IJKD KIDNEY DISEASES

Acute Kidney Injury in Pediatric Patients with COVID-19; Clinical Features and Outcome

Mahbubeh Mirzaee,[1] Mahnaz Jamee,[1,2] Masoumeh Mohkam,[1] Fatemeh Abdollah Gorji,[3] Mitra Khalili,[4] Sedigheh Rafiei Tabatabaei,[2] Abdollah Karimi,[2] Shahnaz Armin,[2] Roxana Mansour Ghanaie,[2] Seyed Alireza Fahimzad,[2] Zahra Pournasiri,[1] Seyed Mohammad Taghi Hosseini Tabatabaei,[1] Reza Dalirani,[1] Nasrin Esfandiar,[1] Mina Alibeik[2]

[1]Pediatric Nephrology Research Center, Research Institute for Children's Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[2]Pediatric Infections Research Center, Research Institute for Children's Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[3]Medical Research Development Center of Mofid Children's Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran
[4]Department of Pediatric Radiology, Mofid Children's Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

Keywords. COVID-19, kidney disease, acute kidney injury, child

Original Paper

Introduction. Renal disorders have been reported as the underlying cause as well as complications of critical COVID-19 in pediatric patients. The purpose of this study was to investigate the pattern of kidney involvement, particularly acute kidney injury (AKI), among pediatric patients with COVID-19.

Methods. In this prospective study, hospitalized pediatric patients with a clinical diagnosis of COVID-19 were enrolled. Demographic, clinical, and laboratory findings were collected and analyzed using a mixed method of qualitative and quantitative approaches and descriptive statistics.

Results. One hundred and eighty-seven patients, including 120 (64.2%) males and 67 (35.8%) females with COVID-19 with a median age (interquartile range) of 60 (24 to 114) months were enrolled in this study. Most patients (n = 108, 58.1%) had one or two underlying comorbidities, mainly malnutrition (77.4%), neurologic/learning disorders (21.4%), and malignancy (10.2%). According to the Kidney Disease Improving Global Outcomes (KDIGO) classification, AKI was detected in 38.5% of patients (stage 1: 55.6%, stage 2: 36.1%, and stage 3: 8.3%) at presentation or during hospitalization. Nine patients (4.8%) required hemodialysis and 16 (8.6%) eventually died. There was no significant association between AKI and admission to the pediatric intensive care unit (PICU) ($P > .05$), a multisystem inflammatory syndrome in children (MIS-C) ($P > .05$), comorbidities ($P > .05$), and mortality rate ($P > .05$).

Conclusion. Kidneys are among the major organs affected by COVID-19. Although kidney abnormalities resolve in the majority of pediatric COVID-19 infections, particular attention should be paid to serum creatinine and electrolyte levels in patients affected by COVID-19, particularly children with a history of malnutrition and kidney disorders.

IJKD 2023;17:20-7
www.ijkd.org
DOI: 10.52547/ijkd.7151

INTRODUCTION

Severe acute respiratory syndrome—coronavirus 2 (SARS-CoV-2) infection or coronavirus disease 2019 (COVID-19) is estimated to affect 2.0 to 7.4% of children, with the majority of cases classified as asymptomatic mild to moderate (24.0 to 26.0%) and severe, observed in 5.9% of patients.[1-5]

Although less common in children than in adults,

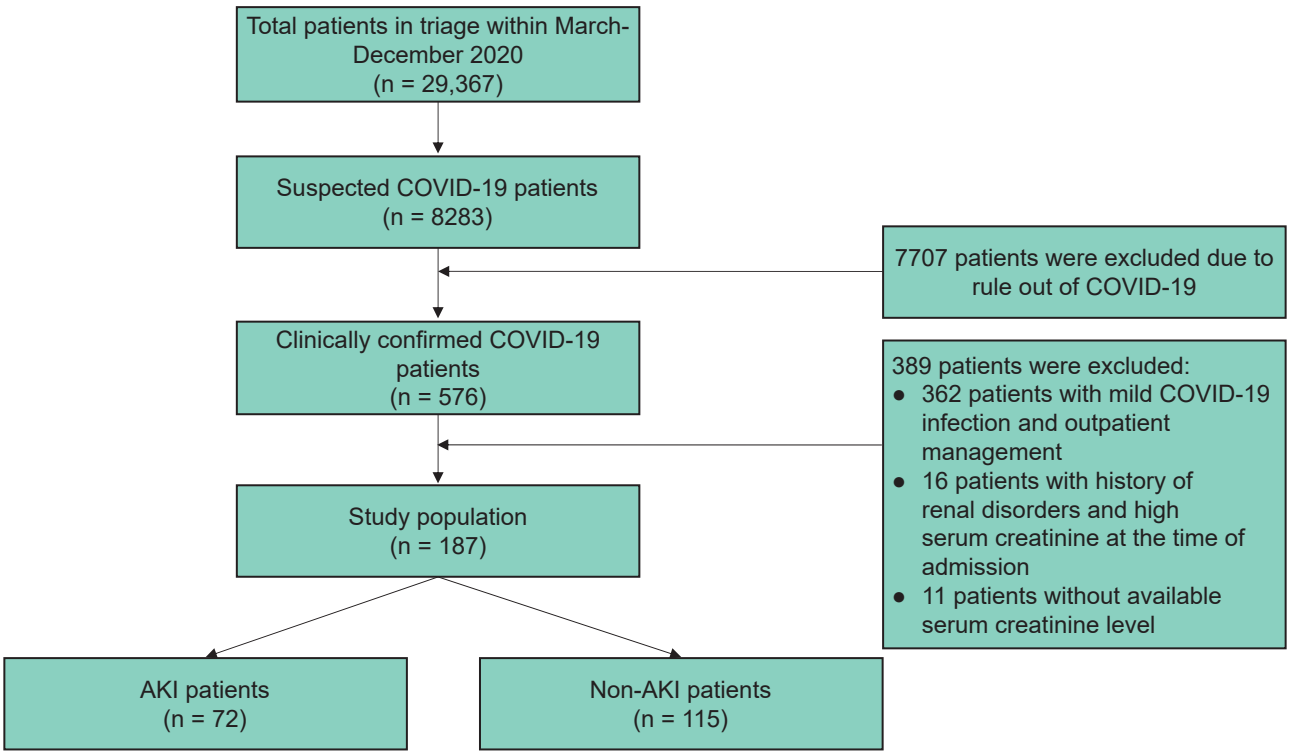
a preexisting medical condition can impact disease severity and prognosis.[6] In critically ill pediatric patients, kidney disorders such as hydronephrosis, chronic kidney disease, and kidney anomalies, have been reported as underlying conditions that predispose them to the development of COVID-19. Kidney disorders such as acute kidney injury, hematuria, proteinuria, and hypertension could also occur as complications of COVID-19.[7-9] However, the prevalence of kidney involvement in COVID-19 might be underestimated, as the available reports are based on hospitalized patients mainly at the beginning of the pandemic, when the pediatric population was considered to be at low risk of infection.[10] Furthermore, the early stages of acute kidney injury may be asymptomatic and baseline kidney function may not be available in most patients.[11]

Internal organ complications may develop slowly in children due to a longer incubation period and milder symptoms compared to adults.[2,12] Therefore, early diagnosis of kidney involvement and implication ofappropriate treatment can help to prevent long-term complications and may be a determining factor in reducing the mortality rate. In this viewpoint, we aimed to investigate the pattern of kidney involvement among pediatric patients with COVID-19, with particular attention to acute kidney injury.

MATERIALS AND METHODS

Participants

We enrolled 187 children with the clinical diagnosis of COVID-19 who were admitted to Mofid Children's Hospital, a teaching and referral hospital for children in Tehran, from March 1, 2020, to December 30, 2020. Patients were selected or excluded based on their COVID-19 status, history of kidney disorders, and creatinine level at admission (Figure). During the study period, 8283 patients with suspected COVID-19 were admitted to the hospital, and the diagnosis of COVID-19 was established in 576 patients, according to the Iranian Ministry of Health's COVID-19 consensus.[13] Patients with a positive test for SARS-CoV-2 nucleic acid in the blood or nasopharyngeal swab samples were considered to have definite COVID-19. Patients without SARS-CoV-2 polymerase chain reaction (PCR) test but with two or more of the following criteria were also enrolled: I) High fever, malaise, gastrointestinal, or respiratory symptoms, II) Leukopenia, lymphopenia, or an



Patients Selection Flowcharts

increase in erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP), III) An atypical chest X-ray or computed tomography (CT) scan. Three hundred and eighty-nine patients including 362 patients with mild COVID-19 treated in the outpatient department, 16 patients with a history of pre-existing kidney disorder and high serum creatinine on admission, and 11 patients without available serum creatinine levels were excluded.

Acute kidney injury was defined according to the KDIGO guideline (Kidney Disease Improving Global Outcomes) for AKI as the following:[14-16]

- An increase in SCr by ≥ 0.3 mg/dL (≥ 26.5 µmol/L) within 48 hours; or
- An increase in SCr to ≥ 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or
- Urine volume of < 0.5 mL/kg/h for 6 hours

The COVID-19 was considered severe if the patient needed admission to an intensive care unit (ICU) or mechanical ventilation.

Data Collection

Patient demographicss, medical comorbidities, clinical presentations, laboratory findings and imagings at the first day of admission including a complete blood count, serum electrolytes (sodium, potassium, calcium, magnesium, phosphorus), urinalysis, urine culture, blood culture, liver function tests, blood urea nitrogen, first and serial serum creatinine levels, lactate dehydrogenase, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) , COVID-19 reverse transcription-polymerase chain reaction (RT-PCR), chest X-ray (CXR), chest CT scan, kidney and urinary tract ultrasound, and outcomes were collected and recorded in a data sheet by a pediatric nephrology fellowship. Patients who met the above mentioned requirements for AKI were identified and enrolled in the study.

Hypertension (HTN) was defined as measured systolic blood pressure (SBP) and/or diastolic blood pressure (DBP) at equal to or more than 95th percentile of age, sex, and height for children up to 12 years of age, while for adolescents aged 13 to 17 years, it was defined as blood pressure ≥ 130/80 mmHg without adjustment for age, sex, or height.[17]

Statistical Analysis

All statistical analyses were performed using SPSS software (v. 26.0, Chicago, IL). Descriptive statistics included means and standard deviation (SD) for normally distributed variables, medians and interquartile range (IQR) for skewed measures, and proportions for categorical variables. Analytical tests including Mann-Whitney, Chi-square, and Fisher exact tests were applied for comparison. The associations between indicators of kidney involvement and in-hospital death were examined using Cox proportional hazard regression analysis. A *P* value < .05 was considered statistically significant.

RESULTS

Overall, 187 pediatric patients, including 120 (64.2%) males and 67 (35.8%) females with COVID-19, were enrolled in this study. The median (Interquartile range: IQR) age of the study population was 60 (24 to 114) months, and the median (IQR) of hospital admission duration was 5 (3 to 8.25) days.

The median (IQR) body mass index (BMI) was 16.0 (13.0 to 18.6). Based on the BMI, patients were classified as underweight (n = 127, 68.3%), normal (n = 42, 22.6%), overweight (n = 13, 7%), and obese (n = 4, 2.2%).

Evidence of COVID-19 was observed in 79 out of 107 (73.8%) CXRs and 85 out of 114 chest CT scans obtained from patients during admission. The SARS-CoV-2 RT-PCR was evaluated in 84 patients and proved positive in about one-third of them (n = 30, 35.7%).

The blood pressure on admission was classified as normal in 126 (85.1%), low in 12 (8.1%), and high in 10 (6.8%) patients, according to the normal range for age, and they were in the normal range for 111 out of 116 (95.7%) patients and high in 5 (4.3%) patients at the time of hospital discharge.

Underlying comorbidities included malnutrition (n = 144, 77.4%), neurologic/learning disorders (n = 40, 21.4%), malignancies (n = 19, 10.2%), inborn errors of metabolism (n = 14, 7.5%), cardiovascular disorder (n = 13, 7%), gastrointestinal/hepatic disorders (n = 10, 5.3%), chronic pulmonary diseases (n = 9, 4.8%), inborn errors of immunity (n = 9, 4.8%), and hematologic disorder (n = 8, 4.3%).

The past medication history included angiotensin-converting enzyme inhibitors (n = 10, 5.3%), nonsteroidal anti-inflammatory drugs (n = 5, 2.7%), trimethoprim/sulfamethoxazole (n = 5, 2.7%), calcineurin inhibitors (n = 2, 1.1%) and vancomycin (n = 1, 0.5%).

Reduced urine volume before admission was reported by 26 (14.3%) patients, edema by 13 (7.1%), urine discoloration by 3 (1.6%), and dysuria by 2 (1.1%) patients.

During hospital admission, the following organs were found to be involved: the lungs (n = 100, 53.5%), the gastrointestinal tract (n = 73, 39%), the skin (n = 7, 3.7%), the heart (n = 5, 2.7%), and the central nervous system (n = 4, 2.1%). In addition, 20 (10.7%) patients developed a multisystem inflammatory syndrome (MIS-C).

Acute kidney injury was present in 187 patients based on the normal range of creatinine levels for age at the time of presentation. Patients diagnosed with AKI were classified into stage 1 (n = 40, 55.6%), stage 2 (n = 26, 36.1%), and stage 3 (n = 6, 8.3%), according to the KDIGO classification. The comparison of the demographic data and clinical and laboratory findings of patients in AKI and non-AKI groups is presented in Table 1.

Table 1. Baseline Characteristics of the Study Population

Baseline Characteristics	COVID-19 Case (n = 187)	AKI (n = 72)	Non-AKI (n = 115)	*P*
Age Group, y				
Infants (0 to 1)	35 (18.7%)	14 (19.4%)	21 (18.3%)	> .05
Toddlers (1 to 5)	63 (33.7%)	27 (37.5%)	36 (31.3%)	
Children (5 to 13)	60 (32.1%)	23 (31.9%)	37 (32.2%)	
Adolescents (≥ 13)	29 (15.5%)	8 (11.1%)	21 (18.3%)	
Median Age, y (IQR)	5 (2 to 9.5)	5 (1.9 to 8.8)	6 (2 to 11)	> .05
Sex				
Male	120 (64.2%)	45 (62.5%)	75 (65.2%)	> .05
Female	67 (35.8%)	27 (37.5%)	40 (34.8%)	
All Comorbidity				
Common Comorbidities	108 (58.1%)	35 (49.3%)	73 (63.5%)	> .05
Neurologic Disorders	40 (21.4%)	14 (19.4%)	26 (22.6%)	> .05
Hematologic Disorders	8 (4.3%)	2 (2.8%)	6 (5.2%)	> .05
Malignancies	19 (10.2%)	5 (6.9%)	14 (12.2%)	> .05
Cardiovascular Disorders	13 (7%)	6 (8.3%)	7 (6.1%)	> .05
Pulmonary Disorders	9 (4.8%)	3 (4.2%)	6 (5.2%)	> .05
Malnutrition	144 (77.4%)	52 (72.2%)	92 (80.7%)	> .05
GI / Hepatic Disorders	10 (5.3%)	3 (4.2%)	7 (6.1%)	> .05
Inborn Errors of Metabolic	14 (7.5%)	4 (5.6%)	10 (8.7%)	> .05
Inborn Errors of Immunity	9 (4.8%)	2 (2.8%)	7 (6.1%)	> .05
Serum Laboratory Findings (Quantitative) Median (IQR)				
Total Leukocyte Count (× 10^3 cell / μL)	8.6 (5.7 to 11.8)	8.5 (5.5 to 12.7)	8.6 (5.9 to 11.5)	> .05
Absolute Neutrophilic Count (cells / μL)	5.2 (2.7 to 8.1)	5.1 (2.5 to 8.0)	5.3 (3.0 to 8.5)	> .05
Absolute Lymphocyte Count (cells / μL)	3 (1.8 to 4.8)	2.9 (2.1 to 4.6)	3.0 (1.7 to 4.8)	> .05
Hemoglobin Level, g/dL	11 (9.9 to 12.4)	10.9 (9.9 to 12.6)	11.3 (10 to 12.4)	> .05
Platelet Count (× 10^3 cell / μL)	222 (145 to 342)	233 (144 to 343)	222 (145 to 345)	> .05
CRP Level, mg/dL	5 (2 to 25)	5 (1.2 to 24)	5 (2 to 34)	> .05
ESR, mg/dL	35 (11 to 56)	29.5 (6.8 to 48)	36 (15 to 60)	> .05
Admission Serum Creatinine Level, mg/dL	0.6 (0.5 to 0.8)	0.8 (0.6 to 1.1)	0.5 (0.5 to 0.6)	< .001
Discharge Serum Creatinine Level, mg/dL	0.5 (0.4 to 0.7)	0.6 (0.4 to 0.8)	0.5 (0.4 to 0.6)	< .05
Admission Serum BUN Level, mg/dL	10 (7.8-15)	12 (8.3-17.7)	10 (7 to 12.8)	< .05
Admission Serum LDH Level, U/L	608 (475 to 944)	620 (479 to 936)	593 (466 to 968)	> .05
Admission Serum Sodium Level, meq/L	136 (134 to 138)	136 (134 to 139)	136 (134 to 138)	> .05
Admission Serum Potassium Level, meq/L	4 (3.7 to 4.4)	4 (3.8 to 4.4)	4 (3.7 to 4.3)	> .05
Admission Serum Calcium Level, mg/dL	8.7 (8.2 to 9.5)	8.9 (8.2 to 9.5)	8.7 (8.2 to 9.4)	> .05
Admission Serum Magnesium Level, mg/dL	2.2 (1.9 to 2.3)	2.2 (2 to 2.3)	2.2 (1.8 to 2.3)	> .05
Admission Serum Phosphorus Level, mg/dL	3.9 (3.1 to 5)	4.2 (3.7 to 4.9)	3.6 (2.9 to 5)	> .05
Duration of Hospital Stay, median (IQR)	5 (3 to 8.25)	6 (3 to 9)	5 (3 to 8)	> .05
Duration of Hospital Stay < 14 days	162 (89%)	63 (91.3%)	99 (87.6%)	> .05
Duration of Hospital Stay ≥ 14 Days	20 (11%)	6 (8.7%)	14 (12.4%)	

Most of the patients (n = 115, 65.7%) had normal leukocyte counts. Leukocytosis and leukopenia were reported in 32 (18.3%) and 28 (16%) of patients, respectively. The majority of patients had normal neutrophil (n = 100, 68.5%), lymphocyte (91, 70%), and platelet (73, 51%) counts. While lymphopenia (n = 19, 14.6%), neutropenia (n = 12, 8.2%), and thrombocytopenia (n = 33, 23.1%) were reported in few patients. Inflammatory markers including ESR (35 of 53, 66%) and lactate dehydrogenase (LDH) (56 of 59, 94.9%), were elevated in most of the evaluated patients.

There was no significant correlation between different stages of AKI and white blood cell (WBC) ($P > .05$), neutrophil ($P > .05$), lymphocyte ($P > .05$), or LDH ($P > .05$) counts at presentation.

Severe COVID-19 was detected in 66 (35.3%) patients. Electrolyte abnormalities were reported in 95 (72.5%) patients, the most common of which were hyponatremia (46, 35.4%), hypernatremia (4, 3.1%), hypokalemia (11, 8.5%), hyperkalemia (22, 16.9%), hypocalcemia (40, 52.6%), hypophosphatemia (38, 59.4%), and hypermagnesemia (38, 62.3%).

Forty-four patients (23.5%) were admitted to the pediatric intensive care unit (PICU) and 27 (14.4%) patients required mechanical ventilation. There was no significant relationship between AKI and Pediatric ICU (PICU) admission ($P > .05$), MIS-C ($P > .05$), or other comorbidities ($P > .05$). Among patients with available serum creatinine levels at the time of hospital discharge, 68 (81.9%) patients had normal serum creatinine level, in 15 patients (18.1%) serum creatinine level rose to 1.5 times higher than baseline and nine patients (4.8%) needed hemodialysis, all of whom were clinically stable. Sixteen patients (8.6%) eventually died. The mortality rate was approximately equal in patients with and without AKI (9.7 vs. 7.8%, $P > .05$) (Table 2).

DISCUSSION

In this study, we investigated the pattern of kidney involvement among pediatric patients with COVID-19 with particular attention to acute kidney injury.

The majority of patients (n = 108, 58.1%) had at least one or two comorbid conditions, mostly malnutrition (77.4%), neurologic/learning disorders (21.4%), and malignancies (10.2%). The association between pre-existing comorbidities and the risk of severe COVID-19 is less established in the pediatric population than in adults, in whom cardiovascular disorders, diabetes, and malignancy are reported to be significantly correlated with severe COVID-19.[18,19] A few studies have reported that severe COVID-19 affects 5.1 and 0.2% of patients with and without comorbidities, respectively, and about two-thirds of patients with the severe form of the infection have underlying comorbidities.[20,21] Therefore, children with underlying comorbidities should receive special attention in terms of protective measurements and diagnostic approaches.

The high prevalence of AKI at presentation or during follow-up (38.5%), as well as high frequency of electrolyte abnormalities (72.5%), are remarkable in this study, in part because the kidneys were not

Table 2. Comparison of Qualitative Variables in COVID-19 Patients

Parameters	Total Case	AKI	Non-AKI	OR	95% CI	*P*
Leukocytosis	32 (18.3%)	15 (22.1%)	17 (15.9%)	1.498	0.692 to 3.245	> .05
Leukopenia	28 (16%)	13 (19.1%)	15 (14%)	1.450	0.642 to 3.273	> .05
Neutrophilia	34 (23.3%)	12 (20.7%)	22 (25%)	0.783	0.352 to 1.738	> .05
Neutropenia	12 (8.2%)	8 (13.8%)	4 (4.5%)	3.360	0.962 to 11.730	< .05
Lymphopenia	19 (14.6%)	4 (7.4%)	15 (19.7%)	0.325	0.102 to 1.043	.05
Thrombocytopenia	33 (23.1%)	13 (22.4%)	20 (23.5%)	0.999	0.466 to 2.141	> .05
High ESR	35 (66%)	11 (61.1%)	24 (68.6%)	0.720	0.220 to 2.359	> .05
Organ's Involvement	157 (84%)	61 (84.7%)	96 (83.5%)	1.098	0.489 to 2.465	> .05
Comorbidities	108 (58.1%)	35 (49.3%)	73 (63.5%)	0.559	0.307 to 1.020	> .05
MIS-C	20 (10.7%)	12 (16.7%)	8 (7%)	2.675	1.036 to 6.909	> .05
Electrolytes Disturbances	95 (72.5%)	36 (73.5%)	59 (72%)	1.080	0.487 to 2.394	> .05
Admission to PICU	44 (23.5%)	22 (30.6%)	22 (19.1%)	1.860	0.939 to 3.685	> .05
Need for Intubation	27 (14.4%)	14 (19.4%)	13 (11.3%)	1.894	0.833 to 4.304	> .05
Mortality	16 (8.6%)	7 (9.7%)	9 (7.8%)	1.268	0.451 to 3.570	> .05

*$P < .05$ is considered significant.

expected to be as involved in the pathogenesis of COVID-19 as much as the lungs and GI tract. In our previous pilot study at the beginning of the COVID-19 outbreak, AKI was reported in 34.5% of patients, half of which were complicated by stage III AKI.[22] The high level of AKI in COVID-19 might be explained by the high expression of ACE2 in renal tubular cells.[23] However, the data regarding COVID-19-related kidney complications in children are lacking, which may suggest that COVID-19 mainly affects the kidneys in an indirect, unmeasurable manner e.g., through dehydration, hypoxia, sepsis-induced cytokine storm, disseminated intravascular coagulation, rhabdomyolysis, or even inappropriate use of non-steroidal anti-inflammatory drugs.[24,25]

The epidemiological characteristics of AKI in pediatric patients with COVID-19 are unknown. According to recent studies, kidney involvement in patients with COVID-19 typically occurs in association with critical situations such as acute respiratory distress syndrome (ARDS) or multi-organ failure. The incidence of COVID-19-associated AKI ranges from 0.5 to 23.0%; these differences could be attributed to the 7 to 15 day interval between the initial assessment and the onset of AKI, as well as the hospital that performed the study, as tertiary referral hospitals are more likely to admit complicated patients.[26,27]

Wang F. *et al.* evaluated 275 adults with COVID-19 and observed AKI in 49.5% of patients during their hospital stay. They showed that patients who developed AKI were older, tended to have some degree of chronic kidney disease, and had sepsis-related multi-organ failure compared to patients without AKI.[27] Bowe *et al.* reported the results of their query on the epidemiology of AKI in 5216 patients with COVID-19 and showed an incidence of 32% for AKI in their study group. In their study, 58, 13, and 16% of the patients met the KDIGO definitions of stages 1, 2, and 3 AKI; respectively, and 12% received renal replacement therapy (RRT).[28]

We did not find any specific correlation between laboratory parameters such as WBC and lymphocyte count, and LDH, and different stages of AKI. However, in another study, the respiratory rate at admission, WBC and lymphocyte count, and LDH level were all linked to stage 2 or 3 AKI.[29] They also demonstrated that patients with COVID-19 and AKI were more likely to requireRRT than those without this COVID-19 and were less likely to recover their kidney function.[29] In another study from the UK, 29% of the 52 pediatric patients developed AKI as part of MIS-C without any need for RRT.[30] In a recent large survey of 41 centers, 106 (44%) critically ill patients were found to have AKI.[31] In a systematic review of twenty-four studies, the AKI incidence among 1247 patients at the median age of 9.1 years was estimated at 30.5%, and RRT was applied to only 0.56% of patients.[32]

Conclusively, AKI appears to complicate one out of every three hospitalized patients with COVID-19, and it is unclear whether the kidney injury will persist or not. In a cohort of 1612 patients with AKI who underwent post-hospitalization follow-up, patients with COVID-19-associated AKI had an 11.3 mL/min/ 1.73 m^2 per year faster decline in GFR. However, further studies are required to provide long-term follow-up for COVID-19 patients in terms of post-infectious kidney function.

LIMITATIONS

This study had some limitations. The research was designed as observational and only evaluated hospitalized patients from a single pediatric hospital; thus, the prevalence of AKI may not accurately reflect its prevalence among all pediatric COVID-19 patients. However, given the rarity of studies on COVID-19-associated AKI in children, this study may be a pioneer in elucidating the prevalence of AKI among this group of patients. This survey will be continued by the authors with a larger sample size, variable underlying disorders, drug histories, and COVID-19 severity, as well as assessment of kidney function in patients complicated by AKI.

CONCLUSION

In conclusion, COVID-19 has a significant impact on a number of organs, including the kidneys. AKI occurred in 38.5% of children admitted to our hospital. There was no significant correlation between the development of AKI and admission to the PICU or the mortality rate, which could be attributed to our previous experience in the management of COVID-19 patients and the timely diagnosis and management of AKI.[22] Although kidney abnormalities improve in the majority of pediatric COVID-19 infections, the long-term outcome of AKI in the post-COVID-19 era is not

clear. Therefore, particular attention should be given to kidney involvement in COVID-19 patients, particularly children with a history of malnutrition and pre-existing kidney disorders.

ACKNOWLEDGMENT

We appreciate the effort of the emergency department and PICU staff at Mofid Children's Hospital, as well as our patients and their families for their participation in this study.

STATEMENT OF ETHICS

The present study was conducted according to the principles expressed in the Helsinki Declaration and approved by the ethics committee of the Pediatric Nephrology Research Center and Research Institute for Children's Health of Shahid Beheshti University of Medical Sciences (Approval code: IR.SBMU.MSP.REC.1399.330). The informed consent was obtained from all individual participants (their parents) included in the study.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

FUNDING SOURCES

The authors received no specific funding for this research.

AUTHPRS' CONTRIBUTIONS

Masoumeh Mohkam, Mahbube Mirzaee, and Mahnaz Jamee developed the original concept and protocol of the study, designed the study, and collected the data. Mahnaz Jamee and Fatemeh Abdollah Gorji wrote the manuscript and designed the statistical tests and analyzed the data. Zahra Pournasiri, Seyed Mohammad taghi Hosseini Tabatabaei, Nasrin Esfandiar, and Reza Dalirani contributed to writing the manuscript. Sedigheh Rafiei Tabatabaei, Abdollah Karimi, Shahnaz Armin, Roxana Mansour Ghanaie, Mina Alibeik and Seyed Alireza Fahimzad collected the data, conceived the project, and supervised and coordinated the study.

Abbreviations

AKI: Acute kidney injury
BMI: Body mass index
COVID-19: Coronavirus Disease 2019
CRP: C-reactive protein
ESR: Erythrocyte sedimentation rate
GFR: Glomerular filtration rate
IQR: Interquartile range
KDIGO: Kidney Disease Improving Global Outcomes
LDH: Lactate dehydrogenase
MIS-C: Multisystem inflammatory syndrome in children
PICU: Pediatric Intensive Care Units
RRT: Renal replacement therapy
RT-PCR: Reverse transcription polymerase chain reaction
SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus-2

REFERENCES

1. Kalantari H, Tabrizi AHH, Foroohi F. Determination of COVID-19 prevalence with regards to age range of patients referring to the hospitals located in western Tehran, Iran. Gene Rep. 2020;21:100910.
2. She J, Liu L, Liu W. COVID-19 epidemic: Disease characteristics in children. J Med Virol. 2020;92(7):747-54.
3. Lee PI, Hu YL, Chen PY, Huang YC, Hsueh PR. Are children less susceptible to COVID-19? J Microbiol Immunol Infect. 2020;53(3):371-2.
4. Chang TH, Wu JL, Chang LY. Clinical characteristics and diagnostic challenges of pediatric COVID-19: A systematic review and meta-analysis. J Formos Med Assoc. 2020;119(5):982-9.
5. Dong Y, Mo X, Hu Y, et al. Epidemiology of COVID-19 Among Children in China. Pediatrics. 2020;145(6).
6. Mehta NS, Mytton OT, Mullins EWS, et al. SARS-CoV-2 (COVID-19): What Do We Know About Children? A Systematic Review. Clin Infect Dis. 2020;71(9):2469-79.
7. Alsohime F, Temsah MH, Al-Nemri AM, et al. COVID-19 infection prevalence in pediatric population: Etiology, clinical presentation, and outcome. J Infect Public Health. 2020;13(12):1791-6.
8. Mahmoudi S, Mehdizadeh M, Shervin Badv R, et al. The Coronavirus Disease 2019 (COVID-19) in Children: A Study in an Iranian Children's Referral Hospital. Infect Drug Resist. 2020;13:2649-55.
9. Chen F, Liu ZS, Zhang FR, et al. [First case of severe childhood novel coronavirus pneumonia in China]. Zhonghua Er Ke Za Zhi. 2020;58(0):E005.
10. Buonsenso D, Zampino G, Valentini P. Novel Coronavirus Disease 2019 Infection in Children: The Dark Side of a Worldwide Outbreak. Frontiers in Pediatrics. 2020;8(215).
11. Pei G, Zhang Z, Peng J, et al. Renal Involvement and Early Prognosis in Patients with COVID-19 Pneumonia. J Am Soc Nephrol. 2020;31(6):1157-65.
12. Guo CX, He L, Yin JY, et al. Epidemiological and clinical features of pediatric COVID-19. BMC Med. 2020;18(1):250.
13. Karimi A, Rafiei Tabatabaei S, Rajabnejad M,

et al. An Algorithmic Approach to Diagnosis and Treatment of Coronavirus Disease 2019 (COVID-19) in Children: Iranian Expert's Consensus Statement. 2020;8(2):e102400.

14. John A Kellum, Norbert Lameire. KDIGO Clinical Practice Guideline for Acute Kidney Injury. Official Journal of the International Society of Nephrology. 2012;2.
15. Laycock J, Baum M, Rees L. KDIGO nomenclature glossary for Pediatric Nephrology. Pediatric Nephrology. 2020;35(12):2201-3.
16. Levey A EK, Dorman N, Christiansen S, et al. Nomenclature for kidney function and disease: report of a kidney disease: improving global outcomes (KDIGO) consensus conference. Kidney Int 2020;97: 1117–1129.
17. Flynn JT, Falkner BE. New Clinical Practice Guideline for the Management of High Blood Pressure in Children and Adolescents. Hypertension (Dallas, Tex : 1979). 2017;70(4):683-6.
18. Guan WJ, Liang WH, Zhao Y, et al. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. Eur Respir J. 2020;55(5).
19. Li X, Xu S, Yu M, et al. Risk factors for severity and mortality in adult COVID-19 inpatients in Wuhan. J Allergy Clin Immunol. 2020;146(1):110-8.
20. Tsankov BK, Allaire JM, Irvine MA, et al. Severe COVID-19 Infection and Pediatric Comorbidities: A Systematic Review and Meta-Analysis. Int J Infect Dis. 2020;103:246-56.
21. Williams N, Radia T, Harman K, et al. COVID-19 Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children and adolescents: a systematic review of critically unwell children and the association with underlying comorbidities. Eur J Pediatr. 2020:1-9.
22. Mohkam M, Mirzaee M, Abdollah Gorgi F, et al. Renal Involvement in COVID-19 Among Iranian Children. Arch Pediatr Infect Dis. 2021;9(1):e106597.
23. Pan XW, Xu D, Zhang H, et al. Identification of a potential mechanism of acute kidney injury during the COVID-19 outbreak: a study based on single-cell transcriptome analysis. Intensive Care Med. 2020;46(6):1114-6.
24. Valizadeh R, Baradaran A, Mirzazadeh A, Bhaskar LV. Coronavirus-nephropathy; renal involvement in COVID-19. J Renal Inj Prev. 2020;9(2):e18-e.
25. Asgharpour M, Zare E, Mubarak M, Alirezaei A. COVID-19 and Kidney Disease: Update on Epidemiology, Clinical Manifestations, Pathophysiology and Management. J Coll Physicians Surg Pak. 2020;30(6):19-25.
26. Gagliardi I, Patella G, Michael A, Serra R, Provenzano M, Andreucci M. COVID-19 and the Kidney: From Epidemiology to Clinical Practice. J Clin Med. 2020;9(8).
27. Wang F, Ran L, Qian C, et al. Epidemiology and Outcomes of Acute Kidney Injury in COVID-19 Patients with Acute Respiratory Distress Syndrome: A Multicenter Retrospective Study. Blood Purif. 2020:1-7.
28. Bowe B, Cai M, Xie Y, Gibson AK, Maddukuri G, Al-Aly Z. Acute Kidney Injury in a National Cohort of Hospitalized US Veterans with COVID-19. Clin J Am Soc Nephrol. 2020;16(1):14-25.
29. Fisher M, Neugarten J, Bellin E, et al. AKI in Hospitalized Patients with and without COVID-19: A Comparison Study. J Am Soc Nephrol. 2020;31(9):2145-57.
30. Stewart DJ, Hartley JC, Johnson M, Marks SD, du Pré P, Stojanovic J. Renal dysfunction in hospitalised children with COVID-19. The Lancet Child & adolescent health. 2020;4(8):e28-e9.
31. Bjornstad EC, Krallman KA, Askenazi D, Zappitelli M, Goldstein SL, Basu RK. Preliminary Assessment of Acute Kidney Injury in Critically Ill Children Associated with SARS-CoV-2 Infection. A Multicenter Cross-Sectional Analysis. 2021;16(3):446-8.
32. Raina R, Chakraborty R, Mawby I, Agarwal N, Sethi S, Forbes M. Critical analysis of acute kidney injury in pediatric COVID-19 patients in the intensive care unit. Pediatric nephrology (Berlin, Germany). 2021:1-12.

Correspondence to:
Mahnaz Jamee, MD
Pediatric Nephrology Research Center, Research Institute for Children's Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran
Pediatric Infections Research Center, Research Institute for Children's Health, Shahid Beheshti University of Medical Sciences, Shariati Street, Mofid Children's Hospital, Tehran, Postal Code: 1551415468, Iran
Tel: 0098 21 2222 9658
E-mail: jamee@sbmu.ac.ir

Received July 2022
Revised September 2022
Accepted November 2022