



# Kidney Health of Refugee Children: An Ongoing Challenge

## Mülteci Çocukların Renal Sağlığı: Süregelen bir Zorluk

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### Abstract

**Aim:** Its geographical proximity to Syria makes Turkey an important destination and transit country for refugees from various countries. The aim of this study is to determine the kidney and urological disease profile and to reveal the ongoing problems of refugee children who applied to a single center in Adana, home to a dense refugee population. To the best of our knowledge, this study is the largest single center experience with the refugee pediatric patient population in this field.

**Material and Method:** Medical records of 614 refugee children who were admitted to the pediatric nephrology and urology clinics between February 2020 and May 2022 were evaluated retrospectively. A total of 530 patients were included in the study.

**Results:** Median age of the 530 patients (301 male/229 female) was 72 months. The median follow-up time was 7 months (IQR 14 months). Congenital anomalies of the kidney and urinary tract with 181 patients (34.2%) is the most common diagnosis. The frequency of chronic kidney disease (CKD) of the patients was determined as 25% with 132 patients. 64 (12%) of the patients required surgical intervention. It was observed that 322 (61%) of the patients did not come to their regular follow-ups and delayed their follow-up.

**Conclusion:** Irregular follow-up and the delay of the treatment can lead to vitally severe consequences in patients with CKD in the long term. We believe that regular patient follow-ups will have a positive impact on the long-term follow-up results of the patients and the health costs of the country hosting the refugee patient profile.

**Keywords:** Refugee, children, acute kidney disease, chronic kidney disease

### Öz

**Amaç:** Suriye'ye olan coğrafi yakınlığı, Türkiye'yi çeşitli ülkelerden gelen mülteciler için önemli bir varış noktası ve geçiş ülkesi yapmaktadır. Bu çalışmanın amacı, yoğun bir mülteci nüfusuna ev sahipliği yapan Adana'da tek merkeze başvuran mülteci çocukların böbrek ve ürolojik hastalık profilini belirlemek ve devam eden sorunlarını ortaya koymaktır. Bildiğimiz kadarıyla bu çalışma, bu alanda mülteci pediatrik hasta popülasyonu ile ilgili en büyük tek merkezli deneyimdir.

**Gereç ve Yöntem:** Şubat 2020 ve Mayıs 2022 tarihleri arasında pediatrik nefroloji ve üroloji bölümlerine başvuran 614 mülteci çocuğun tıbbi kayıtları retrospektif olarak değerlendirildi. Çalışmaya toplam 530 hasta dahil edildi.

**Bulgular:** Beş yüz otuz hastanın (301 erkek/229 kız) ortalama yaşı 72 ay idi. Ortalama takip süresi 7 ay idi (IQR 14 ay). En sık görülen tanı yüz seksen bir hasta (%34,2) ile böbrek ve idrar yollarının konjenital anomalileri idi. Kronik böbrek hastalığı (KBH) sıklığı 132 hasta ile %25 olarak belirlendi. Hastaların 64'üne (%12) cerrahi girişim gerekti. Hastaların 322'sinin (%61) düzenli kontrollerine gelmediği ve takiplerini ertelediği görüldü.

**Sonuç:** Düzensiz takip ve tedavinin geciktirilmesi uzun vadede KBH hastalarında üzücü sonuçlara yol açabilmektedir. Düzenli hasta takibinin, hastaların uzun dönem takip sonuçlarına ve mülteci hasta profilini barındıran ülkenin sağlık maliyetlerine olumlu etki edeceğine inanıyoruz.

**Anahtar Kelimeler:** Mülteci, çocuklar, akut böbrek hastalığı, kronik böbrek hastalığı



## INTRODUCTION

Turkey is a principal destination and transit country for refugees from diverse countries.<sup>[1]</sup> Because of the geographical proximity to Syria Turkey currently hosts more than 60% of the Syrian refugee population and provides free access to shelter, education, and health care since the Syrian civil war (2011).<sup>[2,3]</sup> By January 2019, Istanbul, Sanliurfa, Hatay, Gaziantep and Adana were the five provinces with the highest Syrian populations among the 81 provinces of Turkey. Over half of the refugees are under the age of 18.<sup>[4]</sup> In terms of health and wellbeing, several health risks and other vulnerabilities have been observed to affect Syrian refugee children in the Turkish context since 2011.<sup>[1,2]</sup> Since 2011, healthcare professionals in Turkey have faced a pediatric population with kidney disease with no previous medical records. The hospital where this study was conducted is the largest tertiary hospital in the region where refugee patient referrals are made. Unfortunately, limited data from Syria regarding kidney disease profile of the children makes management of this population challenging. The aim of this study is to determine the kidney and urological disease profile and reveal the ongoing problems in the refugee children who applied to a single center in Adana.

To the best of our knowledge, this study is the largest single center experience with a refugee pediatric patient population in this field.

## MATERIAL AND METHOD

The study was carried out with the permission of Adana City Training and Research Hospital Ethics Committee (Date: 21/04/2022, Decision No: 1911). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

### Participants

The study was carried out in the Pediatric Nephrology and Urology Departments of City Training and Research Hospital, a tertiary medical center bearing the health burden of the vast majority of Syrian refugee patients. Electronic medical records of Syrian refugee children (aged 0-18) were retrospectively analyzed. 614 refugee children were admitted to the pediatric nephrology and urology departments from February 2020 to May 2022. Eighty-four patients with missing medical records were excluded from the study. A total of 530 patients were included in the study.

### Data Collection

The demographic data, clinical and laboratory findings, diagnosis, surgery, hospitalization, intensive care needs, and outcomes of the patients were evaluated retrospectively. Diagnosis and follow-up of glomerular diseases were made in accordance with the KDIGO Glomerulonephritis guideline.<sup>[5]</sup> Chronic kidney disease was defined as the 'The Kidney Disease: Improving Global Outcomes (KDIGO) clinical practice guidelines.<sup>[6]</sup>

## Analyses

This study was performed in retrospective cohort design with Syrian refugee children. Statistical analyses were performed with SPSS version 21 software package. Continuous data were defined by means of mean±SD under parametric conditions and median (interquartile range-IQR) under nonparametric conditions. Normal distribution of numeric variables was tested with Kolmogorov-Smirnov test. Categorical variables were defined by number and percentage. Chi square analysis was used for categorical variables. P values less than 0.05 were considered to be statistically significant.

## RESULTS

Of the 530 patients included in the study, 301 (57%) were male and 229 (43%) were female. Median age of the patients was 72 months (IQR 17-125 months). 445 of the patients were admitted to the pediatric nephrology department, and 85 to the pediatric urology department. The median follow-up time was 7 months (IQR 14 months). Eight of the patients (2%) were diagnosed in their home country, while 522 (98%) diagnosed in Turkey. The median number of applications to nephrology or urology departments was 2 times (IQR 3 times). It was observed that 322 (61%) of the patients did not come to their regular follow-ups and delayed their follow-ups. The frequency of CKD of the patients was determined as 25% with 132 patients. Sixty-four (12%) of the patients required surgical intervention.

Congenital anomalies of the kidney and urinary tract (CAKUT) with 181 patients (34.2%) are the most common diagnoses. It was followed by incontinence/enuresis with 76 patients (14.3%), and nonspecific hydronephrosis in 62 patients (11.7%), respectively. The diagnosis of the Syrian refugee children was shown in **Table 1**. The most common diagnosis in the etiology of CAKUT was vesicoureteral reflux (VUR) with 50 patients (27.6%), followed by neurogenic bladder (NB) in 43 patients (23.8%) and ureteropelvic junction obstruction (UPJO) in 25 patients (13.8%). The etiological classification of the patients with CAKUT is shown in **Table 2**.

**Table 1: The diagnosis of the 530 Syrian refugee children admitted to Pediatric Nephrology and Urology Departments**

Diagnosis	Number of the patients, n (%)
CAKUT	181 (34.2)
Daytime incontinence/ Nocturnal enuresis	76 (14.3)
Nonspecific hydronephrosis	62 (11.7)
Urinary system stone disease	61 (11.5)
Urinary tract infection	46 (8.7)
Glomerular disorders	34 (6.4)
Hematuria/ Proteinuria	23 (4.3)
Hypertension	12 (2.3)
Acute kidney injury	12 (2.3)
Tubular disorders	12 (2.3)
Cystic kidney diseases	7 (1.3)
Others (tumor/nutcracker)	4 (0.8)

CAKUT: Congenital anomalies of the kidney and urinary tract

**Table 2: The etiological classification of the 181 patients with Congenital Anomalies of the Kidney and Urinary Tract**

CAKUT	Number of the patients, n (%)
Vesicoureteral reflux	50 (27.6)
Neurogenic bladder	43 (23.8)
Ureteropelvic junction obstruction	25 (13.8)
Hypodysplasia/ atrophy	13 (7.2)
Agenesis	12 (6.6)
Ectopic kidney	10 (5.5)
Multicystic dysplastic kidney	8 (4.4)
Posterior Urethral Valve	6 (3.3)
Ureterovesical junction obstruction	5 (2.8)
Others	9 (5.0)
- Duplex collecting system	3 (1.7)
- Ureterocele	2 (1.1)
- Megaureter	2 (1.1)
- Bladder diverticulum	1 (0.6)
- Horseshoe kidney	1 (0.6)

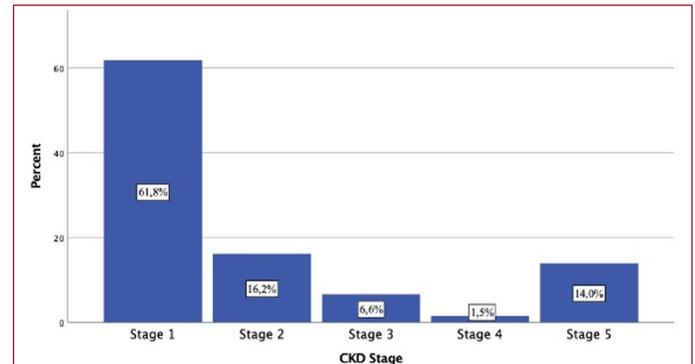
CAKUT: Congenital Anomalies of the Kidney and Urinary Tract

The most common cause in patients, followed up with a diagnosis of glomerular diseases, was nephrotic syndrome (NS) in 28 (82.4%) of the 34 patients. Other causes of glomerular disease were Henoch Schoenlein nephritis with three patients, post streptococcal glomerulonephritis with one patient, hemolytic uremic syndrome with one patient, and Wegener's granulomatosis with one patient, respectively. One of the patients with NS was diagnosed with congenital nephrotic syndrome in his country and was given intermittent albumin infusions. This patient applied only once and did not show up to their follow up. One of the patients was started on prednisolone treatment with a preliminary diagnosis of idiopathic NS. However, the patient did not come to the 1<sup>st</sup> month follow-up to evaluate the steroid response. Of the 26 patients diagnosed with NS with regular clinical follow-up, 35.7% (10 patients) had steroid-sensitive NS, 35.7% (10 patients) had steroid-resistant NS, 17.9% (5 patients) had steroid-dependent NS, and 3.9% (1 patient) was evaluated as frequent relapse NS. Pathological diagnosis of 9 of 10 patients with steroid-resistant NS who underwent kidney biopsy was reported as focal segmental glomerulosclerosis (FSGS), and 1 as membranoproliferative glomerulonephritis (MPGN).

Two (16.7%) of 12 patients diagnosed with acute kidney injury (AKI) had prerenal acute kidney injury. One of these patients developed AKI secondary to dehydration, while the other developed hepatorenal syndrome secondary to neonatal cholestasis. Of the nine (75%) patients with renal AKI, 6 had tubulointerstitial nephritis (TIN) and 3 had acute tubular necrosis (ATN). One of the patients with TIN, had Tubulointerstitial nephritis and uveitis syndrome (TINU). In one (8.3%) patient, post-renal AKI developed secondary to abdominal mass compression. In two of the AKI cases, one with hepatorenal syndrome and the other with cerebral palsy with severe malnutrition diagnosed with ATN, chronic kidney disease was developed.

The frequency of CKD of the 530 patients was determined as 25.6% with 136 patients. The majority of CKD patients were stage 1 patients with a frequency of 61.8%. The distribution of CKD stages of the refugee patients was shown in **Figure 1**. The leading cause of CKD was CAKUT (73.5%), followed by

glomerular diseases (11.8%), tubular diseases (6.6%), urinary system stone disease (3.7%), AKI (1.5%), cystic kidney diseases (1.5%), proteinuria secondary to glycogen storage disease (1.5%) and bilateral Wilms tumor (1.5%). Detailed information of patients with CKD stage 3-5 is shown in **Table 3**.

**Figure 1:** Distribution of chronic kidney disease stages of the refugee patients**Table 3: Detailed information of patients with Chronic Kidney Disease Stage 3-5**

	Sex	Age (month)	CKD Stage	RRT	Etiology	Follow-up	Survival
1	F	88	Stage 5	HD	Urinary system stone disease	No	Alive
2	F	187	Stage 5	HD	NB	No	Alive
3	M	184	Stage 5	-	SB+ NB	Yes	Alive
4	F	186	Stage 5	HD	Anorectal malformation+ NB	No	Alive
5	F	211	Stage 5	HD	Wolfram syndrome+ NB	Yes	Alive
6	M	95	Stage 5	HD	PUV+NB	No	Dead
7	M	195	Stage 5	HD	SB+ NB	Yes	Alive
8	M	175	Stage 5	HD	VUR	No	Alive
9	M	32	Stage 5	HD	VUR	Yes	Alive
10	M	56	Stage 5	HD	PUV	Yes	Alive
11	M	125	Stage 5	HD	PUV	No	Alive
12	F	124	Stage 5	HD	Hypodysplasia/atrophy	Yes	Alive
13	F	62	Stage 5	PD	NS	Yes	Alive
14	M	27	Stage 5	HD	HD	No	Alive
15	M	192	Stage 5	HD	HSP Nephritis	Yes	Alive
16	F	159	Stage 5	HD	Prolonged ATN sequelae	No	Alive
17	F	108	Stage 5	HD	Primary hyperoxaluria	No	Dead
18	F	72	Stage 5	HD	Cystinosis	No	Dead
19	F	9	Stage 5	PD	Polycystic kidney disease	Yes	Alive
20	F	200	Stage 4	-	Hypodysplasia/atrophy	Yes	Alive
21	F	49	Stage 4	-	NS	Yes	Alive
22	F	5	Stage 3	-	HRS sequelae	Yes	Dead
23	F	38	Stage 3	-	VUR	Yes	Alive
24	M	3	Stage 3	-	VUR	Yes	Alive
25	M	31	Stage 3	-	VUR	Yes	Alive
26	M	6	Stage 3	-	VUR	Yes	Alive
27	M	18	Stage 3	-	PUV	No	Alive
28	M	3	Stage 3	-	Hypodysplasia/atrophy	Yes	Alive
29	F	95	Stage 3	-	UVJO	Yes	Alive
30	F	99	Stage 3	-	Bilateral Wilms	No	Alive

F: Female, M: Male, CKD: Chronic Kidney Disease, RRT: Renal replacement therapy, HD: Hemodialysis, PD: Peritoneal dialysis, NB: Neurogenic bladder, SB: Spina bifida, PUV: Posterior urethral valve, VUR: Vesicoureteral reflux, NS: Nephrotic syndrome, HSP: Henoch Schoenlein Purpura, HRS: Hepatorenal Syndrome, UVJO: Ureterovesical junction obstruction

Hospitalization to the inpatient service was required in 18.3% (97 patients) of the 530 refugee children. Of these patients, 16.4% (16 patients) needed follow-up in the pediatric intensive care unit (PICU). Surgical reasons such as urogenital surgery or catheter placement were the most common reason for hospitalization with 93 (47.4%) of 196 hospitalizations. CKD complications such as hypervolemia, hypertensive encephalopathy, acidosis/electrolyte imbalances, and hypertensive cardiomyopathy were the most common causes of PICU hospitalization with a frequency of 66.7%.

CKD was present in 13 (81.3%) of the 16 patients admitted to the PICU. Ten (76.9%) of these patients had stage 5 CKD. In the presence of CKD, hospital and PICU hospitalization rates were 49.3% and 9.6%, those without CKD, these rates were determined as 7.1% and 0.8%, respectively. This difference was found to be statistically significant ( $p < 0.001$ ).

Five patients (0.94 %) died during the follow-up period. Demographic data, primary diagnosis and causes of mortality of these patients are shown in **Table 4**.

**Table 4: Demographic data, primary diagnosis and causes of mortality of the deceased patients.**

	Sex	Age (months)	Diagnosis	CKD	Cause of mortality
1	M	95	PUV+ NB	Stage 5	pulmonary edema
2	F	108	Primary hyperoxaluria	Stage 5	Sepsis
3	F	72	Cystinosis	Stage 5	Sepsis
4	F	4	Bartter Syndrome	Stage 1	Sepsis
5	F	6	Spina bifida+ NB	-	VP shunt dysfunction

M: Male, F: Female, PUV: Posterior urethral valve, NB: Neurogenic bladder, VP shunt: ventriculoperitoneal shunt

## DISCUSSION

In presented study, CKD frequency among refugee children population detected to be 25.6%. Spectrum of kidney problems in the lifetime of the refugee population can vary and may remain permanent in case of inappropriate management. There are few studies evaluating specific diseases in refugee population in Turkey.<sup>[5-8]</sup> Considering that the refugee issue has become a reality not only for cities neighboring Syria, but also for the whole country determining the profile of kidney diseases in the aforementioned population will also make positive contributions to their management.

Kara et al. reported CAKUT to be the most frequent diagnosis among refugee children with a percent of 26.2% in their study conducted in Gaziantep. Neurogenic bladder and VUR were reported to be the most common cause of CAKUT.<sup>[7]</sup> Multicenter retrospective study from Gaziantep reported the frequency of CAKUT in Syrian children to be 31% with non-obstructive hydronephrosis being the main reason.<sup>[8]</sup> As in the literature, in our study, CAKUT with 34.2% was the most common diagnosis among the refugee children, and the most frequent etiology of CAKUT was detected to be VUR. We think that percentages obtained from studies conducted

from border cities are not sufficient for detection of the real incidence of CAKUT because the data in the current studies have been obtained from refugee children population born in Turkey who can access health services. It is a big challenge to determine the real incidence of any disease in this kind of populations, considering that the populations are unable to access healthcare services, give birth at home, prefer to receive health care services from illegal refugee health workers, or refuse to receive any healthcare because of religious/social/trust issues. For instance, in presented study, of 614 patients admitted to Pediatric Nephrology and Urology departments 84 excluded because of the irregular follow-up.

Balat et al.<sup>[8]</sup> reported glomerular diseases as the second most common cause in the refugee population with a frequency of 19.9%, and NS was stated as the most common cause of glomerular diseases. Al Saegh et al.<sup>[9]</sup> published their single center experiences in Iran. In their study, it was reported that NS was the most common clinical presentation and FSGS was the most common glomerulonephritis with a frequency of 30% in 58 kidney biopsies. In our study, the incidence of glomerular disease was 6.4%, and nephrotic syndrome was the most common pathology among glomerular diseases with a percent of 82.4%. FSGS is the leading pathological diagnosis of a small number of biopsies performed. We think that the low rate of glomerular disease, compared to the literature, may be related to the presence of a University Hospital in the city, providing healthcare to the refugee population.

Various etiologies may take role in the development of AKI in children. There is an increased risk of CKD even after several years in patients experienced AKI. Direct or indirect renal injury during armed conflicts in healthy children may cause AKI and , with the most frequent cause reported to be being crush syndrome. Inappropriate management of AKI may increase risk of CKD.<sup>[6]</sup> There were 12 cases diagnosed with AKI. Two of the AKI cases developed CKD in our study. There was only one patient with postrenal AKI who applied with huge intraabdominal mass compression. Common feature of three overmentioned cases with catastrophic results is late admission. Besides proper management of AKI, basic information about basic care, well-being, and access to free health care, defined as a fundamental right for the refugee patient population, can prevent catastrophic consequences.

North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) reported that CAKUT, with 48%, is the leading underlying etiology of CKD.<sup>[10]</sup> This distribution has been reported with similar frequencies in European countries (47-62% in Turkey and other countries in the Middle East).<sup>[11]</sup> One study of 55 pediatric CKD patients from Syria reported NB to be the most frequent reason.<sup>[12]</sup> Multicenter study including data of 633 pediatric refugee children from pediatric nephrology centers in Turkey reported CKD incidence to be 14.8% and CAKUT to be more frequent.<sup>[8]</sup> Celakil et al.<sup>[13]</sup> evaluated 79 refugee pediatric patients with end stage renal disease (ESRD) and diagnosis of various stages of CKD and the

most common cause was reported to be CAKUT (37.9%). In our presented study the frequency of CKD was determined slightly higher (25.6%), with the leading cause being CAKUT (73.5%). There is limited data about exact frequency of CKD or urinary tract anomalies in refugee children population. Due to the prevalence of consanguineous marriages, the frequency of CKD caused by CAKUT may also be expected to be more frequent in this geographical region.

A study from Turkey reported acute community-acquired infections to be the major cause of hospitalization, while the rate of chronic diseases was approximately 16.3%.<sup>[14]</sup> Studies from other countries were also revealed the cause of hospital admission infectious diseases.<sup>[15,16]</sup> Yucel et al.<sup>[17]</sup> presented the largest number of hospitalized pediatric refugee patients' data. Frequency of PICU admission of reported to be 21.9% which was significantly higher than the non-refugee patient population. Gungor et al.<sup>[18]</sup> reported PICU hospitalizations frequency in their study conducted of 623 refugee inpatients, to be 6.7%. In our study, 81% of the patients admitted to the PICU had CKD, and the most common reason for PICU hospitalization was CKD complications. In those without CKD, hospital and PICU admission rates were determined as 7.1% and 0.8%, respectively. These results confront us with the fact that CKD increases the risk of hospitalization and PICU admission, and that the management of complications is more difficult in this patient population.

Sekkarie et al.<sup>[19]</sup> in their study evaluated cultural challenges and tried to suggest approaches to remedy these challenges of ESRD patients. It has been detected that language challenges leading to medical errors, cultural and religious challenges that hinder certain medical practices, trust challenges, dietary and medication challenges, and perception challenges affect the treatment of ESRD patients. A survey conducted by Lemke et al.<sup>[20]</sup> in 2018 showed that the group of refugee children arriving to Germany between 2015–2017 accounts for approximately 20% of the total pediatric dialysis population in Germany. As a conclusion they argue that provision of medical care for these children and their families is often hampered by psychosocial problems, cultural differences, language barriers, and administrative issues. Despite regular financial and logistic resources of the 530 patients 322 (61%) did not come to their regular follow-ups or delayed their follow-up. Etiological causes of mortality in our study were: PUV, NB, Bartter syndrome, cystinosis and primary hyperoxaluria, respectively. Unfortunately, common feature of these patients was non-compliance to treatments and follow-ups.

## CONCLUSION

Children with acute/chronic kidney disease are most vulnerable and most likely to be affected during armed conflict, migration or disaster. Beside experienced specialists well-equipped infrastructure is required for the management of such patient population. Caregivers or families of ESRD and

CKD should be informed in detail about what they should do and where they should apply in overmentioned situations. Considering the socio-economic status of the population, it should be explained that kidney diseases are treatable and preventable, and if the treatment is delayed, it can lead to sad consequences in the long term. We believe that this approach beside prevention from catastrophic health problems will have a positive impact on the health costs of the country that hosts refugee patient profile.

## ETHICAL DECLARATIONS

**Ethics Committee Approval:** The study was carried out with the permission of Adana City Training and Research Hospital Ethics Committee (Date: 21/04/2022, Decision No: 1911).

**Informed Consent:** All patients signed the free and informed consent form.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Author Contributions:** All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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