e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2024; 16(1); 1230-1234

Original Research Article

A Study on Clinical Profile of Autosomal Dominant Polycystic Kidney Disease

Manjuri Sharma[1], Manas Gope[2], Prodip Kumar Doley[3]

[1]Professor and Head of Department of Nephrology, Gauhati Medical College and Hospital, Guwahati, Assam, India

[2]Assistant professor, Department of Nephrology, Agartala Govt. Medical College and GBP Hospital, Agartala, Tripura, India

[3]Associate Professor Department of Nephrology, Gauhati Medical College and Hospital, Guwahati, Assam, India

Received: 25-10-2023 / Revised: 23-11-2023 / Accepted: 26-12-2023

Corresponding Author: Dr. Manas Gope

Conflict of interest: Nil

Abstract:

Background: Autosomal dominant polycystic kidney disease (ADPKD) is the most common hereditary form of kidney disease. Clinical data on this multisystem disorder are scarce from developing countries. We conducted a cross sectional observational study of the clinical profile of ADPKD patients over a period of one year in Gauhati medical college (single centre).

Materials and Methods: A total of 40 patients 24 males and 16 females fulfilled the inclusion criteria of ADPKD, were gathered during the period of 1 year starting from May 2020 to May 2021. All the patients were subjected to a detailed history, clinical examination and laboratory investigations. X-ray chest (PA view), ECG and ultrasound of abdomen, Echocardiography were done. Diagnosis of ADPKD was established by renal ultra-sonography using unified criteria by Pei et al

Results: Mean age was 46.5 ± 12.2 years. About 62.5% had early stage (Stages 1–3) of chronic kidney disease (CKD) and 37.5% had advanced CKD (Stages 4 and 5). Clinical features observed included pain abdomen (47.5%), nocturia (65%), hematuria (22.5%), nephrolithiasis (27.5%), urinary tract infection (UTI) (50%), and hypertension (72.5%). The prevalence of hypertension, nocturia Hematuria, UTI, Hepatic cyst was increased with increasing age which was statistically significant. Extra renal manifestations were polycystic liver disease in 15 patients (37.5%), cysts in pancreas in three (7.5%), and intracranial aneurysm in three (7.5%). A total of 8 patients (20%) developed end-stage kidney disease during the study period. There were statistically significant increased prevalence of mean age, Family h/o early esrd (Age<55 yrs), Smoking, Haematuria, UTI in ESRD group.

Conclusions: In the present study, hypertension was most common presentation of this disease. So, control of hypertension is very important to prevent progression of this disease. Patients who are detected to have ADPKD should be regularly followed-up to pre- vent further progression by timely intervention. Also, family members of patients should be screened for disease and initiate treatment as early as possible.

Keywords: Autosomal Dominant Polycystic Kidney Disease, Chronic Kidney Disease, End-Stage Renal Disease.

Introduction

Autosomal Dominant Polycystic Kidney Disease (ADPKD) is a monogenic, multi-systemic disorder characterized by the development of renal cysts and various extrarenal manifestations, caused by mutations in two genes: PKD1 in 85% and PKD2 in 15% of cases. [1]

Autosomal Dominant Polycystic Kidney Disease (ADPKD) is the fourth common cause of chronic renal failure throughout the world. It accounts for 8-10% of cases of End stage Renal Disease (ESRD) [2]. Cardiovascular abnormalities are the important extra renal manifestations of ADPKD [3,4]. These patients have increased incidence of valvular abnormalities such as mitral prolapse, aortic incompetence and tricuspid prolapse. Aortic aneurysms may also occur with increased frequency in ADPKD. Hepatic cysts arise from dilatation of biliary microhamartomas and from prebiliary glands.

Other uncommon manifestations are pancreatic, splenic, seminal vesical cysts and inguinal hernias. Bladder cysts, arachnoid membrane cysts, spinal

meningeal diverticula are present in 10-40% of asymptomatic patients with ADPKD [5] A single study from India recently reported ADPKD to be the aetiology of chronic kidney disease (CKD) in 2.6% cases. [6] In view of ADPKD being one of the common cause of End Stage Renal Disease (ESRD) and since it has varying clinical presentation we conceptulalized a study to analyse the clinical profile of Autosomal Dominant Polycystic Kidney Disease.

Material and Methods

Study was conducted in the department of Nephrology GMCH, Guwahati. Study subjects were male and female, diagnosed as ADPKD. Total sample size estimated around 40.

Both symptomatic and asymptomatic patients with autosomal dominant polycystic kidney disease meeting imaging criteria were included. Patients with simple cystic kidney disease and patients not meeting imaging criteria were excluded. To recruit 40 study subjects from the patients with ADPKD, approximately monthly Four (4) study subjects were recruited and were selected randomly. Diagnosing ADPKD is generally easy in adults. Ultrasonography (USG) reveals bilateral enlarged kidneys with multiple contiguous cysts of various sizes in cortex and medulla. This is undoubtedly ADPKD if it associated with positive family history and/or cysts in the liver. The diagnosis of ADPKD was established by renal ultrasonography using unified criteria by Pei et al. [7] As per these criteria, the presence of at least three unilateral or bilateral renal cysts in patients aged 15–39 years, two cysts in each kidney in patients aged 40–59 years, and four cysts or more in each kidney in individuals aged ≥60 years are suggestive of a diagnosis of ADPKD.

After obtaining informed consent and Institutional ethical committee approval the Study was conducted. Detail history and physical examination was done with emphasis on Brachial BP, height, weight, BMI. Blood pressure was measured with a standard mercury manometer, sitting position, right arm. Hypertension was diagnosed as blood pressure 140/90 mmHg or the taking of antihypertensive drugs. Body mass index (BMI) was calculated by dividing weight in kilograms by height in meters squared.

Laboratory evaluation included complete haemogram, serum biochemistry including renal function, liver function tests , electrocardiogram, Echocardiography. Urinalysis and Urine culture and sensitivity as and when needed. Renal function was assessed by serum creatinine level, with endogenous creatinine clearance being calculated using the Modification of Diet in Renal Disease (MDRD) study equation. The patients were stratified according to the five stages of CKD listed in the National Kidney Foundation guidelines. [8] Diagnosis of nephrolithiasis was made by a history of stone passage, removal of stone or calcific foci/nephrocalcinosis seen on imaging. Ultrasonography or other imaging reports were also reviewed to identify involvement of other abdominal viscera.

A standardized family history questionnaire was used to screen for a history of ADPKD in first-degree relatives. For each patient, a family tree consisting of parents, siblings, and offspring was prepared. History of polycystic kidney disease (PKD) was explored in these family members. The diagnosis of positive history of PKD in a family member was made on the basis of a known diagnosis of ADPKD or by renal ultrasonography using unified criteria by Pei et al. [7] or kidney failure in that family member.

Details regarding clinical presentation, including renal and non-renal manifestations, detailed family history, co-morbid conditions, other associated conditions, salient laboratory abnormalities, imaging abnormalities, treatment and follow-up were recorded in a structured pro forma. Statistical analyses were performed using the Statistical Package for the Social Science (SPSS). The categorical variables were shown as numbers of cases with percentage, and the continuous variables were shown as mean ± standard deviation (SD). A P value of ≤0.05 was considered statistically significant.

Results and Analysis

A total of 40 study subjects with ADPKD were included randomly from Department of Nephrology, GMCH, Guwahati. Out of 40 patients, 24(60%) men and 16(40%) women. The mean age of the patients was 46.5 ± 12.2 years; 60% belonged to the age group of 40–59 years, 25% to the age group ≥60 years, and 10% to the 15–39 years group and 1% were <15 years.

Twenty seven patients (67.5%) had a positive family history for ADPKD, out of which 18(45%) were male and 9(22.5%) were female. Total number of parents in this study group was 80.Total no of siblings were 142, out of which 81 were brothers and 61 were sisters. Total number of offspring/children was 96, out of which 52 were sons and 44 were daughters. Total number of family members screened for ADPKD was 318.

Out of 40 patients 19 patients (47.5%) had flank pain, 26 patients (65%) had nocturia, 9patients (22.5%) had haematuria, 11 patients (27.5%) had nephrolithiasis, 12(30%) patients had palpable kidney. The prevalence of hypertension was 72.5%, in different CKD stages was CKD Stage 1 (54.5%), Stage 2 (60%), Stage 3 (77.8%), Stage 4 (80%),

and Stage 5 (90%). Mean serum creatinine was 2.84±2.74mg/dl.

Out of 40 patients 19 patients (47.5%) had Left Ventricular hypertrophy (LVH), 7 patients had Mitral valve prolapsed (MVP), 7 patients (22.5%) had Mitral regurtition, 4 patients (10%) had Aortic regurtition, 3 patients (7.5%) had Tricuspid regurtition. The prevalence of hepatic cyst was 37.5%,pancreatic cyst 7.5%, intracranial aneurysm 5%. Out of 40 patients 17 patients (42.5%) had Anemia, mean Hemoglobin (g/dl) value was 11.05+1.84.

Table 1: Comparison of demographic and clinical characteristics between male and female patients (n=40).

Parameter (Mean ± S.D.)	Male(n-24)	Female(n-16)	P value
Age(yrs)	48.54±**13.15**	**47.93±11.23**	0.8672
Hemoglobin(g/dl)	**10.72±1.72**	**9.62±1.8**	0.0699
Creatinine(mg/dl)	**3.19±2.70**	**3.12±3.07**	0.9398
Ckd stage 1	7(29.2%)	4(25%)	0.7736
Ckd stage 2	2(8.3%)	3(18.7%)	0.3353
Ckd stage 3	7(29.2%)	2(12.5%)	0.2213
Ckd stage 4	2(8.3%)	3(18.7%)	0.3353
Ckd stage 5	8(33.3%)	2(12.5%)	0.1416
Flank pain	9(37.5%)	10(62.5%)	0.1883
Nocturia	16(66.7%)	10(62.5%)	0.7876
Hematuria	5(20.8%)	4(25%)	0.7582
Nephrolithiasis	7(19.2%)	4(25%)	0.6659
UTI	11(45.8%)	9(56.2%)	0.5245
Hypertension	19(79.2%)	10(62.5%)	0.2524
Hepatic cyst	8(33.3%)	7(43.7%)	0.5109
Palpable kidney	6(25%)	6(37.5%)	0.4040
Family history of ADPKD present	17(70.8%)	8(50%)	0.1887

Table 2: Comparison of demographic and clinical characteristics in different age groups (n=40).

Parameters	15-39yrs. (n-6)	40-59yrs (n-24)	>60yrs (n-10)	P value
Flank pain	3(50%)	9(37.5%)	7(70%)	0.0883
Nocturia	2(33.3%)	15(62.5%)	9(90%)	0.0218
Hematuria	0	4(16.7%)	5(50%)	0.0483
Nephrolithiasis	0	6(25%)	5(50%)	0.1619
UTI	0	11(45.8%)	9(90%)	0.0187
Hypertension	2(33.3%)	19(79.2%)	9(90%)	0.0218
ESRD	0	0	08(80%)	
Palpable kidney	0	6(25%)	6(60%)	0.0552
Hepatic cyst	0	6(25%)	9(90%)	0.006

The prevalence of hypertension, nocturia Hematuria, UTI, Hepatic cyst were increased with increasing age which were statistically significant.

Table 3: Comparison of prevalence of risk factors responsible for ESRD in esrd and no-esrd group in ADPKD

Parameters	Esrd(n=8)	No-Esrd(n=32)	P value
Age (yrs) (Mean ± S.D.)	64.25 ± 5.53	44.13 ± 9.88	0.001
Male	6 (75%)	18(56.2%)	0.3378
Female	2 (25%)	14(43.7%)	0.3402
Family h/o early ESRD (Age<55 yrs)	8 (100%)	19(59.3%)	0.030
Smoking	7 (87.5%)	20(62.5%)	0.030
Haematuria	6 (75%)	3(9.3%)	0.0001
UTI	8(100%)	12(37.5%)	0.0018
Hypertension	8(100%)	21(65.6%)	0.0543
Diabetes mellitus	2(25%)	4(12.5%)	0.3819

There were statistically significant increased prevalence of mean age, Family h/o early esrd (Age<55 yrs), Smoking, Haematuria, UTI in ESRD group.

Discussion

As far as we know, this is the first study that evalu-

ated the renal and extrarenal clinical manifestations in a cohort of northeast Indian ADPKD population.

The study showed a higher prevalence (60%) of this condition among males, whereas a higher prevalence of 51.4% and 63%, respectively, in female European [9] and Brazilian populations has been reported. Mean age at diagnosis in this study was 46.5 ± 12.2 years, slightly higher in our patients as compared to that in studies by Thong and Ong. [9]

Even the serum creatinine at diagnosis was higher in our study as compared to that in a study by Romão et al. A high prevalence of hypertension, nocturia, abdominal pain, nephrolithiasis, UTI, and renal dysfunction was found in Indian ADPKD patients.

Family history was positive for ADPKD in 67.5% of our study cohort. Family history analysis is a simple and inexpensive approach to identifying individuals at risk for ADPKD. In our study, a high proportion (67.5%) had a positive family history because the instrument used was known history of the disease, and ultrasonography to screen the first-degree relatives for the presence of ADPKD.

An impaired concentrating ability leads to nocturia. It was present in two-third (65%) of our study patients. Recent studies suggest that the urinary concentrating defect and elevated serum concentration of vasopressin may contribute to cystogenesis. They may also contribute to the glomerular hyper filtration seen in children and young adults, development of hypertension, and progression of CKD.10The prevalence of nocturia in 15-39 yrs was 33.3%, in 40-59 yrs was 62.5% and in >60 yrs was 90% (p=0.0218), suggesting the prevalence of nocturia was statistically significant increased with increasing age.

Gross hematuria was reported in 22.5% patients in our study. Nephrolithiasis has been reported in 20%–30% of patients, of whom 50% are symptomatic for stone disease and 20% require definite urologic intervention [11] Nephrolithiasis is more common in male ADPKD patients. Nephrolithiasis was observed in 27.5% of our patients, males (63.6%) had a higher prevalence of nephrolithiasis compared to females (36.4%).

Symptomatic UTI affects 50%–75% of all polycystic patients at some time. [11] Nearly 30% to 50% of patients with ADPKD will have a UTI, either pyelonephritis or cyst infection, during their lifetime. UTI is more common in women with ADPKD. In the current study, 50% of the patients had suffered from at least one episode of UTI, females (56.2%) had a higher prevalence of UTI compared to males (45.8%). In this study, most common organism causing UTI was E.coli (70%) followed by pseudomonas and klebsiella. This is similar to other studies of Salle M et al,[12] which have reported that E.coli (60%) was the most common organism detected among ADPKD patients causing UTI. Hypertension has been known to occur in 70%–80% of adults with ADPKD before loss of kidney function, possibly affecting 80% of the ADPKD patients with renal failure.13 Hypertension is probably the most remediable and serious complication of ADPKD.

In this study, Out of 40 patients 29 patients (72.5%) having Hypertension. Among 29 patients 10 were female (34.4%) and 19 were male (65.6%), means the prevalence of hypertension was higher in male as compared to female patients, though statistically insignificant. The prevalence of hypertension in different CKD stages was CKD Stage 1 (54.5%), Stage 2 (60%), Stage 3 (77.8%), Stage 4 (80%), and Stage 5 (90%), suggesting that the prevalence of hypertension was increased with higher stages. The prevalence of hypertension in 15-39 yrs was 33.3%, in 40-59 yrs was 79.2% and in >60 yrs was 90%, (p=0.0218), hence the prevalence of hypertension was increased with increasing age which was statistically significant.

Hossack KF, et al. studied 163 patients with ADPKD, 26% had mitral valve prolapse, 31% had mitral incompetence, 8% had aortic incompetence, 15% had tricuspid incompetence and 6% had tricuspid valve prolapse. [14]. In our study we reported ICAs in 2 out of 40 patients contributing to 5%, both were presented as subarachnoid hemorrhage even before the diagnosis of ADPKD. The mean age of the patients developing stroke was 47.3 ± 5 years. There was a history of stroke at age below 55 years in first-degree relative in four patients.

Generally, renal function is maintained until the fourth to sixth decade of life. However, once the compensatory mechanism of the kidneys fails, a rapid decline in renal function occurs. The progressive disease ultimately leads to ESRD, and chronic renal failure presents in about 50% of patients by the age of 60 years. [4] Majority of our study patients had elevated serum creatinine level and 37.5% had late CKD Stage (4 and 5) at diagnosis of ADPKD. The mean creatinine at diagnosis was found to be a significant predictor of ESRD. Almost 20% of the study patients having ESRD. The mean age of ESRD patients in ADPKD were 64.25 ± 5.53yrs and in non ESRD group mean age were 44.13 ± 9.88 yrs (p=0.001), mean age were statistically significant high in ESRD group. Majority (75%) of ESRD patients were male.

There was statistically significant increased prevalence of Smoking, Haematuria, UTI in ESRD group. The prevalence of Family h/o early esrd (Age<55 yrs) in ESRD group was 100% and in non ESRD group was 59.3% (p=0.030), suggesting that prevalence of family h/o of early esrd were statisti-

cally significant high in ESRD group.

Polycystic liver disease is the most common extrarenal manifestation of ADPKD. Chauveau et al showed that liver was diffusely cystic in 20% - 50% of patients with ADPKD. 15(37.5%) patients in our study had PLD, and pancreatic cysts were detected in only 7.5% cases. The prevalence of Hepatic cyst was significantly higher with increasing age (p=0.006) and higher in female (43.7%) than in male (33.3%), though statistically insignificant.

Transplantation is the optimal choice of renal replacement therapy in appropriate patients with ADPKD. When transplantation is not an option, or for those waiting for transplantation, either hemodialysis or peritoneal dialysis is a suitable modality.

Bibliography:

1. Hateboer N et al. Comparison of phenotypes of polycystic kidney disease types 1 and 2. Lancet. 1999; 353(9147): 103-7.
2. 2.Spithoven EM, Kramer A, Meijer E, et al.Renal replacement therapy for autosomal dominant polycystic kidney disease (ADPKD) in Europe: Prevalence and survival – Ananalysis of data from the ERA-EDTA Registry. Nephrol Dial Transplant 2014; 29 Suppl 4: iv15-25.
3. Torres VE, Harris PC, Pirson Y. Autosomal dominant polycystic kidney disease. Lancet 2007; 369:1287-301.
4. Martinez-Vea A. Echocardiographic evaluation in patients with autosomal dominant polycystic kidney disease and end stage renal disease. Am J Kidney Dis 1999; 34(2):264-72.
5. Gabow PA. Autosomal dominant polycystic kidney disease-more than just a renal disease. Am J Kidney Dis 1990;14:403-13
6. Rajapurkar MM, John GT, Kirpalani AL, et al. What do we know about chronic kidney disease in India: First report of the Indian CKD registry? BMC Nephrol 2012; 13:10.
7. Pei Y, Obaji J, Dupuis A, et al. Unified criteria for ultrasonographic diagnosis of ADPKD. J Am Soc Nephrol 2009; 20:205-12.
8. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. Am J Kidney Dis 2002; 39 2 Suppl 1:S1-266.
9. Thong KM, Ong AC. The natural history of autosomal dominant polycystic kidney disease: 30-year experience from a single centre. QJM2013; 106:639-46.
10. Nagao S, Nishii K, Katsuyama M, et al. Increased water intake decreases progression of polycystic kidney disease in the PCK rat. J Am Soc Nephrol 2006; 17:2220-7.
11. Baishya R, Dhawan DR, Kurien A, Ganpule A, Sabnis RB, Desai MR. Management of nephrolithiasis in autosomal dominant polycystic kidney disease - A single center experience. Urol Ann 2012; 4:29-33.
12. Sallee M, Rafat C, Zahar JR, Paulmier B, Grunfeld JP, Knebelmann B, Fakhouri F. Cyst Infections in Patients with Autosomal Dominant Polycystic Kidney Disease. Clin J Am Soc Nephrol. 2009; 4: 1183-1189.
13. Patch C, Charlton J, Roderick PJ, Gulliford MC. Use of antihypertensive medications and mortality of patients with autosomal dominant polycystic kidney disease: A population-based study. Am J Kidney Dis 2011; 57:856-62.
14. 14. Hossack KF, et al. Echocardiographic findings in autosomal dominant polycystic kidney disease. N. Engl. J. Med. 1988; 319:907–91.