

Pediatric renal diseases in the Kingdom of Saudi Arabia

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Background: Pediatric nephrology is a growing subspecialty in the Kingdom of Saudi Arabia (KSA). Pediatric nephrologists are challenged with a different spectrum of renal diseases. Moreover, there is a lack of epidemiological studies for most of these diseases. In this article, we discuss the spectrum of renal diseases in KSA and highlight the differences that exist between reports from KSA and those from other countries.

Data sources: PubMed and MEDLINE databases were searched for articles on pediatric renal diseases.

Results: Genetically mediated renal diseases are considerably high in KSA. Congenital and infantile nephrotic syndrome is higher in KSA than in other countries. Post-infectious glomerular pathology is rather common but is declining, while tropical infections such as schistosomiasis have been controlled. Neurogenic bladder caused by spinal lesion is an important cause of chronic kidney disease among pediatric patients. Renal stones are also more frequent in KSA than in other countries.

Conclusions: The spectrum of pediatric renal diseases in KSA is rather different from that reported from Western countries. More epidemiological studies are required to understand the actual incidence and nature of these diseases.

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Introduction

The Kingdom of Saudi Arabia (KSA) is a large country with a high percentage of child population. Children aged 0-14 years represent 29.4% of the population, and the child population growth rate is 1.54%.^[1] The rate of consanguinity is high (52%-56% of marriages) in the Saudi population, and it is associated with a high percentage of genetically mediated renal diseases.^[2-4] Other factors such as infection are still considerably high, leading to a higher incidence of post-infectious glomerular pathology, which was reported to affect 4% of pediatric patients with glomerulonephritis (GN).^[5] The lack of awareness among general pediatricians about the importance of early diagnosis of neurogenic bladder both in patients with spinal cord lesion or non-neurogenic neurogenic bladder contributed to the increased incidence of chronic kidney disease (CKD) in affected children at an early age of the disease as it was reported that they could have end-stage kidney disease (ESKD) before they finished their first decade of life.^[6] In this article, we review the pattern of kidney diseases in Saudi children and compare it with reports from other countries.

We searched the medical databases PubMed and MEDLINE to identify studies that were related to kidney diseases in pediatric patients. We used the search words kidney, renal, children, Saudi and pediatrics. We retrieved 534 articles and reviewed the abstracts of articles that were potentially relevant. We selected the abstracts of 54 articles that were relevant, and obtained the full text of the studies.

Patterns of renal diseases

Glomerular diseases

Nephrotic syndrome (NS) is reported to be more common in Asian children than in Caucasian children.^[7] Similarly, it is thought to be more common in Arab children. However, no epidemiological data are available to confirm this observation. Mattoo et al^[8] reported that Saudi children with primary NS showed no differences in age of onset, male predominance and response to initial prednisolone therapy when compared with published data from other countries. However, they

reported a higher incidence (6%) of familial occurrence. Congenital and infantile nephrotic syndrome was also reported to be higher in KSA than in other countries,^[9] a finding that has also been observed by pediatric nephrologists practicing in KSA. Abdurrahman et al^[9] reported an incidence of 17.0% for infantile nephrotic syndrome and 4.3% for congenital nephrotic syndrome in a cohort of 92 children with nephrotic syndrome. Histopathological reports of Saudi children with glomerular diseases have shown the predominance of focal segmental glomerulosclerosis (FSGS) and mesangial proliferative glomerulonephritis (MesGNS) to be in the range of 24%-39% and 24%-35%, respectively.^[5,7,10] On the other hand, IgA nephropathy was reported in 3%-4% of children with GN, which is less common than in Western countries.^[9,10] Membranoproliferative glomerulonephritis (MPGN) seems to present at an earlier age in Arab children and tends to have a severe course with rapid progression to end-stage renal disease (ESKD).^[11] We reported 8 children with MPGN who presented with steroid-resistant nephrotic syndrome at a mean age of 1.1 years and progressed very quickly to ESKD.^[11] Similar to other parts of the world, it was observed that there was a shift toward an increasing prevalence of FSGS over the recent years in KSA.^[12] Post-infectious GN as a cause of nephrotic syndrome is not common. In a study conducted in 100 patients with nephrotic syndrome, Mattoo et al^[13] found that post-infectious GN was the cause of the condition in only 2% of their study population. Post-streptococcal GN is declining as it was reported as the underlying cause of GN in only 2.7%-2.9% of adult patients^[14] and 4% of pediatric patients.^[5] However, it could present as early as 14 months.^[15] Lupus nephritis (LN) is a cause of glomerular disease in a significant number of children,^[16] and the familial form has been reported in 25 patients from 7 families with the mean age at presentation of 90.6 months (range: 24-144 months).^[17] The authors suggested the mode of inheritance to be autosomal recessive assuming Mendelian inheritance of single gene disorder.^[17] Early onset (<5 years) LN was also reported, and it was associated with poor outcome.^[18]

Structural abnormalities of the renal tract

Similar to reports from other parts of the world, congenital renal anomalies were reported in 45%-64.5% of children as the main underlying cause of CKD and ESKD in KSA.^[19-21] Prenatal (antenatal) ultrasound (US) screening is the routine recommendation in KSA, and this has led to the detection of renal anomalies in 0.7% of screened babies,^[22] similar to the rate (0.76%) reported in a British cohort study.^[23] However, the

availability and accuracy of US screening are varied as this examination is more available and done by more experienced staff in the big cities. This is, unfortunately, not the case in rural areas and small cities where availability and accuracy are limited. A study from Riyadh reported that the antenatal detection rate of posterior urethral valves (PUV) was only 27%, less than the international rate of 70%, despite the fact that most antenatal follow-ups were done in referral centers in the capital.^[24] This was reflected in the delay of the diagnosis in many of those children.

Neurogenic bladder caused by spinal lesion or non-neurogenic neurogenic bladder is an important cause of ESKD in KSA.^[5,19,25] A study from the western province revealed that neurogenic bladder was the underlying cause of ESKD in 19.6% of children with CKD, and in 13.6% of the cases, it was associated with neural tube defects.^[19] The limited awareness of the importance of bladder management in children with spina bifida among pediatricians led to a considerable delay in commencing clean intermittent catheterization (CIC) in the affected children^[5-25] and therefore to early CKD and ESKD. Neel et al^[26,27] reported that although there were many complaints from children and their families, even from patients with sensate urethra, CIC was generally accepted by Saudis. However, most pediatric nephrologists and urologists observe a considerable degree of denial and non-acceptance of CIC in their patients.^[28] The Mitrofanoff principle, which involves the creation of a continent abdominal stoma, provides a satisfactory alternative to children who need CIC.^[29] Unfortunately, this principle is not widely available and in the absence of a clear referral system it is not done for all children who could benefit from it. Reports of other structural abnormalities of the renal tract such as multicystic dysplastic kidney (MCDK) with a natural history of involution are not different from those reported from other countries.^[30,31] Al-Ghwery et al^[30] reported that 86% of children with MCDK in their study had a complete or partial involution at a mean age of 43.6 months. Cultural issues could influence the decision to go for some urological operations such as the repair of anterior hypospadias, which might not be necessary since urination is normally done in a sitting or squatting position in KSA.^[32]

Genetically transmitted renal diseases in children

An estimated 70% of cases of kidney diseases in childhood are congenital with a likely genetic basis.^[33] In KSA, due to the high rate of consanguineous marriages, this percentage is presumably even higher particularly for diseases with an autosomal recessive transmission.^[34] There are few published epidemiological studies on the actual incidence

of various genetically transmitted renal diseases in KSA. Preliminary observations indicate that children in KSA probably have a higher incidence of polycystic kidney disease, familial juvenile nephronophthisis, congenital urological anomalies, familial nephrotic syndrome and tubular diseases such as familial hypomagnesemia hypercalciuria nephrocalcinosis syndrome (FHHNC) and renal tubular acidosis (RTA).^[34] There are few published descriptive and observational studies on various genetically transmitted renal diseases.^[35-37] Collaborative research with researchers from developed countries led to Saudi contribution to a better understanding of some of these diseases, such as FHHNC, congenital nephrotic syndrome, and RTA.^[38,39]

Some renal diseases with a familial predisposition have been reported for the first time from KSA. Ohlsson et al^[40] reported a syndrome of osteopetrosis, renal tubular acidosis and cerebral calcification. The disease, known as "marble brain disease", is associated with stunted growth and mental retardation, and has been linked to carbonic anhydrase II enzyme deficiency.^[41] In a study conducted in KSA, the authors reported that children with a deficiency of this enzyme required a long-term follow-up.^[42] Furthermore, new associations were reported as a possibility of new syndromes.^[43,44] Recently, the availability of new high-throughput genotyping and sequencing technologies have provided help for genetic diagnosis of individuals with an inherited form of kidney disease.^[45] Genetic studies revealed novel mutations of cystinosis^[46] and nephrogenic diabetes insipidus.^[47] Aldahmesh et al^[46] studied the mutation spectrum of CTNS of cystinosis in 21 children from 13 families. Eight mutations were identified, four of which were novel (c.530A>G, c.681G>A, 1013T>G, and c.1018_1041del) with the conclusion that those alleles will provide the basis for routine molecular diagnosis of cystinosis in the region. Two novel mutations were identified in each of AVPR2 and AQP2 underlying nephrogenic diabetes insipidus in Arab families.^[47]

Infections and renal diseases

Urinary tract infections (UTIs) are common in Saudi children, but the exact incidence is unknown. There are cultural issues, which reduce the incidence of UTI in children such as circumcision^[48] done to all children based on Islamic religious instruction, and the standard practice of washing the genital or anal area with water after urination or defecation. However it is believed that structural renal abnormalities are more common in Saudi children. It was reported that vesico-uretral reflux (VUR) is higher (41%) in Saudi children after their first UTI compared with other reports of 25%-30%.^[49]

The commonest causing organism is *Escherichia coli* followed by *Klebsiella*.^[50] Tropical infections such as schistosomiasis have been controlled more than two decades ago in most parts of KSA^[51] and recently even in endemic areas such as Jazan in the south, near Yemen. The success of the interventions, which were based on case finding, treatment of infected individuals, and the chemical and environmental control of freshwater snails, led, in mid-2002, to a strategy to eliminate human infection with *Schistosoma haematobium* from Jazan.^[52]

Renal stones

Renal stones are more common, and they affect up to 20% of the Saudi adult population.^[53] This could be attributed to the hot weather and other environmental factors as well as nutritional and genetic factors.^[54] Similarly, it was reported that nephrolithiasis was not uncommon in children and adolescents.^[55] Calcium oxalate stones are the most common in adults and children.^[54,55] Shock wave lithotripsy is widely used for management, and it is known to have a high rate of success.^[56,57] Vesical calculus due to malnutrition in the very early years of life is currently very rare in KSA. This could be explained by the recent affluence, which has spread to all social classes and with it the tendency to eat "rich" food in large quantities.^[58] Primary metabolic defect as the underlying cause was reported as well in about 11% of the patients in a study conducted at a tertiary hospital in Jeddah,^[59] but the actual percentage could be higher as the sophisticated facilities to diagnose rare inborn errors of metabolism^[60] are available in few referral centers only.

Conclusions

The spectrum of pediatric renal diseases in KSA is rather different from that reported from Western countries. More epidemiological studies are required to understand the actual incidence and nature of these diseases.

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