Eastern Heartland Journal of Medicine
EHJMed 2021;1:105-110
VOL.2.No.1 ISSN -2734-2875

PROFILE OF SUBJECTS WITH ADULT AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE IN A TERTIARY HOSPITAL IN SOUTH EASTERNNIGERIA.

Anyanwu A.C[1], Anaekwe A.N[2], Ngoka S[1], Osineke S.O[1], Oputa R.N[1]

1.Department of Internal Medicine, Federal Medical Center, Owerri
2.Department of Family Medicine, Federal Medical Center, Owerri
Correspondence: Dr Anyanwu A.C
Email: chattony2000@yahoo.com

ABSTRACT

INTRODUCTION

Autosomal dominant polycystic kidney disease (ADPKD) is a systemic disease that affects 1 in 2,000 individuals and is the most common hereditary kidney disease.[1] ADPKD is equally represented among ethnicities and is more common than sickle cell disease, cystic fibrosis, Down syndrome, hemophilia and Huntington disease combined.[2] It is completely penetrant and is characterized by the development of renal cysts and increasing total kidney volume (TKV), leading to urinary concentrating defects, hypertension, polyuria, nocturia, pain, nephrolithiasis, haematuria, infections and progressive loss of kidney function.[2]However, symptoms at disease presentation and the disease course are both highly variable. Patients with ADPKD, on average, progress to end-stage renal disease (ESRD) by the age of 60 years, with 70% of patients requiring renal replacement therapy (RRT) by the age of 70 years. Reducing the incidence of complications related to cyst burden (for example, hypertension, pain, haematuria, infection and nephrolithiasis) or delaying progressive loss of kidney function or the onset of ESRD provides significant improvements in quality of life.[3,4]

Data from randomized controlled trials and observational cohort studies are beginning to affect treatment decisions in an evidence-based fashion.[5-8] As such, the goal of disease management for patients with ADPKD has shifted towards creating meaningful changes in clinical outcomes, and the potential to provide personalized care strategies to delay the onset of ESRD.

ADPKD can have a wide range of clinical presentations: severe cases are diagnosed in utero or neonatally, whereas mild cases can go unrecognized until 60–70 years of age and ESRD might be avoided altogether[2].

Collection of a detailed family history is essential for ADPKD diagnosis and to assess the severity of ADPKD. ADPKD is typically diagnosed following an ultrasound scan that reveals numerous renal cysts, kidney enlargement and liver cysts, which are associated with haematuria, abdominal pain and early-onset hypertension. Alternatively, ADPKD can be diagnosed in the absence of symptoms in individuals with a family history of ADPKD, or coincidentally during medical evaluation of unrelated issues. Renal complications, such as hypertension or proteinuria, cyst pain, infection or gross haematuria, especially occurring before 35 years of age, are predictors of increased disease severity and are the major components of the retrospectively developed predicting renal outcomes in ADPKD (PROPKD) prognostic model.[9,10] All patients should be asked about symptoms, including discomfort, nocturia, polydipsia, dyspareunia or early satiety, as they might not volunteer such details, despite the possibility of a substantial adverse effect on quality of life.

SUBJECTS AND METHODS

This study was a prospective descriptive study carried out over a period of 3 years (2014 to 2017)in the Renal unit of the Federal Medical Centre, Owerri (FMC, Owerri), Nigeria. Patients diagnosed with ADPKD were recruited consecutively from the Nephrology clinic and medical wards. Data was also retrieved from the Medical out-patient records. Diagnosis of ADPKD was made by clinical presentations and presence of multiple cysts in the kidneys on abdominal ultrasound scan. Other relevant information sought include:

Eastern Heartland Journal of Medicine
VOL.2.No.1 ISSN -2734-2875

age at diagnosis, history of hypertension, haematuria, abdominal pain and or swelling, nocturia, family history of cystic kidney disease, presence of cysts in other organs such as the pancreas, liver, spleen and estimated glomerular filtration rate (eGFR)
The objectives were to determine the frequency of ADPKD, the clinical presentations and treatment received by the subjects.

RESULT

Out of a total of three hundred and thirteen (313) patients with renal disease seen over a three year period, sixteen (5%) of them had ADPKD. The male to female ratio of the patients with ADPKD was 1:3, with a mean age of 43.4 +- 11.2 years (range:23 to 60 years).

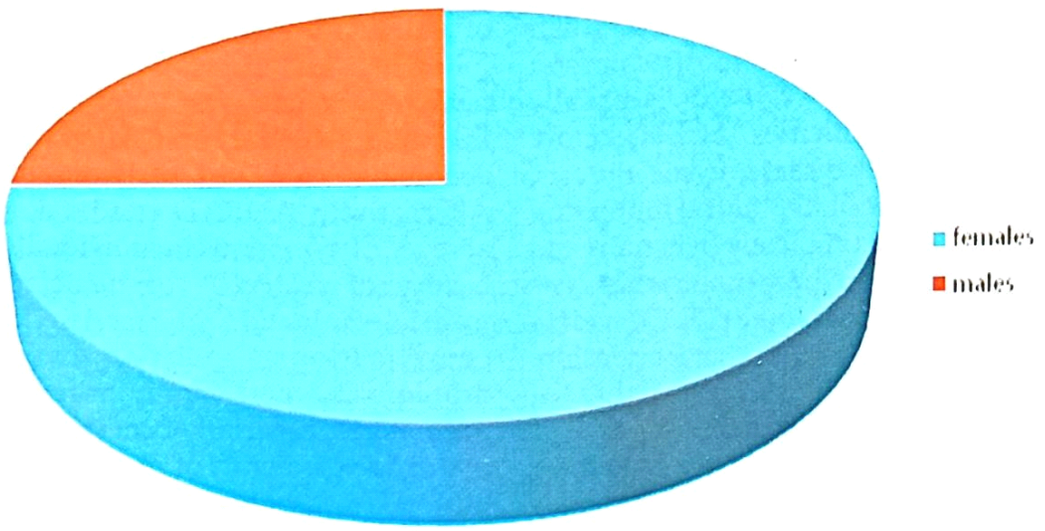

Fig 1: Gender distribution of patients with ADPKD

Table 1: Frequency of co-morbidities

Co-morbidities	Number	Percentage (%)
Hypertension	9	56.3
Diabetes Mellitus	1	8.3

Table 2: Clinical features of study participants

Clinical features	Number	Percentage (%)
Headache	3	18.8
Abdominal swelling	7	43.8
Abdominal/ loin pain	11	68.8
Body swelling	5	31.3
Easy fatigability	4	25.0
Haematuria	3	18.8
Anaemia	4	25.0
Uraemic symptoms	6	37.5

Eastern Heartland Journal of Medicine
VOL.2.No.1 ISSN -2734-2875

Table 3: Investigations

Parameters	Mean	Standard Deviation
Hemoglobin	8.9	2.3
Creatinine	4.6	5.1
Urea	81.5	92.5
eGFR	48.7	45.0
LDL	99.3	34.6
HDL	41.0	12.4
TG	116.8	46.1
TC	173.0	24.0

Other investigations

Ultrasound report: Presence of liver cysts – 4 (25%)
Presence of splenic cysts – 1(8.3%)
Urinalysis: Blood – 3+ (18.8%)
Proteinuria – 1+ (8.3%)

Family and social history

Positive family history of ADPKD – 2 (12.5%)
Intake of herbal medications – 5 (31.3%)

Table 4: Treatment

Treatment	Number	Percentage (%)
Dialysis	4	25.0
Antihypertensive	5	31.3
Hematinic	7	43.8
Blood transfusion	2	12.5
Furosemide	4	25.0

DISCUSSION

The mean age of the ADPKD subjects in this study was 43 years. This finding is similar to that reported in previous studies, as stated in a work done by Graham where kidney dysfunction was not clinically apparent until about the age of forty to fifty years.[11]

This study showed a female preponderance of 3:1 which contradicts the study by Tamparo et al which deduced that it equally affects men and women.[12] This disparity may be explained by the fact that women seek medical attention in comparison to their male counterpart in this part of the world.

With regards to the clinical presentation, the prevalent findings among the study subjects were abdominal pain and swelling, uraemic symptoms, body swelling, anaemia, easy fatigability and headache. Patients with ADPKD can be fairly asymptomatic, especially early in the course of disease, but chronic vague abdominal discomfort, early satiety, polyuria, polydipsia and hematuria remain common. Haemorrhage might be the result of trauma, and is a common cause of presentation in affected children and adolescents following contact sports or falls. Acute adverse events, such as gross haematuria, infections, acute pain syndromes and nephrolithiasis, often require medical attention and lead to increased medical resource utilization and hospital visits compared with that of the general population.[13] The initial management of haematuria is reliant on identifying the underlying aetiology, which can include cyst rupture and/or haemorrhage, infection, nephrolithiasis or an underlying malignancy.

Cyst haemorrhage can be asymptomatic and occur with or without gross haematuria, fever and/or pain.[14,15] Isolated haematuria is usually self-limiting and resolves within a week in the absence of specific treatment.[16]The risks and benefits of delaying the use of anticoagulant or antiplatelet therapies should be determined based upon the specific indication. Patients with non-resolving haemorrhages might develop substantial subcapsular or retroperitoneal haematomas or require blood transfusions, haemostatic agents, interventional embolization, or surgical procedures.[1]

A significant proportion of our study subjects were already in ESRD requiring haemodialysis. Previous studies report that most patients with ADPKD progress to ESRD, with majority requiring renal replacement therapy by the age of 70 years.[4]

Majority of the ADPKD subjects in this studywere hypertensives and the mean eGFR corresponded to stage 3 chronic kidney disease. The work done by Chapman et al showed an early onset of hypertension prior to a measurable reduction in eGFR in 60% of patients with ADPKD.[5,17,18,19] The presence, age of onset, and severity of hypertension is associated with increased TKV[5,19,20] and is a risk factor for younger age at onset of ESRD.[9,21] For every 100 ml increase in TKV, the relative risk of development of hypertension increases by 1.4-fold.[22] Treatment of hypertension in patients with ADPKD should include nonpharmacological interventions, such as weight reduction, exercise and dietary salt restriction. Exclusion of additional secondary causes of hypertension, such as primary hyperaldosteronism, pheochromocytoma or obstructive sleep apnoea, should all be considered with clinical suspicion of their existence.[23,24] Inhibition of the RAAS using angiotensin-converting enzyme (ACE) inhibitors is favoured, as well as the use of angiotensin- receptor blockers (ARBs) and β-blockers[25].

In the study, 8.3% had proteinuria. The Kidney Disease Improving Global Outcome (KDIGO) guidelines recommend the annual assessment of albuminuria and proteinuria in all patients with CKD in order to evaluate disease severity, progression and prognosis.[38] This value was higher among patients with ADPKD with a creatinine clearance >60 ml/min that were enrolled in the TEMPO3:4 trial, >50% had moderately increased albuminuria (3–30 mg/mmol or 30–300 mg/g).[7,26,27] Glomerular-range proteinuria (>1 mg per day) is rarely seen in patients with ADPKD and an alternative glomerular- based diagnosis should be sought.[28,29] Direct evidence that reducing albuminuria in ADPKD affects progression to ESRD is not currently available, but we believe that an elevated ACR is a risk factor for progressive disease and should be included in the decision to target lower blood pressures and increase the dose of Renin-Angiotensin-Aldesterone System (RAAS) inhibitors.

CONCLUSION:

ADPKD, from this study has shown greater prevalence among the female gender and individuals within the middle age bracket. The most common clinical features were abdominal swelling and discomfort, haematuria and hypertension.

REFERENCES

1. Suwabe, T. *et al.* Clinical features of cyst infection and haemorrhage in ADPKD; new diagnostic criteria. Clin. Exp. Nephrol. **16**, 892-902(2012).
2. Gabow, P. A., Autosomal dominant polycystic kidney disease. N. Engl. J. Med. **329**, 332-342(1993).
3. Spithoven, E. M. *et al.* Renal replacement therapy for autosomal dominant polycystic kidney disease in Europe. Prevalence and survival – an analysis of data from the ERA-EDTA Registry. Nephrol. Dial. Transplant. **29**, iv 15 – iv 2 (2014).
4. Fernando, M. R. Dent, H. McDonald, S. P. & Rangan, G. K. Incidence and survival of end-stage kidney disease due to polycystic kidney disease in Australia and New Zealand. Popul. Health Metr. **15**, 7 (2017).
5. Chapman, A B. *et al.* Renal structure in early autosomal-dominant polycystic kidney disease (ADPKD). The consortium for radiologic imaging studies of polycystic kidney disease (CRISP) cohort. Kidney Int. **64**, 1035-1045 (2003).
6. Schrier, R. W. *et al.* Blood pressure in early autosomal dominant polycystic kidney disease. N. Engl. J. Med. **371**, 2255-2266 (2014).

7. Torres, V. E. *et al.* Tolvaptan in patients with autosomal dominant polycystic kidney disease. N. Engl. J. Med. **367**, 2407-2418 (2012).
8. Torres, V. E. *et al.* Multicentre, open-label, extension trial to evaluate the long-term efficacy and safety of early versus delayed treatment with tolvaptan in autosomal dominant polycystic kidney disease. The TEMPO 4:4 Trial. Nephrol. Dial. Transplant.
9. Comec-Le Gall, E. *et al.* The PROPKD score: a new algorithm to predict renal survival in autosomal dominant polycystic kidney disease J. Am. Soc. Nephrol. **27**, 942-951 (2016).
10. Schrier, R. W. *et al.* Predictors of autosomal dominant polycystic kidney disease. J. Am. Soc. Nephrol. **25**, 2399-2418 (2014).
11. Harris, P. C. & Torres, V. E. Genetic measurements and signalling pathways in autosomal dominant polycystic kidney disease. J. Clin. Invest. **124**, 2315-2324 (2014).
12. Leonhard, W. N. *et al.* Scattered deletions of PKD1 in kidneys causes a cystic snowball effect and recapitulates polycystic kidney disease. J. Am. Soc. Nephrol. **26**, 1322-1333 (2015).
13. Knight, T. *et al.* Medical resource utilisation and costs associated with autosomal dominant polycystic kidney disease in the USA: a retrospective matched cohort analysis of private insurer data Clinicoecon. Outcomes Res. **7**, 123-132 (2015).
14. Neuville M., Hustinx, R., Jaques, J., Krzesincki, J. M. & Jouret, F. Diagnostic algorithm in the management of acute febrile abdomen in patients with autosomal dominant polycystic kidney disease. PLOS ONE II e0161277 (2016).
15. Hogan, M. C. & Norby, S. M. Evaluation and management of pain in autosomal dominant polycystic kidney disease. Adv. Chron. Kidney Dis. 17 e1-e161 (2010).
16. Chapman, A. B. *et al.* Autosomal dominant polycystic kidney disease.
17. Lantinga-van Leeuwen, I. S. *et al.* Lowering of PKD 1 expression is sufficient to cause polycystic kidney disease in humans. Mol. Genet **13**, 3069-3077 (2004).
18. Chapman, A. B., Stepniakowski, K. & Rahbari-Oskoui, F. Hypertension in autosomal dominant polycystic kidney disease. Adv. Chron. Kidney Dis. **17**, 153-163 (2010).
19. Chapman A. B. & Gabow, P. A. Hypertension in autosomal dominant polycystic kidney disease. Kidney Int. Suppl. **61**, 571-573 (1997).
20. Irazabal, M. V *et al.* Imaging classification of autosomal dominant polycystic kidney disease: a simple model for selecting patients for clinical trials. J. Am. Soc. Nephrol. **26**, 160-172 (2015).
21. Johnson, A. M. & Gabow, P. A. Identification of patients with autosomal dominant polycystic kidney disease at highest risk for end-stage renal disease. J. Am. Soc. Nephrol. **8**, 1560-1567 (1997).
22. Yu, A. S. *et al.* Trajectory of the GFR in autosomal dominant polycystic kidney disease. J. Am. Soc. Nephrol. **27**, abstr., FR-OR006(2016).
23. Hessheimer, A. J., Vidal, D., Valentini, M. & Garcia-Valdecasas. J. C. Pheochromocytoma as a rare cause of arterial hypertension in a patient with autosomal dominant polycystic kidney disease: a diagnostic and therapeutic dilemma Int. J. Surg. Case Rep. **14**, 85-88 (2015).
24. Hoorn, E. J. *et al.* A case of primary aldosteronism revealed after renal transplantation. Nat. Rev. Nephrol. **7**, 55-60 (2011).
25. Rahbari-Oskoui, F. Williams, O. & Chapman, A. Mechanisms and management of hypertension in autosomal dominant polycystic kidney disease. Nephrol. Dial. Transplant. **29**, 29194-2201 (2014).

26. Kidney disease: improving global outcomes (KDIGO) Chronic Kidney Disease Work Group KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int. Suppl. **3**, 1-150 (2013).

27. Gansevoort, R. T., *et al.* Albuminuria and tolvaptan in autosomal dominant polycystic kidney disease: results of the TEMPO 3:4 Trial. Nephrol. Dial. Transplant. **31**, 1887-1894 (2016).

28. Akinbodewa, A. A., Adejumo, O. A., Ogunsemoyin, A. O. Osasan, S. A. & Adefolalu, O. A. Co-existing autosomal dominant polycystic kidney disease and nephrotic syndrome in a Nigerian patient with lupus nephritis. Am. Afr. Med. **15**, 83-86 (2016).

29. Yenigun, E. C., *et al.* Coexistence of autosomal dominant polycystic kidney disease and amyloidosis in a patient with nephrotic-range proteinuria. Iran. J. Kidney Dis. **8**, 243-245 (2014).