Evaluation of Acquired Cystic Kidney Disease in Patients on Hemodialysis With Ultrasonography

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Introduction. Acquired cystic kidney disease (ACKD) occurs in patients with prolonged uremia, and early detection is important, because clinically significant complications, especially renal cell carcinoma, are associated with ACKD.
Materials and Methods. In a cross-sectional study, we evaluated our patients on hemodialysis, in Ahvaz, Iran, using ultrasonography. The criteria for the diagnosis of ACKD were the presence of at least 4 bilateral renal cysts in patients with noncystic primary kidney diseases as the leading cause of kidney failure.
Results. A total of 148 patients (95 men and 53 women) were included in the study. The prevalence of ACKD was 20.3% (18.9% in men and 22.6% in women). The mean age in patients with and without ACKD was 60.6 ± 16.8 years and 53.6 ± 14.9 years, and the mean hemodialysis duration was 44.2 ± 18.7 months and 34.3 ± 23.5 months, respectively. There were no significant differences in the frequency of ACKD in the men and the women (P = .59) and in the etiology of end-stage renal disease (P = .64). It was significantly more likely to see ACKD in patients with a history of 3 years or longer being on hemodialysis than in those with a shorter dialysis duration (P = .001).
Conclusions. Acquired cystic kidney disease is common in patients on hemodialysis, and we suggest that renal ultrasonography be performed in patients with 3 years or more history of being on renal replacement therapy.

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INTRODUCTION

The number of patients with end-stage renal disease (ESRD) accepted for renal replacement therapy including hemodialysis, peritoneal dialysis, and kidney transplantation increases each year and imposes a major social and economic burden on countries.[1] Acquired cystic kidney disease (ACKD) is a known complication of ESRD. It is characterized by the development of numerous fluid-filled cysts in the kidneys of patients with chronic kidney insufficiency who have no history of hereditary cystic disease.

Patients with primary renal cystic disease, especially autosomal dominant poly cystic kidney disease, should be distinguished from those with ACKD. In ACKD, there is no family history of cystic disease and cysts do not develop in other parts of the body. On the contrary, people with autosomal dominant poly cystic kidney disease often have a family history, and the cysts may occur in the other organs. In addition, the kidneys are normal to small in size with a smooth contour in patients with ACKD, as opposed to usually extreme renal enlargement with autosomal dominant poly cystic kidney disease.[2-4]

Most of the patients with ACKD are asymptomatic.

In one review, for example, only 14% of the patients developed symptoms, with hematuria being the most common, followed by lumbar pain and urinary tract infection.[5] Even in asymptomatic patients, however, sequential radiologic studies demonstrate a progressive increase in the number and size of cysts that may be complicated by severe retroperitoneal or intrarenal hemorrhage with or without hematuria, erythrocytosis, cyst infection, and renal cell carcinoma (RCC) with distant metastasis.[5,6] Therefore, early diagnosis is very important to follow the patients for such complications.

We performed this study to determine the frequency of ACKD among our patients on hemodialysis and its relationship with hemodialysis and kidney disease characteristics in Ahvaz city, Iran.

MATERIALS AND METHODS

This cross-sectional study was conducted on adult patients with ESRD in the hemodialysis center of Emam Khomeini Hospital, in Ahvaz, Iran, from March 2007 to April 2008. Patients with autosomal dominant polycystic kidney disease, medullary sponge kidney, and medullary cystic kidney as the primary renal disease were excluded from this study.

The following data were collected: sociodemographic data, cause of ESRD, date of the onset of hemodialysis, length of time receiving hemodialysis services, and history of a kidney transplant. End-stage renal disease was defined as permanent and irreversible loss of kidney function requiring renal replacement therapy. Hemodialysis was performed for 9 h/w to 12 h/w, three times a week, using semisynthetic (cellulose diacetate) or synthetic (polysulfone) dialysis membranes, and bicarbonate-based dialysis solution at a delivered bicarbonate concentration of 35 mEq/L. Blood flow rate was maintained at 250 mL/min to 400 mL/min, and the dialysis solution flow rate at 500 mL/min.

Renal ultrasonography was performed by the same radiologist for all of the eligible participants. Criteria for the diagnosis of ACKD were the presence of at least 4 bilateral renal simple cysts in small-to-normal sized kidneys with smooth appearance.[7] Five categories of patients, according to the cause of ESRD, were compared in terms of ACKD occurrence: hypertension, diabetes mellitus, glomerular disease, unknown, and miscellaneous. To evaluate the association between hemodialysis duration and the rate of ACKD occurrence, they were also divided into 2 groups of patients on hemodialysis for less than 3 years and those on hemodialysis for 3 years or more.

Data were analyzed using the SPSS software (Statistical Package for the Social Sciences, version 13.0, SPSS Inc, Chicago, Ill, USA). Null hypothesis was tested by 1-sample Kolmogorov-Smirnov procedure. The chi-square test was used for comparisons of dichotomous data. Correlation between quantitative values was tested by the Pearson correlation coefficient test. Comparison of the mean values between these groups was performed by the independent Student *t* test. A *P* value less than .05 was considered significant.

RESULTS

One hundred and fifty-eight patients were on hemodialysis therapy in our dialysis units, of whom 10 had primary cystic kidney disease that were excluded, and the study was performed on 148 patients. They were 95 men (64.2%) and 53 women (35.8%) with a mean age of 55.8 ± 16.4 years (57.1 ± 15.9 years and 53.5 ± 17.3 years in men and women, respectively; $P = .79$). Causes of ESRD were hypertension in 64 patients (43.2%), diabetes mellitus in 45 (30.4%), glomerulopathy in 6 (4.1%), unknown source in 27 (18.2%), and other causes (including obstructive uropathy) in 6 (4.1%).

The mean interval between initiation of hemodialysis and performing ultrasonography was 53.5 ± 17.3 months. Thirty patients (20.3%) had multiple bilateral cystic changes in the kidneys consistent with ACKD. The rates of ACKD in men and women were 18.9% (n = 18) and 22.6% (n = 12), which were not significantly different ($P = .59$). The mean age of the male and female patients with ACKD were 61.7 ± 10.9 years and 59.7 ± 22.7 years, respectively. The mean age in patients with and without ACKD was 60.6 ± 16.8 years and 53.6 ± 14.9 years, respectively. The causes of ESRD in patients with and without ACKD are shown in the Table; there was no significant differences between the two groups ($P = .64$).

Seventy-six patients were on hemodialysis therapy for less than 3 years, of whom only 7 (9.2%) experienced ACKD. In contrast, of 72 patients who were on hemodialysis for 3 years or more,

Cause of Kidney Failure in Patients With and Without Acquired Cystic Kidney Disease (ACKD)*

	Patients on Hemodialysis		
Cause of Kidney Failure	No ACKD	ACKD	Total
Hypertension	53 (44.9)	11 (36.7)	64
Diabetes mellitus	36 (30.5)	9 (30.0)	45
Unknown	21 (17.8)	6 (20.0)	27
Glomerulopathy	6 (5.1)	0	6
Others	2 (1.7)	4 (13.3)	6

*To appraise the association between ACKD and Cause of kidney failure by chi-square test, patients with unknown cause, glomerulopathy, and other reasons were merged together (P = .64).

23 (31.9%) suffered from the ACKD (P = .001). The mean hemodialysis duration in patients with and without ACKD was 44.2 ± 18.7 months and 34.3 ± 23.5 months, respectively (P = .03).

DISCUSSION

Since 1977, when Dunhill and coworkers evaluated necropsy kidney specimens in patients on long-term hemodialysis and discovered extensive bilateral cystic disease in nearly half of the samples,[8] many different studies have been performed about ACKD in patients with ESRD and its prevalence, incidence, and complications.[9-11] In our patients, the frequency of ACKD in patients on hemodialysis was 20.3%, which is comparable with most of the similar reports throughout the world. The rates of occurrence of ACKD, for example, in Pakistan, Jordan, and West Africa was 10%, 22%, and 31%, respectively.[12-14] In a few studies, however, the prevalence of ACKD has been reported to be higher.[15,16] Nonetheless, the diagnosis of ACKD in these studies have been established by more sensitive diagnosis methods such as computed tomography, nephrectomy, or necropsy. Generally, computed tomography is not used as the initial screening method for detection of ACKD.

There were many observational studies that demonstrated male preponderance in the incidence of ACKD, and the authors suggested that male hormones had a role in predisposing or accentuating tubular hyperplasia and cyst formation.[7,10,17] However, in our study, there was no significant difference in percentage of patients diagnosed with ACKD between the genders. Gnionsahe and colleagues also reported that there was no association among gender and incidence of ACKD in their cohort.[11]

In the present study, ACKD was seen more frequently with increasing hemodialysis duration. Seventy-six percent of patients with ACKD were on hemodialysis for more than 3 years, but only one patient was on hemodialysis for less than a year. A similar rise in the incidence of acquired cystic disease with increased duration of dialysis was also observed by some other studies in both adults and children with ESRD.[7,18] In one study of 30 adult patients with chronic kidney disease (who had not started dialysis) and 100 on dialysis, the incidence of multiple cysts was noted to be 7% in those with chronic kidney disease and 22% in those on maintenance dialysis. The mean duration of dialysis in patients with no cysts and those with acquired cystic disease were 15 months and 49 months, respectively.[7] In another study of 54 children on continuous ambulatory peritoneal dialysis, the prevalence of ACKD was 9%, 50%, and 80% among those who had been receiving peritoneal dialysis for 4 years or less, 5 to 9 years, and longer than 10 years, respectively.[18] Other similar studies carried out in different countries confirmed this correlation, too.[15,16] These observations suggest that the duration of kidney failure and dialysis appear to be the major risk factor for cyst formation in both adults and pediatrics.

In our study, ACKD developed regardless of the etiology of kidney failure, and there was not any association between the cause of ESRD and ACKD occurrence. Other authors have also revealed similar observations, suggesting the hypothesis that nephron loss of any etiology leads to compensatory tubular cell hypertrophy and hyperplasia in the intact nephrons.[15,17] This response generally begins by activation of proto-oncogenes and release of growth factors (such as epidermal and hepatocyte growth factors), which accumulate in patients with chronic kidney insufficiency.[19,20] Over a prolonged period of time, these factors can lead to tubular hyperplasia and cyst formation. In addition, one of these proto-oncogenes, called *activator protein 1*, has an important role in the pathogenesis of renal cell carcinoma,[21] which is the most serious complication of ACKD and occurs in 4% to 7% of these patients over a 7- to 10-year period. Metastasis of renal cell carcinoma in ACKD has also been reported in approximately 20% of the cases.[10,22]

In an attempt to detect renal cell carcinoma or premalignant lesions early, it has been suggested that renal ultrasonography be routinely performed

in all patients on dialysis for more than 3 to 5 years. If there is evidence of renal cysts in the initial evaluations, the more sensitive contrast-enhanced computed tomography should be performed annually (particularly in patients with very large cysts), in order to screen for the possible development of carcinoma.[15,23,24]

CONCLUSIONS

Acquired cystic kidney disease is an important and common complication of hemodialysis regardless of the etiology of ESRD. There is an association between ACKD and duration of hemodialysis, and the likelihood of the development of ACKD rises progressively with increasing time being on dialysis. We suggest that renal ultrasonography be performed in patients who are on hemodialysis for 3 years or more.

CONFLICT OF INTEREST

None declared.

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