Original Article

Clinical Characteristics and Outcome of Patients with Autosomal Dominant Polycystic Kidney Disease at a Teaching Hospital in North Central, Nigeria: Eight Year Review

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ABSTRACT

Autosomal Dominant Polycystic Kidney Disease (ADPKD) is a common inherited cause of End Stage Renal Disease (ESRD). However, there is paucity of information on the clinical characteristics in Nigeria. The availability and deployment of ultrasonography has led to an improvement in the diagnosis and recognition of ADPKD in Nigeria. In this study we aimed at determining the clinical characteristics and outcome of ADPKD among patients attending Benue State University Teaching Hospital (BSUTH), Makurdi. This is a retrospective study of all patients with ADPKD seen over an 8 year period between 2013 and 2020 in BSUTH.

Nineteen patients (M/F 9:10) with mean age of 42.79±16.8 were studied. The mode of presentation was loin pain (68.4%), hypertension (42.1%), haematuria (31.6%), oedema (15.8%) and anaemia (10.5%). Three (15.8%) progressed to end stage renal disease/dialysis while three (15.8%) died. ADPKD is common and is an important cause of morbidity and mortality in Nigeria. Clinicians should have a high index of suspicion. Additionally there is need to create awareness among family members with ADPKD stressing the importance and need for screening.

Keyword: Autosomal dominant polycystic kidney disease (ADPKD), Clinical characteristics, Outcomes

INTRODUCTION

Autosomal Dominant Polycystic Kidney Disease (ADPKD) is a multisystem disorder characterized by multiple, bilateral renal cysts and associated with cysts in other organs such as liver, pancreas and arachnoid membranes.[1] It is a genetic disorder caused by mutations in either of two major genes and it is inherited in an autosomal dominant pattern, with variable expression[1].

The common ADPKD proteins, polycystin-1 and polycystin-2, play a critical role in the normal function of

the primary cilium that is essential to maintain the differentiated phenotype of the tubular epithelium.[2]

ADPKD is genetically heterogeneous with two common gens identified PKDI (Chromosome 16p13.3) and PKD2 (Chromosome 4q21). Recently, mutations in a third gene GANNAB have been identified in families with mild polycystic kidney and Polycystic Liver Disease (PLD)[3].

Although mutations in PKD1 and PKD2 lead to the same phenotype, patients with PKD2 mutations have milder disease with fewer kidney cysts, later onset of hypertension and less ESRD than their counterparts with PKD1[2].

PKD1 codes for polycystin-1 an integral membrane protein made up of 4304 amino acids.

PKD 2 codes for polycystin-2, a 968 amino acid protein. Each polycystic affects cell proliferation, differentiation and fluid secretion through G-protein or JAK-STAT mediated signalling pathways[2].

ADPKD is the most common hereditary kidney disorder causing end stage renal disease (ESRD).[4,5,6] It is thus a common cause of morbidity and mortality in Nigeria.[4,5,6] The renal disorder can progress to severe hypertension, renal dysfunction and end stage renal disease requiring renal procedures such as dialysis and renal transplant.

The extra renal complications include subarachnoid haemorrhage, cardiac disorders, enlargement of abdominal organs including liver, pancreases and spleen.[7,8]

Gene technology is still in its infancy in Nigeria and hence diagnosis of ADPKD is mainly by clinical judgment and ultrasonography. As a result there is paucity of data on ADPKD and few studies have been published on it in Nigeria.[9,10] Owing to the above, we therefore sought to evaluate the clinical characteristics and outcome of all patients with ADPKD seen in our centre (BSUTH) over an eight year period.

MATERIALS AND METHODS

It was a retrospective study of all patients with ADPKD seen at BSUTH between 2013 and 2020.

Patients socio-demographic details, laboratory test result, clinical presentation and complications were obtained from the unit's record files and case notes..

The diagnosis of ADPKD was established using the revised unfiled criteria.[11] The eGFR was calculated using CKD-EPI.[12]

Hypertension was defined as systolic blood pressure of $\geq$ 140mmHg or diastolic blood pressure $\geq$90mmHg or use of antihypertensive medication or both irrespective of blood pressure.[13]

The outcomes considered were progression to ESRD/dialysis and death. Data were expressed as mean and percentage and data was analysed using Statistical Package for Social Sciences version (SPSS) 21.0.

RESULTS

A total of 19 patients fulfilled the diagnostic criteria. They included 10 (52.6%) females and 9 (47.4%) males. The age range was 29-60 years with a mean age of 42.79±16.88. This is shown in Table 1. The mean packed cell volume (PCV) was 37.35± 6.21. The mean systolic and diastolic blood pressures were 135.79± 24.11 and 83.68±13.83 respectively. The mean estimated glomerular filtration rate (eGFR) was 260.16 ± 421.76ml/min/1.73m2 while the mean serum creatinine was 77.16 ± 43.51umol/L as shown in table 2. Table 3 reveals that 7(36.8%) patients presented with CKD stage 1, 8 (42.1%) with CKD stage 2, 1(5.3%) with CKD stage 3 and 3 (15.8%) with CKD stage 5(ESRD). Thirteen (68.4%) patients presented with loin pain followed by haematuria 6(31.6%) and oedema 3(15.8%). Hypertension was the most common finding on examination 8(42.1%) followed by pallor (anaemia) with 2 (0.5%). Table 4. Three (15.8%) progressed to end stage renal disease (ESRD) while 3 (15.8%) died as shown in Table 5.

Table1: Socio-Demographics of patients with ADPKD at BSUTH Makurdi

Variable	Frequency	Percent (%)
group		
≤29 years	6	31.6
30 – 39	2	10.5
40 – 49	3	15.8
50 – 59	4	21.1
≥60	4	21.1
Mean ± SD 42.79 ± 16.88		
Sex		
Male	9	47.4
Female	10	52.6

Majority of the patients were females and younger than 30 years.

Table 2: Clinical and laboratory parameters of patients with ADPKD at BSUTH, Makurdi

Variable	Frequency (n = 19)	Mean ± SD
Clinical parameters		
Age (Years)		42.79±16.88
PCV (%)		37.35 ± 6.21
Systolic (SBP)		
Blood Pressure < 140mmHg	11	135.79 ± 24.11
Diastolic (DBP)		
Blood Pressure > 140mmHg	8	83.68 ± 13.83
eGFR		77.16 ± 43.51
Serum Creatinine		260.16 ± 421.76

Keys: *SBP – Systolic Blood Pressure, DBP – Diastolic Blood Pressure, PCV Packed cell volume, eGFR,- Estimated Glomerular Filtration Rate*

The mean diastolic blood pressure was 135.79± 24.1 ml/min/1.73m^2 while the mean diastolic blood pressure was 83.68± 13.8. The mean estimated glomerular filtration rate was 77.16±43.51 while the mean serum creatinine was 260.16± 421.76umol/l.

TABLE 3: Stages of CKD among patients with CKD at BSUTH Makurdi

Stage	eGFR	Frequency	Percent (%)
1	≤90	7	36.8
2	60–89	8	42.1
3	30 –59	1	5.3
4	15 –29	0	0
5	< 15	3	15.8
Total		19	100

TABLE 4: Clinical characteristics of patients with ADPKD at BSUTH Makurdi

Clinical Variable	Frequency	Percent (%)
Haematuria (n=19)		
Yes	6	31.6
No	13	68.4
Loin Pain (n=19)		
Yes	13	68.4
No	6	31.6
Oedema (n=19)		
Yes	3	15.8
No	16	84.2
Hypertension (n=19)		
Yes	8	42.1
No	11	57.9
Anaemia (n=19)		
Yes	2	10.5
No	17	89.5

Loin pain (68.4%), haematuria (31.6%) and oedema (15.8%) were the most common presenting complaints (complaints).

Table 5: Outcome of patients with ADPKD at BSUTH Makurdi

Variable	Frequency	Percent (%)
ESRD/Dialysis (n=19)		
Yes	3	15.8
No	16	84.2
Death (n=19)		
Yes	3	15.8
No	16	84.2

Three patients with ADPKD progressed to ESRD while three died.

DISCUSSION

Autosomal dominant polycystic kidney disease is the most common inherited cause of end stage renal disease in adults[4,5,6]. It accounts for 6-10% of ESRD cases in America and Europe.[4,6,8] A prevalence of 8% has been reported in a hospital based study in Nigeria.[9]

The mean age from our study was 42 ±79 ± 16.88. This compares with that obtained by Pertider O. et al.[14] but was lower than the mean age of 48.6 ± 4.6 and 49.8 ± 3.6 reported by Arogundade *et al*[15]and Chijioke *et al*[9] respectively.

A slight female predominance was noted. This is similar to findings by Awoonidaala *et al.*[16] About 15.8% of the

participant had anaemia (haematocrit less than 30%). This is lower than the 73.2% and 88.2% reported by Arogundade[15] and Itelal T. *et al*.[17,18] This is due to the fact that majority of our patients were relatively younger and presented early. Most of the patients from other studies mentioned above were quite elderly and presented late.

The prevalence of hypertension from our study was 42.1%. This compares with the 42.7% obtained by Perditer et al[14] but lower than the 55.5%, 66.7% and 73.2% by Awororidaa.[17]Everton et al[18] and Arogundade et al[15] respectively.

Hypertension occurs as ADPKD progresses and in most of these studies participants were elderly and presented late compared to the participants in our study.

Hypertension is the most common manifestation of ADPKD and a major contributor to renal disease progression and cardiovascular morbidity and mortality[19-21]. Microalbuminuria, proteinuria and haematuria which are independent risk factors for renal functional decline are more common in hypertensive patients with ADPKD.[21]

Hypertension can also increase mortality from valvular heart disease and intracranial aneurysms which are common in ADPKD[21].

Loin Pain (68.4%) was the predominant symptom among the participants. This compares with the 68.3% reported by Arogundade et al.[15] This is also similar to finding from studies carried out by Perditer *et al*.[14]Aworidaala *et al*.[16], Garbour PA[22], Bajwa *et al*[23]and Deleney et al.[24] Acute Loin Pain may arise from cystic haemorrhage, urolithiasis, mass pressure effect and urinary tract infection[16].

Haematuria was a common mode of presentation (31.6%) among the participants from our study. This compares with 34% obtained by Perditer O *et al*.[14]

Haematuria may be the initial presenting symptom and occurs in up to 35-40% of ADPKD over the course of the disease[25,26]. Many have recurrent episodes and it is usually precipitated by urinary tract infection or strenuous activity[27].

Significant proportion of participants (21.1%) had marked decline in renal function (GFR of 3 and below with 15.8% having ESRD requiring renal replacement therapy).

This value is similar to the 22.9% reported by Everton et al[18] but lower than 33.3% reported by Aworidaala *et al*.[16]

Several factors account for renal function decline. For instance the CRISP study confirmed that kidney and cyst volumes are strongest predictor of renal functional decline.[28,29] Several studies have also confirmed an inverse relationship between size of cyst and level of glomerular filtration[28,29].

Other predictors for progression of renal dysfunction include male gender, PKD1 genotype early age of onset of hypertension, presence of detectable proteinuria, gross haematuria and use of nephrotoxic drugs such as Non-Steroidal Anti-inflammatory drugs (NSAIDS).[29-30]

Mortality from our study was 15.8%. This is lower than the 24% from Chijioke et al[9] and 51.2% by Arogundade *et al*.[15]

Factors that have been associated with mortality in patients with ADPKD include cardiovascular disease and infections (often leading to septicaemia)[31-33]

The cardiovascular causes of death include left ventricular hypertrophy and coronary heart disease.[34] Other causes of death include neurologic causes like ruptured aneurysm and hypertensive intracranial haemorrhage.[35]

CONCLUSION

It is worthy of note that varying patterns of clinical presentations and outcomes have been observed in different studies. ADPKD is an important cause of morbidity and mortality in patients seen in the nephrology clinic.

Recommendation

A high index of suspicion is very important. There is need for early intervention especially for at risk patients that is relatives of ADPKD patients by way of early screening using imaging studies and gene technology.

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