Original Article

Clinical Characteristics and Outcome of Children Requiring First-Time Hemodialysis Over a Year: A Tertiary Center Cohort Study.

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ABSTRACT

Introduction: Acute kidney injury (AKI)and chronic kidney disease (CKD) are serious morbid illnesses with increasing prevalence. Renal replacement therapy is often necessary when kidney function deteriorates, hemodialysis is the most used renal replacement therapy in developing countries.

Aim of the study: The study aims to review the clinical characteristics and outcomes of patients undergoing the first hemodialysis session in our center over one year.

Methods: This is a cohort longitudinal study that included 97 pediatric patients with kidney failure who underwent the first hemodialysis session.

Results: In total, the mean age was 8.84 ± 3.3 years, 53 (54.6%) were males. 42 (43.3%) were offsprings of consanguineous parents and 22.7% had a positive family history of CKD. Acute kidney injury affected thirty-four patients (35%) and chronic kidney disease affected sixty- three patients (65%). The primary causes of AKI and CKD were atypical hemolytic uremic syndrome (aHUS) and unknown kidney disease respectively, and the primary indications of HD were volume overload in AKI and uremic manifestation in CKD. Regarding the AKI group, 61.8% improved, 35.3% progressed to CKD, and 2.9% died. Male sex was more predominant among improved cases (71%), while among non-improved cases, aHUS represented 53% of the etiology with a P-value of 0.043 moreover, anemia and metabolic acidosis were significantly detected with P-values of 0.047 and 0.046 respectively as well as cardiovascular risks.

Conclusion: The main etiology of CKD in our center was unknown. The most important predictors of poor prognostic outcomes in AKI were female sex, anemia, metabolic acidosis, and cardiovascular risks.

KEYWORDS

Children, hemodialysis, clinical profile, outcome

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INTRODUCTION

Chronic kidney disease (CKD) is a major health concern in children and adults worldwide [1]. Chronic kidney disease in children, though sharing the same pathophysiologic mechanisms for deterioration of kidney function as in adults, has distinct characteristics. These include influence on growth and development, underlying etiology, cardiovascular complications, and the psychosocial impact of CKD on the patient and family [2] [3]. The asymptomatic nature of CKD presents diagnostic challenges and children often go unrecognized with progressive deterioration in kidney function [4]. Acute kidney injury (AKI) is a common medical problem among hospitalized patients and may be associated with multiple etiologies [5] [6]. When renal function declines, fluid and metabolic demands are increased, renal replacement therapy (RRT) is the only available treatment for AKI [7].

Hemodialysis (HD) is technically feasible in children of all ages and even in very small neonates. Although the principles of HD are similar for adults and children, there are technical aspects of the procedure and complications that are unique to the pediatric population [8]. Understanding the proximate causes of AKI and potentially modifiable etiologies continues to be the focus of research [9] in addition, the current literature provides little information on children who at first presentation have advanced CKD (GFR < 15 mL/min/1.73 m^2 and rapidly progress to RRT) [4]. The study aimed to describe the clinical characteristics and the outcome of children who underwent their first hemodialysis session over a year.

METHODS

This cohort longitudinal study was conducted on 97 patients with kidney diseases who underwent first-session hemodialysis to describe their characteristics and outcomes. The Research Ethics Committee approved the study (approval code N-206-2023). The patients were recruited and followed up at the acute hemodialysis unit, Center of Pediatric Nephrology and Transplantation (CPNT), Tertiary University Children's Hospital. Inclusion criteria were age between 6 months and 14 years and hemodynamically stable patients with AKI or CKD who were still initiating hemodialysis, we excluded patients referred from other chronic hemodialysis units to focus on first-session hemodialysis. Written consent was taken from caregivers.

Demographic and clinical measures: Full clinical assessment focusing on age, weight, height, body mass index, family history, consanguinity, relevant past history, primary renal disease, and presenting symptoms including (vomiting, fatigue, headache, respiratory symptoms, poor feeding, shortness of breath and fever), review of dialysis indication, hydration status, blood pressure, urine output, and comorbidities including anemia, acidosis, hyperphosphatemia, hypocalcemia, growth failure, and hypertension) and we followed up all patients until they improved, referred, or died

Reviewing of any investigations done: Serum creatinine, estimated GFR using the Schwartz formula (1984) and modified Schwartz formula (2009), for infants (under 1 year of age) and children (over1 year of age) respectively [10],

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Complete blood count, Serum urea, albumin, bicarbonate, calcium, phosphorous, alkaline phosphatase, and serology for collagen vascular diseases as complement levels, Antinuclear antibodies (ANA), Antineutrophilic cytoplasmic antibody (ANCA) , Anti-Streptolysin O titer (ASOT) levels and echocardiographic findings.

Hemodialysis-related data: Vascular access (size, site of insertion, cause of removal), duration of the session, dialyzer size, heparin dose, indication for wash, blood flow rate, and any complication encountered during the session (hypotension, vomiting, muscle cramps, and seizures).The study was conducted over a year and included all patients who required first-session hemodialysis (n=97), we excluded 130 patients who underwent first hemodialysis sessions at their chronic hemodialysis units.

Statistical analysis

Data were verified, coded by the researcher, and analyzed using IBM-SPSS 24.0 (IBM-SPSS Inc., Chicago, IL, USA) *. Descriptive statistics: Means, standard deviations, medians, ranges, frequency, and percentages were calculated. Test of significances: Chi-square/Fisher's Exact/Monte Carlo exact test was used to compare the difference in the distribution of frequencies among different groups. The Shapiro-Wilk test will be used to test data normality. Student t-test/ANOVA test was calculated to test the mean differences in continuous variables between groups. A significant p-value was considered when it was <0.05.

RESULTS

Our study included 97 children who required hemodialysis during the study period, with a mean age of 8.84 ± 3.3 years; 54.6% were males. Of the cohort, 42 patients (43.3%) were off springs of consanguineous parents, positive family history was found in 19 patients (30.2%) of the CKD group and 3 patients (8.8 %) of the AKI one ;2 out of the three AKI patients had a family history of aHUS in their siblings while the last one had a family history of glomerulonephritis.

Four patients had a history of hospital admissions, 2 of them had recurrent urinary tract infections (UTI), one patient had bone marrow transplantation developed AKI secondary to cyclosporin nephrotoxicity, and one child diagnosed with FSGS had a past history of blood transfusion prior to dialysis. Comorbidities represented 25.8% of our cohort, cardiomyopathy was the most common comorbidity affecting about 5.2% of our cases. Comorbidities among the studied group are displayed in **Figure 1.**

Sixty-three patients (64.9%) had chronic kidney disease comprising 34 males and 29 females while 34 patients (35.1%) had acute kidney injury comprising 19 males and 14 females with no statistically significant difference regarding sex between both groups with a P-value of 0.857. By comparing both groups, the mean age was 8.16 ± 1.7 years among the AKI group and 9.20 ± 1.4 among the CKD group with no statistically significant difference regarding age with a P- value of 0.14. There was a statistically significant difference between patients with chronic kidney disease and those in the AKI group regarding history of similar conditions in their families with a P- value of 0.017.

Growth failure (weight or height less than the 3rd percentile) was the most common complication among the study group especially the CKD group , four patients of the study group had a body

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weight of 10 kg or less with a minimum weight of 7 kg, twenty-two patients (22.7%) fell below the 3rd percentile for weight, while 33 patients (34%) fell below the third percentile for height; weight less than the third percentile for age was detected in 19 CKD patients versus 3 AKI patients similarly, height less than the third percentile for age was detected in 30 CKD patients versus 3 AKI patients with a statistically significant difference with P values of 0.017, and < 0.001 respectively.

Most patients were hypertensive (blood pressure > 90th percentile) as 80.4% had systolic hypertension and 74.3% had diastolic hypertension). Presenting symptoms had a wide variation; the most common symptoms at presentation were anorexia (80.4%), lethargy (75.3%), and pallor (69.1). Nearly two-thirds of our study group had a history of upper respiratory tract infection. Oliguria/anuria was exhibited in 49.5% of the study group as shown in **Figure 2**.

By comparing presenting symptoms among both groups, polyurea, polydipsia, and nocturnal enuresis were presented only by the CKD group and not exhibited by the AKI group in addition, the CKD group more commonly suffered vomiting with a statistically significant difference compared to the AKI group with P- values of 0.001 and 0.030 respectively while the AKI group significantly displayed oliguria/anuria and hematuria with a P-value of < 0.001 for each**.**

Upper respiratory tract infection was a common triggering factor in the AKI group compared to the CKD group with a P-value of 0.007. Baseline characteristics and clinical features of both groups are shown in **Table 1.** The predominant two primary etiologies among the CKD group were unknown etiology and cystic kidney disease at about 23.8% each, while atypical HUS (a- HUS) was the predominant cause in the AKI group at about 44% as shown in **Figure 3.**

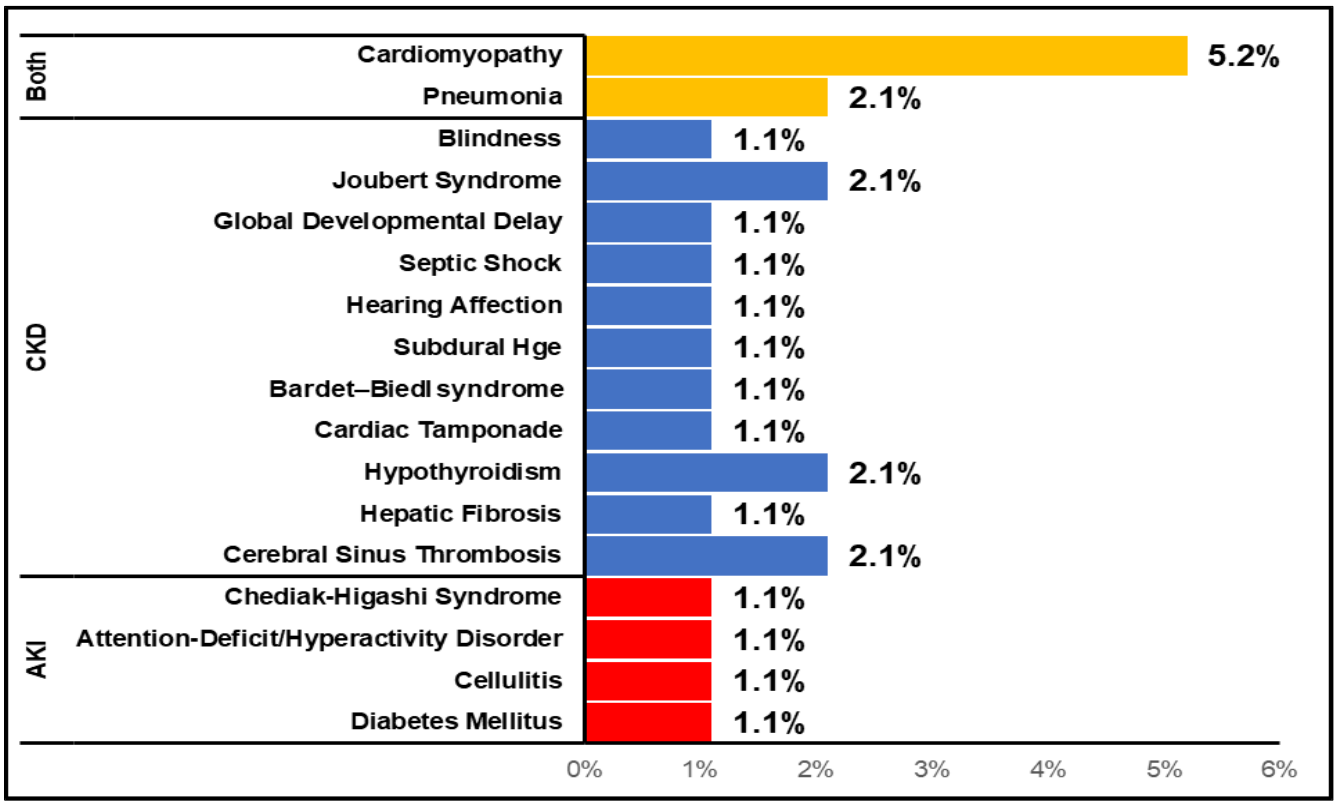

Figure 1: Comorbidities among the studied Cohort

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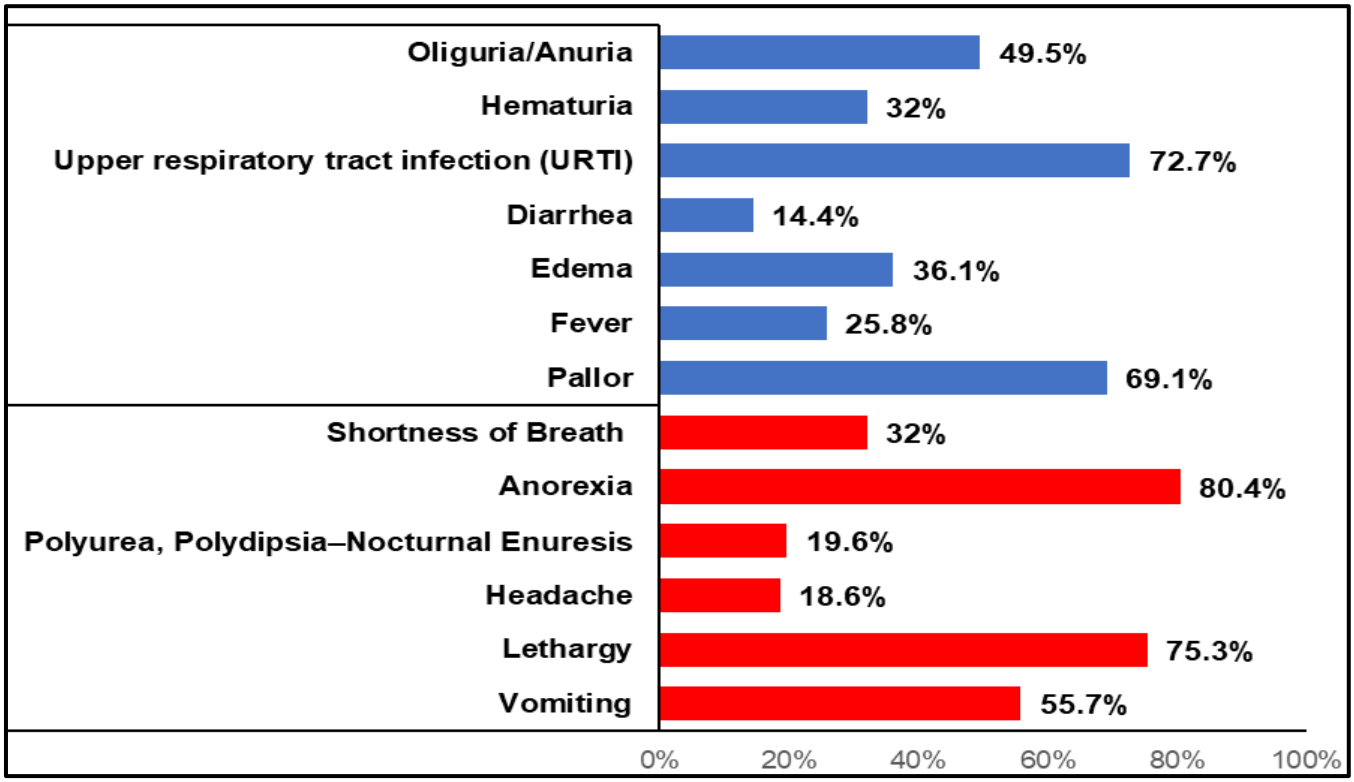

Figure 2: Clinical Presentation of the studied Cohort

Table 1: Comparing clinical characteristics & presenting symptoms between AKI & CKD group

	AKI (n = 34)	CKD (n = 63)	P-value
Age	8.16 ± 1.7	9.20 ± 1.4	= 0.145*
Sex			
Female	15 (44.1%)	29 (46%)	= 0.857**
Male	19 (55.9%)	34 (54%)	
Consanguinity	12 (35.3%)	30 (47.6%)	= 0.242**
Similar Condition	3 (8.8%)	19 (30.2%)	**= 0.017****
Comorbidity	7 (20.6%)	18 (28.6%)	= 0.391**
Past History of Hospital Admission	2 (5.9%)	2 (3.2%)	= 0.522**
Weight<3rd Percentile	3 (8.8%)	19 (30.2%)	**= 0.017****
Height<3rd Percentile	3 (8.8%)	30 (47.6%)	**< 0.001****
BMI	18.34 ± 3.7	18.46 ± 5.1	= 0.905*
Present Symptoms and Signs			
Vomiting	24 (70.6%)	30 (47.6%)	**= 0.030****
Lethargy	27 (79.4%)	46 (73%)	= 0.486**
Headache	5 (14.7%)	13 (20.6%)	= 0.474**
Anorexia	27 (79.4%)	51 (81%)	= 0.855**
Shortness of breath	9 (26.5%)	22 (34.9%)	= 0.394**
Pallor	23 (67.6%)	44 (69.8%)	= 0.823**
Fever	12 (36.4%)	13 (20.6%)	= 0.079**
Polyurea- Polydipsia- Nocturnal Enuresis	0 (0%)	19 (30.2%)	**= 0.001*****
Oedema	15 (44.1%)	20 (31.7%)	= 0.161**
Diarrhoea	7 (20.6%)	7 (11.1%)	= 0.167**
Upper respiratory tract infection	13 (28.2%)	9 (14.3%)	**= 0.007****
Haematuria	25 (75.8%)	6 (9.5%)	**< 0.001****
Oliguria/Anuria	29 (85.3%)	19 (30.2%)	**< 0.001****

AKI; Acute kidney injury, CKD; Chronic kidney disease, BMI; Body mass index.

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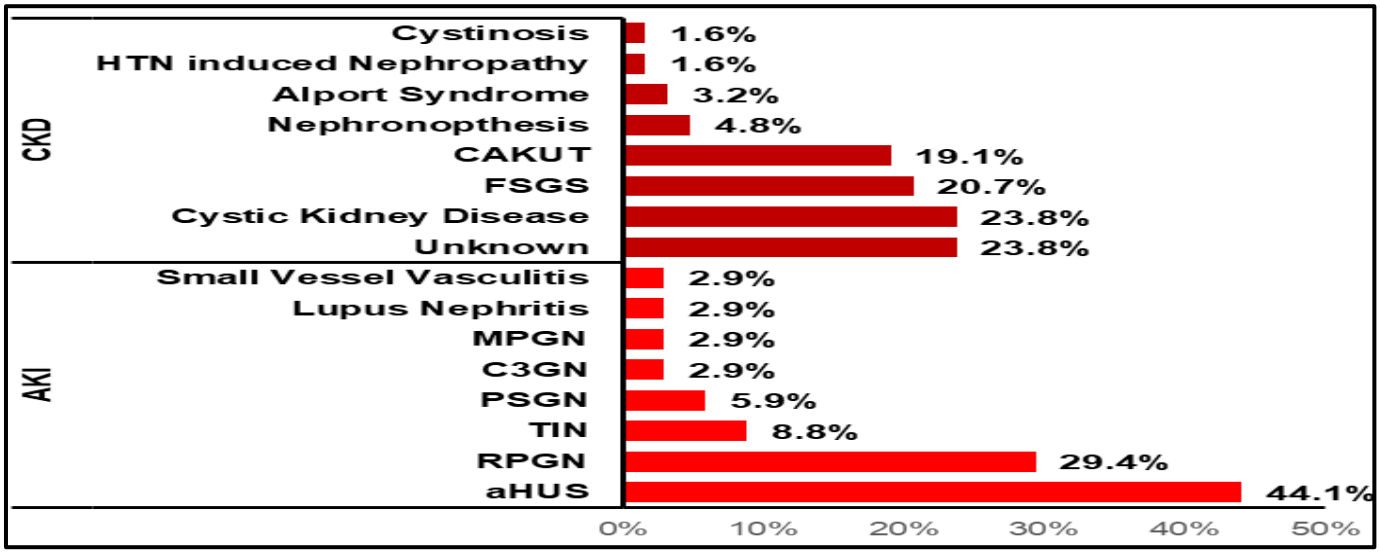

Figure 3: Etiology of Renal Affection among the studied Cohort

HTN: hypertension; CAKUT: congenital anomalies of kidney and urinary tract; FSGS: focal segmental glomerulosclerosis; MPGN: membranoproliferative glomerulonephritis; C3 G: complement 3 glomerulopathy; PSGN: post-streptococcal glomerulonephritis; TIN: tubulointerstitial nephritis; RPGN: rapidly progressive glomerulonephritis; aHUS: atypical haemolytic uremic syndrome.

Peritoneal dialysis was initiated in 17.6% of the AKI group and 14.3% of the CKD group before they started the first HD session. Regarding HD indications, volume overload was more frequent among the AKI group with a P-value of 0.037 in contrast, uremic manifestations were more common among the CKD group with a P-value of 0.042, other indications included persistent metabolic acidosis, persistent hyperphosphatemia, preparation for kidney biopsy to improve the bleeding tendency or to give blood transfusion and 4 patients started hemodialysis based on low glomerular filtration rate.

Regarding vascular access, the right internal jugular vein temporary catheter was the most used site of access insertion in both groups while two patients with CKD started dialysis from arteriovenous fistula (AVF). the mean duration until the removal of vascular access was 9 days (range 2-27), the main causes were improvement of the condition, infection, thrombosis, malfunction, accidental removal, and external hematoma but no statistically significant difference between both groups. Vascular access-related infection was detected in 23.6% of the AKI group, and 17.7% of the CKD group but blood culture was positive in 11.8% of the AKI group and 12.7% of the CKD group.

Nineteen patients (19.5%) of the whole cohort (8 AKI patients and 11 CKD patients) developed dialysis-related complications, of which intra-dialysis hypotension was seen in 5 patients (5%) with no statistically significant difference between both groups as shown in **Table 2.** Regarding the main laboratory data of both groups, platelet count, and serum ALP were significantly higher among the CKD group with P values of 0.004 and 0.007 respectively. In contrast, estimated GFR was significantly lower in this group compared to the AKI group with a P- value of 0.038, while among the AKI group C-reactive protein (CRP) and Antistreptolysin O titer (ASOT) levels were significantly higher compared to the CKD group with P values of 0.010 and < 0.001 respectively as shown in **Table 3.** Concerning the clinical outcome among

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the AKI group, 61.8% improved, 35.3% progressed to CKD, and 2.9% died.

By comparing the clinical and laboratory data between improved cases (n=21) and those who died or progressed to CKD (n=13), we found that sex was a significant factor in predicting prognosis; 15 out of 21 improved patients were males with a P-value of 0.024. aHUS carried the worst prognosis; and represented the etiology of 7 out of 13 non-improved cases with a P value of 0.043. Anemia and metabolic acidosis were the most important medical comorbidities affecting the prognosis with a statistically significant difference with a p-value of 0.047 and 0.046 respectively, furthermore, cardiovascular risks were one of the important predictors of deterioration including volume overload, hypertension, and LV hypertrophy as shown in **Table 4**. While **Table 5** showed the multivariable logistic regression model of the independent predictors of improvement among AKI cases. After adjusting for age and sex, the final model included five independent risk predictors for non-improvement, a-HUS, anemia, high CRP, diastolic hypertension and LV hypertrophy.

Table 2: Dialysis-related data among the Studied Cases

	AKI (n = 34)	CKD (n = 63)	
Dialysis Indications			
Volume overload	12 (35.3%)	11 (17.5%)	**= 0.037***
Uremic manifestations	15 (44.1%)	41 (65.1%)	**= 0.042***
Others	7 (20.6%)	11 (17.5%)	= 0.372*
Mode of Dialysis			
HD from the start	27 (79.4%)	54 (85.7%)	
PD then HD	6 (17.6%)	9 (14.3%)	
CRRT then Conventional HD	1 (2.9%)	0 (0%)	
mporary Catheter Size (French)	8.62 ± 1.2	8.40 ± 1.2	= 0.424***
Site of Insertion			
Rt. Femoral	3 (8.8%)	1 (1.6%)	
Lt. IJV	3 (8.8%)	4 (6.6%)	= 0.077**
Rt. IJV	28 (82.4%)	55 (90.2%)	
Rt. Subclavian	0 (0%)	1 (1.6%)	
Cause of Removal			
Improvement	25 (73.5%)	47 (77.1%)	
Infection	8 (23.6%)	10 (16.4%)	
Thrombosis	0 (0%)	1 (1.6%)	= 0.493**
Malfunction	0 (0%)	2 (3.3%)	
Accidental	1 (2.9%)	0 (0%)	
Haematoma	0 (0%)	1 (1.6%)	
Duration of 1st Session (min.)	137.73 ± 14.2	123.23 ± 10.7	= 0.418***
Blood Flow/min	120.00 ± 35.8	117.74 ± 33.5	= 0.768***
Heparin/Wash			
Heparin	5 (14.7%)	27 (42.9%)	**= 0.007***
Wash	29 (85.3%)	36 (57.1%)	
Positive blood culture	4 (11.8%)	8 (12.7%)	= 0.584*
Complications during 1st Session			
Hypotension	2 (5.9%)	3 (4.8%)	= 0.851*
Cramps	1 (2.9%)	0 (0%)	= 0.901*
Vomiting	1 (2.9%)	2 (3.2%)	= 0.921*
Seizures/Confusion	4 (11.8%)	5 (7.9%)	= 0.759*
Headache	0 (0%)	1 (1.6%)	= 0.901*

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*The Chi-square test was used to compare the difference in frequency between groups
**The Monte Carlo exact test was used to compare the difference in frequency between groups
***Independent Sample t-test was used to compare the difference in mean between group
The total number of CKD group who inserted the catheter was 61 patients as 2 patients had undergone dialysis via arterio-venous fistula.
AKI; Acute kidney injury, CKD; Chronic kidney disease, HD; Haemodialysis, PD; Peritoneal dialysis, CRRT; Continuous renal replacement therapy, LT; Left, RT; Right, IJV; Internal jugular vein.

Table 3: Comparing Laboratory Findings between AKI and CKD group

Parameter (unit)	AKI (n = 34)	CKD (n = 63)	
Hb (g/dl)	8.33 ± 2.1	8.63 ± 1.9	= 0.495*
HCT%	23.89 ± 5.9	26.04 ± 6.1	= 0.147*
MCV (fl)	75.04 ± 6.7	75.94 ± 6.9	= 0.623*
MCH (pg)	29.72 ± 9.1	26.18 ± 2.7	= 0.056*
TLC (Thousands/cmm)	10.94 ± 1.5	9.10 ± 1.3	= 0.066*
Platelet Count (Thousands/cmm)	200.03 ± 29.2	290.09 ± 15.4	**= 0.004***
CRP (mg/dL)	36.97 ± 9.8	9.52 ± 2.4	**= 0.010***
Serum Creatinine (mg/dL)	7.16 ± 0.7	8.22 ± 0.5	= 0.188*
Blood Urea (mg/dL)	234.22 ± 23.9	220.21 ± 17.1	= 0.434*
e-GFR	16.16 ± 5.5	9.17 ± 1.2	**= 0.038***
Albumin (g/dL)	3.39 ± 0.6	3.29 ± 0.7	= 0.542*
PH	7.33 ± 0.1	7.30 ± 0.1	= 0.307*
HCO3 (mEq/L)	15.40 ± 1.6	14.47 ± 1.7	= 0.453*
Ca (mg/dL)	8.54 ± 1.3	7.82 ± 1.9	= 0.061*
Phosphorous (mg/dL)	6.63 ± 1.8	7.13 ± 2.4	= 0.315*
ALP (U/L)	175.67 ± 24.6	346.55 ± 45.5	**= 0.007***
Consumed C3 level (n=39)	12 /32(37.5%)	1/7 (14.3%)	**= 0.001****
Consumed C4 level (n=39)	2/32 (6.3%)	1/7 (14.3%)	= 0.247**
Positive (ANA) (n=34)	6/29 (20.7%)	1/5 (20%)	= 0.732***
Anti streptolysin O- titer (ASOT) (n=39)	165.32 ± 81.1	7.30 ± 1.5	**< 0.001***
Positive (Anti-ds DNA) (n=15)	1/12 (8.3%)	1/3 (33.3%)	= 0.057**
Positive (ANCA) (n=9)	1/9 (16.7%)	1/3 (33.3%)	= 0.571**

Independent Sample t-test was used to compare the difference in mean between groups
****The Chi-square test was used to compare the difference in frequency between groups.**
AKI; Acute kidney injury, CKD; Chronic kidney disease, HB; Hemoglobin, HCT; Hematocrit, MCV; Mean corpuscular volume, MCH; Mean corpuscular hemoglobin concentration, TLC; Total leucocytic count, CRP; C-reactive protein, e-GFR; Estimated Glomerular Filtration Rate, HCO3; Bicarbonate, Ca; Calcium, ALP; Alkaline Phosphatase, C3; Complement Component 3, C4; Complement component 4, ANA; Antinuclear antibody, ASOT; Anti streptolysin O- titer, Anti-ds DNA Ab; Anti double-stranded DNA antibody, ANCA; Antineutrophilic cytoplasmic Antibody.

Table 4: Comparison in Baseline/Clinical/Laboratory Findings among AKI Cases (n=34)

	Improved (n = 21)	Non-Improved[$] (n = 13)	P-value
Age/years	8.43 ± 1.7	7.73 ± 1.4	= 0.637*
Sex			
Male	15 (71.4%)	4 (30.8%)	**= 0.024****
Female	6 (28.6%)	9 (69.2%)	
Etiology			
a-HUS	8 (38.1%)	7 (53.8%)	
RPGN	6 (28.6%)	4 (30.8%)	
TIN	3 (14.3%)	0 (0%)	
PSGN	2 (9.5%)	0 (0%)	**= 0.043****
C3GN	1 (4.8%)	0 (0%)	
MPGN	0 (0%)	1 (7.7%)	
Lupus Nephritis	1 (4.8%)	0 (0%)	
Small Vessel Vasculitis	0 (0%)	1 (7.7%)	
Anemia (Hb<7 g/dl)	5 (23.8%)	7 (53.8%)	**= 0.047****

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Table 4: Comparison in Baseline/Clinical/Laboratory Findings among AKI Cases (n=34). **Continued**			
	Improved (n = 21)	**Non-Improved$ (n = 13)**	**P-value**
Platelet (Thousands/cm)	213.70 ± 38.3	177.25 ± 25.8	= 0.547*
CRP (mg/dL)	46.76 ± 9.4	23.92 ± 4.3	**= 0.039***
Phosphorous (mg/dL)	6.18 ± 1.1	7.30 ± 2.3	= 0.108*
Volume Overload	8 (38.1%)	8 (61.5%)	**= 0.043***
Hypertension			
Systolic Hypertension	3 (14.3%)	4 (30.8%)	**= 0.033***
Diastolic Hypertension	7 (33.3%)	3 (23.1%)	= 0.306*
Comorbidity			
Metabolic Acidosis (PH<7.35)	9 (42.9%)	10 (76.9%)	**= 0.046***
Hyperphosphatemia (> 1.5 mmol/L)	16 (76.2%)	11 (84.6%)	= 0.449*
Hypocalcaemia (< 8.8 mg/dL)	8 (38.1%)	7 (53.8%)	= 0.146*
LV Hypertrophy	1 (4.8%)	3 (23.1%)	**= 0.036***
Growth Failure (Wt.<3rd Percentile)	3 (14.3%)	0 (0%)	= 0.080*
Growth Failure (Ht.<3rd Percentile)	1 (4.8%)	2 (15.4%)	= 0.322*

***Independent Sample t-test was used to compare the difference in mean between groups**
****The Chi-square test was used to compare the difference in frequency between groups**
***** The Monte Carlo exact test was used to compare the difference in frequency between groups**
$Non-improved=Progression to ESKD/Dead
AKI; Acute kidney injury, a-HUS; Atypical hemolytic uremic syndrome, RPGN; Rapidly progressive glomerulonephritis, TIN; Tubulointerstitial nephritis, PSGN; Poststreptococcal Glomerulonephritis, C3GN; Complement 3 Glomerulonephritis, MPGN; Membranoproliferative glomerulonephritis, Hb; Hemoglobin, CRP; C reactive protein, LV; Left ventricular.

Table 5: Independent Predictors of Improvement among AKI cases: Multivariable Logistic Regression Model.

	OR (95% CI) *	**P-value**
Age/years	1.056 (0.921 – 1.212)	= 0.433
Sex (Male)	1.953 (0.755 – 5.025)	= 0.167
a-HUS	3.501 (1.152 – 9.633)	**= 0.027**
Anemia	1.549 (1.021 – 6.454)	**= 0.039**
CRP	1.015 (1.004 – 1.104)	**= 0.044**
Diastolic Hypertension	2.408 (1.017 – 4.745)	**= 0.042**
LV Hypertrophy	3.042 (1.059 – 7.125)	**= 0.024**

a-HUS=atypical hemolytic uremic syndrome, LV =left ventricular,CRP =C-reactive protein

DISCUSSION

Hemodialysis is an important life-saving procedure in patients with AKI and CKD requiring renal replacement therapy [11]. Growth failure is a hallmark in children with CKD and its pathogenesis is multifactorial including nutritional, hormonal, hematological, and metabolic disorders, such as electrolyte imbalance, acidosis, mineral and bone disorder (CKD-MBD), anemia, birth parameters, associated syndromes and parental height [12].

According to the registry of the North American Pediatric Renal Transplant Cooperative Studies (NAPRTCS) [13], growth failure was found in 35% of the cohort, Our CKD group, had a similar percentage of growth failure (30.2% for weight and 47.6% for height), in contrast to another study evaluating children presenting with advanced CKD where growth failure detected only in 19% of cases [4], that could be explained by the difference in the etiology of CKD in both cohorts.

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The etiology of renal disease in almost a quarter (23.8%) of the CKD group was unknown similar to what was reported by earlier multi-center research from our country which suggested that low health awareness, inaccessibility to medical centers, and the lack of antenatal screening caused the delayed diagnosis [14]. On the other hand, a study in Brazil in 2019, shows only 11% of pediatric CKD patients with unknown etiology [15].

Diversity of etiologies of AKI is seen in developing countries, A review of Nigerian publications regarding pediatric AKI from 1990 to 2012 postulated nephrotoxins and infections as predominant AKI etiology [16]. *Krishnamurthy et al.* reported infections, PSGN, and HUS as common causes of AKI [17] while PSGN and crescentic glomerulonephritis were the most common etiologies in another study [18]. We found that atypical HUS in 44.1% followed by RPGN in 29.4% of the cases were the main etiologies in the AKI group.

The prevalence of consanguinity in African countries drives the spectrum of kidney diseases in children [19], nearly half (43.3%) of our cohort were offsprings of consanguineous parents, in addition to a positive family history of CKD that increase the risk of autosomal recessive diseases. Another interesting finding was the presence of a positive family history of similar conditions in 3 cases of the AKI group; two of them were diagnosed as a-HUS which progressed to ESKD raising the possibility of genetic background, and the last one with PSGN improved completely. Lethargy and anorexia were the most common presenting symptoms in both groups which are non-specific manifestations that could delay the diagnosis of kidney diseases and this finding is similar to a previous study [4].

Regarding the AKI group; Oliguria/anuria and edema were the main presentations similar to a study conducted in Pakistan [18]. It could be explained by the high prevalence of glomerular diseases in our AKI group which is characterized by oliguria and resulting edema. In addition, vomiting was more common in patients with AKI with a prevalence of 70.6% which is higher than the same study that reported a prevalence of only 36.2% [18]. This could be due to congestive gastropathy or uremia, while cases with CKD had presenting symptoms of polyuria, polydipsia, and nocturnal enuresis, this could be explained by defective urine concentration capacity in addition to the majority of cases had non-glomerular kidney diseases.

Kidney diseases are often precipitated by infections that are more prevalent with low socioeconomic conditions [19], we reported fever, diarrhea ,and URTI in 25.8%, 21.6% and 14.4% respectively but with a higher incidence of URTI in the AKI group that could be the precipitating factor for cases with a-HUS, PSGN, and RPGN. Cardiovascular disease (CVD) has been recognized as one of the most important complications of CKD and one of the leading causes of death. It develops early and progresses through CKD stages [20]. Cardiomyopathy was the most common comorbidity in our cohort and the majority of the patients had systolic and diastolic hypertension (80.4% and 74.3% respectively). This should be addressed and managed timely to prevent mortality and morbidity.

An average of 15 patients (6 patients with AKI and 9 patients with CKD) initially started peritoneal dialysis (PD) before hemodialysis. According to our unit's protocol, for patients with uremic encephalopathy or body weight less than

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10 kg, it is preferred to start PD first to avoid hemodynamic instability or dialysis disequilibrium while only one girl diagnosed with crescentic glomerulonephritis due to ANCA-associated vasculitis started initially CRRT as she had ultrafiltarion intolerance (manifested hypotension) due to significant weight gain (>10%) and cardiomyopathy.

The most common indications for starting HD were volume overload in the AKI group and uremic manifestations in the CKD one. This was anticipated given the etiologies of the two groups and presenting symptoms, which comprised non-glomerular diseases in the CKD group, where polyuria predominated, and glomerular diseases in the AKI group, where oliguria was more prevalent.

Published clinical practice guidelines vary concerning eGFR cutoffs below which dialysis therapy should be initiated but they recommend assessing symptoms or signs of uremia [21], we reported eGFR at the initiation of hemodialysis of 9.17 ± 1.2 in our CKD group out of which four patients started hemodialysis based on low eGFR; only two of them underwent dialysis through AVF because most of our CKD cohort was accidentally discovered and this emphasizes the importance of early detection of cases and planning for permanent vascular access.

In the present study, the main cause for vascular access removal was improvement in 72 patients (25 cases with AKI and 47 cases with CKD). Regarding the CKD group, these patients were presented with acute conditions requiring dialysis on top of CKD, they did not require dialysis again until their discharge. Vascular access-related infection is a major cause of hospitalization in hemodialysis patients[22]. In our cohort, presumed infection in 18 patients was the second cause of catheter removal. Out of which, 12 patients had positive blood cultures that yielded gram-positive bacteria (coagulase-negative and methicillin-resistant staphylococci) which comes in concordance with results reported by *Weldetensae and his colleagues* [11].

Regarding laboratory findings, we found significantly higher CRP and ASOT levels in the AKI group compared to the CKD group which may be caused by the higher rate of URTI in the AKI group. Despite plasma therapy, ~48% of children with aHUS die or develop ESRD [23], we reported similar results as 46% of aHUS patients died or progressed to CKD, and this could also explain why anemia (hemoglobin less than 7 gm/dl) was significantly higher in the (non-improved) group. Many reports suggest that fluid overload at initiation of renal replacement therapy is associated with increased mortality [24]. In our cohort, volume overload and hypertension were found to have statistically significant ($p < 0.05$) associations with the non-improved AKI cases in agreement with the findings concluded by *Tresa et al* [18].

LIMITATIONS OF THE STUDY

This study is limited by the brief follow-up period of AKI patients. The clinical features and presentation were the main emphasis of this study not the course of treatment.

RECOMMENDATIONS

Accurately diagnosing pediatric AKI patients enables appropriate patient management. Using monoclonal therapy for atypical hemolytic syndrome (a-HUS) cases can improve patient outcomes.

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Preparing CKD patients with A-V fistula before dialysis could avoid catheter-related complications. Proper data recording and setting up a registry for ESRD in pediatrics.

CONCLUSION

We concluded that the main cause of CKD in our center was unknown while a-HUS was the most common cause of AKI which carried the worst prognosis. Severe anemia, volume overload, and systemic hypertension are predictors of poor prognosis among AKI cases. Hemodialysis was initiated based on symptoms without a cutoff value for eGFR.

ABBREVIATIONS

a-HUS	atypical hemolytic uremic syndrome
AKI	Acute kidney injury
ANA	anti-nuclear antibodies
ANCA	anti neutrophil cytoplasmic antibodies
ASOT	anti-streptolysin O titer
AVF	Arterio-venous fistula
CKD	chronic kidney disease
CRRT	continuous renal replacement therapy
CRP	C-reactive protein
eGFR	estimated glomerular filtration rate
ESKD	end stage kidney disease
FSGS	focal segmental glomerulosclerosis
HD	hemodialysis
LV	left ventricle
MBD	mineral bone disorders
NAPRTCS	North American Pediatric Renal Transplant Cooperative Studies
PD	peritoneal dialysis
PSGN	post-streptococcal glomerulonephritis
RPGN	rapidly progressive glomerulonephritis
RRT	renal replacement therapy
URTI	upper respiratory tract infections
UTI	urinary tract infections

REFERENCES

1. Coresh J. Update on the Burden of CKD. J Am Soc Nephrol. 2017 Apr;28(4):1020–2.
2. Becherucci F, Roperto RM, Materassi M, Romagnani P. Chronic kidney disease in children. Clin Kidney J. 2016 Aug;9(4):583–91.
3. Atkinson MA, Ng DK, Warady BA, Furth SL, Flynn JT. The CKiD study: overview and summary of findings related to kidney disease progression. Pediatr Nephrol. 2021 Mar;36(3):527–38.
4. Abukwaik WM, Baracco R, Jain A, Gregory M, Valentini RP, Kapur G. Clinical profile of children incidentally found to have advanced kidney failure. Pediatr Nephrol [Internet]. 2022;37(5):1097–103. Available from: https://doi.org/10.1007/s00467-021-05293-4
5. Mahmoud L Ben, Pariente A, Kammoun K, Hakim A, Ghozzi H, Sahnoun Z, et al. Risk factors for acute decompensation of chronic kidney disease in hospitalized patients in the nephrology department: a case-control study. Clin Nephrol. 2014 Feb;81(2):86–92.
6. Naicker S, Aboud O, Gharbi MB. Epidemiology of acute kidney injury in Africa. Semin Nephrol. 2008 Jul;28(4):348–53.
7. Christiansen S, Christensen S, Pedersen L, Gammelager H, Layton JB, Brookhart MA, et al. Timing of renal replacement therapy and long-term risk of chronic kidney disease and death in intensive care patients with acute kidney injury.

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Crit Care. 2017 Dec;21(1):326.

8. Rees L. Paediatrics: Infant dialysis--what makes it special? Nat Rev Nephrol. 2013 Jan;9(1):15–7.
9. Nie S, Tang L, Zhang W, Feng Z, Chen X. Are There Modifiable Risk Factors to Improve AKI? Biomed Res Int. 2017;2017:5605634.
10. Mian AN, Schwartz GJ. Measurement and Estimation of Glomerular Filtration Rate in Children. Adv Chronic Kidney Dis. 2017 Nov;24(6):348–56.
11. Weldetensae MK, Weledegebriel MG, Nigusse AT, Berhe E, Gebrearegay H. Catheter-Related Blood Stream Infections and Associated Factors Among Hemodialysis Patients in a Tertiary Care Hospital. Infect Drug Resist. 2023;16(May):3145–56.
12. Haffner D. Strategies for Optimizing Growth in Children With Chronic Kidney Disease. Front Pediatr. 2020;8:399.
13. Seikaly MG, Salhab N, Gipson D, Yiu V, Stablein D. Stature in children with chronic kidney disease: analysis of NAPRTCS database. Pediatr Nephrol. 2006 Jun;21(6):793–9.
14. Safouh H, Fadel F, Essam R, Salah A, Bekhet A. Causes of Chronic Kidney Disease in Egyptian Children. Saudi J Kidney Dis Transplant [Internet]. 2015;26(4). Available from: https://journals.lww.com/sjkd/fulltext/2015/26040/causes_of_chronic_kidney_disease_in_egyptian.30.aspx
15. Nogueira PCK, Konstantyner T, De Carvalho MFC, De Xavier Pinto CC, De Pádua Paz I, Belangero VMS, et al. Development of a risk score for earlier diagnosis of chronic kidney disease in children. PLoS One. 2019;14(4).
16. Olowu WA. Acute kidney injury in children in Nigeria. Clin Nephrol. 2015;83(7 Suppl 1):70–4.
17. Krishnamurthy S, Narayanan P, Prabha S, Mondal N, Mahadevan S, Biswal N, et al. Clinical profile of acute kidney injury in a pediatric intensive care unit from Southern India: A prospective observational study. Indian J Crit care Med peer-reviewed, Off Publ Indian Soc Crit Care Med. 2013 Jul;17(4):207–13.
18. Tresa V, Yaseen A, Lanewala AA, Hashmi S, Khatri S, Ali I, et al. Etiology, clinical profile and short-term outcome of acute kidney injury in children at a tertiary care pediatric nephrology center in Pakistan. Ren Fail [Internet]. 2017;39(1):26–31. Available from: https://doi.org/10.1080/0886022X.2016.1244074
19. Esezobor CI, Alakaloko AE, Admani B, Ellidir R, Nourse P, McCulloch MI. Paediatric Nephrology in Africa. Curr Pediatr Rep. 2021;9(4):134–41.
20. Mitsnefes MM. Cardiovascular Disease Risk Factors in Chronic Kidney Disease in Children. Semin Nephrol. 2021 Sep;41(5):434–8.
21. Susantitaphong P, Altamimi S, Ashkar M, Balk EM, Stel VS, Wright S, et al. GFR at initiation of dialysis and mortality in CKD: a meta-analysis. Am J kidney Dis Off J Natl Kidney Found. 2012 Jun;59(6):829–40.
22. Agrawal V, Valson AT, Mohapatra A, David VG, Alexander S, Jacob S, et al. Fast and furious: a retrospective study of catheter-associated bloodstream infections with internal jugular nontunneled hemodialysis catheters at a tropical center. Clin Kidney J. 2019 Oct;12(5):737–44.
23. Loirat C, Fakhouri F, Ariceta G, Besbas N, Bitzan M, Bjerre A, et al. An international consensus approach to the management of atypical hemolytic uremic syndrome in children. Pediatr Nephrol. 2016 Jan;31(1):15–39.
24. Selewski DT, Cornell TT, Lombel RM, Blatt NB, Han YY, Mottes T, et al. Weight-based determination of fluid overload status and mortality in pediatric intensive care unit patients requiring continuous renal replacement therapy. Intensive Care Med. 2011 Jul;37(7):1166–73.

AUTHORS' CONTRIBUTIONS

The submitted manuscript is the work of the author & co-author. All authors have contributed to authorship, have read, and approved the manuscript.

Conception and design of study: RG

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Acquisition of data: FA and EE
Analysis and/or interpretation of data: RG *and FA*
Drafting the manuscript: EE
Revising the manuscript critically for important intellectual content: RG
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STATEMENTS

Ethics approval and consent to participate

This study protocol and the consents were approved and deemed sufficient by the Ethical Research Committee of Kasr Al Ainy Faculty of Medicine, Cairo university and informed written consent was obtained in every case from their legal guardians.

Consent for publication

The contents and material of the manuscript have not been previously reported at any length or being considered for publishing elsewhere.

Availability of data and material

"Not applicable"

Conflict of interest

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