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ORIGINAL ARTICLE

Insight into prevalence, etiology, and modalities of pediatric chronic dialysis: a comprehensive nationwide analysis

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Abstract

Background This study aimed to determine the prevalence and etiology of kidney failure (KF) among children below 15 years of age receiving chronic dialysis in Saudi Arabia and describe their dialysis modalities.

Methods This cross-sectional descriptive study was conducted on 8 August 2022, encompassing all 23 pediatric dialysis centers in Saudi Arabia. Data gathered comprised patient demographics, causes of KF, and the dialysis methods employed. Collected data underwent analysis to determine prevalence of children undergoing chronic dialysis, discern underlying causes of KF, and evaluate distribution of patients across different dialysis modalities.

Results The prevalence of children on chronic dialysis is 77.6 per million children living in Saudi Arabia, equating to 419 children. The predominant underlying cause of KF was congenital anomalies of the kidneys and urinary tract (CAKUT), representing a substantial 41% of cases. Following this, others or unknown etiologies accounted for a noteworthy 25% of cases, with focal segmental glomerulosclerosis (FSGS) comprising 13%, glomerulonephritis at 11%, and congenital nephrotic syndrome contributing 10% to etiological distribution. Regarding dialysis modalities employed, 67% of patients were on peritoneal dialysis (PD), while the remaining 33% were on hemodialysis (HD).

Conclusions This first nationwide study of pediatric chronic dialysis in Saudi Arabia sheds light on the prevalence of children undergoing chronic dialysis and underlying causes of their KF, thereby contributing to our understanding of clinical management considerations. This research serves as a stepping stone for the development of national registries.

Keywords Childhood kidney failure · Prevalence · Etiology · Peritoneal dialysis · Hemodialysis · Saudi Arabia

Introduction

Kidney failure (KF) poses a significant risk of morbidity and mortality among pediatric patients [1]. As pediatric patients reach KF, they require chronic kidney replacement therapy (KRT) to sustain life. Data on KRT in the Kingdom of Saudi Arabia (KSA) are scarce and mostly regional or institutional based. Two regional studies conducted in the Asir area and the Western region reported a mean annual incidence of KF in 9.2 per million children, with the most common cause being congenital anomalies of the kidney and urinary tract (CAKUT) [2, 3]. The Saudi Center of Organ Transplantation (SCOT) report that in 2019, 21,068 patients underwent chronic dialysis in the KSA. The majority received hemodialysis (HD), with 112 of them under 15 years old. Peritoneal dialysis (PD) was administered to 1546 patients, including 213 under 15 years old. The KSA had 8165 HD machines across 6920 outlets and 36 PD facilities. Automated peritoneal dialysis/continuous cycling peritoneal dialysis (APD/CCPD) was the preferred PD modality for 76% of patients, followed by continuous ambulatory peritoneal dialysis (CAPD) for 15% and intermittent peritoneal dialysis (IPD)

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for 9%. Additionally, there were 1121 kidney transplants in the KSA in the same year, with 981 from living donors and 140 from deceased donors [4].

Kari published a review in 2012 that shed light on the distinctive spectrum of KF among children in KSA, which differs from reports in other countries [5]. Genetically inherited glomerular diseases have been described with higher prevalence in pediatric Saudi populations; this includes congenital and infantile nephrotic syndrome in familial patterns [6, 7], a predominance of focal segmental glomerulosclerosis (FSGS) and mesangial proliferative glomerulonephritis in histological reports [8–10] and presence of familial lupus nephritis with worse outcomes described with disease onset younger than 5 years [11–13]. The elevated rate of consanguinity among the Saudi population, surpassing 50% of marriages, also carries clinical implications for potential early detection and genetic counseling [14, 15].

Additionally, the delayed diagnosis of posterior urethral valves (PUV), with many cases going undetected antenatally compared to the higher international detection rate of up to 70%, has resulted in delayed management, leading to CKD and poorer outcomes [16, 17]. The neurogenic bladder has also emerged as a significant contributor to CKD and KF, primarily due to late identification and a lack of awareness among pediatricians regarding spina bifida, resulting in delayed relief of urinary back pressure and recurrent urinary tract infections, thus advancing CKD [3, 8, 18]. Other studies showed a probability of a higher prevalence of cystic diseases, including polycystic kidney disease and juvenile nephronophthisis [19, 20]. Furthermore, stone-forming illnesses that can lead to CKD and KF are anticipated to have a higher incidence, including familial hypomagnesemia hypercalciuria nephrocalcinosis, renal tubular acidosis, and primary metabolic defects, which can be underestimated due to the requirement of advanced screening and diagnostic methods [21–23].

Saudi Arabia, through its Vision 2030 initiative, aims to address chronic diseases comprehensively and provide top-tier healthcare throughout the kingdom. The healthcare system in KSA serves more than 31 million citizens and residents, as well as several million visitors during tourism, Hajj and Umrah, with state-of-the-art university hospitals, medical cities, specialized hospitals, and widespread primary care centers [24]. Moreover, the unique background and etiological factors of CKD and KF in Saudi pediatric patients, as revealed in the literature, highlight the imperative for further advanced research and targeted national investments. This study represents the inaugural step in a broader initiative aimed at collaborating with all Saudi healthcare centers to address critical questions in pediatric kidney disease. It serves as a pioneering investigation into CKD and KF prevalence, KRT implementation, etiology, and regional distribution in Saudi Arabia's pediatric population.

Methods

This study was conducted with the approval of the Institutional Review Board (IRB) at King Saud University (IRB Approval # 22/0457/IRB). On the 8th of August 2022, the data was collected from all 23 pediatric kidney centers that offer chronic dialysis in Saudi Arabia. The aim was to describe the etiologies and prevalence of KF among children living in Saudi Arabia and their dialysis modalities. Our age limit for children was below 15 years of age, in accordance with Ministry of Health laws and regulations. Prevalence was calculated based on the 2022 Census of the General Authority for Statistics per million age-related population (pmarp).

The data includes patients' demographic information and etiologies of KF, which were classified as CAKUT, FSGS, glomerulonephritis, congenital nephrotic syndrome, and other or unknown etiologies. Modalities of chronic dialysis, either peritoneal dialysis (PD) or hemodialysis (HD), were also collected. Also, we recorded the number of centers offering pediatric kidney transplantation.

The authors represented the data collected from the five regions of Saudi Arabia: Northern (NR), Southern (SR), Eastern (ER), Western (WR), and Central Regions (CR). The data was analyzed to estimate the prevalence of children with KF on dialysis in Saudi Arabia and to identify the most common etiologies and the distribution of patients on different dialysis modalities.

Statistical analysis

The collected data was analyzed using SPSS version 21 [25]. Descriptive statistics were calculated for patient demographics, etiologies of KF, and dialysis modalities. Frequencies and percentages were used to describe categorical variables. The prevalence of children on chronic dialysis was calculated per million children living in Saudi Arabia.

Results

The study included all 23 national centers across Saudi Arabia. Due to the considerable size difference between centers, the authors represented data from the five different regions of Saudi Arabia. Of the 23 participating centers, seven were from WR, six from CR, six from ER, three from SR, and one from NR. We identified 419 children with KF on chronic dialysis (Table 1). The prevalence was estimated to be 77.6 pmarp in Saudi Arabia [26].

Most of our dialysis patients were in the age group between 6 and 12 years (45%), followed by those above

Table 1 Characteristics of the dialysis centers in Saudi Arabia ($N=23$)

	CR ($N=6$)	NR ($N=1$)	SR ($N=3$)	ER ($N=6$)	WR ($N=7$)	All ($N=23$)
Most frequent age group (%)	6–12 years (39%)	> 12 years (54%)	6–12 years (63%)	2–5 and 6–12 (34.5%)	6–12 years (55%)	6–12 years (45.6%)
CAKUT, *n* (%)	90 (44.3%)	2 (18.2%)	20 (43.6%)	24 (43.6%)	42 (40.4%)	178 (42.5%)
Unclassified/unknown etiology, *n* (%)	38 (18.7%)	2 (18.2%)	15 (32.6%)	16 (29.1%)	32 (30.8%)	103 (24.6%)
FSGS, *n* (%)	27 (13.3%)	2 (18.2%)	6 (13%)	2 (3.6%)	14 (13.5%)	51 (12.2%)
GN, *n* (%)	30 (14.8%)	2 (18.2%)	1 (2.2%)	3 (5.5%)	9 (8.6%)	45 (10.7%)
CNS, *n* (%)	18 (8.9%)	3 (27.2%)	4 (8.7%)	10 (18.2%)	7 (6.7%)	42 (10%)
HD centers, *n* (%)	6 (100%)	1 (100%)	3 (100%)	3 (50%)	5 (71.4%)	18 (78.3%)
PD centers, *n* (%)	6 (100%)	1 (100%)	3 (100%)	6 (100%)	7 (100%)	23 (100%)
Transplant centers, *n* (%)	3 (50%)	0	1 (33.3%)	1 (16.7%)	2 (28.6%)	7 (30.4%)
HD patients, *n* (%)	60 (29.6%)	8 (72.7%)	13 (28.3%)	14 (25.5%)	41 (39.4%)	136 (32.5%)
PD patients, *n* (%)	143 (70.4%)	3 (27.3%)	33 (71.7%)	41 (74.5%)	63 (60.6%)	283 (67.5%)

n number, % percentage, *CAKUT* congenital anomalies of the kidney and urinary tract, *FSGS* focal segmental glomerulosclerosis, *GN* glomerulonephritis, *CNS* congenital nephrotic syndrome, *HD* hemodialysis, *PD* peritoneal dialysis, *CR* Central region, *NR* Northern region, *SR* Southern region, *ER* Eastern region, *WR* Western region

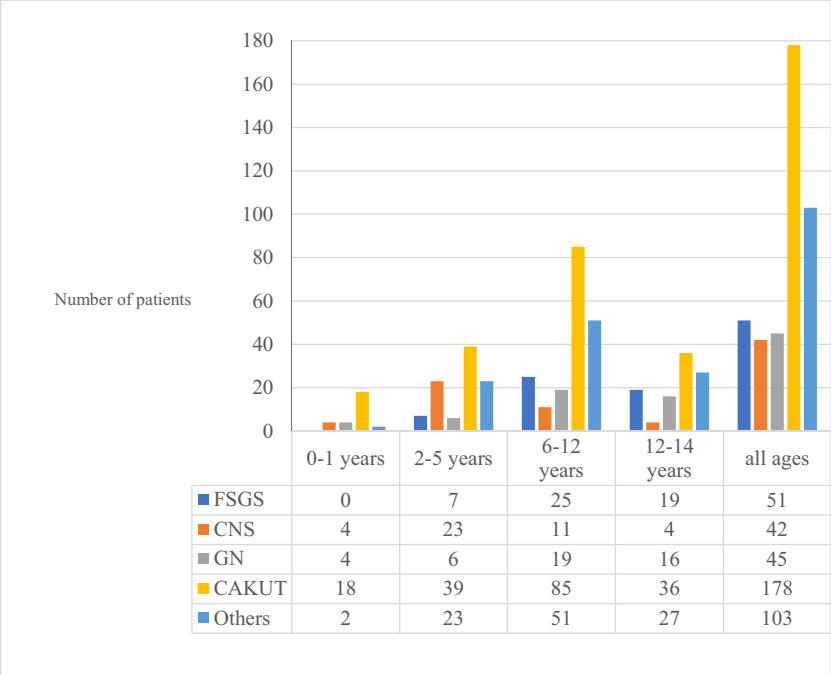

Fig. 1 Etiologies of kidney failure among children treated in dialysis centers throughout Saudi Arabia ($N=419$). *FSGS*, focal segmental glomerulosclerosis; *CNS*, congenital nephrotic syndrome; *GN*, glomerulonephritis; *CAKUT*, congenital anomalies of the kidney and urinary tract

12 years of age and 2 to 5 years of age, 24.5% and 23.5%, respectively. The youngest age group (0–1 years) was less prevalent, accounting for around 9% in CR and ER regions, 4% in SR, and 3% in WR, while no patients were identified in NR. The most common etiology of KF in our population was CAKUT, accounting for 168 patients (41%). The second most common etiology was due to unclassified or unknown etiologies, accounting for 25%, followed by FSGS, representing 13%. Then, glomerulonephritis was 11%, and congenital nephrotic syndrome was 10% of all etiologies (Fig. 1).

Regarding the modalities of chronic KRT, all centers had a PD option, in contrast to HD; three centers in ER (50%) and two in WR (29%) did not have an HD option, while all other centers had an HD option (Fig. 2). 67.5% of patients with KF on chronic dialysis in KSA were on PD, while 32.5% were on HD. All regions had around two-thirds of their dialysis population on PD except NR, which had one

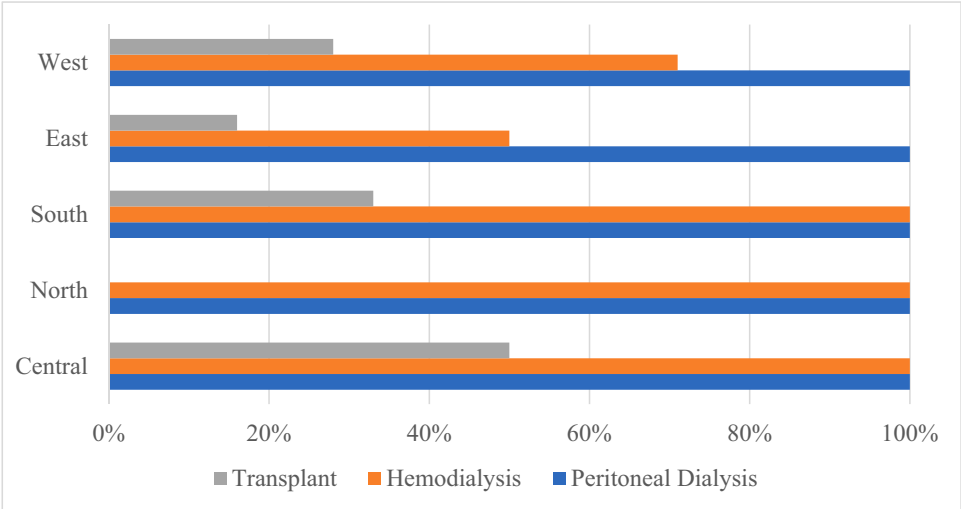

Fig. 2 Availability of different modalities of kidney replacement therapies at each region in Saudi Arabia

third on PD. Furthermore, we identified seven centers that offer pediatric kidney transplantation across the kingdom: CR has three centers, followed by WR with two centers, while ER and SR have one center each.

Discussion

Over the past 30 years, significant improvements have been made in caring for children with KF [27]. However, most available data stems from KF registries, and information is still limited. This scarcity of data is more problematic in areas such as central and southern Africa or in the Arab countries of North Africa and the Middle East [28]. The first pediatric KRT in Saudi Arabia was performed in June 1982 at King Khalid University Hospital in Riyadh. Initially, only a few HD centers treated children under 10 years old, and none accepted infants [29]. However, this changed over time, with two studies published in the Asir and Western regions of Saudi Arabia, reporting the causes and prevalence of KF among children in those areas, which were single center and enrolled only a small number of patients [2, 3]. This research will be the first national project to evaluate the epidemiology of KF in children and the use of KRT in Saudi Arabia.

A look at population-based studies and national registries is worthwhile, comparing the results of our research to those of other countries in the world. The data published in the US Renal Data System (USRDS) annual report in 2022 reveal that the adjusted incidence and prevalence of KF in pediatric patients (< 18 years) were 11 and 76 pmarp, respectively. The leading cause of KF among children aged < 6 years was CAKUT, replaced by glomerulonephritis and other causes in those older than 6. The leading modality used as KRT was HD (46.9%), followed by PD (38.8%), followed by kidney transplant (14.3%) [30, 31].

In Europe, the European Dialysis and Transplant Association (EDTA) initially relied on patient questionnaires and renal unit reports as the primary way to gather data. However, this was later supplanted by collecting data from national and regional European registries [28, 32, 33]. In 2004, van der Heijden et al. published a report based on 12 Western European registries showing an increase in the prevalence of KRT in children and adolescents aged below 20, from 22.9 pmarp in 1980 to 62.1 pmarp in 2000 [34]. HD was the most common initial form of KRT (48%), followed by PD (34%), followed by pre-emptive transplantation (18%). The primary renal causes of KF were glomerulonephritis, pyelonephritis, and miscellaneous causes [34]. In 2021, Bonthius et al. published another report reviewing the last 10 years' trends from 2007 to 2016 in 22 Western and Eastern European countries participating in the ESPN/ERA-EDTA Registry since 2007. It showed that the prevalence of KRT in children below 15 has increased by 2% annually from 26.4 pmarp in 2007 to 32.1 pmarp in 2016 [35]. The difference in the reported prevalence between van der Heijden (2004) and Bonthius (2021) reflects an expansion in the targeted population to include Eastern European countries and a methodological shift from questionnaire-based data to registry-based data. PD increased to be equal to HD (both 40%) as the initial KRT, followed by pre-emptive kidney transplant (20%). CAKUT replaced glomerulonephritis as the leading cause of KF requiring KRT.

In Japan, a nationwide survey of patients under 20 years of age with KF was conducted in 1998. The prevalence rate of KF among pediatric patients already on treatment in 1998 was 22 per million population. The most common diseases causing KF were renal hypoplasia/dysplasia (28.9%) and FSGS (19.2%). The methods and frequencies of KRT of the treated KF patients were as follows: PD at 42%, kidney transplant at 41%, and HD at 17% [36]. In 2012, JSPN led a nationwide cross-sectional survey to explore the incidence,

primary kidney disease, initial treatment modalities, and survival in Japanese children with KF who were less than 20 years of age from 2006 to 2011. CAKUT remained the most common cause of KF (39.8%). Initial treatment modality in patients who commenced KRT consisted of PD (61.7%), HD (16%), and pre-emptive transplantation (22.3%) [37]. A recent nationwide cross-sectional survey was conducted in 2023 by Hirano et al. identifying 701 Japanese children younger than 20 with CKD stage 5. Again, CAKUT was the leading primary kidney disease (37.4%), and PD was the most common initial modality of KRT (60.3%) [38].

In Australia and New Zealand, the annual ANZDATA report published in 2021 showed a prevalence of KRT in Australia of 17 and 58 pmp in the age groups 0–4 and 5–14 years, respectively, and in New Zealand of 20 and 62 pmp in the same age groups [39]. The leading cause of KF was miscellaneous and others (25%), followed by hypoplasia/dysplasia and glomerulonephritis (17%). The modality most often used as an initial KRT was PD (56%), followed by HD (23%), followed by transplant (21%). In comparison, the most prevalent modality by 2020 was kidney transplant (82%) [40].

We compare our data to those previously mentioned four nationwide surveys and national registries from America, Europe, and Asia. It appears that the prevalence of KF on chronic dialysis in Saudi children (77.6 pmp) is higher than those reported in Japan, Australia, New Zealand, and Europe and comparable to that reported in America. CAKUT seems to be the leading etiology of KF in children, both in our study and the four registries we compare our data to, with a tendency to be supplanted in older ages by glomerulonephritis (especially FSGS) and other miscellaneous and unclassified causes. In our study, PD is by far the most applied modality of KRT in all areas of Saudi Arabia except the Northern Region (NE), and this propensity to use PD more than HD was also found in Japan, Australia, and New Zealand. On the other hand, HD seems to be the predominant KRT in the USA, while in Europe, an equal proportion of children are treated with either HD or PD. Given their differences in methodological approaches, pediatric age groups, socioeconomic status, and the non-inclusion of kidney transplants in our study, we realize the difficulty in comparing our data to those nationwide registries. Nonetheless, it helps us to understand where we stand in the services we provide to our children with KF as compared to other parts of the world and to guide policy-making and clinical practice guidelines in Saudi Arabia in targeting CAKUT as a leading cause of KF in children in the antenatal and postnatal national programs.

The etiology of 25% of our cohort was under the category of others or unknown, which is almost similar to the NAPRTCS 2011 annual dialysis report [30]. In our study, this might be attributed to the late presentation of patients from rural areas with a higher incidence of genetic diseases. Many referred to a well-equipped center with advanced CKD and atrophied kidneys with likely low-yield kidney biopsies. We recognize this as one of the weaknesses of our study.

Study strengths, limitations, and future research

Our study has several strengths and limitations to highlight. This study is the first nationwide analysis of pediatric KF in Saudi Arabia, providing a comprehensive overview of the prevalence, etiologies, and dialysis modalities. This information will help nephrologists and providers taking care of children with kidney disease in Saudi Arabia and the Middle East and add much to the advancement of diagnosis, treatment modality, and, eventually, the outcome of management of children with KF. Also, it represents the first data registry in the area, which might help participation in global projects.

Including all pediatric nephrology centers in Saudi Arabia ensures a representative sample, enhancing the study's generalizability. Also, the data collected covers both etiologies and dialysis modalities, providing valuable information for healthcare professionals and policymakers to develop targeted interventions at a national level.

Our study has several limitations. Firstly, it is retrospective and relies on medical records, which may contain missing or incomplete data. Additionally, our cohort did not include post-kidney transplant patients, potentially affecting the accuracy of the overall prevalence of KF in children undergoing KRT in the kingdom. Furthermore, the study's cross-sectional nature precludes the determination of causality or temporal relationships between variables. The sum of the unclassified or unknown etiologies accounted for 25% of cases, which may limit the complete understanding of the actual distribution of KF causes. Also, it is important to note that our study primarily focuses on dialysis patients, and we do not have data on prevalent kidney transplant recipients. As a result, we cannot accurately estimate the true prevalence of KRT in Saudi Arabia, which includes both dialysis and kidney transplant.

Future research with longitudinal studies and national registries could explore temporal relationships and assess the effectiveness of interventions in improving patient outcomes. As the incorporation of digital health and artificial intelligence continues to become an increasingly essential component of healthcare, the potential for personalized healthcare will expand significantly [41–43]. Further research is needed to identify the factors contributing to unclassified or unknown etiologies and better understand the causes of KF in children.

Conclusion

This study provides first-time insights into the prevalence, etiology, and dialysis modalities of children on chronic dialysis living in Saudi Arabia with a critical comparison to other

parts of the world. The prevalence of children on chronic dialysis is 77.6 per million in Saudi Arabia, with CAKUT as the most common etiology. Moreover, the study findings provide valuable insights for healthcare professionals and policymakers to address KF-related challenges and enhance patient outcomes. Based on these results and the literature review, we strongly recommend having a national registry to further the care of our pediatric patients and direct proper healthcare support toward deficient areas.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00467-023-06245-w.

Author contribution KA and M-HT conceptualized and designed the study, drafted the initial manuscript, and critically reviewed and revised the manuscript. All other coauthors contributed to the data extraction from their centers, shared in drafting the original manuscript, and approved the submitted version. RR reviewed and revised the manuscript.

All authors have read and agreed to the published version of the manuscript.

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Data availability All original data presented in the study are included in the article; further inquiries can be directed to the corresponding authors.

Declarations

Ethical approval The studies involving human participants were reviewed and approved by the IRB of King Saud University, Riyadh, Saudi Arabia (Ref IRB Approval # 22/0457/IRB, date June 2, 2022). Written informed consent from the participant's legal guardian/next of kin was not required to participate in this study in accordance with the national legislation and the institutional requirements.

Consent to participate Not applicable.

Competing interests The authors declare no competing interests.

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