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ORIGINAL ARTICLE

Etiology and pediatric chronic kidney disease progression: Taiwan Pediatric Renal Collaborative Study

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Background/Purpose: This study aims to examine the characteristics of Taiwanese children with chronic kidney disease (CKD) and delineate the factors that lead to disease progression in this population.
Methods: We reviewed the records of the Taiwan Pediatric Renal Collaborative Study, a multicenter database of Taiwanese children with CKD. Multivariate regression analysis was used to identify the main factors associated with disease progression.
Results: A total of 382 children aged 1–18 years were included in the study (median age was 10.6 years; interquartile range: 6.4–13.8). There were 197 males (51.6%) and 185 females. CKD Stage 1 was diagnosed in 159 children (41.6%), Stage 2 in 160 (41.9%), Stage 3 in 51 (13.4%), and Stage 4 in 12 (3.1%). Fifty-six children (14.7%) experienced CKD progression. A multivariate analysis for all patients indicated that the risk for disease progression was increased in children

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with CKD secondary to a structural abnormality, genetic disease, anemia, elevated diastolic blood pressure, or elevated blood urea nitrogen. Compared with children with Stage 1 CKD, those with Stage 2 and Stage 4 CKD had decreased risk for CKD progression in this short-term cohort follow-up.

Conclusion: CKD etiology affects disease progression. Careful monitoring and treatment of anemia and elevated blood pressure in children with CKD may slow disease progression.

Introduction

Chronic kidney disease (CKD) is characterized by decreased renal function. CKD can be progressive and may ultimately result in end-stage renal disease. To date, the majority of research into CKD has focused on adults. Little information is available about CKD in a pediatric population, particularly for early-stage disease, despite the fact that CKD is not uncommon in children (3.0–12.1 cases per million)[1,2] and the incidence of pediatric CKD is increasing.[3] This is concerning not only because CKD can progress to end-stage renal disease, but also because CKD in children can alter nutrition and bone and mineral metabolism,[4] thereby affecting growth. It can also have a negative effect on the quality of life of the afflicted children and their families.[5,6]

There are many differences in the etiology, progression, and treatment of CKD in adults compared with that in children,[3] and what we know about CKD in adults may not apply to children. Additional information on CKD in children is needed to improve diagnosis, maximize treatment, and potentially slow the progression of the disease in this population.

Although studies have recently begun to examine the epidemiology and clinical characteristics of pediatric CKD,[7–11] very little information has been published describing the factors associated with disease progression in children,[8] and there are no data about the epidemiology and clinical characteristics of East Asian children with CKD. As there are ethnic differences in the incidence of end-stage renal disease,[12] it is important to determine the epidemiology and clinical characteristics of East Asian children with CKD.

We reviewed the Taiwan Pediatric Renal Collaborative Study (TAPRC) database, which contains the records of children with CKD treated at the major centers that serve Taiwan. We present the patients' demographic and clinical characteristics, factors associated with disease progression, and data on CKD etiology. We analyzed children who had CKD due to structural abnormalities of the genitourinary tract or genetic diseases,[13] and those who had CKD due to nephritis and hemodynamic changes following previous acute renal failure.

Patients and methods

Study design

We conducted a retrospective review of the TAPRC central database (Table S1). The study included Taiwanese children aged 1–18 years who received treatment for CKD between January 2009 and June 2012. The inclusion criteria were as follows: study participants could not be older than 20 years at follow-up (age at first visit was <17.5 years); they had to have a diagnosis of broad-spectrum renal disease for more than 3 months; they had to meet the criteria for categorization in accordance with the staging system of the Kidney Disease Outcomes Quality Initiative[14]; and the participants had to have between 0.5 and 1.5 years of follow-up data available in the database. Children aged 1–2 years were eligible for enrollment despite the fact that the Kidney Disease Outcomes Quality Initiative staging system is not applicable to children <2 years of age.

Table S2 shows the differences between children who were included in the study and those who were excluded. In brief, children who were included tended to be older and to have higher ages at the onset of disease, as well as higher systolic blood pressure, height, weight, body mass index, estimated glomerular filtration rate (eGFR), and hemoglobin and hematocrit levels. In addition, a greater proportion of study patients presented with proteinuria, autoimmune disease, hyperlipidemia, or gout.

Patients not requiring drug therapy were followed once every 6 months. Stable patients requiring continuous drug therapy were followed every 3 months, as required by Taiwan's National Health Insurance system.

Renal function was assessed using the eGFR calculated using the new Schwartz equation.[15] An eGFR of <90 mL/min/1.73 m^2 or a CKD of >90 mL/min/1.73 m^2 in the presence of persistent proteinuria or a renal structure abnormality was considered to indicate CKD.[13] Children were excluded from the study if they had Stage 5 CKD at diagnosis, were transplant recipients, had previously received maintenance dialysis, or were pregnant. Hypertension[16] and anemia[17] were defined as previously described. The study was approved by the Institutional Review Board of National Cheng-Kung University Hospital (A-BR-101-082).

Data extraction

We examined patient demographics, clinical characteristics, CKD etiology, symptoms at diagnosis, comorbidities, family history of disease, and disease progression as indicated by an increase in CKD stage from the time of diagnosis to follow-up. All biochemical analyses were performed using standard techniques. Serum creatinine was calibrated using isotope dilution mass spectrometry. All laboratories in Taiwan use this method to determine serum creatinine levels, which enabled us to reliably compare values analyzed by different laboratories.