[Downloaded free from http://www.sjkdt.org on Sunday, December 06, 2009]

Saudi J Kidney Dis Transplant 2009;20(5):806-810
© 2009 Saudi Center for Organ Transplantation

Saudi Journal of Kidney Diseases and Transplantation

Original Article

Analysis of Causes of Mortality in Patients with Autosomal Dominant Polycystic Kidney Disease: A Single Center Study

Ebadur Rahman, Faraz A. Niaz, Abdulkareem Al-Suwaida, Shahpar Nahrir, Mohammed Bashir, Habibur Rahman, Durdana Hammad

Department of Medicine, King Khalid University Hospital, Riyadh, Saudi Arabia

ABSTRACT. This study was aimed at determining the median survival and most frequent causes of death in patients with the Autosomal Dominant Polycystic Kidney Disease (ADPKD). A retrospective, observational analysis was made on patients registered with a diagnosis of ADPKD, in the computer records of the Sheffield Kidney Institute (SKI), United Kingdom, during the years 1981 to 1999. Data on 363 patients were analyzed from these computer records and further information, if any, was obtained from the patients' clinical notes. During this period, 88 patients died. The median age of the patients who died was 60.5 years, with the youngest being 37 years old and the oldest being 82 years. The major causes of death in this study group were cardiovascular (46.6%), infection (15.9%), central nervous system (CNS) disorders (11.36%), and miscellaneous causes (11.36%). Our study suggests that the major cause of death in patients with ADPKD was cardiovascular followed by infection, of which 42% of the deaths were due to septicemia. CNS causes of death comprised 11.36% of whom 60% had cerebrovascular events including subarachnoid hemorrhage in 20% of the patients. Uremia was the cause of death in only 2.2% of the patients in this series.

Introduction

Autosomal Dominant Polycystic Kidney Disease (ADPKD)) is the most common hereditary kidney disease,[1] characterized by replacement of functioning renal parenchyma with cysts and increase in the volume of the kidney. Patients with ADPKD are at high risk for renal and extra-renal complications, resulting in high morbidity and mortality, especially due to cardiovascular complications.[2]

The reported mortality rate in patients with ADPKD ranges between 1.6 and 2.88 folds (95% confidence interval, R/R 1.3-2.0) in comparison with the general population.[3] ADPKD patients accounts for nearly 10% of all cases of Chronic Renal Failure (CRF) requiring dialysis or renal transplantation.[1,4] They are prone to end-stage renal disease (ESRD) and carry a

Correpondence to:

Dr. Ebadur Rahman
Senior Registrar
Department of Medicine (38)
Division of Nephrology
King Khalid University Hospital
P.O. Box 2925, Riyadh 11461, KSA
E-mail: ebadurmr@yahoo.com

[Downloaded free from http://www.sjkdt.org on Sunday, December 06, 2009]

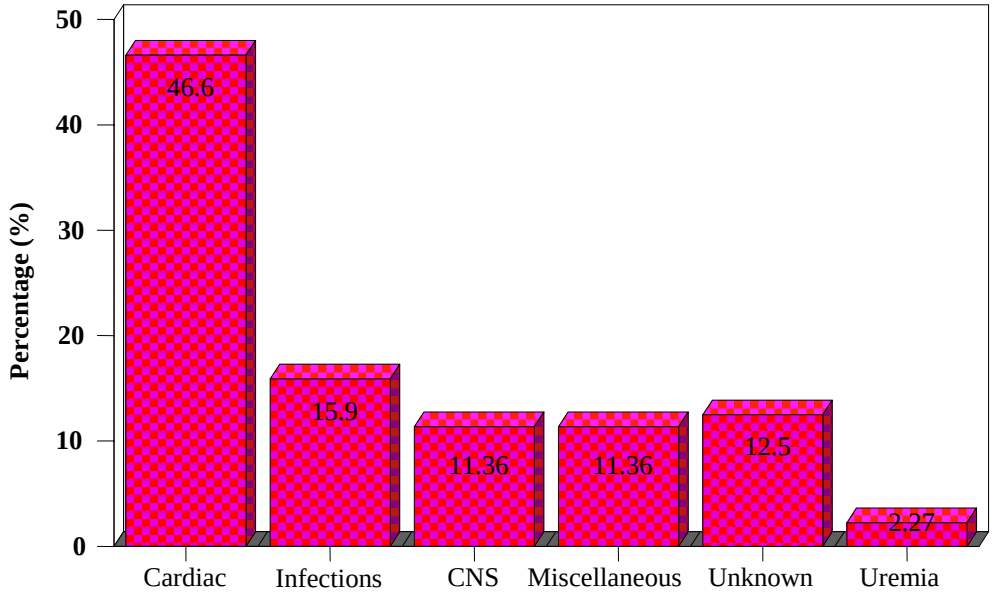

Figure 1. The causes of death in the study patients (n=88)

poor survival rate.[5] Hypertension occurs at an early age in such patients.[6]

Cysts in the liver and hepatic failure are among the common extra-renal manifestations adding to morbidity and mortality.[7] Cardiovascular complications are common, progressive and often fatal; thus, ADPKD patients have an unfavorable risk profile.[8] There is a progressive increase in ventricular mass index, left ventricular hypertrophy (LVH), valvular prolapse and hypertension.[9,10] Coronary and intracranial aneurysms and their rupture contribute further to mortality.[11] Complications are more commonly seen in whites.[12,13] Acute coronary dissection, although rare, is a dreaded complication.[14] Infections also add to fatality in patients with ADPKD.

Materials and Methods

This is a retrospective, observational study using computer records of the Sheffield Kidney Institute (SKI), the United Kingdom. A total of 363 patients with a diagnosis of ADPKD were registered between 1981 and 1999. Further information on these patients, if required, was obtained from their clinical notes. The total number of patients who died of ADPKD during the study period was 88. The diagnosis of ADPKD was made by clinical examination, urography, and ultrasound or CT scan of abdomen. The dominant inheritance of polycystic kidney disease was diagnosed from positive family history. However, the gene distinguishing the two variants of ADPKD was not looked for.

Statistical Analysis

The median age of survival in this group and distribution of causes of death was calculated using Microsoft Excel. The incidence of different associations and complications were also calculated using the same program.

Results

The median age at death of the study patients was 60.5 years, with the youngest being 37 years and the oldest, 82 years. The major causes

[Downloaded free from http://www.sjkdt.org on Sunday, December 06, 2009]

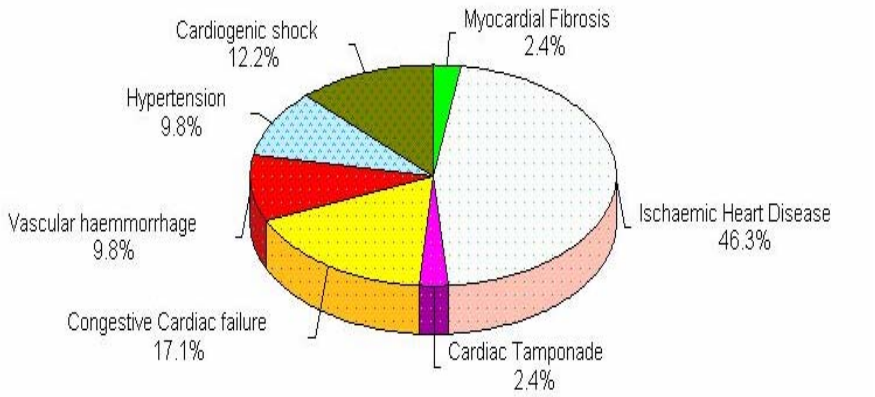

Figure 2. Cardiovascular causes of death in the study patients (n= 41)

of death in this group of patients included cardiovascular in 46.6% of the patients, infection in 16%, central nervous system (CNS) disorders in 11.36% and miscellaneous causes in 11.36% of the patients (Figure 1). The miscellaneous group included one patient who was found not suitable for dialysis, one patient committed suicide, one patient died of gastrointestinal (GI) bleeding and one other patient died of rheumatoid arthritis. Uremia caused death in only 2.2% of the patients in this series. In both cases, death occurred due to voluntary refusal to undergo dialysis.

Cardiovascular causes of death

The principal cardiovascular causes of death included Ischemic Heart Disease (IHD) in 46.3%, Hypertensive Heart Disease (HHT) in 8.8% and Congestive Cardiac Failure (CCF) in 17.1% (Figure 2). Two patients died of retroperitoneal hemorrhage secondary to aortic dissection.

CNS causes of death

In order of decreasing frequency, the CNS causes of mortality included cerebrovascular accidents (CVA) in 60%, sub-arachnoid hemorrhage (SAH) in 20% and brain-stem hemorrhage and intracerebral hemorrhage in 10% each. The distribution of different CNS causes of death is shown in Figure 3.

Infectious causes of death

Infections accounted for 15.9% of the causes

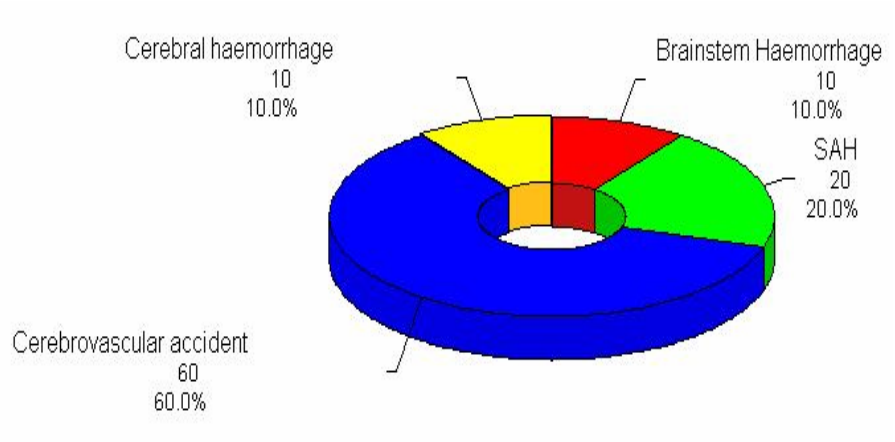

Figure 3. Central nervous system causes of deaths among the study patients (n=10)

[Downloaded free from http://www.sjkdt.org on Sunday, December 06, 2009]

Table 1. Miscellaneous causes of death in the study patients

Trait	Total number of patients	Percentage out of 10 patients
Pulmonary		
Respiratory failure	1	40%
Chronic obstructive airway disease	2	
Pulmonary embolism	1	
Malignancy		
Bronchogenic carcinoma	2	30%
Ovarian carcinoma	1	
Graft failure	1	10%
Suicide	1	10%
Femoral embolism	1	10%

of death in this series. The leading cause was septicemia (42.9%) followed by pneumonia (35.7%), peritonitis (14.3%) and infective endocarditis in 7.1% of the patients.

Miscellaneous causes of death

This series comprised 11.36% of the study patients. Their distribution is summarized in Table 1.

Discussion

Mortality in patients with ADPKD is higher than in the general population. The present study reveals that the median age at death was 60 years while life span as low as 37 years was observed. The most frequent cause of death was cardiovascular events, accounting for 46.6% of the total mortality. Amongst them, IHD seen in 46.3% and CHF, seen in 17.1%, were the common causes. Similar results have been reported by Fick GM et al from Colorado, USA. In their study, cardiovascular diseases were responsible for 36% of deaths; followed by infection in 24%.[13] Cardiac hypertrophy was found in 89% of patients in their study.

In another study from the Netherlands, Florijin KW et al demonstrated a relative risk of 2.88 (95% CI: 1.41-5.9) for cardiovascular mortality after adjustment for age. In a report from Canada in 2006, Handa SP described an unfavorable cardiovascular risk profile responsible for increased risk for cardiovascular mortality.[9]

Infection was another important cause of death in the present study, accounting for 42.9% of total deaths; pneumonia was seen in 35.7%, peritonitis in 14.3% and infective endocarditis in 7.1% of the patients. Previous studies have also reported infection as a major cause of mortality, being responsible for 24-30% of deaths.[4]

Deaths due to CNS causes accounted for 11.36% in this series. Patients with ADPKD are at increased risk of cranial and extracranial aneurysms and rupture of these aneurysms are responsible for increased mortality in these patients.[12] Rivera M,[13] reported the occurrence of acute cerebrovascular events in 9.8% of their patients with ADPKD including ischemia, ruptured aneurysms, cerebral and intracranial hemorrhage.

A high incidence of ESRD is associated with ADPKD patients (57.9%).[6] Uremia accounted for 2.2% of deaths in our study.

A total of 11.3% of the deaths were due to miscellaneous causes. Malignancies and respiratory causes for death accounted for 70% of the miscellaneous group.

Conclusion

Our study suggests that cardiovascular disease, infection and cerebrovasular diseases are the common causes of mortality in patients with ADPKD. Constant vigilance and aggressive management of blood pressure, prompt control of infection if it occurs, and frequent screening for malignancies can improve the outcome of these patients.

References

1. Schrier RW. Optimal care of autosomal dominant

[Downloaded free from http://www.sjkdt.org on Sunday, December 06, 2009]

polycystic kidney disease patients. Nephrology (Carlton) 2006;11(2):124-30.
2. Florijin KW, Chang PC, Van der WoudeFJ, van Bockel JH, van Saase JL. Long-term cardiovascular morbidity and mortality in autosomal dominant polycystic kidney disease patients after transplantation. Transplantation 1994;57(1):73-81.
3. Florijin KW, Noteboom WM, Van Saase JL, et al. A century of mortality in five large families with polycystic kidney disease. Am J Kidney Dis 1995;25(3):370-4.
4. Fick GM, Johnson AM, Hammond WS, et al. Causes of death in autosomal dominant polycystic kidney disease. J Am Soc Nephrol 1995; 5(12):2048-56.
5. Sotirakopoulos N, Tsitsios T, Stambolidou M, Cristodoulidou C, Spaia S, Mavromatidis K. Anticipation of end stage renal disease in patients with autosomal dominant polycystic kidney disease in successive generations. Ren Fail 2001;23(5):715-20.
6. Fourtounas C, Panteris V, Valis D. Survival after end stage renal disease in autosomal dominant polycystic kidney disease. Am J Kidney Dis 2002;39(3):660.
7. Schrier R, Kimberly M, Johnson A, et al. Cardiac and renal effects of standard versus rigorous blood pressure control in autosomal dominant polycystic kidney disease: Results of a seven year prospective randomized study. J Am Soc Nephrol 2002;13:1733-9.
8. Elias TJ, Bnnister KM, Clarkson AR, et al. Progressive hepatic failure secondary to adult polycystic kidney disease. Aust NZJ Med 1999;29(2):282-3.
9. Handa SP. Cardiovascular manifestations of autosomal dominant polycystic kidney disease in young adults. Clin Invest Med 2006;29(6): 339-46.
10. Bardaji A, Martinez-Vea A, Valero A. Cardiac involvement in autosomal dominant polycystic kidney disease: A hypertensive heart disease. Clin Nephrol 2001;56(3):211-20.
11. Chapman AB, Johnson AM, Rainguet S, et al. Left ventricular hypertrophy in autosomal dominant polycystic kidney disease. J Am Soc Nephrol 1997;8(8):1292-7.
12. Hadimeri H, Lamm C, Nyberg G. Coronary aneurysms in patients with autosomal dominant polycystic kidney disease. J Am Soc Nephrol 1998;9(5):837-41.
13. Riviera M, GonzaloA, Gobernado JM, et al. Stroke in Adult polycystic kidney disease. Postgrad Med J 1992;68(803):735-8.
14. Fredman BI, Souci JM, Chapman A, et al Racial variation in autosomal dominant polycystic kidney disease. Am J Kidney Dis 2000;35(1):35-9.
15. Kaehny WD, Everson GT. Extra renal manifestations of autosomal dominant polycystic kidney disease. Semin Nephrol 1991;11(6): 661-70.
16. Yiyum J, Gabow P, Johnson A. autosomal dominant polycystic kidney disease in blacks. J Am Soc Nephrol 1994;4(9):1670-4.
17. Pecczkowska MJ, Anuszewiez A, Grzeszczak W, et al. The coexistence of acute aortic dissection with autosomal dominant polycystic kidney disease. Blood Press 2004;13(5):283-6.