Pattern of Referral and outcome of Childhood Nephro-urologic Disorders: A 6-year-follow up report in a single Centre in Khartoum

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Abstract

Background: previous patterns and outcomes of nephro-urologic disorders in children in Khartoum might have been influenced by establishment of tertiary care renal services. The aim of this study was to re-study these parameters to determine if any changes towards improvement of child healthcare have occurred.

Methods: We retrospectively reviewed case records of all children with renal disorders who were referred to the paediatric nephrology unit, Soba University Hospital, Khartoum, during the period January 2006 to December 2012.

Results: A total of 800 children with 1121 renal disorders were seen forming 5.5% of the paediatric unit cases ; 61% males and 38.8% females . Mean age at diagnoses was 7.73 years (±5.35) .Common causes of renal disorders were chronic kidney disease (24.1%), acute glomerulonephritis (14.9%) and nephrotic syndrome (14.8%) followed by urinary tract infections (11.3%) and acute kidney injury (10.5%). Renal calculi, hereditary diseases, congenital anomalies of kidney and urinary tract, multisystem diseases and renal tumors were: recorded in 7.7%, 7.6%, 5.1%, 3.1%, and 0.8% respectively. On short term follow-up 59.2% recovered renal function, 22% progressed to CKD, 6.2% died, 5% referred to other centers and 7.5% were lost to follow-up.

Conclusion: Glomerular diseases and CKD were the most common causes of referral of children with nephro-urologic disorders in Sudan. These findings reflect the referral pattern in a centre where tertiary care paediatric renal services are developing and patient care is improving. The high prevalence of CKD with a potentially treatable causes calls for more efforts to early detect and refer CKD patients.

Introduction

In developing and underdeveloped countries, endemic diseases continued to be the leading causes of high childhood morbidity and mortality and to be top priories in health budget allocations. However, chronic renal disease in children is a growing health problem worldwide especially in countries with resource-poor settings. Improvement in renal services in a given area is usually paralleled by changes in prevalence rates, patterns and outcomes of renal disorders. Hence, re-studying these parameters is useful in assessing changes in child health care and providing basic data for the health care planners. Several studies from different parts of the world have reported different prevalence rates, patterns and outcomes of nephro-urologic disorders in children [(1-6)]. Delayed referral, genetic and environmental factors might have predisposed to these variations. Lack of advanced diagnostic and treatment facilities usually lead to suboptimal treatment of renal disorders and therefore progression to CKD is inevitable with consequent high morbidity and mortality [(7, 8)]. Many of these renal diseases are potentially treatable if detected and treated early and hence the risk of permanent kidney damage could be reduced by early referral. Previous data from Sudan was largely derived

from secondary care settings. Establishment of specialized tertiary care paediatric renal unit in Soba Hospital, Khartoum State in 2005 has increased the referrals of patients with various renal diseases who were in need of advanced management. In this centre all treatment modalities including RRT are provided free by well-trained paediatric nephrology and surgery teams. Since then, our patients care and data registry have markedly improved. We took this opportunity to retrospectively restudy the prevalence, pattern of referral, and short-term outcome of nephro-urologic disorders in children in a single Centre in Khartoum State.

Patients & methods:

We retrospectively reviewed the case records of all children with nephro-urologic disorders, who have been referred and managed in the paediatric nephrology unit in Soba University Teaching Hospital, Khartoum State in the period between January 2006 and December 2012. Re-admissions and patients with incomplete records were not included. Data was abstracted from the records using standard data collection sheet. Data pertaining to age, gender, residence, history, clinical signs and diagnosis were recorded. Laboratory tests used in diagnosis were all recorded. These included urine tests (urinalysis, cultures, urine albumin/creatinine ratio [UACR]), blood tests (urea, creatinine, albumin, electrolytes, serological tests (Anti-streptolysin O [ASO] titre, compliment C3, C4, antinuclear antibody [ANA], Anti-double stranded [anti-ds] DNA, hepatitis B surface antigen [HBs Ag], hepatitis C virus [HCV] antibody and human immunodeficiency virus [HIV]), and kidney histopathology. Other investigations including imaging studies (ultrasound scan [USS] computed axial tomography [CT], voiding cysto-urethrogram [VCUG] and isotope scans) were also recorded. The diagnosis of glomerular diseases, nephrotic syndrome, hereditary diseases and urologic disorders was based on their relevant clinical and laboratory criteria[10-13]. Hypertension was defined as blood pressure higher than 95th percentile for age[14]. Acute kidney injury (AKI) was diagnosed on the basis of serum creatinine levels ≥150% above normal levels for age and oliguria (≤ 0.5 ml/Kg per hour for 6 hours) and/or occurrence of acidosis, and/or urea, phosphate and potassium outside the normal range for age[15]. CKD was defined as glomerular filtration rate (GFR) < 60 ml/min/1.73m2 for ≥ 3 months and CKD stage 5 requiring RRT as GFR < 15 ml/min/1.73 m2[16]. Our centre provides medical treatment for primary renal diseases, surgery for urologic disorders and renal replacement therapy (RRT) for ARF and CKD5. RRT modalities were: peritoneal dialysis [PD], haemodialysis [HD]), and transplantation. Following discharge, all patients were seen for follow-up in the outpatient clinic. Cases requiring management in specialized centres e.g. oncology centres were referred.Outcome measures were the recovery of a normal renal function with/without persistence of proteinuria, progression to CKD, or death. The study was approved by the Hospital Research and Ethics Committee.

Data analysis:

Data was analyzed using the Statistical Package for Social Science (SPSS) software version 18. Descriptive statistics used comprised means ± standard deviation or medians for continuous data, and percentages for categorical data. The prevalence of paediatric renal disease was calculated as a percentage of total paediatric admissions and mortality as percentage of total renal disease admissions.

Results:

Over 7 years our centre received 800 children in whom 1121 nephro-urologic disorders were recorded. The overall prevalence was 5.5% (800 out of 14545 patients admitted to the paediatric wards). There were 494 males (61.8%) and 306 females (38.2%). The mean age (± SD) at presentation was 7.73 ± 5.35 (range 0.4 – 13.1) years with the majority (61.6%) being in the age group 5-15 years. Most of the patients were originally from the Central State: 307 (38.4%),followed by Western: 215 (26.9%), and Northern State: 194 (24.3%). Among the study group 1121 nephro-urologic disorders were recorded.

The presenting features are shown in table.1.In order of frequency were: oedema (46.8%), proteinuria (34.8%), haematuria (33.6%) hypertension (31.6%)

and oliguria/ anuria (28.1%), table 1. Other presenting features were urinary symptoms (9.5%) and abdominal masses (3.3%). At admission, the mean blood urea (±SD) was 130±76 (range 20 - 350) mg/dl and mean serum creatnine (±SD) was 3.4±4.1 (range 1.0- 19) mg/dl. The mean haemoglobin level (±SD) was 9.9±2.7 (range 2.6 – 12.9) gm/dl.

The profile of nephro-urologic disorders is shown in table 2. Common causes of nephro-urologic disorders were chronic kidney disease (CKD): 270 (24.1%), acute glomerulonephritis (AGN): 168 (14.9%) and nephrotic syndrome: 166 (14.8%). Urinary tract infections (UTIs) and acute kidney injury (AKI) were recorded in 127 cases (11.3%) and 118 (10.5%) respectively. Renal calculi, hereditary nephropathies, congenital anomalies of kidney and renal tract (CAKUT), multisystem diseases and renal tumors were recorded in 86 (7.7%), 85 (7.6%), 57 (5.1%), 35 (3.1%), and 9 (0.8%) cases respectively. Aetiology of CKD was unknown in 28.1%. Identifiable causes of CKD in order of frequency were: glomerulopathy (27.9%), CAKUT (19.3%), renal calculi (10.4%) hereditary nephropathies (7.8%), and multisystem diseases (6.4%). The majority of AGN cases (62.8%) were due to post-infectious GN. Less frequent causes of AGN were: rapid progressive GN (17%), mesangioproliferative GN (14%), membranoproliferative GN (4.7%) and IgA nephropathy (1.5%). Steroid - sensitive NS (SSNS) was more common than steroid-resistant NS (SRNS) (72.3% versus 27.7% respectively). Minimal change diseases (MCD), focal segmental glomerulosclerosis (FSGS) and mesangioproliferative GN were detected in 49.4%, 34.3% and 16.3% of biopsied patients respectively. The majority of UTIs cases (68.5%) had an associated co-morbidity. Urine culture isolates showed Escherichia coli in 55.2%, Klebsiella species 24.4%, pseudomonas 15.7% and Staphylococcus aureus in 4.7%. AKI was recorded in 118 patients and causes in order of frequency were severe sepsis and/or gastroenteritis (31.5%), acute GN (27.2%), HUS (14.5%), malaria-associated (12.9%) obstructive uropathies (6.9%), sickle cell nephropathy and lupus nephritis (2.6% each), and hair dye poisoning (1.7%). Renal calculi were detected in 86 patients in various sites of the renal tract (pelvis and/or calyces in 65.5%, ureters 23.2% and bladder 11.6%). Hereditary renal disorders were recorded in 85 patients. Types in order of frequency were: polycystic kidney disease (PCKD) (28.2%), renal tubular acidosis (RTA) (18.8%), nephronophthisis (16.5%), Alport syndrome (14.1)%, congenital NS (10.6%), sickle cell nephropathy (4.7%) and Barter's syndrome and primary hyper-oxaluria (3.5% each). CAKUT were recorded in 57 cases and types were: posterior urethral valve (PUV) (36.4%), kidney hypoplasia/ dysplasia and nephrocalcinosis (18.3% each), vesico-ureteric reflux (VUR) (16.5%), neurogenic bladder (7.3%) and Brune Belly syndrome (3.2%). Renal tumors were recorded in nine patients; nephroblastoma in seven and lymphoma in two.

The short -term outcome of patients in the study is shown in table 3. The mean follow- up period ± SD was 2.83 ± 1.82 (range 0.6 – 6) years. The results showed that 474 patients (59.2%) recovered normal renal function, 176 (22%) developed CKD, 40 (5%) were referred to other centers, 50 (6.2%) died and 60 patients (7.5%) were lost to follow up. Out of 176 cases with CKD, 137 were CKD3-4 on conservative treatment and 39 CKD5 on chronic dialysis. Common causes of death were: severe sepsis in 50% and dialysis complications (32%).

The outcome of children with CKD is shown in table 4. About half of patients with CKD remained on conservative treatment; about 25% were either transplanted or remained alive on maintenance dialysis. Mortality from CKD was 6.3%

Table1. Presenting features of nephro-urologic disorders in children in Khartoum (n=800)

Features	Frequency	Percent
Oedema	374	46.8%
Proteinuria	278	34.8%
Haematuria	269	33.6%
Hypertension	253	31.6%
Oliguria/Anuria	225	28.1%
Urinary symptom	76	09.5%
Abdominal masses	27	03.3%

Table 2. Types of renal disorders (n=1121) in children in Khartoum

Renal diagnosis	Frequency	percent
Chronic kidney disease (CKD)	**270**	**24.2%**
Acute glomerulonephritis (AGN)	**168**	**14.9%**
Nephrotic syndrome (NS)	**166**	**14.8%**
Urinary tract infections (UTIs)	**127**	**11.3%**
Acute kidney injury (AKI)	**118**	**10.5%**
Renal calculi	86	7.7%
Hereditary nephropathy	85	7.6%
Polycystic kidney disease (PCKD)	24	
Renal tubular acidosis (RTA)	16	
Nephronopthisis	14	
Alport syndrome	12	
Congenital nephrotic syndrome	9	
Sickle cell nephropathy	4	
Barter's syndrome	3	
Primary hyper-oxaluria	3	
Congenital anomalies of kidney and renal tract (CAKUT)	**57**	**5.1%**
Posterior urethral valve (PUV)	20	
Hypoplastic/ Dysplastic kidneys	10	
Nephrocalcinosis	10	
Vesico-ureteral reflux (VUR)	9	
Neurogenic bladder	6	
Brune Belly syndrome	2	
Multisystem diseases	**35**	**3.1%**
Haemolytic uraemic synd. (HUS)	22	
Lupus nephritis	13	
Renal tumors	**9**	**0.8%**
Nephroblastoma	7	
Lymphoma	2	
Total	1121	**100.0%**

Table 3. Short-term outcome of children with nephro-urologic disorders in Khartoum

Outcome	Frequency	Percent
Recovered normal renal function	**474**	**59.2%**
Without proteinuria	196	
With persistent proteinuria	278	
Chronic kidney disease (CKD)	**176**	**22.0%**
CKD3-4 on conservative treatment	137	
CKD5 on chronic dialysis	39	
Referred to other Centers	**40**	**5.0%**
Lost to follow-up	**60**	**7.5%**
Death	**50**	**6.3%**
Total	**800**	**100.0%**

Table 4.Short-term outcome of children with chronic kidney disease (CKD) in Khartoum

Outcome	Frequency	Percent
CKD3-4 on conservative treatment	137	50.7%
CKD5 on chronic dialysis	39	14.4%
Received kidney transplantation	32	11.9%
Died	16	5.9%
Lost to follow-up	46	17.1%
Total	270	100.0%

Discussion:

Previous data[9] did not define the prevalence of paediatric renal disorders in Khartoum. In our centre, over 6 years, we reported an overall prevalence of 5.5% indicating that substantial number of children with renal disorders had been managed in hospital. This prevalence is comparable to reports in other developing countries: Nepal (6.3%), Nigeria (4.5% & 3.2%), and Iraq (5.8%)[4,17-19]. Our data also showed the wide spectrum of renal disorders as has been described in these countries[4,17-19]. However, the pattern has changed as we recorded chronic kidney disease (CKD), acute glomerulonephritis (AGN) and nephrotic syndrome (NS) in more than half of our patients. The recently established specialized centre in Soba Hospital had attracted more patients with such complicated disorders who were in need of advanced management. These findings are comparable to reports in Jos, Nigeria, Nepal, and Iran[3-6] where similar settings of renal care have been developing. In this study the aetiology of CKD was unknown in 28% which is similar to reports from Sudan and other developing countries[3, 20, 21]. This is due to the late referral at an advanced stage of the disease when no cause could be identified. The most common identifiable causes of CKD in this study were AGN and NS which is similar with studies from other countries (3,6,22). and Sudan [21]. AGN in this study was less prevalent (14.9%) than in other countries (Nigeria; 37.7%, Nepal 28.7% & 30.7%, and Iran 23%) [3-6] but comparable to a previous study from Sudan (12%) [9].This may be due to current pattern of referral, uncontrolled use of antibiotics and improved personal hygiene. In this study nephrotic syndrome accounted for 14.8% of the cases whereas in other studies the prevalence varied from 16% to 34%[3- 6, 18, 22,) This variation may be related to genetic and/or environmental factors. A previous study from Sudan and other studies from Africa[9,23,24] reported that steroid- resistant NS (SRNS) was more common than steroid-sensitive NS (SSNS). In contrast, our results showed predominance of SSNS (72.3%) over SRNS (27.2%) . Better management of SSNS with recent generation of immunosuppressive drugs in our centre had increased the referral of such cases particularly those with frequently relapsing course. UTIs were less common in this study (11.3%) compared to other studies (18%-30%)[5,6,19] and a previous study (68.5%)[9].This difference may be due to high rate of negative urine cultures resulting from prior use of antibiotics. The lower prevalence of renal calculi and CAKUT might have played a role. Improvement in detection and treatment of UTIs at secondary care levels may be another factor. The commonest causative organism of UTIs was E. coli which is similar to other studies[25]. In this study the prevalence of acute renal injury (AKI) has increased to 10.5% compared to 6% in the previous study[9]. This is due to improvement in provision of acute dialysis services and other supportive measures. Similar prevalence was reported in countries where renal care settings have been developing; Nigeria 9.5% and 10.5%[1,22] and Iraq 11.3%[19]. As in other studies (4), AGN and haemolytic uraemic syndrome (HUS) were among the leading causes of AKI (26.2% and 14.5%) respectively. This finding reflects the improving methods of diagnosis and the high index of suspicion. In this study, hereditary renal diseases were rare disorders (7.6%). In contrast, these disorders were the leading causes in Arab countries like Saudi Kingdom, Jordan and Iraq[2,8,19]. This may be related to the high rate of consanguinity among their populations. CAKUT were also rare renal disorders (5.1%) in our series. Similar finding was shown in other studies from Nigeria and Iran[3, 6]. This may be due to the limited distribution of prenatal kidney scanning services. Renal tumors were rare renal disorders among our children (0.8%) which is comparable to data from Iraq (1.4%)[19]. In contrast, two studies from Nigeria and a previous study showed a higher prevalence of renal tumors (11.1%, 7.2%, 6.2% respectively) [1,3,9]. These variations could be related to ethnic and or environmental factors e.g. .prevalence of Epstein Barr virus. The outcome on latest follow-up is comparable to the previous study[9] when comparing progression to CDK and mortality. However, more patients had access to renal replacement therapy

compared to a previous data[21]. In spite of available renal replacement, the unchanged mortality may be explained by the increased number of AKI and CKD cases in whom mortality is usually high particularly in those with late referral.

In conclusion; This study documented the wide spectrum of childhood nephro-urologic disorders in Khartoum and showed that significant proportion of children with such disorders had been managed in hospital. The high prevalence of CKD is most likely due to the late referral and/or the recent improvement of renal replacement therapy services. The unchanged mortality may be due to increasing numbers of AKI and advanced CKD cases. The high cost of management calls for more efforts for training of health personnel and increasing their awareness about the importance of early detection and referral.

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