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Etiology and outcome of chronic renal failure in Indian children

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Abstract A prospective analysis of all new pediatric cases of chronic renal failure (CRF) was performed at our hospital over a 1-year period. The diagnosis of CRF was based on serum creatinine >2 mg/dl with supportive clinical, laboratory, and radiological findings. There were a total of 48 patients with CRF with a median age of 13 years (range 10 days to 16 years). The causes of CRF included glomerulonephritis (37.5%), obstruction and interstitial (52%), hereditary (6.3%), and undetermined (4.2%). Patients were symptomatic for a mean of 33.2 months (range 10 days to 11 years) at presentation. Eight patients (16.7%) had acute reversible deterioration of renal function at presentation. This was due to accelerated hypertension in 2, infection in 3, volume depletion in 2, and nonsteroidal antiinflammatory drugs in 1 patient. At presentation, 22 (46%) children had mild to moderate renal failure and 26 (54%) had end-stage renal disease. Twenty-one children (43.7%) had associated illness at presentation. Mean follow-up was 22.9 weeks (range 2–126 weeks). At the end of the study period, 10 (21%) patients were on conservative treatment, 7 (14.6%) on maintenance dialysis, 8 (16.7%) patients had functioning allografts, 4 (8.3%) patients had died, and 19 (39.6%) opted against further therapy. We conclude that CRF in Indian children carries a poor prognosis due to late referral and the limited availability and high cost of renal replacement therapy.

Key words Chronic renal failure · Dialysis · Transplantation · Indian children

Introduction

Chronic renal failure (CRF) is an important renal cause of morbidity and mortality in children. Most of the data on CRF in children are registry based and hence deal only with children accepting renal replacement therapy (RRT) [1–3]. Some studies have documented the problem of CRF in children [4–11], however, very few have prospectively evaluated the magnitude of CRF, associated conditions, factors causing acute deterioration, and the overall outcome, especially in the developing countries. In our country there is no national or regional registry collecting data on CRF on end-stage renal disease (ESRD). Thus the incidence and prevalence of pediatric CRF, its burden on the health care system, and its outcome are not known. Hence we prospectively studied all children with CRF presenting to our hospital over a 1-year period to analyze the etiology, spectrum, and outcome.

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Patients and methods

A prospective analysis was carried out on all the new cases of pediatric CRF (≤16 years), including those seen in the renal outpatient clinic and all inpatients and inservice referrals over a 1-year period at our hospital. The hospital is the only tertiary care pediatric nephrology referral center for the state of Uttar Pradesh, which has a total population of about 150 million [12]. It has all modern biochemical, immunological, radiological, scintigraphic, and histopathological facilities for the diagnosis of various renal disorders. Standard biochemical (serum and urine) and radiological investigations were performed in these patients. The diagnosis of CRF was based on clinical, laboratory, and radiological findings, i.e., all patients presenting with serum creatinine >2 mg/dl with no evidence of recovery over the ensuing 3 months, other clinical features of CRF, and evidence of bilateral contracted kindeys and/or azotemic symptoms of more than 3 months' duration. Kidney biopsy was performed in other patients with normal-sized kidneys to establish the diagnosis of CRF.

The patients with CRF were subdivided into the various etiological subgroups. A definitive diagnosis of chronic glomerulonephritis (CGN) was made when it was confirmed by biopsy. In patients where biopsy was not performed, a probable diagnosis of CGN was based on the presence of a long history of edema and nephrotic proteinuria before the onset of CRF, active urinary sediment, and/or urinary protein excretion >1 g/m^2 per day at the time of diagnosis at our center. A definitive diagnosis of chronic interstitial nephritis (CIN) was based on demonstration of vesicoureteric reflux (VUR) on micturating cystourethrogram or when the child had neurogenic bladder leading to secondary VUR. In other cases it was confirmed by biopsy. A probable diagnosis of CIN was made

when at least three of the following features were present: (1) signs and symptoms of VUR, (2) a history of recurrent urinary tract infection with reflux or history of pyelonephritis, (3) a history of exposure to nephrotoxic drugs, toxins, or indigenous medications, (4) urinary protein <1 g/m^2 per day except when secondary focal segmental glomerulosclerosis was suspected, (5) demonstration on ultrasonography or intravenous pyelography of irregular renal outline or hydronephrosis, and (6) the absence of glomerular disease, as described above. The diagnosis of obstructive nephropathy was based on the presence of hydronephrosis and demonstration of an associated obstructive condition. Alport syndrome was diagnosed in the presence of sensorineuronal deafness and lenticonus, or a family history of nephritis and deafness. Patients who did not fall into defined categories were classified as "CRF due to unknown causes." In all patients we looked for potentially reversible factors. We also looked for various associated conditions. At the end of the study period the outcome was analyzed.

Results

There were a total of 48 patients with CRF with a median age of 13 years (range 10 days to 16 years). Only 3 of these were younger than 5 years at presentation. The male to female ratio was 2.2. The etiology of CRF is shown in Table 1. Patients were symptomatic for a mean of 33.2 months (range 10 days to 11 years) at presentation. Eight patients (16.7%) had acute reversible deterioration of renal function on an underlying CRF. This was due to accelerated hypertension in 2, infection in 3, volume depletion in 2, and antiinflammatory drugs in 1 patient. Twenty-one children (43.7%) had associated illness at presentation, including renal tubular acidosis in 10 (47.6%), epilepsy in 5 (23.8%), tuberculosis in 4 (19%), and hepatitis B infection in 2 (9.5%) patients.

At presentation, 22 (46%) children had mild to moderate renal failure and 26 (54%) had ESRD. The mean follow-up in our study was 22.9 weeks (2–126 weeks). Of the 22 patients with mild to moderate renal failure at presentation, 7 (31.8%) continued to have mild to moderate renal failure and were on conservative treatment at the last follow-up, 4 (18.2%) progressed to ESRD, 1 (4.5%) patient died, and the parents of 10 (45.4%) children with relatively advanced renal failure opted against further treatment after diagnosis. One patient who had progressed to ESRD received a renal allograft and the parents of another 3 decided against any definitive form of RRT; these patients remained on conservative treatment. Of the 26 patients with ESRD at presentation, 7 (26.9%) were on some form of maintenance dialysis, 9 (34.6%) received renal allografts, 1 (3.8%) died, and the parents of 9 (34.6%) children opted against medical treatment. Two children died after renal transplantation, 1 within 1 month due to septicemia, and the other patient who was hepatitis B surface antigen positive died after 2 months due to pneumonia. Thus there were a total of 3 (11.5%) deaths in the ESRD group. Hence at the end of the study period, 10 (21%) patients were on conservative treatment, 7 (14.6%) on maintenance dialysis, and 8 (16.7%) patients were alive with a functioning allograft. Four patients (8.3%) died and 19 (39.6%) opted against further treatment.

Table 1 Etiology of chronic renal failure

Etiology	*n* (%)
Glomerulonephritis	18 (37.5)
CGN	8
FSGS	4
IgAN	3
MPGN	3
Obstruction/interstitial nephritis	25 (52)
Primary VUR	10
PUV	5
Solitary kidney stone	2
NTD VUR	2
GUTB	1
Rhabdomyosarcoma of urinary bladder	1
Crossed fused ectopia with hydronephrosis	1
CIN (unknown)	3
Hereditary	
Alport syndrome	3 (6.3)
Unknown	2 (4.2)

NTD, Neural tube defects; PUV, posterior urethral valve; GUTB, genitourinary tuberculosis; CGN, chronic glomerulonephritis; FSGS, focal segmental glomerulosclerosis; IgAN, IgA nephropathy; MPGN, mesangioproliferative glomerulonephritis; VUR, vesicoureteric reflux; CIN, chronic interstitial nephritis

Discussion

Children constitute about 44% (66 million) of the total population of our state, the most populous in the country [12]. The number of children with CRF in our country is not known, but is likely to be large. The reported incidence of acceptance of RRT in children is about 5–10 per million child population [4]. As most of these data are registry based they do not include information about patients who receive only conservative management or those who receive no treatment at all. A few studies have reported a much higher prevalence of CRF, of the order of 18.5–58.3 per million child population [10, 13]. Unfortunately, there are few reports from other centers in India and those deal mainly with children accepting RRT [3]. In an analysis of 174 children seen over 10 years, Srivastava et al. [14] found that advanced irreversible renal failure constituted 0.8% of total admissions to pediatric wards. As this was a retrospective study and dealt only with admitted patients it may not reflect the true extent of CRF in children. In addition the outcome of these children was not evaluated. The incidence of CRF in our study is lower than that reported in Swedish and French series [9, 10]. In a previous study we observed that children constituted 5.3% of total CRF cases referred to our hospital [15]. This may be an underestimation due to underdiagnosis and under-referral of children with CRF because of lack of awareness, limited availability and high cost of RRT. In this study we have analyzed in detail the etiology, spectrum, and outcome of these children.

The median age of our patients was 13 years and only 3 (6.25%) patients were under 5 years of age. This is in contrast to an earlier report from our country, in which

study 58 (33%) patients were under 5 years of age [11]. In a previous study of Turkish children the mean age was 9.5 years [5]. The reason for fewer children under 5 years in our study could be that very young children with CRF are usually not considerable suitable for dialysis and transplantation, and hence are not referred to tertiary centers for further management. These data are similar to the initial experience of the Swedish group [10]. In our study glomerulonephritis (37.5%) was the most-common cause of CRF. The incidence of hereditary nephropathies in our series is lower than in other studies [8–10]. Interstitial nephritis and obstructive nephropathy were together responsible for 52% of cases. This is much higher than that in Swedish and Turkish children [8, 9]. Another important observation was that posterior urethral valve (PUV) was responsible for half of the cases of obstructive nephropathy. The prevalence of PUV has not been reported in other studies from India [3, 11]. Hence there should be greater awareness of PUV amongst pediatricians, surgeons, and urologists to allow early diagnosis. In 3 children the etiology of CIN was not apparent from clinical history and investigations. There was a history of intake of indigenous medicines that may have a contributory role in the etiology, but in view of absence of further details these patients have been classified as unknown CIN.

One sixth of our children had acute deterioration of renal function with underlying chronic renal insufficiency at presentation. A large number of these were reported to have associated conditions, such as renal tubular acidasis and tuberculosis. Early and effective treatment in these conditions often leads to dramatic improvement in these children. The mean duration of symptoms prior to diagnosis was 33.2 months. More than half of the children had ESRD at presentation. This highlights the problem of delayed diagnosis and referral. It has been shown that prompt therapy for chronic renal insufficiency may retard progression is terminal renal failure [9, 10]. An additional advantage is the economic benefit of postponing the development of ESRD. This may help buy sufficient time for the child, to attain an age at which dialysis and transplantation is easier and long-term results better.

In our study a high proportion of families of children even with mild or moderate renal failure opted against further treatment. This is possibly due to lack of awareness both amongst the families and the referring physicians of the available therapeutic interventions at this stage. An overriding factor is the expense involved in RRT. In the absence of state funding, RRT remains unaffordable for the vast majority of the population. In a developing country like India, governmental support for an ESRD program is obviously difficult in the context of current health care priorities. However, RRT is not entirely beyond the reach of children from developing countries, as has been shown by the Brazilian experience. As RRT becomes more easily available and awareness increases, the acceptance rate also rises [2]. Greater involvement of non-government and charitable organizations and the creaton public funds for management of serious diseases could help in providing much needed financial support without burdening the exchequer [16]. A total of 10 (21%) children received a renal allograft in our study. This is an encouraging figure and indicates an increasing acceptance of transplantation in children both by nephrologists and parents.

To conclude, obstructive nephropathies and interstitial nephritis constitute a large subgroup of CRF in Indian children. Delayed referral, limited availability, and high cost of RRT leads to a much poorer outcome than in developed countries. An active effort should be made to identify associated conditions and reversible factors in these children. There is increasing acceptance of RRT, but the overall figure is much lower than from other countries. A greater awareness needs to be created amongst patients as well as the referring physicians.

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