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Original article

Children with chronic renal failure in Sweden 1978–1985

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Abstract. A survey of chronic renal failure (CRF) in Swedish children was carried out for the period 1978–1985, using age-related cut-off levels for creatinine concentrations corresponding approximately to a glomerular filtration rate of 30 ml/min per 1.73 m^2. The mean annual incidence of CRF was 6.9 and of terminal renal failure (TRF) 4.4/million children. The prevalence increased during the study period, for preterminal renal failure from 14.1 (1978) to 26.1 (1985) and for TRF from 12.4 to 16/million children. The main groups of primary renal disease were malformations (42%), hereditary disorders (27%), and glomerular diseases (14%), while pyelonephritis with vesico-ureteral reflux only made up 5%.

Key words: Chronic renal failure – Epidemiology

Introduction

The treatment of chronic renal failure (CRF) with diet, dialysis and renal transplantation offers improved survival and quality of life for children as well as adults. Epidemiological data are essential for the planning of renal replacement programmes. Retrospective studies covering well-defined populations [1–4] and reports from referral centres [5, 6] have provided such information. Since the previous Swedish report covering the years 1974–1977 [2], a continued registration of incidence and prevalence of CRF in Swedish children has been carried out and the results from the period 1978–1985 are reported here. Since there has been a general tendency in Sweden during the last 15 years towards more active treatment of children with CRF, a higher prevalence of terminal renal failure (TRF) could be expected.

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Methods

Questionnaires concerning children with CRF were sent, on two occasions, to all Swedish departments of Paediatrics, Paediatric Surgery, and Nephrology, and all units replied. Children from 6 months to 16 years of age were included in the study.

CRF was defined as a glomerular filtration rate (GFR) below 30 ml/min per 1.73 m^2 for at least 6 months. When a GFR determination was not available, the serum creatinine (SCR) concentration was used; greater than 120 µmol/l for children aged 6 months to 3 years, greater than 150 µmol/l from 3 to 10 years, and greater than 180 µmol/l from 10 to 16 years.

TRF was defined as death from CRF or a need for active treatment, i.e. dialysis or transplantation. Children with a functioning renal transplant were included in this group. Preterminal renal failure (*preTRF*), was thus CRF before entering TRF.

All children that fulfilled the diagnostic criteria for CRF for the first time during the year were included in the annual incidence of CRF. Most of these were preterminal, some already terminal at diagnosis. The annual incidence of TRF included all children entering TRF, both earlier known as *preTRF* and newly diagnosed during the year.

For the final classification of the primary renal disease, the case records were reviewed, and in some patients additional information was obtained by re-evaluation of X-ray films and biopsy specimens. The diagnoses of renal hypoplasia and dysplasia were mostly based on urographies performed during the 1st year of life, showing small kidneys and often abnormal numbers of calyces. Differentiation between the two conditions was not carried out. In the group hypo-/dysplasia and obstruction children were included with unilateral agenesis or early nephrectomy of a dysplastic kidney, and obstruction of the urethra or the remaining ureter. The prune belly syndrome and neurogenic bladder disorders were included in the group of obstructive conditions because of the functional obstruction present in these states. Patients with vesico-ureteral reflux were registered as pyelonephritis and not as malformation as in the report of Habib et al. [5]. The term pyelonephritis, was thus used in children with urinary tract infection and renal scarring, with or without vesico-ureteral reflux.

Results

A total of 146 children, 76 boys and 70 girls, with CRF were detected. Of these, 99 were diagnosed during 1978–1985. In the remaining 47, CRF was verified earlier, but the patients were still below 16 years of age at the beginning of 1978.

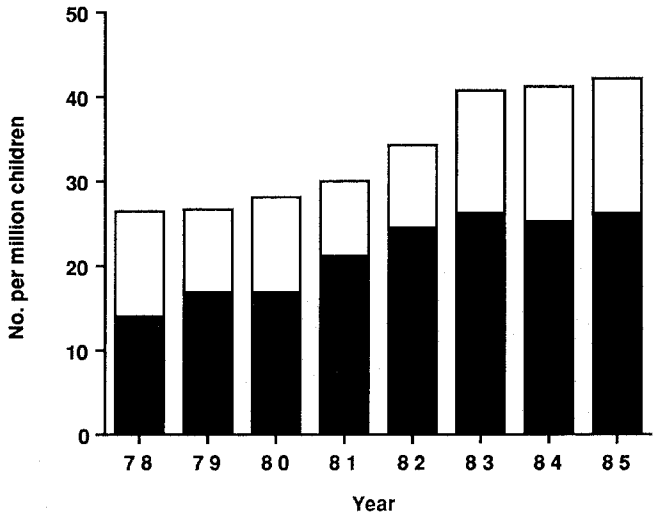

Fig. 1. The prevalence of terminal (TRF) and preterminal (*preTRF*) renal failure at the end of each year. □ TRF; ■ *preTRF*

The mean annual incidence of CRF was 6.9 (range 4.3–10.8)/million children in the same age group. This corresponds to 12 new cases/year in Sweden with a population of 8.3 million people (1.44/million total population). The mean annual incidence of children reaching TRF was 4.4 (range 1.1–8)/million children or 7 new cases/year (0.84/million total population). The incidence of both CRF and TRF varied from year to year without any tendency for increase or decrease.

The prevalence of CRF increased continuously during the study period. The same tendency was observed for both *preTRF*, from 14.1 at the end of 1978 to 26.1 at the end of 1985, and TRF, from 12.4 to 16/million children (Fig. 1).

Nineteen children died from CRF (2.4/year or 1.3/million children per year). Eight had been treated by dialysis or transplantation, while 11 were not actively treated. The reasons for withholding active therapy were severe mental retardation in 3 cases and other complicating conditions in 3 cases (multiple malformations, juvenile chronic arthritis with renal amyloidosis and polycystic kidney disease with severe liver fibrosis). Doctors and parents had together decided not to start active treatment in the remaining 5 children.

The primary renal disease of patients with CRF is presented in Table 1. Malformations accounted for 42%, glomerular diseases for 14%, and hereditary disorders for 27%. The most common disease entities were renal hypo-/dysplasia without urinary tract infection ($n = 25$), juvenile nephronophthisis ($n = 16$), urethral valve ($n = 13$), and polycystic disease ($n = 11$). There were 8 children with a diagnosis of pyelonephritis. Three of these patients had established renal damage before emigrating to Sweden. All 8 children had vesico-ureteral reflux with dilatation.

Among the 77 children reaching TRF, malformations were less and glomerular diseases more common than in the whole group of CRF (32% compared with 42% and 19% compared with 14%, Table 1). The diagnosis of CRF was established earlier in the children with malformations than in those with hereditary disorders and glomerular diseases (Table 2).

Table 1. Primary renal disease in children with chronic renal failure (CRF) and terminal renal failure (TRF) during the period 1978–1985

Renal disease	No. of patients	
	All CRF $n = 146$	TRF $n = 77$
Hypo-/dysplasia	**30 (21%)**	**14 (18%)**
- without UTI	25	
- with UTI	5	
Hypo-/dysplasia and obstruction	**6 (4%)**	**1 (1%)**
Obstructive conditions	**25 (17%)**	**10 (13%)**
– Urethral valve	13	
– Bilateral ureteral stenosis	2	
– Other obstructive malformations	5	
– Prune-belly syndrome	3	
– Neurogenic bladder	2	
Glomerulopathies	**21 (14%)**	**15 (19%)**
– Focal segmental glomerulosclerosis	6	
– Systemic lupus erythematosus	3	
– Schönlein-Henoch syndrome	3	
– GN with advanced diffuse sclerosis	3	
– Diffuse proliferative GN	1	
– Focal segmental proliferative GN	1	
– Mesangioproliferative GN	1	
– Rapidly progressive GN	1	
– IgA nephropathy	1	
– Anti-basement membrane GN	1	
Hereditary disorders	**40 (27%)**	**23 (30%)**
– Juvenile nephronophthisis	16	
– Polycystic disease	11	
– Laurence-Moon-Biedl syndrome	3	
– Cystinosis	2	
– Congenital nephrotic syndrome	2	
– Alport's syndrome	1	
– Hereditary glomerulopathy	5	
Vascular nephropathies	**8 (5%)**	**3 (4%)**
– Haemolytic uraemic syndrome	4	
– Renal damage associated with birth asphyxia	3	
– Renal circulatory disturbances due to septicaemia	1	
Pyelonephritis	**8 (5%)**	**5 (6%)**
– Pyelonephritis with vesico-ureteral reflux	8	
Other kidney disorders	**8 (5%)**	**6 (8%)**
– Drash syndrome	2	
– Wilms' tumour (bilateral)	1	
– Interstitial nephritis	1	
– Renal amyloidosis	1	
– Wegener's granulomatosis	1	
– Unclassified nephropathy + mental retardation +chromosomal aberration	1	
– Nephrotic syndrome + renal tuberculosis	1	

The children with TRF are included also in the group with CRF
UTI, *U*rinary tract infection; GN, *g*lomerulonephritis

Discussion

Under-reporting is a problem associated with this type of study and the results therefore represent minimum figures. We do believe, however, that this survey includes practically all children in whom a diagnosis of CRF was made,

Table 2. Age at diagnosis of CRF in 99 children during the period 1978–1985

Primary renal disease	No. of patients		
	<5 years $n=36$	5–10 years $n=26$	10–16 years $n=37$
Hypo-/dysplasia	15	2	3
Hypo-/dysplasia and obstruction	4	1	1
Obstructive conditions	8	0	4
Glomerulopathies	1	5	10
Hereditary disorders	4	11	12
Vascular nephropathies	2	3	2
Pyelonephritis	0	3	2
Other kidney disorders	2	1	3

since there is good co-operation between doctors treating such children in Sweden. Only a few centres perform qualified diagnostic investigations of TRF and give treatment by diet, dialysis and transplantation, and thus the reporting in this group is probably complete.

Previous investigations have used an SCR of 180 µmol/l (2 mg/dl) as the cut-off level for CRF [1–3]. We chose age-related cut-off levels of the SCR that would roughly correspond to a GFR of 30 ml/min per 1.73 m^2. This may, to some extent, have increased the number of children with *preTRF*, in comparison with previous studies. Twelve of the 69 children with *preTRF* had an SCR below 180 µmol/l. Seven of these had a GFR below 30 ml/min per 1.73 m^2, while in the remaining 5 no GFR determination was available. The prevalence of *preTRF* was indeed considerably higher (14.1 in 1978 increasing to 26.1 in 1985) than that reported for 1975 in the German survey [3] (6.5/million children). The Swiss [1] and the previous Swedish [2] investigations, however, gave figures of the same order as the present study despite having an SCR of 180 µmol/l as cut-off level.

The mean annual incidence of TRF was 4.4/million children. This figure was similar to that of the previous Swedish study (4.17, [2]), but lower than in the Swiss [1] and the German [3] reports (5.6 and 5.05, respectively). These findings can hardly be explained by methodological differences but may reflect different spectra of primary renal diseases. An explanation could be that renal disease was detected earlier in Swedish children, through health service programmes at well-baby clinics and schools, as well as through careful investigation of children with urinary tract infections. Early detection of *preTRF*, supervision of diet and metabolic disturbances, prevention of infections and control of blood pressure might delay progression to TRF, perhaps until adulthood.

The prevalence of TRF increased during the study period, which is to be expected with the more active treatment and survival of children with TRF. Unfortunately no comparable figures are available from the previous Swedish study [2]. However, in 1985 the prevalence of 16/million children had not reached the German figure for 1977 (22/million children [3]). Programmes for active treatment of children with CRF by dialysis and transplantation were started earlier in the Federal Republic of Germany than in Sweden and this probably, at least partly, explains the higher prevalence of TRF.

The major groups of primary renal disease, in our study, were malformations and hereditary disorders, together accounting for 69% of the total number of children with CRF, which is exactly the same as in the earlier Swedish study [2]. The corresponding figure in a paper from Paris was 66% (9.6% vesico-ureteral reflux included [5]) but only 47% in the German study [4]. Glomerulonephritis was the primary renal disease in only 14% in the present study but 27% in the previous one [2], while vascular nephropathies and reflux nephropathies were more common. A diminished proportion of CRF was caused by glomerulopathies in several other studies [7–9]. Such a decrease may also be noted when the studies are arranged according to year of publication: 26% in 1973 [5], 23% in 1980 [1], 20% in 1985 [4] and 14% in the present study.

There was a remarkable difference in the figures reported for pyelonephritis or reflux nephropathy: 21% for children with TRF in Great Britain, 1968–1978 [6] and 16.3% in the registry of the European Dialysis and Transplant Association, 1981 [7], compared with 6% in Sweden, 1978–1985. Pyelonephritis, without associated obstructive conditions or urolithiasis, was reported as the cause of CRF (both *preTRF* and TRF) in 16% in the Federal Republic of Germany, 1969–1975 [4], 9.6% in France, 1961–1971 [5] and 5% in the present study. Our study is more recent than the others, which may explain some of the differences. However, in the previous Swedish study, covering the years 1974–1977, no child was detected with CRF due to pyelonephritis. The differences may also reflect variations in the classification of the primary renal disorders, illustrated by the problem of distinguishing renal hypo-/dysplasia from reflux nephropathy at a late stage of the disease. It should be pointed out, however, that 25 of our 29 cases with the diagnosis of hypo-/dysplasia never had a urinary tract infection. Thus, the present and previous Swedish studies suggest that a smaller proportion of CRF cases are caused by infections in Sweden than in the other countries studied. In Sweden urine cultures are routinely performed in infants and small children with fever of unknown origin. A diagnosis of pyelonephritis leads to radiographic examination of the kidneys and lower urinary tract, as well as a thorough follow-up of the child [10]. It is possible that swift medical intervention prevents the development of progressive renal disease in these children.

In conclusion, this study shows a higher prevalence of *preTRF* in Swedish children than that reported from other countries. In contrast, the prevalence of TRF was lower. This might be due to earlier detection of the primary renal disease. The treatment of CRF by dialysis and transplantation has previously not been as active in Sweden as in many other countries, resulting in a lower prevalence of TRF. During the last few years an increasing number of renal transplantations have been performed, especially in younger children. This will probably result in a further increase in the prevalence of TRF.

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Ask the expert*

An 11-year-old boy from Ghana presented in September 1988 with a 1-year history of recurrent haematuria. Initially there had been some dysuria and frequency. A 24-h collection of terminal samples of urine in hospital revealed schistosomes. An intragtvegtnous pyelogram showed nodular filling defects in the bladder mucosa in keeping with cystitis. He was treated with praziquantel 50mg/kg per day in three divided doses for 1 day. His haematuria has not recurred and repeat early morning urine collections revealed no evidence of schistosomes. A repeat ultrasound showed a normal bladder with no evidence of thickening and a normal bladder capacity. There were no areas of calcification within the bladder wall. The Schistosoma *enzyme-linked immunosorbent assay (ELISA) test was positive at presentation at level 4 (predicted value 82%). The repeat test 1 month after treatment revealed that this had dropped to level 2 (predicted value 76%). Is one 1-day course of praziquantel sufficient for this condition? Is it worth repeating the* Schistosoma *ELISA test at intervals to show that it continues to fall, or will it remain positive for a long time following irradication of the* Schistosoma *from the bladder? What follow-up should we perform from the point of view of the known long-term complications of carcinoma of the bladder; should we check for microscopic haematuria every 6 months or so, or should we even consider routine cystoscopy at regular intervals?*

Key word: Schistosomiasis

This is the classical presentation and course of recent *Schistosoma haematobium* infection. According to WHO reports, this parasitic infection is fairly common in Ghana, as well as in many other African countries [1]. The nodular bladder lesions are characteristic and are, in fact, submucosal granulomatous masses [2] formed by the immune-mediated tissue response against the parasite [3]. These are composed of one or more ova surrounded by large numbers of lymphocytes, eosinophils, mast cells and a few neutrophils and macrophages, and shelled off by a peripheral condensation of fibroblasts

These granulomata respond quite readily to treatment with praziquantel [4]. Unless considerable fibrosis has already taken place before treatment, they usually leave no residual damage. Even much more advanced pathology in the lower urinary tract, with alarming radioloical appearances in an intravenous urogram, may completely resolve with schistosomicidal therapy [5]. The 1-day course of treatment is sufficient. Out of all species of schistosomes pathogenic to man, *S. haematobium* is the most vulnerable to the effect of the drug [4].

The ELISA test is a good indicator of active disease. It usually takes 3–4 months before it turns negative, depending on which ELISA technique is being used, and whether it is looking at worm or egg antigens or at antibodies against the parasite [6]. Repetition of the test in another couple of months will probably show complete regression. If it remains significantly positive, another single-dose treatment with praziquantel is indicated.

It is unnecessary to do any further follow-ups unless the patient is reinfected. The possibility is always there, as long as the socioeconomic factors leading to initial exposure are still the same. Reinfection is usually detected by recurrence of haematuria and reappearance of eggs in the urine. Whether a regular check-up for reinfection is indicated is a matter of general health policy in the country. This particular patient is not more vulnerable to reinfection when compared with the general population. Indeed, his first infection may confer partial immunity against reinfection [7].

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* The editors invite questions for this section