

Intracranial Aneurysms in Patients with Kidney Disease

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Abstract: This literature review focuses on aneurysms in patients with ADPKD in a series of cases reported in retrospective and prospective studies to monitor responses recorded from different hospitals in Iraq were included, where information and demographic data about patients were collected for a period of two years, from January 2019 to March 2021. patients' information was collected, which included (age, gender, aneurysm size and location, morbidity and mortality, and estimates related to surgical and rupture risks obtained from a set of predictive factors) In the analysis of logistic regression to risk factors, we find that the most important factors that posed a high risk of mortality are age, in addition to ADPKD patients, smoking patients, and a statistically significant relationship was found, that is, there is an association between the incidence of mortality and the above factors with a p-value < 0.001. Genetic etiology in intracranial aneurysms is suggested as this hypothesis is supported by the appearance of several patients in the same family or in patients with associated genetic diseases, such as adult polycystic kidney disease (ARPKD).

Keywords: Mortality, ARPKD, BMI, MCA, Aneurysms.

INTRODUCTION

Autosomal dominant polycystic kidney disease (ADPKD) is a monogenic polycystic disease, mostly characterized by the presence of multiple bilateral renal cysts, as well as external manifestations (cysts in other organs, blood vessels, heart, gastrointestinal tract, and musculoskeletal malformations), which evolve to a variable degree [Irazabal, M.V. *et al.*, 2011; Xu, H.W. *et al.*, 2011; Flahault, A. *et al.*, 2018].

Epidemiology of ADPKD is the most common hereditary kidney disease, with an estimated prevalence of between 1:400 and 1:1000, and is the third leading cause of end-stage kidney disease (ESKD) [Schievink, W.I. *et al.*, 1992; Nurmonen, H.J. *et al.*, 2017; Flahault, A. *et al.*, 2016; Chapman, A.B. *et al.*, 2015]. It is a disease that spreads all over the world and affects all races equally [Chauveau, D. *et al.*, 1994; Malhotra, A. *et al.*, 2019]. Worldwide, the annual incidence of ADPKD-induced ESRD is 8.7 and 6.9 cases per million (1998-2001 in the US), 7.8 and 6.0 cases per million (2005-2006 in Asia) for men and women, respectively [Rozenfeld, M.N. *et al.*, 2016; Agrawal, A. *et al.*, 2012]

Previous studies on this topic have shown that the likelihood is increased in cases of a family history of intracranial aneurysm and/or subarachnoid hemorrhage (SAH) [Huston, J.I.I. *et al.*, 1993; Chauveau, D. *et al.*, 1994], which are often asymptomatic but can produce focal symptoms due to compression of adjacent structures or SAH due to rupture, with A morbidity and mortality rate of 35-55%, [Belz, M.M. *et al.*, 2001] with a

median age of rupture less than the general population (39 vs. 51 years) [Graf, S. *et al.*, 2002]. The purpose of sharing this case is to emphasize the importance of screening patients with ADPKD and a family history of aneurysms— intracranial or SAH, [Johnston, S.C. *et al.*, 1998] previous aneurysm rupture, preparation for major surgery, and high-risk occupations. Among the diagnostic techniques, MRI is the preferred method.

MATERIAL AND METHODS

Patient Sample

In this study, 100 patients from different hospitals in Iraq were included, where information and demographic data about patients were collected for a period of two years, from January 2019 to March 2021. were included Patients who suffer from Aneurysms and intracranial hemorrhages with kidney disease

Study Design

One hundred patients from different hospitals in Iraq were included, and the patients' ages ranged between 30 to 50 years, and demographic information and data were collected for patients, laboratory data and echocardiography were also collected.

The patients were also classified on the basis of comorbidities, which included blood pressure diseases and diabetes when the glucose level was read ≥ 126 mg/dL.

The diagnostic criteria for hypercholesterolemia were based on LDL \geq 100 mg/dL with cad, <130 mg/dL with two or more risk factors, 160 LDL-C mg/dL with one risk factor included.

Patients were classified as having a family history of the disease through a questionnaire distributed to patients, which states that there are first-degree relatives previously diagnosed with ADPKD.

Study Period

Through cooperated with the work ethics committee, all necessary licenses were obtained for the purpose of collecting information and demographic data for patients. This study was conducted in two years, from 2019-2021.

Purpose of Study

This study aims to know the effect and assessment outcomes of Aneurysms and intracranial hemorrhages in patients with kidney disease.

RESULTS

Table 1: Main demographic characteristics of patients

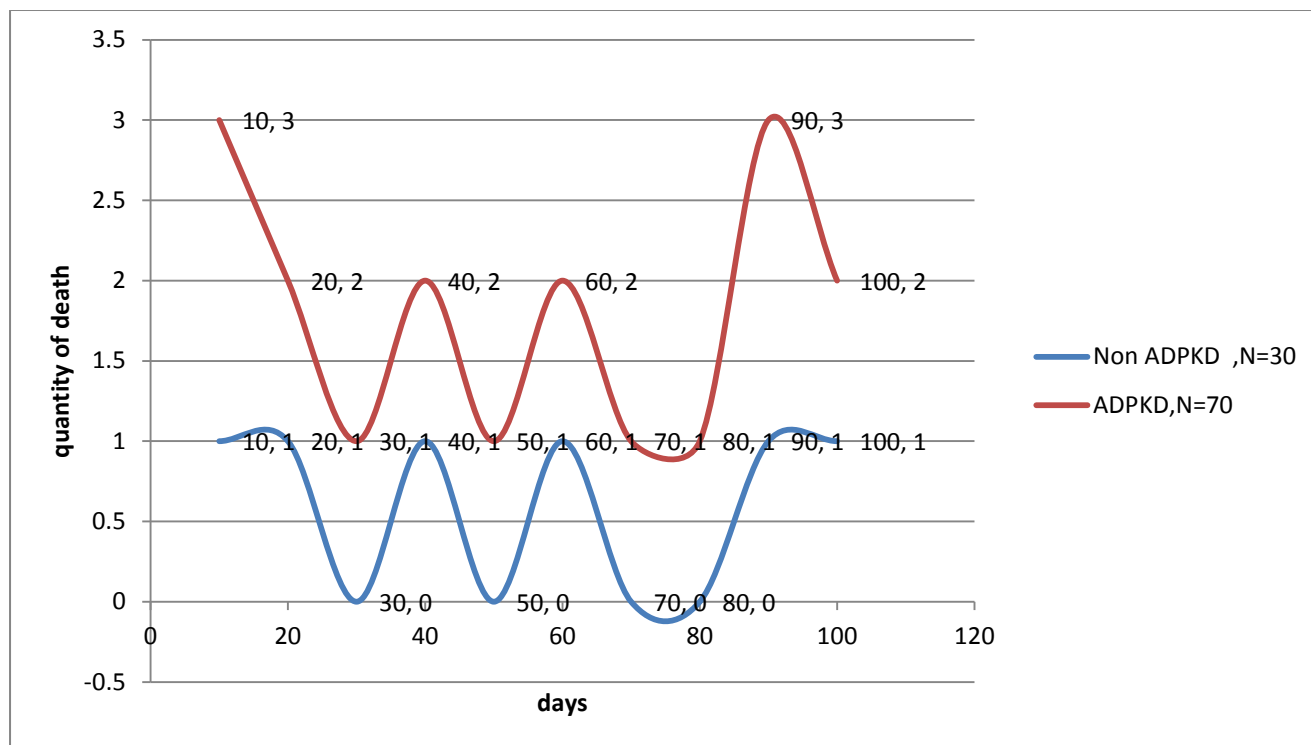
	Non ADPKD, N=30	ADPKD, N=70	P-value
Age			
30-34	4	15	
35-39	10	20	0.87
40-44	9	20	
45-50	7	15	
SEX			
Male	19	40	0.55
Female	11	30	0.02
BMI, mean sd	26 \pm 3.3	27.33 \pm 4.1	0.08
comorbidities			
Hypertension	10	30	<0.001
Diabetes mellitus	7	22	<0.001
Atrial fibrillation	6	10	0.77
Ischemic heart disease	7	8	0.95
Tobacco use			
Yes	12	25	0.4
No	17	45	0.66
Family history			
Yes	11	40	<0.001
No	19	30	<0.001
Mean hemoglobin (g/dL)	10.21 (9.11-10.34)	10.99 (10.44 -11.33)	<0.001
Mean serum albumin (g/dL)	3.11(2.98-3.22)	3.25 (3.1-3.45)	<0.001
Mean total cholesterol (mg/dL)	145.11 (140 -151.22)	160 (155.22-169.3)	<0.001
Mean low density lipoprotein (mg/dL)	85.55 (82.22-88.4)	95.11 (83.39-97.34)	<0.001
WBC, \times 103/ μ L	4.6 \pm 2.1	6.6 \pm 1.8	<0.001

Table 2: Distribution of patients according to Size of aneurysm and Location of aneurysm

Variable	Value
Size	
< 5 mm	20
5–9 mm	30
10–24 mm	22
> 25 mm	28
Location	
anterior communicating artery	33
MCA	40
internal carotid artery	12
posterior circulation	11

Table 3: Outcomes of Echocardiography of patients

	ADPKD, N=70	Non ADPKD, N=30	P-value
Aortic diameter, mm	35±2.2	31.2±1.7	0.55
Mitral inflow E, m/s	0.9±2.1	0.3±0.0.2	0.001
Mitral inflow A, m/s	0.1±0.1	0.5±0.1	0.94
Mitral inflow DT, ms	190±33	211±44	0.23
Mitral inflow E/A	0.5±0.6	1.1±0.1	0.18

**Figure 1:** outcomes of the mortality rate according to the Kaplan Meier scale**Table 4:** Logistic regression of patient risk factors

	CR (95%)	P-value
Age	2.2 (1.8-2.7)	0.001
ADPKD VS non ADPKD	3.8 (2.6-4.4)	<0.001
Size of aneurysm	1.8 (0.9-2.6)	<0.001
comorbidities	1.1 (0.8-1.2)	0.05
Location of aneurysm	0.8 (0.4-1.3)	0.88
Echocardiography	1.4 (0.8-1.9)	0.55
Smoking	2.44 (1.98-2.97)	<0.001
Family history	3.2 (2.4-6.8)	<0.001

DISCUSSION

In this study, 100 patients from different hospitals in Iraq were collected and distributed into two groups according to the presence or absence of ADPKD.

Seventy patients were included in the patient group and 30 in the control group.

The most common ages in this study were from 35 to 39 years for ten patients in a control group and 20 in a group of patients, followed by 40-44 years

for 20 patients, 30-34 years for 15 patients, and 45-50 years for 15 patients.

Patients were distributed according to gender, and males were more prevalent in this study, with 40 patients in the group of patients and 30 patients with females. The most common comorbidities were Hypertension for 30 patients, Diabetes mellitus for 22 patients, and the majority of patients had a family history of the disease, as 40 patients were diagnosed by distributing a questionnaire to patients in the diagnosis of family history of the first degree.

It was reported that 30 patients had a size of aneurysm of 5-9 mm, and 28 patients were >25 mm. The most common distribution according to aneurysm site was MCA for 40 patients and ACA for 33 patients. The least common in this study was posterior circulation for 11 patients.

SAH due to ruptured intracranial aneurysm and ADPKD is a devastating event associated with high rates of morbidity and mortality.

Wilson, F. *et al.*, conducted a prospective study in England between January 1985 and March 1988 on patients admitted to a neurology unit in which SAH was suspected and who underwent CT and cerebral angiography studies. Of the total 254 patients aged between 15 and 76 years (median 49.1 years), a total of 414 aneurysms were found, of which 114 patients (44.9%) had multiple aneurysms. Among the risk factors that were found were smokers and female sex.

In the analysis of logistic regression to risk factors, we find that the most important factors that posed a high risk of mortality are age, in addition to ADPKD patients, smoking patients, and a statistically significant relationship was found, that is, there is an association between the incidence of mortality and the above factors with a p-value < 0.001.

In a longitudinal study of the evolutionary control of factors that impede the formation and growth of intracranial aneurysms, Juvela, *et al.*, conclude that the greatest risk in the formation and development of aneurysms occurs in females and tobacco smokers as it can lead to a plasma arterial wall imbalance indicated in elastase. alpha antitrypsin Japanese authors, led by Shujima, conducted a computerized fluid dynamic study in 20 middle cerebral artery aneurysms and developed a concept called "WSS," which they came up with through a formula related to the frictional force generated by viscosity and blood pressure and its effect on the development of intracranial aneurysms [Ferro, J.M. *et al.*, 2007; Van Gijn, J. *et al.*, 2009]. These authors recommend that computational studies of aneurysms in terms of flow would constitute another tool for predicting the initiation, growth, and rupture of intracranial aneurysms, such that a high degree of WSS is valuable in shaping the stage of the aneurysm while a low degree of the aneurysm [Van Asch, C.J. *et al.*, 2010; Feigin, V.L. *et al.*, 2009].

CONCLUSION

According to the reviewed literature, this patient has four risk factors for developing intracranial aneurysms in ADPKD patients, which are: female, menopause, hypertension, and family history of cerebrovascular disease.

RECOMMENDATION

Although it is indisputable that bleeding prevention is the best strategy, this does not hide the importance of long-term comparative studies as presenters of scientifically based conclusions about different treatment options while at the same time, optimal management of unruptured aneurysm is the possibility of its insurance before ruptured.

REFERENCES

1. Irazabal, M.V., Huston, J., Kubly, V., Rossetti, S., Sundsbak, J.L., Hogan, M.C., Harris, P.C., Brown, R.D. and Torres, V.E. "Extended follow-up of unruptured intracranial aneurysms detected by presymptomatic screening in patients with autosomal dominant polycystic kidney disease." *Clinical Journal of the American Society of Nephrology* 6.6 (2011): 1274-1285.
2. Xu, H.W., Yu, S.Q., Mei, C.L. and Li, M.H. "Screening for intracranial aneurysm in 355 patients with autosomal-dominant polycystic kidney disease." *Stroke* 42.1 (2011): 204-206.
3. Flahault, A., Trystram, D., Nataf, F., Fouchard, M., Knebelmann, B., Grünfeld, J.P. and Joly, D. "Screening for intracranial aneurysms in autosomal dominant polycystic kidney disease is cost-effective." *Kidney international* 93.3 (2018): 716-726.
4. Schievink, W.I., Torres, V.E., Piepgras, D.G. and Wiebers, D.O. "Saccular intracranial aneurysms in autosomal dominant polycystic kidney disease." *Journal of the American Society of Nephrology* 3.1 (1992): 88-95.
5. Nurmonen, H.J., Huttunen, T., Huttunen, J., Kurki, M.I., Helin, K., Koivisto, T., von und zu Fraunberg, M., Jääskeläinen, J.E. and Lindgren, A.E. "Polycystic kidney disease among 4,436 intracranial aneurysm patients from a defined population." *Neurology* 89.18 (2017): 1852-1859.
6. Flahault, A., Trystram, D., Fouchard, M., Knebelmann, B., Nataf, F. and Joly, D. "Screening for unruptured intracranial aneurysms in autosomal dominant polycystic kidney disease: a survey of 420 nephrologists." *PLoS one* 11.4 (2016): e0153176.

7. Chapman, A.B., Devuyt, O., Eckardt, K.U., Gansevoort, R.T., Harris, T., Horie, S., Kasiske, B.L., Odland, D., Pei, Y., Perrone, R.D., Pirson, Y., Perrone, R.D., Pirson, Y., Schrier, R.W., Torra, R., Torres, V.E., Watnick, T. and Wheeler, D.C. "Conference Participants: Autosomal-dominant polycystic kidney disease (ADPKD): Executive summary from a Kidney Disease: Improving Global Outcomes (KDIGO) controversies conference." *Kidney Int* 88.1 (2015): 17-27.
8. Chauveau, D., Pirson, Y., Verellen-Dumoulin, C., Macnicol, A., Gonzalo, A. and Grünfeld, J.P. "Intracranial aneurysms in autosomal dominant polycystic kidney disease." *Kidney international* 45.4 (1994): 1140-1146.
9. Malhotra, A., Wu, X., Matouk, C.C., Forman, H.P., Gandhi, D. and Sanelli, P. "MR angiography screening and surveillance for intracranial aneurysms in autosomal dominant polycystic kidney disease: a cost-effectiveness analysis." *Radiology* 291.2 (2019): 400-408.
10. Rozenfeld, M.N., Ansari, S.A., Mohan, P., Shaibani, A., Russell, E.J. and Hurley, M.C. "Autosomal dominant polycystic kidney disease and intracranial aneurysms: is there an increased risk of treatment?." *American Journal of Neuroradiology* 37.2 (2016): 290-293.
11. Agrawal, A., Dwivedi, S., Singh, B.R. and Banode, P.J. "Simultaneous hemorrhage in intracranial aneurysms and in renal cyst in a case of polycystic kidney disease." *Saudi Journal of Kidney Diseases and Transplantation* 23.4 (2012): 794-798.
12. Huston, J.I.I.I., Torres, V.E., Sullivan, P.P., Offord, K.P. and Wiebers, D.O. "Value of magnetic resonance angiography for the detection of intracranial aneurysms in autosomal dominant polycystic kidney disease." *Journal of the American Society of Nephrology* 3.12 (1993): 1871-1877.
13. Chauveau, D., Pirson, Y., Verellen-Dumoulin, C., Macnicol, A., Gonzalo, A. and Grünfeld, J.P. "Intracranial aneurysms in autosomal dominant polycystic kidney disease." *Kidney international* 45.4 (1994): 1140-1146.
14. Belz, M.M., Hughes, R.L., Kaehny, W.D., Johnson, A.M., Fick-Brosnahan, G.M., Earnest, M.P. and Gabow, P.A. "Familial clustering of ruptured intracranial aneurysms in autosomal dominant polycystic kidney disease." *American journal of kidney diseases* 38.4 (2001): 770-776.
15. Graf, S., Schischma, A., Eberhardt, K.E., Istel, R., Stiasny, B. and Schulze, B.D. "Intracranial aneurysms and dolichoectasia in autosomal dominant polycystic kidney disease." *Nephrology Dialysis Transplantation* 17.5 (2002): 819-823.
16. Johnston, S.C., Selvin, S. and Gress, D.R. "The burden, trends, and demographics of mortality from subarachnoid hemorrhage." *Neurology* 50.5 (1998): 1413-1418.
17. Ferro, J.M., Canhao, P. and Peralta, R. "Update on subarachnoid haemorrhage." *Journal of neurology* 255.4 (2008): 465-479.
18. Van Gijn, J., Kerr, R.S. and Rinkel, G.J. "Subarachnoid haemorrhage." *The Lancet* 369.9558 (2007): 306-318.
19. Van Asch, C.J., Luitse, M.J., Rinkel, G.J., van der Tweel, I., Algra, A. and Klijn, C.J. "Incidence, case fatality, and functional outcome of intracerebral haemorrhage over time, according to age, sex, and ethnic origin: a systematic review and meta-analysis." *The Lancet Neurology* 9.2 (2010): 167-176.
20. Feigin, V.L., Lawes, C.M., Bennett, D.A., Barker-Collo, S.L. and Parag, V. "Worldwide stroke incidence and early case fatality reported in 56 population-based studies: a systematic review." *The Lancet Neurology* 8.4 (2009): 355-369.

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