

Aetiology of Paediatric End-stage Renal Failure in Jordan: A Multicentre Study

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ABSTRACT

Objective: The purpose of this study was to find out the aetiology of end-stage renal failure (ESRF) in children in Jordan.

Subjects and Methods: This was a multicentre retrospective study at five participating hospitals. Data collection included medical record review for age, gender, aetiology of ESRF, modality of renal replacement therapy (RRT) and outcome. End-stage renal failure was defined as estimated glomerular filtration rate < 15 mL/min/1.73m².

Results: There were 275 children with ESRF: 131 males and 144 females. The most common causes of ESRF in children were congenital anomalies of the kidney and urinary tract (CAKUT), 45.8%, hereditary disorders, 23.2% and glomerulopathies, 26.2%. Neurogenic bladder, reflux nephropathy and posterior urethral valve accounted for 16.8%, 12.7% and 4.0%, respectively. Amongst the hereditary disorders, primary oxalosis and cystic disease accounted for 8.0% and 7.2% of the aetiologies of ESRF, respectively. Focal segmental glomerulosclerosis was the most common histological type amongst the glomerulopathies (10.2%), followed by mesangiocapillary glomerulonephritis (4.7%) and chronic glomerulonephritis (3.0%). The aetiology was unknown in 4% of the cases. The modality of dialysis included isolated peritoneal dialysis (PD) in 30.9%, isolated haemodialysis (HD) in 49.1%, alternating peritoneal and haemodialysis in 9.1%, transplanted in 8.7% and conservative treatment in 1.8%. Death occurred in 57.3% of PD patients versus 34.4% in HD patients.

Conclusion: This is the first report on the aetiology of ESRF in children in Jordan. The most common aetiologies of ESRF were CAKUT 45.8%, hereditary disorders 23.2% and glomerulopathies 22.9%.

Keywords: Aetiology, children, chronic kidney disease, end-stage renal failure, Jordan

Etiología de la insuficiencia renal pediátrica en fase final en Jordania: un estudio multicéntrico

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RESUMEN

Objetivos: El propósito de este estudio fue investigar la etiología de la insuficiencia renal en fase terminal (IRFT) en niños en Jordania.

Sujetos y métodos: Se trató de un estudio retrospectivo multicéntrico en los cinco hospitales participantes. La recopilación de datos incluyó la revisión de las historias clínicas por edad, sexo, etiología de la IRFT, modalidad de terapia de reemplazo renal (TRR) y resultados. La insuficiencia renal en fase terminal fue definida como la tasa de filtración glomerular estimada < 15 mL/min/1.73m².

Resultados: Participaron 275 niños con IRFT: 131 varones y 144 hembras. Las causas más comunes de IRFT en niños fueron: las anomalías congénitas del riñón y las vías urinarias (ACRVU), 45.8%; los trastornos hereditarios, 23.2%; y las glomerulopatías, 26.2%. La vejiga neurogénica, la nefropatía por reflujo y la válvula de uretra posterior representaron 16.8%, 12.7% y 4.0%, respectivamente. Entre los trastornos hereditarios, la oxalosis primaria y la enfermedad quística representaron el 8.0% y 7.2% de las etiologías de la IRFT, respectivamente. La glomeruloesclerosis

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focal y segmentaria fue el tipo histológico más común entre las glomerulopatías (10.2%), seguido por la glomerulonefritis mesangiocapilar (4.7%) y la glomerulonefritis crónica (3.0%). La etiología era desconocida en el 4% de los casos. La modalidad de diálisis incluía diálisis peritoneal aislada (DP) en 30.9%, hemodiálisis aislada (HD) en el 49.1%, hemodiálisis alternativa y peritoneal en 9.1%, trasplantadas en 8.7% y tratamiento conservador en 1.8%. La muerte ocurrió en el 57.3% de los pacientes de DP en comparación con el 34.4% en los pacientes de HD.

Conclusión: *Este es el primer reporte sobre la etiología de la IRFT en niños en Jordania. Las etiologías más comunes de la IRFT fueron las ACRVU (45,8%), los trastornos heredofamiliares (23.2%), y las glomerulopatías (22.9%).*

Palabras claves: etiología, niños, insuficiencia renal crónica, insuficiencia renal en fase final, Jordania

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INTRODUCTION

Besides being a financial burden, end-stage renal failure (ESRF) in children is a cause of morbidity and mortality, especially in developing countries. The incidence of ESRF in Jordanian children in 2006 was estimated to be 7.5 new cases per million child population per year, and the prevalence was 14.5 patients per million children population (1). There is no accurate registry for children with ESRF in Jordan. The renal registry documents adults and older children on haemodialysis. Data obtained from single tertiary care centres remain incomplete (2). Many infants with chronic kidney disease remain undiagnosed, especially if they die in infancy from other causes such as sepsis and dehydration. The purpose of this multicentre study was to get, as accurate as possible, information on the aetiology of ESRF in children in Jordan.

SUBJECTS AND METHODS

The study was a multicentre retrospective review of the aetiology of ESRF in children in Jordan. The participating centres included Jordan University Hospital, Queen Rania Children's Hospital (Armed forces), Al-Bashir Government Hospital, Prince Hamzeh Hospital (Hashemite University) and Mutah University. The study period was from January 2003 to December 2012. Data collection included medical record review for age, gender, aetiology of ESRF, modality of renal replacement therapy (RRT), age at starting RRT and outcome. Since some patients visited more than one hospital, care was taken to avoid duplication of data. The estimated glomerular filtration rate (eGFR) was calculated by using the Schwartz formula (3). In addition to information from medical records, outcome was checked by calling parents and interviewing dialysis nurses. The study was approved by the Institutional Review Board (IRB) of the different hospitals.

End-stage renal failure was defined as eGFR < 15 mL/1.73m²/minute, according to the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (4). Patients who presented with ESRF but the diagnosis of the primary disease remained undiagnosed were categorized as unknown. Descriptive statistics and Chi-squared test were used for statistical analysis.

RESULTS

There were 275 children with ESRF: 131 (47.6%) males and 144 (52.4%) females. Age at diagnosis for chronic kidney disease (CKD) and age at reaching ESRF were 4.20 ± 2.95 (0.08–17) years and 5.86 ± 3.37 (0.17–19) years, respectively. Aetiology is shown in the Table.

Table: Aetiology of end-stage renal failure in Jordanian children

Aetiology	Number of cases (%)	Total
Congenital anomalies of the kidney and urinary tract	126 (45.8%)	126 (45.8%)
Neurogenic bladder	46 (16.7%)	
Reflux nephropathy	35 (12.7%)	
Posterior urethral valve	11 (4%)	
Renal hypo/dysplasia	34 (12.4%)	
Hereditary nephropathy	64 (23.3%)	64 (23.3%)
Oxalosis	22 (8%)	
Cystic kidney disease	20 (7.2%)	
PCKD	11 (4%)	
Nephronophthisis	7 (2.5%)	
BBS	2 (0.7%)	
CNS	11 (4%)	
Cystinosis	5 (1.8%)	
Bartter syndrome	3 (1.1%)	
Epstein syndrome	3 (1.1%)	
Glomerulopathies	72 (26.2%)	72 (26.2%)
Multisystem disease	9 (3.3%)	
HUS	6 (2.2%)	
SLE	2 (0.7%)	
HSP	1 (0.4%)	
Miscellaneous	3 (1.1%)	3 (1.1%)
Unknown	10 (3.6%)	10 (3.6%)
Total	275 (100%)	100%

PCKD: polycystic kidney disease; BBS: Bardet Biedel syndrome; CNS: congenital nephrotic syndrome; HUS: Haemolytic uraemic syndrome; SLE: systemic lupus erythematosus; HSP: Henoch-Schönlein purpura

Associated vesico-ureteral reflux (VUR) was present in 47.8% of the 46 patients with neurogenic bladder. Mean age at reaching ESRF for reflux nephropathy was seven years.

The frequency of acquired glomerulopathies was as follows: focal segmental glomerulosclerosis (FSGS) 28 (10.2%), Mesangiocapillary glomerulonephritis (MCGN) 13 (4.7%), rapidly progressive glomerulonephritis (RPGN) 7 (2.5%),

mesangial proliferative glomerulonephritis 5 (1.8%) and poststreptococcal glomerulonephritis 2 (0.7%). Eight (3.0%) were classified as chronic glomerulonephritis. Kidney biopsies were mainly done for steroid resistant nephrotic syndrome. Genetic testing was not routinely done because of the high cost.

Mean age at reaching ESRF for FSGS and MCGN was 6.7 years and 7.5 years, respectively. Only 21.4% of patients with FSGS reached ESRF after the age of 10 years. Diarrhoea positive haemolytic uraemic syndrome (D+HUS) occurred in 5/6 and atypical haemolytic uraemic syndrome (aHUS) in 1/6.

One female with post salmonella HUS reached ESRF by the age of 10 years.

Two patients had amyloidosis, one secondary to familial Mediterranean fever, and the other with hyper IgD syndrome.

Outcome

Eighty-five patients (30.9%) and 135 patients (49.1%) were put on peritoneal dialysis (PD) and haemodialysis (HD), respectively. Twenty-five patients (9.1%) had alternating PD and HD. Family refused dialysis in five. In general, infants were put on PD and older children on maintenance HD. Transfer from PD to HD was done because of recurrent peritonitis.

Among the PD patients, 43 (57.3%) died and 32 (42.7%) were alive, versus HD 45 (34.4%) and 86 (65.6%) dead and alive, respectively. Odds ratio (OR) was 2.6; 95% confidence interval (CI) was 1.4, 4.6 and *p*-value < 0.001.

The majority of children with oxalosis and congenital nephrotic syndrome died while on RRT. Twenty-four patients (8.7%) had a renal transplant and one patient was lost to follow-up.

Most transplants done in Jordan were harvested from living related donors. The few who went abroad had non-related renal transplant.

DISCUSSION

The most common causes of ESRF in children were CAKUT (45.8%), hereditary disorders (23.3%), and glomerulopathies (26.2%). In the present study, CAKUT was aetiologic in 56% of the cases, which is similar to other parts of the Middle East (5, 6), Western Europe (7, 8) and North America (9–11). Neurogenic bladder, reflux nephropathy and posterior urethral valve accounted for 16.8%, 12.7% and 4.0%, respectively. The frequency of neurogenic bladder was similar to other parts of Saudi Arabia [19.6%] (12), but more frequent than Slovakia [1.9%] (13). Neurogenic bladder is a frequent cause of ESRF in developing countries (14). Reflux nephropathy was similar to Kuwait (5) but more frequent than in North America [5%] (15). In our study, reflux nephropathy was the second cause of ESRF in childhood which was similar to the North American Paediatric Renal Trials and Collaborative Studies [NAPRTCS] (15). The contribution of posterior urethral valve was higher in Saudi Arabia [17%] (16) and rare in Slovakia [0.8%] (13). Renal hypo/dysplasia was responsible for 12.4% of cases of ESRF, which is comparable to Kuwait [14.6%] (5). There is an overlap amongst the various aetiologies of CAKUT. Many patients with reflux nephropathy and obstruc-

tive uropathies have an associated renal dysplasia. Together, these were responsible for 32.8% of childhood ESRF in the United Kingdom (17). There is no evidence that urinary tract infections (UTI) per se are a cause of ESRF (18); however, a UTI infection is a warning sign that the child may have an underlying congenital renal anomaly. While VUR is common in childhood, not all patients with VUR develop renal failure. Those doing so most likely have it secondary to the damaging effect of intrauterine reflux on the developing kidney, culminating in renal hypo/dysplasia (18).

Hereditary nephropathy accounted for 23.3% of the causes of ESRF, which is similar to Kuwait [21%] (5, 19) and Iran [21%] (19) but less than Slovakia [77%] (13). Among the hereditary disorders, primary oxalosis and cystic disease accounted for 8.0% and 7.2% of aetiologies of ESRF, respectively. Primary oxalosis is prevalent in Middle Eastern countries (5, 19), probably due to the high rate of parental consanguinity. While hereditary disorders accounted for 23.3% of cases of ESRF, the prevalence is probably much higher. Many cases in the CAKUT and glomerulopathies groups have an underlying genetic basis, especially in the presence of high consanguinity rates in the Jordanian population.

Glomerulopathies accounted for 26.2% of the aetiologies, which was higher than Iran [10.2%] (19), Kuwait [5.2%] (5), Italy [6.8%] (20), Slovakia [15.4%] (13) and North America [14%] (16) but less than France [30.7%] (8) and Jamaica [33%] (21). Focal segmental glomerulosclerosis was the most common histological type amongst the glomerulopathies (10.2%), followed by MCGN (4.7%) and chronic glomerulonephritis (3.0%). The frequency of FSGS was similar to Slovakia [9.6%] (13). In NAPRTCS data, CAKUT predominated in younger patients, and most cases of FSGS reached ESRF after the age of 12 years (9, 22). Focal segmental glomerulosclerosis was the most common aetiology of ESRF amongst the glomerulopathies, which is similar to our results. It is interesting to note that in addition to CAKUT, most cases of FSGS reached ESRF before the age of 10 years. The reason could be that many cases of FSGS had an undiagnosed genetic basis, due to the high rate of consanguinity. While the aetiology remained unknown in 4% in our series, it accounted for 1.7% of the cases in Kuwait (5), 50% in Vietnam (23) and 39.1% in Sudan (24). This is most likely due to late referral to paediatric nephrology services. Even in young adults, aetiology of ESRF labelled as unknown could be due to undiagnosed CAKUT in childhood (10).

CONCLUSION

This is the first report on the aetiology of ESRF in children in Jordan. The most common causes of ESRF were CAKUT (45.8%), hereditary disorders (23.3%) and acquired glomerulopathies (26.2%).

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