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ORIGINAL ARTICLE

Chronic renal failure in Sudanese children: aetiology and outcomes

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Abstract The provision of tertiary paediatric nephrology facilities has led to increasing referrals of children with chronic renal failure (CRF). We report the aetiology and outcomes over 5 years, during which period the improving socio-economic situation has allowed increasing provision of dialysis and transplantation. The records of 205 children (124 male; 60.5%) who were referred to a tertiary paediatric nephrology unit in Khartoum between 2001 and 2006 with a glomerular filtration rate of less than 50 ml/min per 1.73 m^2 body surface area were reviewed. The mean age at the time of diagnosis with CRF was 9.8 years (range 3 months–17 years). The aetiology was chronic glomerulonephritis in 52 (25.4%), congenital urological malformations in 36 (17.5%), urolithiasis in 19 (9.3%), hereditary nephropathy in 14 (6.8%), multisystem diseases in 4 (2%), and cause unknown in 80 (39.1%). Of the 205 children, 136 (63%) had reached end-stage renal failure, with chronic haemodialysis being undertaken in 48 (35.3%), intermittent peritoneal dialysis in 43 (31.6%), continuous ambulatory peritoneal dialysis in 17 (14.7%), and no treatment in 25 (18.4%). At the end of the study period 53 of the 205 (25.9%) remained on dialysis, 51 (25%) were on conservative treatment, 8 (3.9%) had received transplants, 48 (23.4%) had died, and 45 (22%) had been lost to follow-up. The results illustrate the geographical variations in CRF aetiology in different countries, which may be influenced by current patterns of referral as well as environmental and society factors. The large number with an unknown aetiology for their CRF requires further prospective investigation. We hope the current high mortality rate will improve with earlier referral, improved nutrition, family support, and better access to treatment modalities, especially the provision of kidney transplantation from living related donors.

Keywords Chronic renal failure · Children · Transplantation · Dialysis

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Introduction

Sudan is the largest country in Africa, with a land area of approximately 2.5×10^6 km^2 and a total population of about 36 million, 60% of whom live in rural areas. The annual population growth is 2.2%, with children under 15 years old constituting approximately 45% of the total population. Public expenditure on health is 1% of gross domestic product (GDP) or US$ 3.88 per capita. This is far less than suggested by the Commission on Microeconomics and Health for low income families [1].

The care of children with chronic renal failure (CRF) imposes a burden on the health care budget of developing and underdeveloped countries like Sudan. However, the peace settlement in southern Sudan and exploitation of oil reserves has significantly improved the economic status of the country, with consequent improvement in the health care budget. Comprehensive paediatric renal services have developed in the capital, Khartoum, and, currently, dialysis and transplantation are provided free of charge to children who are eligible.

The aetiology of CRF in children is different from that in adults, and congenital dysplasia/hypoplasia account for the highest frequency of paediatric CRF cases in the developed world, where facilities generally allow early diagnosis [2–4]. In contrast, infections and acquired causes are responsible for most CRF cases in developing countries, where patients are often referred late and at a terminal stage [5–8]. As well as socio-economic factors, there may be environmental and genetic factors which lead to these variations in aetiology.

The paediatric nephrology service was started in Khartoum in 2001, and, before then, older children were treated in renal centres supervised by adults' nephrologists. Continuous intermittent peritoneal dialysis was used for some patients but with high morbidity and mortality rates. Chronic haemodialysis became available in 2004, followed by continuous ambulatory peritoneal dialysis (CAPD) in 2005. These are provided free at our unit, but renal transplantation is only available within adults' units in the locality.

The establishment of a specialised unit was accompanied by maintenance of a patient data registry. We report data on the aetiology and outcomes for CRF that are used for ongoing audit, so that treatment priorities can be set and a reasoned case made for more resources.

Methods

We reviewed the records of patients with a diagnosis of CRF who were seen at the paediatric nephrology unit at Soba University Hospital and the Dr. Salma Dialysis and Transplant Kidney Centre between 2001 and 2006. CRF was defined as glomerular filtration rate (GFR) less than 50 ml/min per 1.73 m^2 body surface area, estimated by the Schwartz formula [9] when an accurate height had been recorded. The value of k varies as a function of age and gender, being 0.33 in preterm infants, 0.45 in full-term infants, 0.55 in children and adolescent girls, and 0.70 in adolescent boys [9]. Alternatively, we used serum creatinine values above 178.8 μmol/l (2 mg/dl) for 0–2 year olds, 221 μmol/l (2.5 mg/dl) for 3–10 year olds, and 265 μmol/l (3 mg/dl) for 10–15 year olds [10, 11].

Results

There were 205 children (124 male, 60.5%) enrolled in the study. The male:female ratio was 1.5:1, and the average age at the time of diagnosis was 9.8 years (range 3 months–17 years). There were 33 patients (16%) below 5 years of age, 52 (25.4%) were within the age range 5–10 years, and 128 patients (58.5%) were more than 10 years of age, of whom 86 (40.9%) were aged between 10 years and 15 years.

Aetiology

The aetiology of CRF in the 205 patients is shown in Table 1. In 80 patients (39.1%) the aetiology could not be identified, as biopsy was felt to be inappropriate, due to the need for general anaesthesia or because of small kidneys where it was felt the risk outweighed potential benefit. Fifty-two children (25.4%) had a biopsy proven diagnosis of chronic glomerulonephritis, which was difficult to characterise completely in 20 of 52 cases due to the limited histology methods available at the time. All biopsies were examined by light microscopy, but immunofluorescence was being introduced during this period. Electron microscopy was only available for suspected Alport's syndrome, with specimens being sent abroad as part of a research project.

Dipsticks for urinalysis, full biochemistry facilities, and renal ultrasonography were freely available in Khartoum during the study period, but they were of limited availability and variable quality in other centres, especially in rural areas.

Table 1 Aetiology of CRF in 205 Sudanese children, 2001–2006

Primary renal disease	Frequency	Percentage of total %
Glomerulopathy	52	25.4
Rapidly progressive glomerulonephritis	17	
Focal segmental glomerulonephritis	8	
Membranoproliferative glomerulonephritis	6	
Minimal change disease	1	
Unspecified glomerulonephritis	20	
Congenital urological malformation	36	17.5
Congenital obstructive uropathy		
– associated with neurogenic bladder	17	
– not associated with neurogenic bladder	5	
Reflux nephropathy	5	
Nephrocalcinosis	4	
Dysplasia/hypoplasia/aplasia	5	
Urolithiasis/stones	19	9.3
Hereditary nephropathy	14	6.8
Polycystic kidney disease	4	
Congenital nephrotic syndrome	3	
Juvenile nephronophthisis	5	
Medullary sponge kidney	1	
Sickle cell disease	1	
Multisystem disease	4	2
Haemolytic uraemic syndrome	3	
Systemic lupus erythematosus	1	
Cause unknown	80	39.1
Total	205	100

Treatment modalities

Of the 205 patients, 136 (66%) reached end-stage renal failure (ESRF) requiring dialysis (Table 2). Haemodialysis was the treatment modality employed for the majority of patients from 2004 onwards. Intermittent peritoneal dialysis was employed early in the programme, with dialysis sessions through an acute peritoneal catheter (Peritocat®, B. Braun) for 3–5 days per week. This was subsequently replaced by the development of a CAPD programme, with percutaneous placement of double-cuffed curled catheter by the paediatric nephrologist and development of specialised nursing support.

No dialysis was undertaken by 25 children after extensive discussions with the families. Usually, this occurred when the child lived in the rural community some distance from the hospital, under poor associated economic circumstances.

Outcomes

The outcomes for the 205 patients at the end of 2006 are shown in Table 3; 25.9% remained on dialysis, 24.9% were being maintained on conservative treatment, and 23.9% had died. Twenty-seven out of 49 (55.1%) had died on dialysis, and 22/49 (44.9%) had died due to inability to access or travel to the centre for care. A large number of patients are referred from long distances throughout the country and are lost to follow-up when they return to their referral centre. Only seven children (3.4%) had received transplants from living related kidney donors in local adult centres at the time of study, with 100% patient survival. No programme for renal transplantation from deceased donors exists yet in Sudan.

Discussion

This study defines for the first time the aetiology and treatment outcomes in children with CRF in Sudan, based on the population of children referred to a newly established tertiary paediatric renal unit. The study period encompassed a time when the unit had been developing comprehensive treatment facilities, including renal biopsy, dialysis, and liaison with adults' units for renal transplantation. Socio-economic conditions in many parts of the world mean that many children with CRF have little or no prospects of treatment, particularly if dialysis and transplantation are required [5, 7, 12]. A combination of improving economic circumstances, two paediatric nephrologists who had received sponsored training abroad, and the support of adult colleagues led to the establishment of our paediatric renal unit. There was also the additional support provided by an overseas benefactor who contributed to the building of a haemodialysis unit and establishment of 'sister-unit' links with UK paediatric renal units.

Table 2 Treatment modalities in patients with ESRF (n=136)

Type of dialysis	Frequency	Percentage
Chronic haemodialysis (CHD)	48	35.3
Continuous ambulatory peritoneal dialysis (CAPD)	20	14.7
Chronic intermittent peritoneal dialysis (CIPD)	43	31.6
No dialysis	25	18.4
Total	136	100

Table 3 Treatment outcome of patients with CRF (n=205)

Outcome measure	Frequency	Percentage
Chronic haemodialysis	41	20
Continuous ambulatory peritoneal dialysis	12	5.9
Living related donor transplantation	7	3.4
CRF on conservative treatment	51	24.9
Died	49	23.9
Lost to follow-up	45	22
Total	205	100

The true incidence and prevalence of CRF in Sudanese children is difficult to determine, because of the current pattern of referral and lack of a national database. An increasing prevalence in children of 62.1 per million age-related population requiring renal replacement therapy (RRT) was noted in European data in 2001 [4]. Since 45% of the Sudanese population of 36 million are under 15 years of age, then the number of Sudanese children requiring RRT could be as high as 1,000, compared with the 136 reported in this initial series.

There was an obvious male predominance in our series, as has been described in other similar studies from different parts of the world [2, 13, 14]. These studies have related male predominance to the high rate of congenital urological anomalies, which was not shown in our study. Chronic glomerulonephritis accounted for 25.4% of our patients with CRF and was the commonest identifiable aetiology. Similar reports from adult Sudanese patients reported the predominance of chronic glomerulonephritis as a cause of CRF in 33% and 38% of patients [15, 16]. Studies from other developing countries in Asia, Latin America, and Africa have shown a high prevalence of glomerulonephritis in their patients, with rates of over 50% in Nigeria and China [5, 7, 14, 17]. In many of these countries, the high incidence of infections such as malaria, schistosomiasis, tuberculosis, hepatitis C and HIV might have led to infection-related glomerulonephritis. However, another report about the

nephrotic syndrome in African children showed lack of evidence for tropical nephrotic syndrome [18]. Similarly, but unexpectedly, other reports from Japan, Australia and New Zealand have shown a higher incidence of ESRF due to chronic glomerulonephritis in their child population [19, 20].

Congenital urological malformations, including dysplasia, were detected in only 36 of our patients (17.5%). This incidence is far below what has been reported in Western and Asian countries, including many Arab countries. In those areas such anomalies constituted the major cause of CRF in their child population [3, 4, 10, 21, 22]. There may be differences in classification between registries and countries in this respect, especially with patients previously described as having reflux nephropathy as opposed to renal dysplasia or obstructive uropathy with associated reflux. However, neither of these conditions figures prominently in our series, and this may reflect on patterns of referral. Children with obstructive uropathy, which, in many cases, is being detected on antenatal scans in developed countries, may die from urosepsis before referral for chronic kidney disease (CKD) care in underdeveloped countries.

In about 40% of our children with CRF we were uncertain of the aetiology. High rates have also been reported in Africa and Asia [12, 13]. Reports from adult Sudanese patients also showed high frequencies of cause unknown, at 16% and 20% [15, 16]. This could have been due to the pattern of late referrals, with failure of detection of the primary cause and lack of intensive imaging modalities. If more detailed ultrasound methods were available to define renal size, it is possible that renal dysplasia/hypoplasia might be diagnosed more frequently. Other, as yet unidentified, environmental or genetic factors may also be responsible for the lower incidence of congenital anomalies in our population and would require further investigation to define.

We diagnosed renal calculi in 19 of our patients (9.3%) with CRF. This finding is lower than that in the Syrian population (18%) but approximately similar to that reported in Kuwaiti children (10.4%) [11, 22]. The hot weather, high rate of consanguinity, or other as yet unknown factors might have a role in this respect.

Only 14 patients (6.8%) in this series had hereditary nephropathy. This incidence is low in comparison with many published data, especially from the Arab world and Iran [10, 13, 23, 24]. This difference cannot be explained by the a high rate of parental consanguinity in our community. However, our findings are similar to published data from Bangladesh and Indian populations [14, 17, 25].

Multisystem disease accounted for only 2% of patients with CRF in our study, similar to published data from Indian and Kuwaiti populations [25–27]. Most of our patients with haemolytic uraemic syndrome recovered completely, and most of our systemic lupus erythematosus patients remained with normal function up to the time of the study.

Most of our patients (66%) with CRF presented with, or reached, ESRF requiring dialysis. Similar findings have been reported in other developing countries in which most of the CRF patients present at an advanced stage of CRF [12, 14, 17, 28]. In Sudan the availability of renal replacement therapy (RRT), namely chronic dialysis or transplantation, has been limited. Although the majority (81.6%) of our children with ESRF were offered some sort of dialysis treatment, only 25.9% were on regular dialysis, and only 3.4% had undergone kidney transplantation from a living related donor at the end of the study period. The majority of patients who died had inadequate dialysis with intermittent peritoneal dialysis in the early days of our programme or opted for conservative treatment at home. Sudan has only two paediatric dialysis centres, two trained paediatric nephrologists and five paediatricians with a special interest in nephrology. All these facilities are centred in the capital, Khartoum, and patients from different parts of the country have to travel to these centres for specialised nephrology care. Although the dialysis treatments are provided free, the family still have to pay for additional medicines at present and support themselves in the hospital vicinity. Chronic peritoneal dialysis at home is being developed with increasing nursing expertise but still with many restrictions due to socio-economic factors. Good communication with families and within the multiprofessional team are essential to resolve many of the logistical and ethical issues posed by the current restrictions on provision of care, not only in Sudan but in many parts of the world [29, 30].

In conclusion, most of the Sudanese children with CRF present at a later stage with a terminal stage of the disease. Our results also reflect the geographical variations in the aetiology of CRF, which may be due to the present pattern of referral. The large number with an unknown aetiology is under further investigation. Most of our children with ESRF had had either inadequate dialysis or no dialysis treatment, leading to a high mortality rate. Our aspirations are to continue to develop the comprehensive diagnostic and treatment facilities at our unit at the same time as educating paediatricians countrywide in better recognition and management of CRF. We have been helped by close collaboration between our unit and a ‘sister unit’ in the UK with respect to training of key personnel, teaching and registry development as well as adult colleagues locally. A deceased-donor transplant programme is currently not available in Sudan, and so major efforts are being made to provide living related donor transplant programmes for children, as we support the view that transplantation is the best treatment modality for children.

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