Original Article

Clinical Spectrum of Autosomal Dominant Polycystic Kidney Disease (ADPKD)

1. Abdul Kareem Zarkoon 2. M. Saleem Khan Barrech 3. Zahir Khan Mandokhail 4. Azimullah Asif Jah Gorya

1. Assoc. Prof. of Nephrology 2. Assoc. Prof. of Neurology 3. Assoc. Prof. of Neurology 4. Incharge PMRC, Bolan Medical College Quetta.

ABSTRACT

Objective: To evaluate the clinical spectrum of autosomal dominant polycystic kidney disease (ADPKD).

Design of study: Hospital base perspective and retrospective study.

Place and duration of study: This study was conducted in Department of Nephrology Sandeman, Provincial Hospital Quetta, from Nov. 2008 to Dec. 2010.

Patients and Methods: In this study, 50 patients were taken with autosomal dominant polycystic kidney disease diagnosed by abdominal ultrasonography which were evaluated for their clinical spectrum by symptoms, clinical examination, ultrasonography, urine detailed report, urea, creatinine, 24 hours urinary creatinine and also evaluate for the extra-renal manifestation by abdominal utrasonography, gastrointestinal endoscopy and computed tomography (C.T Scan) of brain.

Key Words: Polycystic kidney, hypertension, haematuria, UTI, flank pain, hepatic cyst, diverticular disease

INTRODUCTION

Autosomal dominant polycystic kidney disease is defined genetically by its dominant inheritance and pathologically by cystic dilatation of nephrons. ADPKD is world wide distribution, its exact incidence in Pakistan is not known but seen quite frequently. Most of the cases of ADPKD became clinically apparent after the age of40 years but may present at the age of 8-80 years. The diagnosis of the ADPKD is usually made during evaluation of the patient for abdominal pain or flank pain, haematuria or hypertension. Less frequent patient may present with sign and symptoms of urinary tract infection or renal insufficiency or aware of abdominal mass or during investigation because of a strong family history. The most frequented highly sensitive method for diagnosing of ADPKD is abdominal ultrasonography which shows bilaterally enlarged kidneys with multiple contiguous cyst of various sizes in the cortex medulla. However computed tomography (C.T Scan) and Magnetic Resonance Imaging (MRI) can be used. The system effected in ADPKD include, besides kidneys are gastrointestinal tract in which hepatic cysts and diverticular disease are most common. In cardiovascular system mitral valve prolapsed and intracranial aneurysm in brain is most common.

MATERIALS AND METHODS

This study includes 50 Cases of ADPKD. Diagnosis of ADPKD was established on detailed history, physical examination and ultrasonography. All 50 patients entered into the study were diagnosed ADPKD, documented by ultrasonography studies as defined by the presence of at least four renal cortical cyst bilaterally[1].

The Diagnosis of ESRF in ADPKD was made on the basis of:

1. Bilateral renal cortical cysts leading to distortion of renal parenchyma on Ultrasound.
2. Creatinine clearance less than 10ml/mint.
3. Serum creatinine more than 10 mg/dl.
4. Gradual progression of renal failure.
5. Exclusion of other conditions causing acute on chronic renal Impairment e.g., sepsis, uncontrolled hypertension, volume depletion and drug induced There was no exclusion criteria. Other initial laboratory workup included complete blood picture, serum urea, creatinine level, serum electrolytes, routine urine examination and liver function test, urine C/S. ECG, Echocardiography and in suspected cases investigate through barium meal to rule out diverticular disease. C.T. Scan of the brain was also done in a patient with a family history of CVA. All the cases were assessed by neurologist. The findings of history, physical examination, extra-renal manifestation and other related laboratory work up were recorded on a comprehensive Performa especially designed for this study. Majority of the patients were followed up for up to more than six month.28 patients are still visiting our OPD. 10 patients were kept on .maintenance HD during 2 years period. Four of them died because of other complications related to ESRD. transplant was not done in any patient because of restricted hospital policy, only for live related donor.

RESULTS

In our study 50 cases of ADPKD were entered. They were between 30-70years of ages with a mean age of 44 years.32 were Male and 18 were female. Majority of ADPKD patients 38 (76%) were having Impaired renal function and of which 21(42%) has reached end Stage renal failure and remaining 17 (34%) patients were having chronic renal failure but not reached the ESRD. 12 patients (24%) were having normal function. Two Commonest clinical findings were flank pain in 22 cases (44%), Gross haematuria was present in 11 cases (22%) and microscopic haematuria was present in 17 cases (34%) so the overall case of haematuria were 28 (56%). urinary tract infection were found in12 cases (24%). The most common clinical finding was hypertension and in 35 cases (70%).Palpable flank masses were found in 13cases (26%). Polycythemia was noted in 6 cases (12%).

Renal calculi were detected in 16 cases (32%). Hepatic cyst was the commonest extra-renal manifestation of ADPKD and were found in 19 cases (38%). Intestine diverticular were detected in11 cases (22%) and mitral valve prolapsed in 10 cases (20%).

DISCUSSION

ADPKD is a disorder characterized by remarkable cysts formation with in the Kidney. It is one of the most common human genetic diseases[2]. It is estimated that about 8-10 % of the patients in the dialysis population belongs to ADPKD[3]. In this study total 50 cases of ADPKD were studied for their clinical spectrum and has been observed that the disease is more common in male (32 cases) as compared to females (18cases) where according to previous report.[4] There is no sex differentiation. It is not known the exact explanation of the higher incidence of ADPKD in males our study but it is probably related to the fact that our society is male dominated and opportunities to seek medical advice as compared to female. In onset of disease, presentation is almost parallel to the previous studies done regarding the age. It has been observed that majority of patient (42) out of total 50 cases were between the age of 40 – 70 years with the maximum numbers (24) who presented with the disease in the 4th decade. In our study we were only able to get strong evidence of family history of ADPKD in 18 cases (36%). We were not able to find familial history of ADPKD in 32 (64%) cases after through interrogation with their families. These are quite significant numbers and explain the fact that most of the families do not know the cause of death of their immediate ancestors. In the western literature the incidence of positive family history is about more than 60%.[5] Another important factor regarding the higher incidence of positive family history of ADPKD in western society is related to the better health care delivery system to the common people. Whereas in the developing countries like Pakistan, the health care system is very poor and there is no facility of screening of the families with such a common genetic disease. In our study 21 cases (42%) had end stage renal disease (ESRD) while 17 cases (34%) showed impaired renal function manageable by conservative treatment. Out of 50 ADPKD patients only 12 cases (24%) were of normal renal functions manageable by conservative treatment. The number of ESRF patient in our study is higher as compared to 25%[5.] This possibly due to delayed diagnosis and delay in seeking medical advice. For the purpose of description of all 50 patients are divided into two groups according to the age of patient at the time of presentation. There were 32 patients who are less than 50 years age, only 9 patients (28%) presented with ESRF. In second group, there were 19 patients with more than 50 years of age, 12 cases (67%) having ESRF. We also observed nearly the same incidence of CRF (manageable conservatively) age wise. These result showed that increased age is major risk factor for ESRF in ADPKD[5]. The incidence of ESRF is 50% between 50 and 60 years of age and 75% by the age of 70 years. Flank pain was the commonest presenting symptom of ADPKD in our study. It was present in 22 cases (44%) for which they came to the hospital to see medical advice. There are conflicting reports regarding the commonest presentation of ADPKD in the western literature. In a study showed the incidence of flank pain in 30% while it is 50-60% as reported[6,7]. The second most common presentation of ADPKD was urinary Tract Infection (UTI) and it is seen in 12 cases (24%) in the study. A study reported 19% incidence of UTI in ADPKD[6]. Gross haematuria was the third commonest presenting feature in ADPKD patients in the study. It was the presenting feature in 11 cases (22%). A study reported 15-20% incidence of gross haematuria[7]. Hypertension is commonest occurrence in ADPKD patients. It is noticed in 35 cases (70%). There were 17 cases with impaired renal function but not reached the ESRF out of which 18 (85%) were having hypertension. There were 17 cases with impaired renal function but not reached the ESRF, 12(70%) have had hypertension where as there were 12 cases with normal renal function out of which 5(41%) were found hypertensive. 50-70% incidence of hypertension that occurs in early course of ADPKD[8]. Cyst enlargement causing bilateral renal ischemia and subsequent release of rennin is proposed in this study is the cause of hypertension in ADPKD patients. Our present results of hypertensive population in ADPKD patient also show nearly parallel incidence of hypertension as in above mentioned studies[9, 10, 11]. In our study it also appears that hypertension is an early event in natural history of ADPKD. Renal calculi has been reported in 16(32%) cases associated with ADPKD. In a study, reported renal calculi in 34% of

the cases[6]. Palpable renal masses were found at the time of presentation in 13(26%) in our study. It is higher as compared to previous studies by Delaney in which he reported palpable renal masses in 15% of the cases. The higher incidence in our study is possibly due to delay in the referral of the patients, as the most of the patients were presented in very advanced renal disease. Polycythemia was associated with ADPKD in 6(12%) in our study. It is observed in non-azomatic patients on dialysis than other dialyzed patients, reflecting the presence of higher level of erythropoietin. Hepatic cysts were found to be associated with ADPKD in total 19(38%) cases out of which 13(26%) patients who were having hepatic cyst (2 patients also had pancreatic cyst) were more than 50 years age, being extremely uncommon before the age of 30 years. Although there were sizeable structure involvement of the liver, did not show abnormal liver function test. According to a study, the increase incidence of hepatic cysts with the increasing age[7]. The principle non-cystic gastrointestinal manifestation in our study was colonic diverticular. It is reported in 11(22%) of cases. None of the patients in our study had colonic Perforation, although it has been reported in few cases[12]. In the western literature incidence of diverticular disease in ADPKD patients is reported 83% of patient on heamodialysis. The lower incidence in our study is due to the fact that we had performed barium studies only selected symptomatic cases. Mitral valve prolapsed (MVP) was found to be associated in 10 cases(20%) in our study, which near to the prospective studies[13] in which they reported 26% frequency of MVP in ADPKD, as compared with frequency of 20% in control population, palpitation and non-exertional chest pain were the main symptoms in our patients of mitral valve prolapsed. One of the most devastating extra-renal manifestation is intra-cranial secular aneurysm (ICA), which has not been observed in our study. The reason of not finding ICA is that we have not performed C.T or MRI in all our cases studied. The exact frequency of ICA varies from (0-41%)[14]. There is three recent American prospective studies, one found no aneurysm in 96 patient on either C.T Scan or MRI studies[10]. The second found aneurysms in 4 of 92 patients, 3 of whom had multiple aneurysms. This study use C.T scan with 2mm cuts in the axial and corneal planes, angiography, or both[16]. The third study used magnetic resonance angiography and detected aneurysms in 9 of 85 asymptomatic patients with ADPKD[17].

CONCLUSION

Autosomal Dominant Polycystic Kidney Disease (ADPKD) is the one of the common hereditary disorders. Our experience in this study confirmed that the ADPKD is one of the important causes of ESRD in our country. The most common findings were hypertension, flank pain and heamaturia. Large number of patient with ADPKD presented with end stage renal failure which reflects a delay in diagnosing this disease. About half of our total patients at the time of presentation were more than 40 years of age. We have also observed a higher incidence in males. In one third of the cases there was a strong evidence of family history, while remaining two third of the patients were not able to document family history of ADPKD. The most common extra-renal manifestation were hepatic cysts, colonic diverticular and Mitral Valve Prolapse in decreasing order. There is no published local data available regarding this common hereditary disorder to help us to compare the clinical spectrum of this disorder. In this study we have observed that Ultrasonography is a valuable diagnostic tool ADPKD and that a relationship exists between structural and function abnormalities suggesting a pathogenic role of cysts in the development of signs and symptoms. These observations provide important counseling information for physicians caring for these patients, and they enable investigators to develop criteria upon which to base future interventional studies.

RECOMMEDATIONS

On the basis of our experience in ADPKD, our recommendation for patients with this disease are:

1.Blood pressure should be closely and regularly monitored and it should be maintained as normal as possible.
2. Yearly renal function test in non-azotemic patients and quarterly in Azomatic patients.
3. UTI should be treated with appropriate antibiotics.
4. Instrumentation of urinary tract should be avoided.
5. For heamaturia bed rest, hydration and pain control will improve the symptom within a week.
6. Avoid strenuous physical exercise or trauma.
7. Screening of family members.
8. Counseling for family planning.

The risk of transfer of ADPKD gene to fetus should be explained to the parents. If the facilities of gene linkage techniques are available then either amniocentesis chronic villous sampling can be used for DNA analysis. In fetus is fond with defected gene then the parents should be informed and the choice to terminate the pregnancy should be discussed or another option although practically difficult in our society would be to avoid conception and to consider an adopted child.

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Address for Corresponding Author:
Abdul Kareem Zarkoon,
Assoc. Prof. of Nephrology,
Bolan Medical College Quetta.