macroscopic hematuria	39 (28.67%)
Urinary tract infection	22 (16.17%)
Renal calculi	39 (28.67%)

Seventeen (12.5%) cases were on renal replacement therapy among whom 11 (8.08%) were on hemodialysis and 5 (3.67%) on peritoneal dialysis (Table 3).

Table 3. Renal replacement therapies

Renal replacement therapy	Number of patients
Hemodialysis	11 (8.08%)
Peritoneal dialysis	5 (3.67%)
Transplantation	1 (0.73%)

Discussion

Polycystic kidney disease is characterized by countless epithelium-lined cysts containing urine-like fluid that is diffusely scattered throughout the renal cortex and medulla. The disease occurs worldwide in all races and ethnic groups. Approximately one-half of affected subjects will experience minimal morbidity, whereas the remainder will have complications to a variable degree (3). Autosomal dominant polycystic kidney disease (ADPKD) is a dominantly inherited systemic disorder equally inherited in men and women but ADPKD women have a slower rate of progression to renal failure, with a later age of entry into ESRD as compared with men (8). Most affected patients do not experience symptoms and escape detection until middle age. During the silent years, the renal cysts progressively expand. The kidney enlargement may not be noticed until the seventh or eighth decade of life (3). Our patients were aged 47.31±16.34 (65 men, 71 women) years and they knew their diagnosis for 2.78 years.

Even though we do not have enough scientific data about smoking and its specific effect on polycystic kidney disease, we predict that by increasing cardiovascular morbidity and mortality rates, smoking may accelerate the transition phase to an ESRD besides being a risk factor in ESRD (9). A retrospective multi-center European case-control study showed that smoking is an independent risk factor for ESRD in patients with inflammatory and non-inflammatory renal disease, i.e. polycystic kidney disease. The pathogenesis of the smoking-related renal damage is largely unknown. The intermittent increase in blood pressure during smoking seems to play a major role in causing renal damage (9, 10). Among our study population 11.76% were smoking, 29.41% had quitted smoking. All of our patients were inferred about the potential effects of smoking and advised about quitting. According to an analysis of the Turkish Society of Nephrology Polycystic Kidney Disease Working Group, 923 polycystic kidney disease patients were examined and it was found that 20.5% the patients were smoking and 17.2% had quitted smoking (11).

Hypertension accelerates the transition of polycystic kidney disease to ESRD (1, 2, 6, 12). Hypertension was the most common symptom among our patients (72.05%), correlating with Schrier's study results demonstrating hypertension in 578 patients (71%) (7). The hypertension is associated with a substantial incidence of left ventricular hypertrophy (5). Increased left ventricular mass and hypertrophy have been found in early stages of ADPKD. The mechanism that leads to an increase in left ventricular mass in this population is largely unknown but hypertension facilitates this process (13). Since cardiovascular events are the most common cause of death in ADPKD patients, the occurrence of hypertension and left ventricular hypertrophy are extremely important cardiovascular risk factors for ADPKD patients (5). A prospective 7-year randomized study showed that rigorous control of hypertension in hypertensive subjects with ADPKD, decreased left ventricular mass index to a greater extent than standard therapy (<140/90 mmHg) (7). So, hypertension should be treated effectively (1, 2, 13). Early intervention in diagnosing and aggressively treating blood pressure in patients with ADPKD therefore has the potential of preventing left ventricular hypertrophy, cardiovascular complications, and mortality (7). Only 42.85% of our patients were at the target blood pressure. Similarly Ecker et al. determined hypertension prevalence as 71.8% in Turkish APKD patients. Among the hypertensives only 45.1% were controlled (11).

There are several experimental and clinical observations that show an increased activity of the renin-angiotensin-aldosterone system in ADPKD patients. Given the potential detrimental renal and cardiac effects of angiotensin II, it is reasonable to treat hypertensive ADPKD patients with angiotensin converting enzyme (ACE) inhibitors (14). Inhibitors of the renin-angiotensin-aldosterone system decrease and prevent left ventricular hypertrophy and cardiac complications as they slow the progression to ESRD (1, 14). Thirty-three of our patients (42.85%) were taking renin angiotensin system blockers such as ACE inhibitors or angiotensin receptor blockers.

Patients frequently present with hematuria as the initial manifestation of ADPKD. Hypertensive ADPKD subjects were more likely to have gross hematuria than normotensive subjects and those with gross hematuria had larger renal size (15). Nephrectomy might be considered, if life threatening hematuria develops. Thirty-nine (28.67%) of our patients had macroscopic hematuria and most were hypertensive but none of them needed nephrectomy. It was reported that only 29.4% patient had macroscopic hematuria in Turkish patients (11).

Symptomatic lower urinary tract infection affects 50-75% of all polycystic patients at some time (16). In our study, 22 patients were confirmed to have (16.17%) urinary tract infections by urinary culture. According to the report of the TSN, PKD Working Group, 29.4% patients were confirmed to have urinary tract infections (11). On the other hand, no statistically significant differences in the frequency of any manifestations of ADPKD between men and women were found, although the frequency of symptoms consistent with urinary tract infections tended to be higher in women than in men (17). Most of the patients with urinary infection were women similar to literature.

The prevalence of nephrolithiasis is considerably greater in patients with ADPKD than in the general population (18). The composition of stones is most frequently based on uric

acid and/or calcium oxalate. Metabolic factors are important in their pathogenesis. Distal acidification defects may be important in a few patients, while an abnormal transport ammonium, low urine pH, and hypocitraturia are the most common abnormalities (19). Nephrolithiasis precipitates the onset of the renal failure (18) but the treatment of nephrolithiasis in patients with ADPKD is not different from that in patients without ADPKD (19). Ultrasonography is necessary and useful procedure to determine nephrolithiasis. We determined nephrolithiasis in 39 patients (28.67%) by ultrasonographic examination. Turkish PKD Working Group found existence of renal calculi in 28% of their patients (11). End stage renal disease develops sooner in the patients with progressive factors and they will need renal replacement therapy within shorter period of time (1, 2, 6, 13). While 11 of our patient required haemodialysis, 5 of them were treated with peritoneal dialysis. Only one patient underwent renal transplantation.

Conclusion

In conclusion, since penetrance of polycystic kidney disease is 100%, it should definitely be investigated in suspected cases and among their family members, at the same time. The presence of potential risk factors such as gender, age, smoking and clinical renal manifestations as well as renal replacement therapy, and presence of hypertension should be questioned and investigated at the first appointment in order to as much as possible slow the progression of the disease.

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