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ACUTE KIDNEY INJURY IN CHILDREN WITH COVID-19

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ABSTRACT

Background: Renal dysfunction in coronavirus disease 2019 (COVID-19) can result from the direct invasion of renal tissue by the virus or the cytokine storm caused by the disease. We aimed to evaluate renal involvement in the form of acute kidney injury (AKI) in children with COVID-19 admitted to Bandar Abbas Children's Hospital. **Methods:** This descriptive-analytical study retrospectively evaluated 135 children with confirmed COVID-19 admitted to Bandar Abbas Children's Hospital, in 2020-2021. Patients' information including age, gender, weight, blood pressure, heart rate, respiratory rate, white blood cell (WBC) count, platelet count, hemoglobin concentration, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), lactate dehydrogenase (LDH), blood urea nitrogen (BUN), and creatinine were extracted from their medical files. Also, admission to the intensive care unit (ICU), hospital length of stay, death, dialysis, edema, and comorbidities were recorded. AKI was diagnosed based on the Kidney Disease Improving Global Outcomes (KDIGO) criteria. **Results:** The mean age of the participants was 53.29 ± 47.57 months, of whom 68 (50.4%) were male. AKI was found in 9 patients (6.7%). Edema/proteinuria was observed in 3% and oliguria/hematuria in 4.4%. 1Also, 36.3% of the patients had comorbidities, 14.8% were admitted to ICU and 2 patients (1.5%) died. There was no statistically significant difference between children with and without AKI regarding age, weight, blood pressure, heart rate, respiratory rate, CRP, ESR, WBC and platelet count, hemoglobin, and hospital length of stay ($P>0.05$), while mean BUN and creatinine levels were significantly higher in the AKI group ($P=0.032$ and $P<0.001$, respectively). On the other hand, although comorbidities, ICU admission, and edema/proteinuria were higher in patients with AKI, the differences between groups regarding gender, comorbidities, ICU admission, edema/proteinuria, oliguria/hematuria, glucosuria, and death were not statistically significant ($P>0.05$). **Conclusions:** Overall, 6.7% of children with confirmed COVID-19 had AKI. Baseline creatinine and BUN levels were significantly higher in children with AKI compared to those without AKI; however, there was no correlation between AKI and other factors.

KEYWORDS: COVID-19, acute kidney injury, children.

INTRODUCTION

Children and adolescents with coronavirus 2019 (COVID-19) usually have a better clinical course compared to adults. The death rate in the pediatric population was <1% in the initial studies.[1, 2] The most common clinical features of COVID-19 in children include fever, dry cough, and pneumonia.[1] However, multi-system involvement such as hyperinflammatory shock is also increasing.[3]

Acute kidney injury (AKI) in COVID-19 can result from the direct invasion of the renal tubular cells by the virus or the cytokine storm associated with the disease.[4-6] Some studies have reported high rates of AKI in both children and adults with COVID-19.[7-9] [s]Moreover, in a large multi-center study on children with COVID-19 admitted to the pediatric intensive care unit (PICU), 37% developed AKI, which was similar to children with sepsis.[7] Similarly, a study in the United Kingdom reported that critically ill children with COVID-19 and having the clinical features of multisystem inflammatory syndrome in children (MIS-C) were at higher risk of AKI.[3] However, another study from New York showed that all COVID-19 pediatric patients who are hospitalized are at increased risk of AKI.[10]

Overall, a relatively limited number of studies have been carried out for the evaluation of COVID-19 renal involvement in children both globally and in Iran. Thus, we aimed to evaluate renal involvement in the form of AKI in children with COVID-19 admitted to Bandar Abbas Children's Hospital.

METHODS

Participants and study design

This descriptive-analytical study retrospectively evaluated 135 children with confirmed COVID-19 admitted to Bandar Abbas Children's Hospital, in 2020-2021. The inclusion criteria were age<18 years and COVID-19 diagnosis based on the reverse transcriptase-polymerase chain reaction (RT-PCR) test results. Patients with incomplete medical records were excluded from the study.

The study was approved by the Ethics Committee of Hormozgan University of Medical Sciences (IR.HUMS.REC.1400.221). Patients' information including age, gender, weight, blood pressure, heart rate, respiratory rate, white blood cell (WBC) count, platelet count, hemoglobin concentration, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), lactate dehydrogenase (LDH), and blood urea nitrogen (BUN) were extracted from their medical files. Also, admission to the intensive care unit (ICU), hospital length of stay, death, dialysis, edema, and comorbidities were recorded. Serum creatinine levels on admission, 48 hours after admission, the highest value of serum creatinine within 7 days, and urine output during the first 48 hours of hospitalization were noted.

AKI was diagnosed based on the Kidney Disease Improving Global Outcomes (KDIGO) criteria.[11] Serum creatinine levels of 0.5-1 mg/dL was considered normal for children 3-18 years and 0.3-0.7 for those <3 years.[12] Oliguria was defined as <0.5 ml/kg/h.

Data analysis

We used the Statistical Package for the Social Sciences (SPSS) software (version 26.0, Armonk, NY: IBM Corp., USA) for data analysis. Quantitative variables were described using means and standard deviations. Qualitative variables were described using frequencies and percentages. Based on the results of the Kolmogorov-Smirnov normality test, the independent t-test was used for the comparison of hemoglobin between children with and without AKI, while the Mann-Whitney test was used for other quantitative variables. The Chi-squared and Fisher's exact tests were used to compare qualitative variables between groups. P-values <0.05 were regarded as statistically significant.

RESULTS

Of a total of 135 children with confirmed COVID-19 evaluated in this study with a mean age of 53.29 ± 47.57 months, 68 (50.4%) were male and 67 (49.6%) were female. Overall, AKI was observed in 9 patients (6.7%). There was no statistically significant difference between children with and without AKI regarding age, gender, weight, comorbidities, systolic and diastolic blood pressure, heart rate, and respiratory rate (Table 1).

All laboratory findings were comparable in children with and without AKI, except for serum BUN and creatinine levels which were significantly higher in children with AKI (P<0.001 and P=0.032, respectively) (Table 2).

Overall, 20 children (14.8%) were admitted to the ICU and 2 (1.5%) died. However, there was no difference between children with and without AKI regarding ICU admission or death (P=0.130 and P=1.000, respectively). Moreover, although hospital length of stay was slightly higher in the AKI group, the difference was not statistically significantly compared to children without AKI (P=0.209) (Table 3).

Table 1: Comparison of general characteristics between children with and without AKI.

Variables	Total (n=135)	No AKI (n=9)	AKI (n=126)	P-value*
Age (month) mean ± SD	53.29 ± 47.57	54.40 ± 48.00	37.67 ± 39.99	0.239
Gender N (%)				
Male	68 (50.4)	63 (50.0)	5 (55.6)	1.000†
Female	67 (49.6)	63 (50.0)	4 (44.4)	
Weight (kg) mean ± SD	17.04 ± 11.27	16.64 ± 10.75	22.61 ± 16.81	0.363
Comorbidities N (%)	49 (36.3)	45 (35.7)	4 (44.4)	0.723‡
SBP (mmHg) mean ± SD	96.52 ± 9.09	96.59 ± 9.22	95.59 ± 7.27	0.937
DBP (mmHg) mean ± SD	63.41 ± 7.19	63.33 ± 7.09	64.44 ± 8.82	0.832
HR (/min) mean ± SD	105.90 ± 17.76	106.18 ± 18.08	102.00 ± 12.52	0.485
RR (/min) mean ± SD	27.64 ± 8.82	27.92 ± 9.01	23.67 ± 3.84	0.202

Abbreviations: N, number; SD, standard deviation; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; RR, respiratory rate; AKI, acute kidney injury.
*Analyzed by the Mann-Whitney test.
†Analyzed by the Chi-squared test.
‡Analyzed by the Fisher's exact test.

Table 2: Comparison of laboratory findings between children with and without AKI.

Variables	Total (n=135)	No AKI (n=9)	AKI (n=126)	P-value*
Hemoglobin (g/dL) mean ±	10.49 ± 1.57	10.46 ± 1.57	10.98 ± 1.58	0.902†
WBC count (/µl) mean ± SD	9407.04 ± 4665.35	9292.86 ± 4697.22	11005.56 ± 4091.95	0.207
Platelet count (/µl) mean ± SD	288805.19 ± 140119.60	287942.06 ± 139779.96	300888.89 ± 152961.14	0.902
Cr (mg/dL) mean ± SD	0.54 ± 0.28	0.50 ± 0.13	1.07 ± 0.85	0.032
BUN (mg/dL) mean ± SD	14.27 ± 6.97	13.18 ± 4.69	29.53 ± 13.74	<0.001
CRP (mg/L) mean ± SD	31.24 ± 49.46	31.26 ± 50.54	30.83 ± 32.71	0.566
ESR (mm/h) mean ± SD	25.20 ± 26.56	24.31 ± 25.97	37.67 ± 32.96	0.178
LDH (U/L) mean ± SD	516.56 ± 188.89	515.64 ± 193.44	529.44 ± 112.92	0.445
Edema/proteinuria N (%)	4 (3.0)	3 (2.4)	1 (11.1)	0.244‡
Oliguria/hematuria N (%)	6 (4.4)	6 (4.8)	0 (0.0)	1.000‡
Glucosuria N (%)	5 (3.7)	5 (4.0)	0 (0.0)	1.000‡

Abbreviations: N, number; SD, standard deviation; WBC, white blood cell; Cr, creatinine; BUN, blood urea nitrogen; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; LDH, lactate dehydrogenase; AKI, acute kidney injury.
*Analyzed by the Mann-Whitney test.
†Analyzed by the independent t-test.
‡Analyzed by the Fisher's exact test.

Table 3: Comparison of outcomes between children with and without AKI.

Variables	Total (n=135)	No AKI (n=9)	AKI	P-value*
Hospital length of stay (days) mean ± SD	4.29 ± 2.64	4.19 ± 2.55	5.67 ± 3.57	0.209†
ICU admission N (%)	20 (14.8)	17 (13.5)	3 (33.3)	0.130
Death N (%)	2 (1.5)	2 (1.6)	0 (0.0)	1.000

Abbreviations: N, number; SD, standard deviation; ICU, intensive care unit; AKI, acute kidney injury.
*Analyzed by the Fisher's exact test.
†Analyzed by the Mann-Whitney test.

DISCUSSION

In the current study, we observed AKI in 6.7% of the children admitted to hospital with confirmed COVID-19. The rate of AKI was 21% in Kari et al.'s study[13], 1.3% in Wang et al.'s study[14], 30.51% in the systematic review and meta-analysis of Raina et al.[15], 34.5% reported by Mohkam et al.[16], 8.2% in the study by Basaley et al.[17], and 37.5% in that of Basu et al.[18] The various rates of AKI reported in these studies can be due to the difference in AKI diagnostic criteria, the severity of COVID-19 in each study population, the accuracy and method of measurement for variables involved in the diagnosis of AKI, and different demographic characteristics of the study populations.

We also found that ICU admission rate did not differ between children with and without AKI. Moreover, these children were comparable in terms of hospital length of stay. On the contrary, admission to the PICU was higher in children with AKI in Kari et al.'s study; however, in line with our findings, they reported no association between AKI and prolongation of hospital stay.[13] A reason behind the discrepancy between the two studies can be that a high percentage of children with AKI in their study also had MIS-C. This can also be the cause of significantly higher death rate of children with AKI in Kari et al.'s study, while there was no statistically significant difference between children with and without AKI in our study. Similar to Kari et al., Wang et al. reported AKI only in critically ill children admitted to PICU. They attributed the development of AKI to the cytokine storm and complement-mediated injury in children with COVID-19.[14] Raina et al. demonstrated a high prevalence of MIS-C in children with COVID-19 and AKI, which confirms the potential role of MIS-C and the high prevalence of AKI in these patients.[15] Comparable results were reported by Basalely et al.[17]

In another study, Mohkam et al. evaluated kidney involvement in children with COVID-19 and showed that on admission, 10% of the patients had oliguria, 7.7% had edema, and 3% had hypertension. In the first urinalysis, proteinuria, leukocyturia, and hematuria was found in 46%, 24%, and 23% of patients, respectively.[16] Contrarily, edema/proteinuria and oliguria/hematuria were found in 3% and 4.4% of our patients, respectively. This disparity can be justified by the previous renal status of patients before COVID-19; in other words, baseline creatinine levels of the children.

In a different study by Sambas et al., the association of renal function with the severity of COVID-19 was evaluated. They illustrated that COVID-19 severity can affect children's kidneys, presenting with a decrease in

the glomerular filtration rate.[19] Thus, COVID-19 severity can influence the incidence of AKI in children and may be a reason for different findings of the previous studies.

COVID-19 was confirmed by RT-PCR in all the children evaluated in our study, while Basu et al. assessed AKI in children and adolescents suspected of COVID-19, and were not able to confirm the diagnosis by laboratory tests in approximately half of their patients.[18] Nevertheless, AKI was reported in 41.3% of their confirmed COVID-19 cases, which is much higher compared to our results. Basu et al. concluded that AKI and severe AKI commonly occurs in critically ill children with COVID-19 and the rate is two-fold higher than what is usually observed in critically ill children due to other diseases.[18] Their results confirm the impact of COVID-19 severity on the incidence of AKI in children.

Our study had some limitations. First, we retrospectively evaluated the patients and a retrospective design fails to establish a cause-and-effect correlation. Second, our sample size was relatively small, which limits the generalizability of our findings.

CONCLUSIONS

Based on the results of the current study, 6.7% of children with confirmed COVID-19 had AKI. Baseline creatinine and BUN levels were significantly higher in children with AKI compared to those without AKI; however, there was no correlation between AKI and other factors. Future studies with larger sample sizes and longitudinal designs are required to confirm the findings of the current study.

Declarations

Ethics approval and consent to participate

The study received ethics approval from the Ethics Committee of Hormozgan University of Medical Sciences under the ethics code: IR.HUMS.REC.1400.221 and it complies with the statements of the Declaration of Helsinki. The retrospective design of the study waived the need for obtaining informed consent from the patients.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Consent for publication

Not applicable.

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Author's contributions

Conceptualization and study validation: MM
Implementation and supervision: MM
Data analysis and interpretation: KG
Writing and reviewing: KG

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