Original Article

# Clinical manifestations, imaging findings and laboratory abnormalities in 51 patients with autosomal dominant polycystic kidney disease: Experience at Tirupati, South India

K. M. Bhargav[1], B. Siddhartha Kumar[1], Alladi Mohan[1], L. R. Aramadhaka[1], B. Manoj Prajwal[1], D. Prabath Kumar[1], B. Vijayalakshmi Devi[2], V. Sivakumar[3]

Departments of [1]Medicine, [2]Radiodiagnosis and [3]Nephrology, Sri Venkateswara Institute of Medical Sciences, Tirupati, Andhra Pradesh, India

## Abstract

**Background:** Autosomal dominant polycystic kidney disease (ADPKD) is an important cause of renal failure. Sparse recent data are available on clinical presentation ADPKD from India.

**Methods:** We retrospectively studied the clinical presentation, imaging findings and laboratory abnormalities in 51 patients diagnosed to have ADPKD at our tertiary care teaching hospital at Tirupati, South India.

**Results:** Their mean age at presentation was 49.1± 13.2 years; there were 32 (63%) males. Salient renal clinical manifestations at initial presentation included abdominal pain (47%); fever (35%), shortness of breath (33%); palpable mass per abdomen (25%); burning micturition (20%); haematuria (10%); and renal/ureteric caliculi (12%). Other manifestations were headache (21%); altered sensorium (12%); intracerebral bleed (8%) and chest pain (8%). Family history of ADPKD was present in 13 (26%) patients. On imaging studies kidneys were normal sized in 39%, enlarged in 59% and small sized in one patient; co-existent liver cysts were found in 12 patients. Hypertension ($n$ = 20, 40%); chronic kidney disease (CKD) ($n$ = 36, 71%) were evident at initial presentation. Other associated co-morbid conditions were type 2 diabetes mellitus ($n$ = 6); Marfan's syndrome with mitral valve prolapsed and renal cell carcinoma (one patient each).

**Conclusions:** In Tirupati, South India, ADPKD most commonly presented in fourth or fifth decade of life. Males were affected more frequently than females. Presence of CKD, hypertension at the time of inital diagnosis suggests that ADPKD is diagnosed late in the course of the disease. A high index of suspicion, specific diagnostic work-up including abdominal ultrasonography is required to diagnose ADPKD.

**Keywords:** Autosomal dominant polycystic kidney disease, diagnosis, India

**Address for correspondence:** Dr K. M. Bhargav, Assistant Professor, Department of Medicine, Sri Venkateswara Institute of Medical Sciences, Tirupati - 517 507, Andhra Pradesh, India.
E-mail: bhargavkm2002@gmail.com

## INTRODUCTION

Autosomal dominant polycystic kidney disease (ADPKD) is a genetic disease affecting the kidney and is one of the leading causes of kidney disease requiring dialysis. The cystic diseases of the kidney may be broadly classified into ADPKD, nephronopthisis and medullary cystic diseases. Polycystic kidney disease is inherited predominantly in

| Access this article online | |
|---|---|
| Quick Response Code: | Website: www.jcsr.co.in |
| | DOI: 10.4103/JCSR.JCSR_28_18 |



**How to cite this article:** Bhargav KM, Kumar BS, Mohan A, Aramadhaka LR, Prajwal BM, Kumar DP, *et al*. Clinical manifestations, imaging findings and laboratory abnormalities in 51 patients with autosomal dominant polycystic kidney disease: Experience at Tirupati, South India. J Clin Sci Res 2018;7:165-9.

two forms: autosomal dominant and autosomal recessive. ADPKD is a common genetic disease affecting the renal system.[1] Rarely, it occurs in an individual sporadically. The mechanism for the sporadic presentation is not known. ADPKD is characterised by fluid-filled sacs called cysts, occurring predominantly in the kidney, but also occurs in the liver, brain, blood vessels and organs in the decreasing order.

The incidence of ADPKD worldwide is not known, and it is 2.6% according to a study conducted on chronic kidney disease (CKD) in India.[2] According to a US study, it is 1.7 in symptomatic patients with family history, while the predicted incidence is 2.75 based on the autopsy.[3] The disease usually occurs between the third and sixth decade of the life. However, it may occur in both the extremities of life. There is no gender predilection. Hypertension is the most common presentation of ADPKD, followed by proteinuria.[4] Many extrarenal complications occur in these patients such as hepatic cysts, pancreatic cysts, berry aneurysms and others.

It is a ciliopathy and transmitted in the individuals as monogenic disease. Two loci polycystic kidney disease (PKD) 1 and PKD2 are affected in the disease. The patients with PKD1 allele progress to end-stage renal disease (ESRD) earlier than the patients bearing PKD2 gene. The allele PKD1 is responsible for 85% of the cases of ADPKD.[5] A sound knowledge about the clinical features, genetics, radiological features and management of ADPKD is of critical importance as it accounts for a major portion of the end-stage renal failure.

## MATERIAL AND METHODS

We retrospectively studied the clinical presentation, various imaging findings and laboratory abnormalities in patients diagnosed to have ADPKD ($n$ = 51) at the Medicine, Nephrology Outpatient service, Medicine and Nephrology Wards at Sri Venkateswara Institute of Medical Sciences, Tirupati, during the period 2009–2018.

The study was approved by the Institutional Ethics Committee. Written informed consent was obtained from all the study participants. In all patients, a detailed history was obtained and a thorough physical examination was carried out. Laboratory evaluation included complete haemogram, serum biochemistry including renal function and liver function tests and electrocardiogram. All patients had undergone abdominal ultrasonography; findings regarding renal involvement, associated hepatic involvement, were documented in detail. Computed tomography of the abdomen and head, diagnostic workup for acute undifferentiated febrile illness and echocardiography were done where appropriate.

On abdominal ultrasonography, specifically, all patients were evaluated for the presence of cysts in one or both kidneys, their number and location. The diagnosis of ADPKD was made as per the criteria described by Ravine *et al*.:[6] (i) the presence of at least two renal cysts (unilateral or bilateral) in individuals at risk and younger than 30 years, (ii) in individuals aged 30–59 years-at least two cysts in each kidney and (iii) in individuals aged 60 years and above the presence of at least four cysts in each kidney.

All patients received medical treatment for co-morbid conditions, such as diabetes mellitus and hypertension; patients with CKD received conservative management. All patients were followed up in Medicine and Nephrology Outpatient Service.

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 analysis

Data were recorded in a structured pro forma and were managed with Microsoft Excel 2010 (Microsoft Corp, Redmond, USA). Continuous variables were summarised as mean ± standard deviation or median (interquartile range) as appropriate. Categorical variables were summarised as percentages. The statistical software IBM SPSS Statistics Version 20 (IBM Corp, Somers, USA) was used for statistical analysis.

## RESULTS

The mean age of the patients at presentation was 49.1 ± 13.2 years; there were 32 (63%) males. Age group-wise distribution of patients was as follows: 30–40 years ($n$ = 15); 40–50 years ($n$ = 18); 50–60 years ($n$ = 10) and more than 60 years ($n$ = 8). Documented family history of ADPKD was present in 13 (26%) patients.

Salient renal manifestations at initial presentation included abdominal pain ($n$ = 24, 47%), fever ($n$ = 18, 35%), shortness of breath ($n$ = 17, 33%), burning micturition ($n$ = 10, 20%) and haematuria 5 (10%). A palpable mass per abdomen was evident in 13 (25%) patients. Major non-renal clinical manifestations included headache ($n$ = 11, 21%), altered sensorium ($n$ = 6, 12%), intracerebral bleed ($n$ = 4; 8%) and chest pain ($n$ = 4; 8%). These patients had presented with acute onset of symptoms to the emergency room and

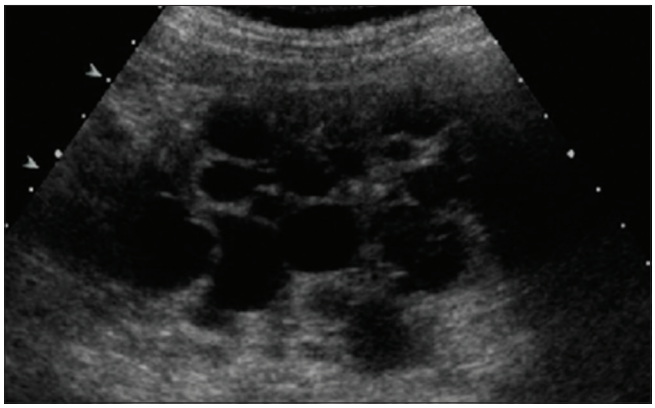

**Figure 1:** Ultrasonography of the abdomen showing polycystic kidney disease

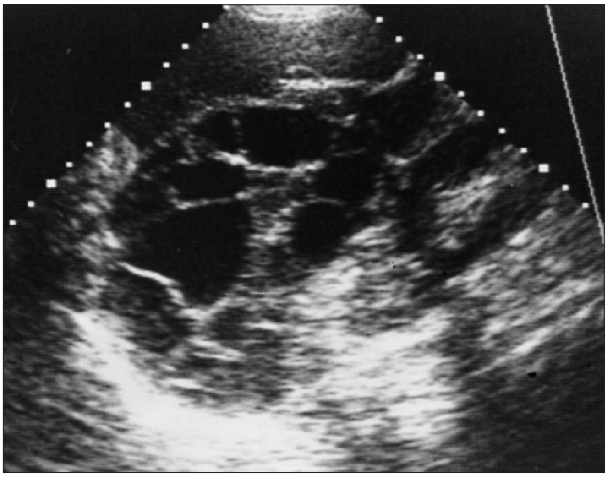

**Figure 3:** Ultrasonography showing polycystic liver disease

**Table 1: Clinical presentation in 51 patients with autosomal dominant polycystic kidney disease**

| | *n* (%) |
|---|---|
| Chronic symptoms | |
| Abdominal pain | 24 (47) |
| Fever | 18 (35) |
| Shortness of breath | 17 (33) |
| Burning micturition | 10 (20) |
| Haematuria | 5 (10) |
| Acute symptoms | |
| Headache | 11 (21) |
| Altered sensorium | 6 (12) |
| Intracerebral bleed | 4 (8) |
| Chest pain | 4 (8) |

diagnostic workup established the diagnosis of ADPKD in these. These details are summarised in Table 1.

Imaging studies [Figures 1 and 2] revealed that the kidneys were normal sized in 20 (39%) patients. The kidneys were enlarged in 30 patients (59%) and small sized in 1 (2%) patient. Among patients with enlarged kidneys ($n$ = 30), the right kidney was enlarged in 25 (83%), left kidney was enlarged in 30 (100%) and both kidneys were enlarged

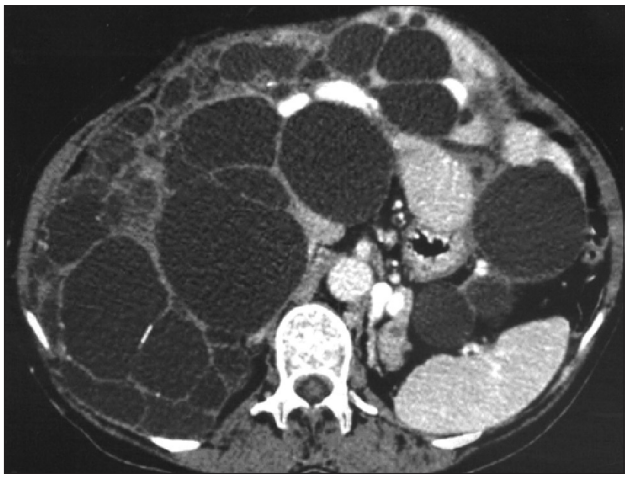

**Figure 2:** Computed tomography scan abdomen showing polycystic kidneys

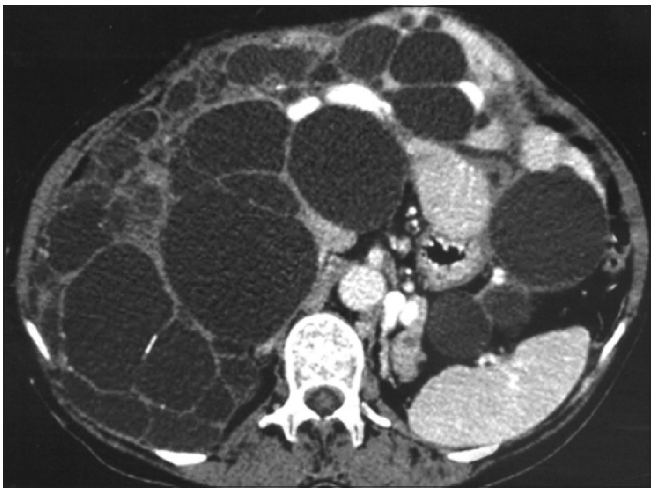

**Figure 4:** Computed tomography showing polycystic liver disease

in 25 (83%) patients. Renal/ureteric calculi were seen in 6 (12%) patients. Co-existent liver cysts were found in 12 (24%) patients [Figures 3 and 4].

Anaemia occurred in 26 of the 48 patients tested (54%); none of the patients had polycythaemia. CKD was present in 36 (71%) patients at the time of initial diagnosis. Type 2 diabetes mellitus was an important co-morbid illness that was observed in 6 (12%) patients; hypertension was evident in 20 (40%). Other associated conditions included Marfan's syndrome with mitral valve prolapse and renal cell carcinoma seen in one patient each. The patient with Marfan's syndrome had presented to the outpatient service for evaluation of breathlessness. Clinical examination confirmed the presence of Marfan's syndrome, clinical examination and echocardiography confirmed the diagnosis of mitral valve prolapse in this patient. Diagnostic workup in the patient with renal cell carcinoma established the diagnosis of ADPKD.

## DISCUSSION

The ADPKD is the most prevalent hereditary disease affecting the renal system in the world as well as India, and there are only limited data available about ADPKD in the Indian subcontinent, particularly in Southern India. Hence, to know the incidence, clinical features, extrarenal manifestations and radiological features, the present study was conducted. In the cystic disease of the kidney, ADPKD is the most common one and it is characterised by distribution of cysts entirely in both the cortex and medulla.

The average age of ADPKD presentation in the present study was 49 ± 13.2 years. In other studies, it was 50 ± 20[7] and 45.8 ± 14.5 years.[8] All the three studies showed a similar trend in the average age of presentation. Hence, it is evident that the onset of ADPKD globally is around 45 years.

In the present study of 51 patients of ADPKD, 32 were male patients which account for 63%, and it is in concordance with the study done by Vikrant and Parashar,[8] where it was 60.3% and Rabbani *et al*.[9] found a ratio of 5:2 male to female in a Pakistan-based study in 2008. However, in a study conducted by the Australian research group on CKD, there was no sex predilection.[10] Hence, there is a need to do continuation studies on ADPKD worldwide to know whether there is any gender difference with geographical variation. Rabbani *et al*. reported 44.6% of patients of ADPKD had a family history.[9] The family history of ADPKD was present in 43.9 patients in the study conducted by Kumar *et al*.[7] However, in the present study, it was only 26%. The difference may be due to the small size of the population in the said three studies.

Hypertension manifests in the beginning course of the disease in ADPKD;[11] 40% of the patients in the present study had hypertension; while in other studies, it was found to be 78%[4] and 67.9%.[9]

There are some co-morbidities that are common in ADPKD patients, one of the co-morbidities is diabetes. Type 2 diabetes mellitus was present in 12% of the patients in the present study, on the other hand, it was 12.5% in another study.[9] Going by the prevalence of diabetes mellitus in India (7.5%),[12] a higher proportion of patients with ADPKD seems to have diabetes mellitus. This issue merits further study.

Abdominal pain is a common presenting symptom by the ADPKD patients. Abdominal pain was the major manifestation in the current study with 47% of the individuals suffering. In another study,[7] 53.7% patients had abdominal pain. Causes of pain are multiple and can include consequences related to cysts – cyst enlargement, cyst rupture and cyst infection. Low back pain, flank and abdominal pain are known symptoms as a result of cyst growth and proliferation in ADPKD patients.

ADPKD that patients develop hypertension early in the disease leading to ESRD.[13] CKD was present in 36 (71%) patients in the present study, whereas in another study,[14] it was 28%. There is wide variation in the above studies probably due to the fact that patients were not thoroughly followed up in the group.

Headache may be due to uncontrolled hypertension in these patients. Headache was the dominant non-renal symptom occurring in 21% of the patients suffering from ADPKD in the present study. In another study,[7] headache was present in that is 18 of the 51 patients (43.9%).

Renal stones were present in 6 of the 51 (14.6%) patients in the present study which is similar to 25.6%[15] and 20%[16] reported in other studies. However, a higher figure (38.9%) was observed in another study; the difference in the studies may be due to the variation in the choice of investigation for diagnosing renal calculi.

Of the myriad of ADPKD manifestations, cardiovascular problems occur in a significant amount of patients such as left ventricular hypertrophy and mitral valve prolapsed. The murmur of mitral valve prolapse was found in 2 out of 51 (4.9%) patients which was confirmed on echocardiography in a study.[7] We observed mitral valve prolapse in 2% of the patients. In another study,[17] 26% of patients were found to have mitral valve prolapse. Whether these variations reflect the true epidemiology of the condition requires further study.

Coexistence of liver cysts along with the renal cysts is a well-known entity. The liver is diffusely cystic in 20%–50% of patients with ADPKD.[18] The liver cysts were coexisting in 24.3% of the patients in our study, which is much less compared to 83%[19] and 75% reported in other studies.[19] Cysts in the kidney substance frequently rupture and result in haematuria. Haematuria has been described in 64% of the patients with ADPKD urinalysis.[20] In comparison, in the present study, only 10% of patients had haematuria, while other studies showed a higher incidence of haematuria with 18%[14] and 21%.[8] The discrepancy in the incidence may be due to difference in the investigation method and size of the study population. Further, the continuation of the present study is required to know the exact incidence.

There is an increased risk of malignancy in ADPKD individuals. In a retrospective study on a histopathological registry, the prevalence of ADPKD is 5%,[21] whereas in the present study, it is 1 out of 51 patients.

One of the major complications of kidney disease is anaemia. There are various reasons for the development of anaemia in CKD patients, such as lack of erythropoietin, uremic inhibitors of erythropoiesis, decreased absorption of iron and others.[22] In a prospective observational study conducted in a tertiary care centre in Kerala in India, the prevalence of anaemia is 90.39% in CKD patients.[23] In the present study, out of the 48 patients tested, 26 had anaemia. Other studies, however, quoted lesser incidence of anaemia.[24] Further, the study is required to clarify the issue.

Association between Marfan's syndrome and ADPKD is seldom reported in the literature. However, in the present study, there was one case of Marfan's syndrome out of 51 patients. This issue merits further study.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

## REFERENCES

1. Mallett A, Patel C, Salisbury A, Wang Z, Healy H, Hoy W, *et al*. The prevalence and epidemiology of genetic renal disease amongst adults with chronic kidney disease in Australia. Orphanet J Rare Dis 2014;9:98.
2. Rajapurkar MM, John GT, Kirpalani AL, Abraham G, Agarwal SK, Almeida AF, *et al*. What do we know about chronic kidney disease in India: First report of the Indian CKD registry. BMC Nephrol 2012;13:10.
3. Christopher MB, Matter S, Chawla A, Nellesen D, Rossetti S, Benjamin G. Burden of autosomal dominant polycystic kidney disease: Systematic literature review. Am J Pharm Benefits 2015;7:e27-36.
4. Ratnam S, Nauli SM. Hypertension in autosomal dominant polycystic kidney disease: A clinical and basic science perspective. Int J Nephrol Urol 2010;2:294-308.
5. Igarashi P, Somlo S. Genetics and pathogenesis of polycystic kidney disease. J Am Soc Nephrol 2002;13:2384-98.
6. Ravine D, Gibson RN, Walker RG, Sheffield LJ, Kincaid-Smith P, Danks DM, *et al*. Evaluation of ultrasonographic diagnostic criteria for autosomal dominant polycystic kidney disease 1. Lancet 1994;343:824-7.
7. Kumar A, Zaffar K, Sajad H, Kumar BS, Hamid S, Akhter M. A prospective study on clinical profile of autosomal dominant polycystic kidney disease (ADPKD) in Jammu for a period of 1 year. Open J Nephrol 2012;2:123-35.
8. Vikrant S, Parashar A. Autosomal dominant polycystic kidney disease: Study of clinical characteristics in an Indian population. Saudi J Kidney Dis Transpl 2017;28:115-24.
9. Rabbani MA, Ali SS, Murtaza G, Ahmad B, Maria Q, Siddiqui BK, *et al*. Clinical presentation and outcome of autosomal dominant polycystic kidney disease in Pakistan: A single center experience. J Pak Med Assoc 2008;58:305-9.
10. Ecder T, Schrier RW. Hypertension in autosomal-dominant polycystic kidney disease: Early occurrence and unique aspects. J Am Soc Nephrol 2001;12:194-200.
11. Nunes AC, Milani V, Porsch DB, Rossato LB, Mattos CB, Roisenberg I, *et al*. Frequency and clinical profile of patients with polycystic kidney disease in Southern Brazil. Ren Fail 2008;30:169-73.
12. Ramachandran A. Epidemiology of diabetes in India – Three decades of research. J Assoc Physicians India 2005;53:34-8.
13. Gabow PA, Johnson AM, Kaehny WD, Kimberling WJ, Lezotte DC, Duley IT, *et al*. Factors affecting the progression of renal disease in autosomal-dominant polycystic kidney disease. Kidney Int 1992;41:1311-9.
14. Syed T, Thakuriya R, Rishi JP. The profile of autosomal dominant polycystic kidney disease (ADPKD) patients in rural areas of North India. J Sci Innov Res 2016;5:119-21.
15. Nishiura JL, Neves RF, Eloi SR, Cintra SM, Ajzen SA, Heilberg IP, *et al*. Evaluation of nephrolithiasis in autosomal dominant polycystic kidney disease patients. Clin J Am Soc Nephrol 2009;4:838-44.
16. Segal AJ, Spataro RF, Barbaric ZL. Adult polycystic kidney disease: A review of 100 cases. J Urol 1977;118:711-3.
17. Hossack KF, Leddy CL, Johnson AM, Schrier RW, Gabow PA. Echocardiographic findings in autosomal dominant polycystic kidney disease. N Engl J Med 1988;319:907-12.
18. Chauveau D, Fakhouri F, Grünfeld JP. Liver involvement in autosomal-dominant polycystic kidney disease: Therapeutic dilemma. J Am Soc Nephrol 2000;11:1767-75.
19. Bae KT, Zhu F, Chapman AB, Torres VE, Grantham JJ, Guay-Woodford LM, *et al*. Magnetic resonance imaging evaluation of hepatic cysts in early autosomal-dominant polycystic kidney disease: The Consortium for Radiologic Imaging Studies of Polycystic Kidney Disease Cohort. Clin J Am Soc Nephrol 2006;1:64-9.
20. Delaney VB, Adler S, Bruns FJ, Licinia M, Segel DP, Fraley DS, *et al*. Autosomal dominant polycystic kidney disease: Presentation, complications, and prognosis. Am J Kidney Dis 1985;5:104-11.
21. Jilg CA, Drendel V, Bacher J, Pisarski P, Neeff H, Drognitz O, *et al*. Autosomal dominant polycystic kidney disease: Prevalence of renal neoplasias in surgical kidney specimens. Nephron Clin Pract 2013;123:13-21.
22. Babitt JL, Lin HY. Mechanisms of anemia in CKD. J Am Soc Nephrol 2012;23:1631-4.
23. Sathyan S, Sunil G, Poornima V. Prevalence of anemia and cardiovascular diseases in chronic kidney disease patients: A single tertiary care centre study. Int J Adv Med 2017;4:247-51.
24. Mao Z, Xie G, Ong AC. Metabolic abnormalities in autosomal dominant polycystic kidney disease. Nephrol Dial Transplant 2015;30:197-203.