Prevalence of complications in children with chronic kidney disease according to KDOQI

H Wong[1], K Mylrea[1], J Feber[1], A Drukker[2] and G Filler[1]

[1]Department of Pediatrics, Division of Nephrology, Children's Hospital of Eastern Ontario, Ottawa, Ontario, Canada and [2]Shaare Zedek Medical Center, Jerusalem, Israel

The Kidney Disease Outcome and Quality Initiative (KDOQI) Group recommended guidelines for the monitoring and treatment of chronic kidney disease (CKD) in 2002. These recommendations were based on the prevalence of known complications as seen in adults. In children, the exact prevalence of these complications is unknown. We therefore conducted a cross-sectional study of 366 patients with CKD in a single center to analyze the prevalence of these complications across all stages of kidney disease. Patients were categorized to their KDOQI stage of CKD according to their estimated renal function as determined from serum cystatin C. Fifty seven percent of patients had CKD stage 1, 29.0% stage 2, 10.4% stage 3 and 4.1% stages 4 + 5. Uropathies (31%) were the most prevalent causes of CKD. Glomerular disease accounted for 27%. The overall prevalence of complications was as follows: hypertension 70.2%, anemia 36.6%, proteinuria 11.5%, and metabolic bone disease 16.9%. Metabolic bone disease and anemia occurred frequently, even with a glomerular filtration rate >60 ml/min/1.73 m^2. Growth failure (11.5%) was also common and is not a component of the KDOQI guidelines for CKD in children. The prevalence of all complications increased with worsening stage of kidney disease (all *P*-values significant). In summary, this study supports the KDOQI guidelines in defining and staging CKD in children. This study also highlights the differences in the causes and complications that occur in CKD between adults and pediatrics. We recommend modification of the KDOQI guidelines for children to reflect the differences described in this paper.

Kidney International (2006) **70,** 585–590. doi:10.1038/sj.ki.5001608; published online 21 June 2006

KEYWORDS: KDOQI; chronic kidney disease; prevalence; complications; cystatin C; glomerular filtration rate

Correspondence: *G Filler, Department of Pediatrics, Division of Nephrology, Children's Hospital of Eastern Ontario, 401 Smyth Road, Ottawa, Ontario, Canada K1H 8L1. E-mail: filler@cheo.on.ca*

Received 31 January 2006; revised 14 March 2006; accepted 28 March 2006; published online 21 June 2006

Recent publications by the Kidney Disease and Outcome Quality Initiative (KDOQI) Group have suggested guidelines for the treatment of patients with chronic kidney disease (CKD).[1] In 2003, these guidelines were reviewed and recommended for the same use in children with CKD.[2] Complications of CKD may include hyperkalemia, proteinuria, hypertension, anemia, acidosis, and metabolic bone disease.[3,4] In addition to these complications, pediatric CKD patients have problems such as growth failure and cognitive impairment,[5,6] which are not included in the KDOQI guidelines. Few studies have reported the prevalence of these abnormalities in childhood onset CKD.[7]

The aim of the study was to assess the prevalence of complications that occurred in our children with CKD. We hypothesized that there would be a child-specific pattern of complications of CKD based on the differences in physiology and underlying diagnosis.

RESULTS

Three hundred and sixty-six patients were included in this study, 221 patients were male and the mean age was 9.9 ± 5.1 years. The seven most common CKD diagnoses included non-syndromic renal dysplasia ($n = 47$), autosomal-dominant polycystic kidney disease ($n = 29$), renal scarring ($n = 28$), renal transplant recipients ($n = 25$), posterior urethral valves ($n = 24$), reflux nephropathy ($n = 23$), and Alport's disease ($n = 20$). Sixty-two different diagnoses accounted for the remaining children with CKD. We classified these diagnoses according to the following headings: cystic ($n = 47$), tubular ($n = 30$), glomerular diseases ($n = 100$), uropathies ($n = 114$), and renal hypoplasia or dysplasia ($n = 75$). The distribution of patients according to these headings and the CKD stages is listed in Table 1. Overall, the prevalence of glomerular disease decreased and the prevalence of tubular disease increased with increasing stage of CKD ($P = 0.01$ and 0.0002). Glomerular disease accounted for 27.0% of the overall causes of CKD compared with uropathies, which accounted for 31.1% (Table 1).

The cystatin C (CysC)-based glomerular filtration rate (GFR) was compared with 346 patients who had sufficient information to calculate a Schwartz-based GFR, using the published constants[8] −20% because of the measurement of creatinine with an enzymatic method. The median Schwartz

Table 1 | Prevalence of CKD according to KDOQI stage of kidney disease and pathophysiological cause

	Number	Overall %	% Stage 1	% Stage 2	% Stage 3	% Stages 4 and 5
Cystic	47	12.81	15.94	6.60	15.79	6.67
Tubular	30	8.17	3.38	14.15	10.53	26.67
Glomerular	100	27.25	33.33	18.87	23.68	13.33
Uropathy	114	31.06	34.30	30.19	26.32	6.67
Dysplastic	75	20.44	13.04	30.19	23.68	46.67
	366					

CKD, chronic kidney disease; KDOQI, Kidney Disease and Outcome Quality Initiative.

GFR (94.3) and median CysC GFR (93.6) were compared with the Wilcoxon's matched pairs test and we found no statistical difference ($P = 0.9855$). Bland–Altman analysis of the two methods for calculating GFR showed an overall bias of 0.01% and s.d. of the bias of 28%. Surprisingly, these results suggest good agreement between the two methods of calculating GFR. The mean GFR of our renal transplant patients was 69.5 ml/min/1.73 m^2 (range 34.4–124.7). There were six patients treated with dialysis: two with peritoneal dialysis and four with hemodialysis. Fifteen patients less than 1 year of age with a mean age-corrected GFR of 88 ml/min/1.73 m^2 (range 24–151) were included in the study.

Anemia (using the KDOQI cutoff of a hemoglobin <120 g/l) was present in 36.6% of the overall cohort. The prevalence of anemia increased from 31% at stage 1 to 93.3% at stages 4 and 5 ($P<0.001$). Treatment with either iron or hormone therapy correlated closely with the stage of kidney disease (both $P<0.0001$), whereas hemoglobin <120 g/l did not correlate with the stage of kidney disease.

Hypertension, as expected, was the most common complication to occur in CKD across all five stages (70.2%). It is noteworthy that even in CKD stage 1, 63% of patients had hypertension. Angiotensin-converting enzyme inhibitors and/or angiotensin II type I receptor blockers were used in 61.7%. These drugs were most often utilized in CKD stage 3 with 76.3%, whereas only 66.6% of patients received angiotensin II type I receptor blockers or angiotensin-converting enzyme inhibitors in CKD stages 4 and 5. We did not evaluate whether concerns about hyperkalemia may have contributed to this lower percentage.

The prevalence of proteinuria (>1 g/day) increased across all stages of CKD ($P<0.0001$). This prevalence ranged between 5.8% in stage 1 and 40% in stages $4+5$. The overall prevalence of proteinuria >1 g/day was 11.5%.

One-sixth (16.9%) of patients had metabolic bone disease. Intact serum parathyroid hormone (PTH), treatment with 1,25-dihydroxy vitamin D, phosphate binders, and phosphate dietary restrictions increased with severity of disease. The prevalence of metabolic bone disease was as high as 15.09% in stage 2 disease, 47.37% in stage 3, and 100% in stages 4 and 5 CKD. Interestingly, 6.28% of patients with CKD stage 1 also fit the criteria of metabolic bone disease.

Growth failure occurred in 11.5% of patients. The prevalence of growth failure increased with increasing stage of CKD ($P = 0.0001$). The overall use of growth hormone in our patients was 3% and was highest in patients with CKD stages 4 and 5 (20%).

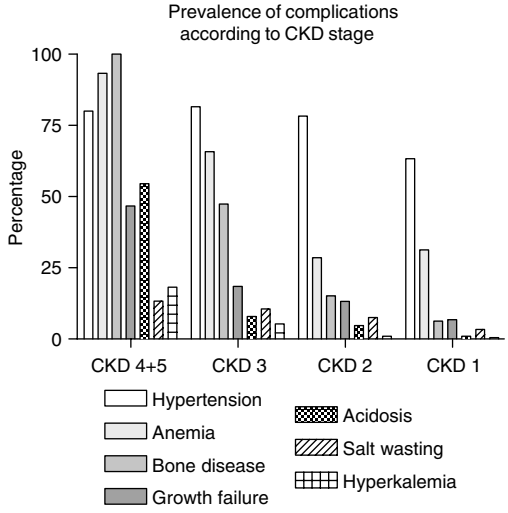

Figure 1 | Prevalence of complications according to KDOQI stage of CKD. The following complications were analyzed: hypertension, anemia, proteinuria, growth failure, metabolic bone disease, hyperkalemia, electrolyte wasting, and acidosis. Overall, the prevalence of complications increased with declining kidney function. In addition, the prevalence of anemia and metabolic bone disease occurred earlier and higher in children than previously reported in adults compared with hypertension which occurred less frequently.

The prevalence of hyperkalemia (overall 1.6%), acidosis (overall 4.4%), and electrolyte wasting (5.7%) requiring supplementation all increased with severity of disease. Patients on dialysis were excluded from the analysis for hyperkalemia. These results are summarized in Table 2 and Figure 1.

DISCUSSION

This paper describes the prevalence of complications that occur in children with CKD according to the stages proposed by the KDOQI guidelines. These stages were based in part on the increasing prevalence of abnormalities associated with CKD in adults.[9] KDOQI recommended the same definitions and staging criteria for children with CKD older than 2 years of age.[2] However, application of these guidelines according to CKD stage in children has never been validated. This paper therefore represents the first attempt to describe the