A Comparative Analysis of Clinical Characteristics and Laboratory Findings of COVID-19 between Intensive Care Unit and Non-Intensive Care Unit Pediatric Patients: A Multicenter, Retrospective, Observational Study from Iranian Network for Research in Viral Diseases (INRVD)

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Abstract

Background: To date, less is known about the clinical features of COVID-19 pediatric patients admitting to ICUs. Herein, we aimed to describe the differences in demographic characteristics, laboratory findings, clinical presentations, and outcomes between COVID-19 pediatric patients admitting to ICU and non-ICU settings.

Methods: This multicenter study involved 15 general and pediatrics hospitals on confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection by positive real-time reverse transcription polymerase chain reaction (RT-PCR) between March 19 and May 31, 2020, during the initial peak of the COVID-19 pandemic in Iran.

Results: Overall, 166 patients were included, of which 61 (36.7%) required ICU admission, especially in <5 years old age group. Malignancy and heart diseases were the most frequent underlying condition. There was significant decrease in platelet counts, PH, HCO3 and base excess as well as increases in creatinine, creatine phosphokinase and potassium levels between ICU-admitted and non-ICU patients. Dyspnea was the major symptom for ICU group patients. Acute respiratory distress syndrome (ARDS), shock and acute cardiac injury were the most common features among ICU-admitted patients. The mortality rate was substantially higher in the ICU than in non-ICU patients (45.9% vs. 1.9%, respectively; P<0.001).

Conclusions: Underlying diseases were the major contributing factors in COVID-19 pediatric patients for the increased ICU admissions and mortality rates. There are few paraclinical parameters for differentiating pediatrics in terms of prognosis and serious outcomes of COVID-19. Healthcare providers should consider children as a high-risk group, especially those with younger age and underlying medical conditions and define strategies to control and prevent COVID-19 transmission in this population.

Background

The current Coronavirus Disease 2019 (COVID-19) pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) generally causes mild to moderate respiratory tract diseases in humans, and patients usually recover without any special treatment. However, older people and especially those with underlying medical conditions are at an increased risk of developing severe disease outcomes [1].

Several studies on COVID-19 infection among pediatric patients have revealed differences in clinical signs and symptoms, prevalence rates, and mortality rates compared to adults [2, 3]. Children are less affected than older individuals by SARS-CoV-2 in the aspect of the number of infected persons and the incidence of serious adverse outcomes [4, 5]. Based on the results of previous epidemiological investigations, the prevalence of children affected by COVID-19 was 2.2% and 1.7% in China and the USA, respectively [3, 6]. SARS-CoV-2 is transmitted among the pediatric population mainly through direct contact, contaminated droplets, and perhaps aerosols [7, 8].

Like adults, children can also experience a severe form of COVID-19 infection, leading to intensive care unit (ICU) admission. In previous studies, the ICU admission rate among children with COVID-19 varied from 1.7–16% [9–12]. However, the rate is lower than those reported for adults (ranged from 5–32%) [13–17]. To date, limited studies have been carried out to characterize the clinical, laboratory, and demographic features of pediatric COVID-19 patients in Iran [18–21]. Among four studies reporting epidemiological and clinical data of pediatric patients with COVID-19 infection, the largest sample size was 35 cases in the survey conducted by Mahmoudi et al. [19].

Herein, we aimed to conduct a large multicenter study to compare demographic characteristics, laboratory findings, clinical features, and outcomes between pediatric COVID-19 patients admitted to the ICU versus non-ICU cases.

Methods

Study design, setting, and participants

The current survey was a retrospective cross-sectional study carried on a total of 325 pediatric patients diagnosed with COVID-19 infection who admitted to 15 general and pediatrics hospitals collaborative to the Iranian Network for Research in Viral Diseases (INRVD) between March 19th and May 31th 2020. Overall results have been submitted elsewhere (under revision). A proportion of this population in whom COVID-19 was confirmed by positive real-time reverse transcription polymerase chain reaction (RT-PCR) for SARS-CoV-2, according to WHO interim guidance [22] was selected for further analysis (n = 166). The major inclusion criteria were patients who needed ventilation support either invasive mechanical ventilation or extra corporeal membrane oxygenation (ECMO) and/or organ dysfunction development who were transferred into the ICU. All other patients were transferred to wards for specialist care and were included as non-ICU cases. This study was approved by the Institutional Review Board of Tehran University of Medical Sciences (Ethics code number: 1399.378) and was conducted in compliance with the principles of the Declaration of Helsinki. Written informed consent was obtained from parents of pediatric patients.

Molecular Detection Of SARS-CoV-2

Throat and nasal samples were obtained using flocked swabs immediately after admission. Laboratory confirmation of the SARS-CoV-2 was performed using the RT-PCR assay [22]. RT-PCR was carried out using the diagnostic kits approved by the Iranian Pasture Institute, targeting the E and RdP genes, along with the same protocol for all laboratories across the country. The samples were deemed positive if the cycle thresholds (Ct) value was ≤ 37 and negative if the Ct value was > 40. Samples with a Ct value between 37–40 was considered as a borderline result and were repeated.

Laboratory And Imaging Indicators

Laboratory examinations including routine blood tests, hematological, biochemical tests and assessment of biomarkers for monitoring lung, liver, and renal functions along with blood saturation parameters were

performed in hospitals' laboratories. According to the guidelines issued by The Ministry of Health, all COVID-19 confirmed cases with any respiratory symptoms underwent a chest X-ray upon admission. A chest CT scan usually applied in the case of either the presence of any abnormality in their X-ray or for the patients who progress to the severe form of the disease.

Data Collection

The epidemiological and demographic data, comorbidity, clinical symptoms, and signs on the admission of all laboratory-confirmed COVID-19 pediatric patients were retrospectively extracted from electronic medical records, according to predefined standardized data collection forms provided by INRVD.

Statistical analysis

Statistical analyses were performed using R software (R Foundation for Statistical Computing, Vienna, Austria; http://cran.r-project.org/). Continuous variables were presented as medians and interquartile ranges (IQR), and categorical variables were expressed as counts (%). Fisher's exact test and chi-square test of independence were used to compare categorical variables, and Wilcoxon's rank-sum test was used for continuous variables. For comparative analyses, a *P*-value less than 0.05 was considered statistically significant.

Results

Demographic characteristics and associated comorbidities

Table 1 presents demographic characteristics and related comorbidities of pediatric patients with COVID-19 at hospital admission. Out of 166, 61 (36.7%) were admitted in ICU, and 105 (63.3%) were non-ICU cases. According to the age group, the highest and the lowest numbers of admitted cases to ICU were in the age group of 1–5 and 5–10 years, respectively (31.1% *vs* 14.7%, $P = 0.02$, Table 1). Males were more infected in both ICU and non-ICU settings compared to the females (62.8% *vs* 37.1% and 59.0% *vs* 40.9%, respectively, $P = 0.7$, Table 1). Malignancies and heart were the most common underlying conditions; each affecting 11.4% of ICU-admitted patients (Table 1). 21.3% of ICU-admitted patients and 39.0% of non-ICU patients had histories of antibiotic use ($P = 0.02$, Table 1). However, there were no significant differences in influenza vaccination history, corticosteroid therapy, and chemotherapies between two groups (Table 1).

Table 1
Demographic characteristics and associated comorbidities of pediatric patients with COVID-19

Admission detail	Overall (N = 166)	Non-ICU (N = 105)	ICU (N = 61)	*P* value
Age group (Year), No. (%)				0.02*
0–1	28 (16.8)	11 (10.4%)	17 (27.8%)	
1–5	53 (31.9%)	34 (32.3%)	19 (31.1%)	
5–10	26 (15.6%)	17 (16.3%)	9 (14.7%)	
10–15	56 (33.7%)	41 (39.0%)	15 (24.5%)	
Gender, No. (%)				0.7
Male	102 (61.4%)	66 (62.8%)	36 (59.0%)	
Female	64 (38.5%)	39 (37.1%)	25 (40.9%)	
Associated comorbidities, No. (%)				
Asthma	4 (2.4%)	3 (2.8%)	1(1.6%)	< 0.001*
Cystic fibrosis	1 (0.6%)	1 (0.9%)	0 (0%)	
Chronic kidney disease	4 (2.4%)	1 (0.9%)	3 (4.9%)	
Diabetes	1 (0.6%)	1 (0.9%)	0 (0%)	
Failure to thrive	4 (2.4%)	2 (1.9%)	2 (3.2%)	
Heart diseases	9 (5.4%)	2 (1.9%)	7 (11.4%)	
Immune suppression	2 (1.2%)	0 (0%)	2 (3.2%)	
Malignancy	20 (12.0%)	13 (12.3%)	7 (11.4%)	
Other	24 (14.4%)	7 (6.6%)	17 (27.8%)	
No comorbidity	97 (58.4%)	75 (71.4%)	22 (36.0%)	
Patient history, No. (%)				
History of antibiotic use	54 (32.5%)	41 (39.0%)	13 (21.3%)	0.02*
History of flu vaccination	22 (13.2%)	13 (12.3%)	9 (14.7%)	0.8
History of corticosteroid therapy	16 (9.6%)	9 (8.5%)	7 (11.4%)	0.7
History of chemotherapy	15 (9.0%)	9 (8.5%)	6 (9.8%)	0.9

Clinical Characteristics

Fever and cough were the most frequent clinical symptoms among both groups. However, dyspnea was more prevalent among the ICU than non-ICU cases (50.8% *vs* 26.6%, respectively, $P = 0.003$, Table 1). Signs such as grunting and nasal flaring were seen more frequently in ICU versus non-ICU patients (0.01 and < 0.001, respectively, Table 2).

Table 2
Clinical characteristics and outcomes of pediatric patients with COVID-19

Admission Detail	Overall (N = 166)	Non-ICU (N = 105)	ICU (N = 61)	*P* value
Symptoms, No. (%)				
Fever	122 (73.4%)	81 (77.1%)	41 (67.2%)	0.2
Fatigue	27 (16.2%)	19 (18.0%)	8 (13.1%)	0.5
Cough	89 (53.6%)	59 (56.1%)	30 (49.1%)	0.5
Anorexia	42 (25.3%)	26 (24.7%)	16 (26.2%)	0.9
Dyspnea	59 (35.5%)	28 (26.6%)	31 (50.8%)	0.003*
Sore throat	7 (4.2%)	6 (5.7%)	1 (1.6%)	0.4
Diarrhea	30 (18.0%)	18 (17.1%)	12 (19.6%)	0.8
Nausea/Vomiting	55 (33.1%)	37 (35.2%)	18 (29.5%)	0.6
Headache	10 (6.0%)	10 (9.5%)	0 (0%)	0.01*
Abdominal pain	9 (5.4%)	7 (6.6%)	2 (3.2%)	0.5
Myalgia	3 (1.8%)	3 (2.8%)	0 (0%)	0.3
Rhinorrhea	3 (1.8%)	2 (1.9%)	1 (1.6%)	0.9
Drowsiness/Loss of consciousness	9 (5.4%)	2 (1.9%)	7 (11.4%)	0.01
Seizures	11 (6.6%)	4 (3.8%)	7 (11.4%)	0.1
Skin rash	6 (3.6%)	4 (3.8%)	2 (3.2%)	0.9
Clinical signs, No. (%)				
Cyanosis	7 (4.2%)	2 (1.9%)	5 (8.1%)	0.1
Grunting	9 (5.4%)	2 (1.9%)	7 (11.4%)	0.01*
Nasal flaring	19 (11.4%)	3 (2.8%)	16 (26.2%)	< 0.001*
Wheezing	18 (10.8%)	9 (8.8%)	9 (14.7%)	0.3
Respiratory fine crackles	30 (18.0%)	15 (14.2%)	15 (24.5%)	0.1
Respiratory Coarse Crackles	21 (12.6%)	12 (11.4%)	9 (14.7%)	0.7
Shock	9 (5.4%)	3 (2.8%)	6 (9.8%)	0.07
Arrhythmia	4 (2.4%)	1 (0.9%)	3 (4.9%)	0.1

Admission Detail	Overall (N = 166)	Non-ICU (N = 105)	ICU (N = 61)	*P* value
Acute kidney injury	2 (1.2%)	0 (0%)	2 (3.2%)	0.1
Acute respiratory distress syndrome	19 (11.4%)	2 (1.9%)	17 (27.8%)	< 0.001*
Acute cardiac injury	4 (2.4%)	0 (0%)	4 (6.5%)	0.01*
Clinical outcome, No. (%)				
Death	30 (18.1%)	2 (1.9%)	28 (45.9%)	< 0.001*
Recovered	136 (81.9%)	103 (98.1%)	33 (54.1%)	

Among a list of complications, the acute respiratory distress syndrome (ARDS), shock and acute cardiac injury were the most common features among ICU-admitted patients compared to non-ICU patients with significant associations ($P < 0.001$, $P = 0.07$ and $P = 0.01$, respectively, Table 2). The mortality rate was significantly higher in the ICU than in non-ICU patients (45.9% vs. 1.9%, respectively; $P < 0.001$, Table 2).

Laboratory Data

There were no substantial differences between both groups in terms of WBC counts, serum inflammatory indexes (CRP and ESR) and other hematological parameters (Table 3). Exceptionally, 19 (32%) of patients admitted to the ICU had normal platelet counts compared to 46 (51%) of those with non-ICU patients ($P = 0.08$, Table 3). Regarding biochemistry parameters, significant increases in creatinine, creatine phosphokinase (CPK) and LDH levels were observed in ICU compared to non-ICU admitted patients, ($P = 0.06$, 0.01 and 0.06, respectively, Table 3). An elevated level of potassium was seen in 25% and 6.9% of ICU and non-ICU admitted patients, respectively, while it was decreased in 7.0% and 2.3% of ICU-admitted and non-ICU patients, respectively ($P = 0.002$, Table 3).

Table 3
Laboratory findings of pediatric patients with COVID-19

	Overall (N = 166)	Non-ICU (N = 105)	ICU (N = 61)	*P* value
White blood cell				0.1
Decreased	36 (22%)	27 (27%)	9 (15%)	
Increased	23 (14%)	11 (11%)	12 (20%)	
Normal	102 (63%)	63 (62%)	39 (65%)	
Neutrophil				0.1
Decreased	19 (12%)	15 (16%)	4 (7.1%)	
Increased	24 (16%)	12 (12%)	12 (21%)	
Normal	109 (72%)	69 (72%)	40 (71%)	
Lymphocyte				0.1
Decreased	52 (34%)	38 (39%)	14 (25%)	
Increased	15 (9.7%)	11 (11%)	4 (7.1%)	
Normal	87 (56%)	49 (50%)	38 (68%)	
Hemoglobin				0.2
Decreased	68 (44%)	37 (39%)	31 (53%)	
Increased	3 (1.9%)	2 (2.1%)	1 (1.7%)	
Normal	83 (54%)	57 (59%)	26 (45%)	
Platelet				0.08
Decreased	27 (18%)	15 (16%)	12 (20%)	
Increased	58 (39%)	30 (33%)	28 (47%)	
Normal	65 (43%)	46 (51%)	19 (32%)	
C-reactive protein				0.5
Increased	34 (72%)	22 (69%)	12 (80%)	
Normal	13 (28%)	10 (31%)	3 (20%)	
Erythrocyte sedimentation rate				0.3
Increased	52 (37%)	36 (40%)	16 (31%)	
Normal	89 (63%)	54 (60%)	35 (69%)	

	Overall (N = 166)	Non-ICU (N = 105)	ICU (N = 61)	*P* value
Blood urea nitrogen				0.2
Increased	35 (23%)	18 (20%)	17 (28%)	
Normal	117 (77%)	74 (80%)	43 (72%)	
Creatinine				0.06
Increased	70 (46%)	48 (52%)	22 (37%)	
Normal	82 (54%)	44 (48%)	38 (63%)	
Sodium				0.1
Decreased	13 (9.0%)	6 (6.9%)	7 (12%)	
Increased	2 (1.4%)	0 (0%)	2 (3.4%)	
Normal	130 (90%)	81 (93%)	49 (84%)	
Potassium				0.002*
Decreased	6 (4.2%)	2 (2.3%)	4 (7.0%)	
Increased	20 (14%)	6 (6.9%)	14 (25%)	
Normal	118 (82%)	79 (91%)	39 (68%)	
Prothrombin time				0.07
Decreased	0 (0%)	0 (0%)	0 (0%)	
Increased	17 (35%)	4 (19%)	13 (46%)	
Normal	32 (65%)	17 (81%)	15 (54%)	
Partial thromboplastin time				0.5
Decreased	21 (43%)	8 (38%)	13 (46%)	
Increased	12 (24%)	7 (33%)	5 (18%)	
Normal	16 (33%)	6 (29%)	10 (36%)	
International normalized ratio				0.08
Decreased	0 (0%)	0 (0%)	0 (0%)	
Increased	11 (24%)	2 (10%)	9 (35%)	
Normal	35 (76%)	18 (90%)	17 (65%)	
Lactate dehydrogenase				0.06
Decreased	2 (2.3%)	1 (1.8%)	1 (3.1%)	

	Overall (N = 166)	Non-ICU (N = 105)	ICU (N = 61)	*P* value
Increased	57 (65%)	32 (57%)	25 (78%)	
Normal	29 (33%)	23 (41%)	6 (19%)	
Creatine phosphokinase				0.01*
Decreased	0 (0%)	0 (0%)	0 (0%)	
Increased	22 (42%)	9 (27%)	13 (65%)	
Normal	31 (58%)	24 (73%)	7 (35%)	
Aspartate aminotransferase				0.8
Decreased	0 (0%)	0 (0%)	0 (0%)	
Increased	34 (40%)	19 (38%)	15 (42%)	
Normal	52 (60%)	31 (62%)	21 (58%)	
Alanine aminotransferase				0.4
Decreased	4 (4.7%)	2 (4.1%)	2 (5.6%)	
Increased	21 (25%)	15 (31%)	6 (17%)	
Normal	60 (71%)	32 (65%)	28 (78%)	
Alkaline phosphatase				0.9
Decreased	4 (44%)	3 (43%)	1 (50%)	
Increased	2 (22%)	2 (29%)	0 (0%)	
Normal	3 (33%)	2 (29%)	1 (50%)	
D-dimer				0.9
Increased	6 (38%)	3 (38%)	3 (38%)	
Normal	10 (62%)	5 (62%)	5 (62%)	
Total Bilirubin				0.6
Increased	4 (27%)	3 (38%)	1 (14%)	
Normal	11 (73%)	5 (62%)	6 (86%)	
Calcium				0.3
Decreased	26 (47%)	14 (54%)	12 (41%)	
Increased	1 (1.8%)	1 (3.8%)	0 (0%)	
Normal	28 (51%)	11 (42%)	17 (59%)	

	Overall (N = 166)	Non-ICU (N = 105)	ICU (N = 61)	*P* value
Phosphorus				0.9
Decreased	2 (67%)	2 (67%)	0 (NA%)	
Increased	1 (33%)	1 (33%)	0 (NA%)	
Normal	0 (0%)	0 (0%)	0 (NA%)	
pH				0.002*
Decreased	41 (50%)	15 (34%)	26 (68%)	
Increased	5 (6.1%)	5 (11%)	0 (0%)	
Normal	36 (44%)	24 (55%)	12 (32%)	
PCo2				0.6
Decreased	35 (43%)	17 (39%)	18 (49%)	
Increased	30 (37%)	18 (41%)	12 (32%)	
Normal	16 (20%)	9 (20%)	7 (19%)	
HCo3				< 0.001*
Decreased	44 (54%)	16 (36%)	28 (76%)	
Increased	7 (8.6%)	2 (4.5%)	5 (14%)	
Normal	30 (37%)	26 (59%)	4 (11%)	
Po2				0.5
Decreased	48 (62%)	26 (60%)	22 (63%)	
Increased	6 (7.7%)	2 (4.7%)	4 (11%)	
Normal	24 (31%)	15 (35%)	9 (26%)	
Base excess				0.09
Decreased	46 (73%)	23 (64%)	23 (85%)	
Increased	8 (13%)	5 (14%)	3 (11%)	
Normal	9 (14%)	8 (22%)	1 (3.7%)	

Blood Saturation Indexes

In terms of blood saturation values, PH was decreased in 26 (68%) of ICU patients compared with 15 (34%) of non-ICU cases ($P = 0.002$, Table 3). Moreover, HCo3 was decreased in the former group

compared with the latter group (76% and 36%, respectively, Table 3). Lastly, Base Exess decrease observed in ICU (85%) more than non-ICU groups (64%) (P = 0.09, Table 3).

Radiological Features

The CT scan results performed on admission showed bilateral and unilateral ground glass opacity among 32% and 7.7% of non-ICU-admitted patients, respectively, and 25% and 6.8% of ICU admitted patients, respectively (P = 0.7). Bilateral and unilateral lung consolidation were also observed in 12% and 6.7% of non-ICU-admitted patients, respectively, and 21% and 12% of ICU admitted patients, respectively (P = 0.3). Bilateral and unilateral pleural effusion was found in 5.1% of non-ICU admitted patients, and 7% and 2.3% of ICU admitted patients, respectively (P = 0.8). In ICU admitted cases, unilateral and bilateral white lung were seen in 2.3% of cases and these findings were not observed in non-ICU cases (P = 0.2).

Discussion

Iran is considered one of the most affected countries by COVID-19 globally, with high incidence and mortality rates. To date, several studies have reported clinical parameters associated with COVID-19 infection in children; however, data on pediatric patients in Iran are still scarce. On the other hand, there are minimal published data on pediatric patients requiring ICU worldwide. This descriptive cross-sectional country-wide investigation compared the epidemiologic and clinical features of ICU admitted and non-admitted pediatric patients with confirmed COVID-19 in Iran.

Present survey showed that malignancies and cardiac disorders were the most common underlying disease in ICU-admitted pediatric patients. Similar results were found in the surveys conducted by Shekerdemian et al. [23] and Alfraij et al.[24], where malignancy was the most frequent underlying disease among children with COVID-19 admitted to the ICU. Prata-Barbosa et al. and Alfraij et al. also reported that heart disease was amongst the most frequent comorbidities among COVID-19 pediatric patients admitted to the ICU [24, 25]. According to these results, children with cancers and heart diseases were associated with increased risk of severe complications of COVID-19.

Investigators observed that COVID-19 patients with cancer had higher ICU admission rates, severe complications, invasive mechanical ventilation, and mortality rate compared with COVID-19 patients without cancer. The higher susceptibility of cancer patients to severe COVID-19 infection might be explained in part by their systemic immunocompromised status induced by the underlying malignancy and anticancer therapy. Furthermore, most childhood malignancies have aggressive behavior and require prolonged periods of intensive therapy, which are potentially associated with long-term side-effects such as severe impairment of innate and adaptive immunity [26–28]. On the other hand, some other studies suggested that children with cancer are not more susceptible to severe COVID-19 infection than other children [12, 28–31]. This controversy stems at least in part from the fact that different kinds of cancers have distinct clinical features such as different growth rates, different responses to treatment, and different prognoses. Unfortunately, we could not be able to find the data about the type of tumor in our

patients due to the retrospective design of our study and so, further conclusions cannot be drawn at this stage.

A proportion of ICU admitted patients were children less than five years old. Similar findings were reported in two studies conducted by Dong et al. [2, 9], in which infants and younger children were more likely to develop severe clinical manifestations of COVID-19 infection compared with children higher than five years old. A potential explanation for this phenomenon might be the immaturity of the immune system. The immune system of neonates and young children is underdeveloped and subdued, which might render them more susceptible to most infections, including SARS-CoV-2.

Among different clinical symptoms, dyspnea was significantly frequent in pediatric patients admitted to ICU than the non-ICU patients. This finding was consistent with the result of a survey conducted in New York City [32]. As reported, dyspnea was the only clinical symptom, which was significantly more frequent in pediatric patients admitted to the ICU than those admitted to the medical wards (92.3% vs. 30.3%, respectively). Similar results were obtained in the study conducted by Bhumbra et al. [33], where 71% and 58% of COVID-19 pediatric patients admitted to the ICU and general ward presented dyspnea, respectively. Thus, it seems that in most cases, the severe form of COVID-19 in children is associated with lung involvement. This interpretation is supported by another finding: ARDS was substantially higher in patients admitted to the ICU (27.8%) than those patients who were not admitted to the ICU (1.9%). Moreover, Chao et al. reported that the rate of ARDS was higher in patients admitted to the ICU (76.9%) compared with patients admitted to the medical unit (0%) [32]. Present survey showed that acute cardiac injury and acute kidney injury cases were only seen among ICU patients. In parallel, Stewart et al. reported that most acute kidney injury cases (93%) were found in those admitted to the pediatric ICU [34]. Chao et al. also showed a significantly higher rate of acute kidney injury among pediatric patients admitted to the ICU than non-ICU patients (38.5% vs. 0%, respectively) [32]. Alfraij et al. also reported that circulatory failure is significantly associated with pediatric death in their study cohort [24]. It has been reported that heart failure and acute cardiac injury are significantly associated with in-hospital death [35]. Taken together, these findings indicate that acute cardiac injury and acute kidney injury are associated with severe COVID-19 infection among children.

With exception of few blood test parameters abnormalities (such as decrease in platelet, increases in creatinine, LDH, CPK and potassium) and also some atypical blood saturation indexes, the difference in the rest of indexed were not substantial between ICU and non-ICU individuals. These findings shed important light on the nature of the disease in this population. Unlike in the adults, no significant laboratory parameters could be characterized for the prognosis of COVID-19 clinical outcomes in pediatrics worldwide.

Conclusions

In conclusion, this multicenter study demonstrates that underlying diseases were the major contributing factors in COVID-19 pediatric patients for the increased ICU admissions and mortality rates. There are few

paraclinical parameters for differentiating pediatrics in terms of prognosis and serious outcomes of COVID-19. Our findings emphasize that healthcare providers should consider children as a high-risk group, especially those with younger age and underlying medical conditions and define strategies to control and prevent COVID-19 transmission in this population.

List Of Abbreviations

SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; ICU: Intensive care unit; RT-PCR: Reverse transcription polymerase chain reaction; ARDS: Acute respiratory distress syndrome; COVID-19: Coronavirus Disease 2019; INRVD: Iranian Network for Research in Viral Diseases; ECMO: Extra corporeal membrane oxygenation; IQR: Interquartile ranges; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; CPK: Creatine phosphokinase; LDH: Lactate dehydrogenase;

Declarations

Ethics approval and consent to participate

The project was approved by the ethics committee of Tehran University of Medical Sciences (No. 1399.378) and followed the Declaration of Helsinki. Written consent was obtained from the guardians of the patients.

Consent for publication

Not applicable

Availability of data and materials

All data generated or analyzed during this study are included in this article.

Competing interests

The authors have no conflict of interest.

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Authors ‘contributions

Study inception and design: S.M.J, A.F, I.S; Data collation: A.F, N.P, M.K, M.R.S, H. H, Z.M, A.S.D, F.C, A.S, M.M, M.A, H.H, J.S, A.H, A.H, M.S.R, S.S, M.K, A.A, A.A, H.R.S, A.A.R, M.A, S.O.M, Z.S, A.S, V.P, D,Y; Statistical analysis: M.F; Drafting of the manuscript: A.T; Sorting data: P.K.A, F.N.M, S.M, R.K; Interpretation of data:

B.S, A.T, S.A.R, M.R.K, A.J, S.S, A.G, R.D, S.A, S.S.M, F.A; Supervision: S.M.J, A.F, A.T; All authors have read and approved the manuscript.

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