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DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF PATIENTS WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASES IN ISTANBUL FACULTY OF MEDICINE

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ABSTRACT

Aims: Autosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary renal disease which affects about 1 in 400 to 1 in 1000 people worldwide. Therefore it is vital to know the natural course of the disease elaborately. The aim of this study is to assess the demographic and clinical characteristics of patients with Autosomal dominant polycystic kidney disease (ADPKD).

Methods: Medical records of 144 patients with Autosomal dominant polycystic kidney disease (ADPKD) were examined and the data were acquired from these records. The investigated demographic and clinical characteristics were age, gender, history of smoking, hypertension, types of antihypertensive drugs used, macroscopic hematuria, urinary tract infection, urinary tract stones, renal replacement therapy, cysts found in other organs, and results of the patients' blood and urine tests such as blood urea nitrogen (BUN), creatinine, cholesterol, albumin, hemoglobin and proteinuria. Patients who had a blood pressure (BP) of 140/90 mmHg or greater and/or using antihypertensive medications were considered as hypertensive.

Results: The study included 61 male and 83 female patients. The mean age of patients was 44.9 years. 11.9% of the patients were smokers whereas 4.2% were ex-smokers. The mean systolic and diastolic blood pressures (BP) were 139.2 mmHg and 89.5 mmHg, respectively. The mean arterial pressure was 106.1 mmHg. 82.4% of the patients had hypertension. 71.5% used antihypertensive drugs and 49.5% of those used renin-angiotensin-aldosterone system (RAAS) blockers (angiotensin converting enzyme inhibitors or angiotensin receptor blockers). 13.2% of the patients had macroscopic hematuria and 16.7% had urinary tract stones. Liver cysts were found in 27.1% of the investigated patients. Out of patients, 11.2% had end stage renal disease and were treated with hemodialysis.

Conclusion: This study showed that hypertension is the most common clinical finding in Autosomal dominant polycystic kidney disease (ADPKD) patients and renin-angiotensin-aldosterone system (RAAS) blockers are widely used. The presence of potential risk factors such as age, smoking, clinical renal manifestations, hypertension and disease in family members should be questioned and investigated for the early diagnosis and treatment of this disease.

Keywords: Autosomal dominant polycystic kidney disease, hypertension, angiotensin-converting enzyme inhibitor, angiotensin receptor blocker

INTRODUCTION

Autosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary renal disorder and it affects between 1 in 400-1000 individuals (1, 2). ADPKD is caused by mutations in two different genes, PKD1 and PKD2. The gene PKD1, which is localized to the short arm of chromosome 16, is associated with polycystin-1 protein and is responsible for 85% of the ADPKD patients. The gene PKD2 found on the long arm of chromosome 4 accounts for 15% of ADPKD cases and is associated with polycystin-2 protein (1). These gene products, polycystins, are membrane glycoproteins and are expressed in a wide variety of tissues and cell types (1, 2).

Autosomal dominant polycystic kidney disease (ADPKD) is a systemic disorder which has both renal

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and extrarenal manifestations, such as renal cysts, nephromegaly, hypertension, hematuria, polyuria, urinary tract stones, urinary infections, cysts in the liver and other organs, intracranial aneurysms, mitral valve prolapse, abdominal or inguinal hernias and colonic diverticuli. Multiple renal cysts and progressive renal enlargement are the main clinical features present in all of the patients. Extrarenal manifestations occur with variable frequency and in various combinations (1, 2).

Autosomal dominant polycystic kidney disease (ADPKD) causes renal failure in 50% of affected persons by the age of 60 years. It is responsible for 5-10% of end-stage renal disease (ESRD). Patients who are diagnosed before the age of 30 have a worse renal survival. Male sex, PKD1 gene mutation, episodes of hematuria and the precocity and severity of hypertension are important risk factors for ESRD (3).

The aim of this retrospective study was to investigate the demographic and clinical characteristics of patients with ADPKD followed in Istanbul Faculty of Medicine.

MATERIAL AND METHODS

Intellectual impairments in older patients are frequently the result of two other syndromes, each of which frequently coexists with dementia: depression and delirium. Depression is commonly accompanied by to dementia, but it can also masquerade as dementia. Moreover, a patient with depression and cognitive impairment, whose intellectual functions improve with treatment of the mood disorder, has an almost five-fold greater risk of suffering irreversible dementia later in life. Several factors are related to dementia: age, head injury, genetic factors, black race, higher LDL cholesterol levels, physical activity, male gender, smoking, drug use, education level. There are also many factors that decrease risk, such as NSAID use, HMG-CoA reductase inhibitor use, moderate alcohol intake and strong social supports.

A total of 144 patients with ADPKD who have been examined in Istanbul Faculty of Medicine Nephrology Outpatient Clinic from 1995 to 2014 were included in our study. Medical records of these individuals were studied and the data for the research were acquired from these records.

The diagnosis of ADPKD was confirmed by the presence of 5 or more renal cysts found in both kidneys. The examined demographic characteristics were age, gender, smoking history (smoker, non-smoker, ex-smoker). Renal manifestations (macroscopic hematuria, urinary system infection, urinary tract stones and renal replacement therapy), hypertension, types of antihypertensive drugs (diuretics, beta blockers, calcium channel blockers, angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers, alpha blockers and others), extrarenal manifestations (liver cysts, cysts in other organs, umbilical or inguinal hernias) were also studied.

The results of the patients' blood and urine tests such as blood urea nitrogen (BUN), creatinine, cholesterol, albumin, hemoglobin and proteinuria were recorded. The glomerular filtration rates were calculated by using the CKD-EPI formula (4).

Patients who had a blood pressure of 140/90 mmHg or greater and/or using antihypertensive medications were considered as hypertensive. The target blood pressure was <130/80 mmHg.

Urinary tract infection was defined as an infection confirmed by positive urinary culture. The presence and absence of urinary tract stones had been confirmed by ultrasonographic examination and/or a history of passing stones. Abdominal ultrasonography was used to evaluate liver cysts.

RESULTS

The study included 144 (61 male, 83 female) patients and 84 (58.3%) patients had a positive family history for ADPKD. The mean age of patients was 44.9 years. Among these patients, 30.8% of the patients had no history of smoking; 12% were current smokers whereas 4.2% were ex-smokers.

The mean systolic and diastolic blood pressures were 139.2 mmHg and 89.5 mmHg, respectively. The mean arterial pressure was 106.1 mm Hg. The mean serum creatinine was 1.9 ± 2.1 mg/dl and glomerular filtration rate was 65.7 ± 37.4 ml/min/1.73m^2.

A total of 117 (82.4%) patients had hypertension and 25 (17.6%) patients were normotensive. Among the hypertensive patients, 98 (83.8%) were taking antihypertensive drugs. Blood pressure was under control in 40.8% of the subjects (Figure 1).

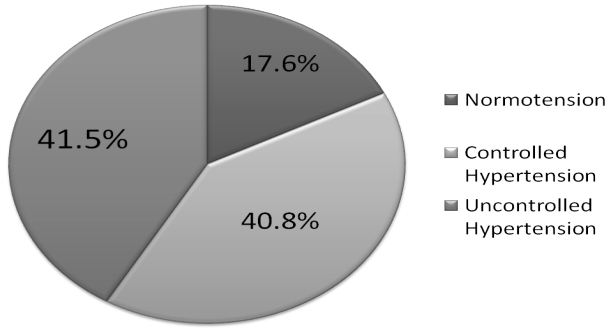

Figure 1: The presence of controlled and uncontrolled hypertension

The use of antihypertensive drugs was as follows: 5.5% diuretics, 7.4% beta blockers, 32.1% calcium channel blockers, 28.5% ACE inhibitors, 21.1% angiotensin receptor blockers and 5.5% alpha blockers (Figure 2).

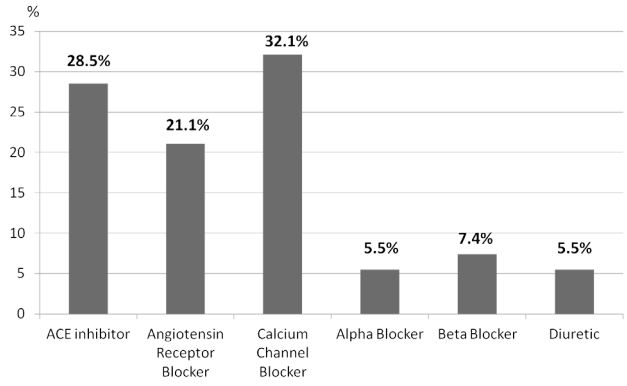

Figure 2: The antihypertensive agents used in the patients with ADPKD

Regarding other manifestations of ADPKD, 13.2% (n=19) of the patients had a history of macroscopic hematuria, 2.2% (n=14) had documented urinary tract infections, 16.7% (n=24) had urinary tract stones and 4.9% (n=7) of the patients had hernias. Liver cysts were detected in 39 patients (27.1%) (Figure 3).

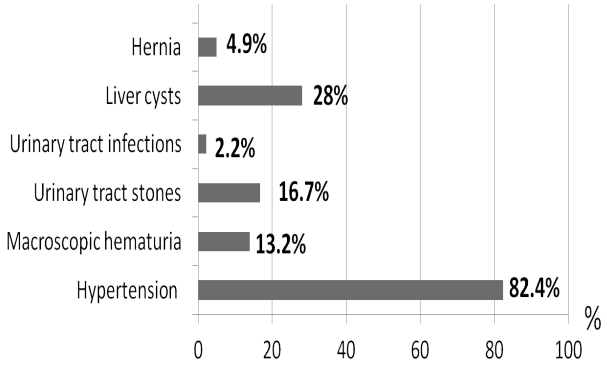

Figure 3: Prevalence of clinical findings

88.8% of the study population did not need any renal replacement therapy, 11.2% had ESRD and were treated with hemodialysis.

DISCUSSION

Autosomal dominant polycystic kidney disease is the fourth common cause of ESRD. Hypertension is a common finding of ADPKD, affecting both renal and patient survival. Left ventricular hypertrophy, intracranial and extracranial aneurysms and cardiac valvular abnormalities are other cardiovascular manifestations of this disease (5).

The present study showed that hypertension is the most common clinical finding in our patients. Activation of the renin-angiotensin-aldosterone system (RAAS) seems to play a major role in the pathogenesis of hypertension in ADPKD (5). Thus, it is reasonable to treat hypertension in ADPKD with ACE inhibitors and angiotensin receptor blockers. In the present study, ACE inhibitors and angiotensin receptor blockers were the most commonly used antihypertensive agents.

There is an increasing number of studies showing the detrimental effects of smoking on kidney functions in patients with chronic kidney disease (6, 7). Chapman et al. (8) reported that smoking history was a significant independent variable in determining the level of proteinuria in patients with ADPKD. Furthermore, in a cohort of 323 patients with ADPKD, Ozkok et al. (9) found that the frequency of smoking and amount of cigarettes smoked (package/year) were significantly higher in rapid progressors compared to slow progressors. Among our patients, 12% were current smokers. The patients should be strongly advised to quit smoking in order to slow the progression of the disease and decrease the cardiovascular risk.

Patients frequently present with hematuria as the initial manifestation of ADPKD. Hypertensive ADPKD subjects are more likely to have gross hematuria than normotensive subjects and those with gross hematuria have larger renal size (10). In the present study, 13.2% of the patients had a history of a macroscopic hematuria.

Symptomatic lower urinary tract infection affects 50–75% of all polycystic patients at any given time (11). Our study demonstrated that 2.25% patients had a confirmed urinary tract infection.

The prevalence of urinary tract stones is considerably greater in patients with ADPKD than in the general population. The composition of the stones is most frequently 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 ammonium transport, low urine pH and hypocitraturia are the most common abnormalities (1, 2, 11).

Urinary tract stones precipitate the onset of renal failure. The treatment of these stones in ADPKD patients is not different from that in patients without ADPKD. Ultrasonographic examination of the urinary system is a necessary and useful procedure to determine urinary tract stones (12). We determined these stones in 16.7% of the patients by ultrasonographic examination.

End-stage renal disease develops sooner in the patients with progressive factors. The PKD1 gene, younger age at diagnosis, male gender, hypertension, increased left ventricular mass, hepatic cysts in women, 3 or more pregnancies, gross hematuria, urinary tract infections in men and increased renal volume are factors associated with worse renal function in ADPKD (1-3). Among our patients with ADPKD, 11.2% had ESRD.

In conclusion, ADPKD is a systemic hereditary disease associated with a high risk of morbidity and mortality. Hypertension is the most common clinical manifestation of this disease. Early detection and treatment of hypertension, with drugs that block the RAAS, has the potential to decrease the cardiovascular complications and slow the progression of renal disease in ADPKD.

Ethics Committee Approval: This study was approved by Istanbul University Faculty of Medicine Scientific Researches Ethics Committee.
Informed Consent: Written informed consent was obtained from the participants of this study.
Conflict of Interest: The authors declared no conflict of interest.
Financial Disclosure: The authors declared that this study received no financial support.

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