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Pediatrik Yoğun Bakım Ünitesindeki COVID-19 Hastalarının Değerlendirilmesi

Evaluation of COVID-19 Patients in The Pediatric Critical Care Unit

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ÖZ

Amaç: Genel popülasyondaki toplam vaka sayısı ile karşılaştırıldığında, çocuklarda az sayıda ağır akut solunum sendromu koronavirüs 2 (SARS-CoV-2) enfeksiyonu bildirilmiştir. Hiçbir çocuk çalışması (veya vaka) ağır koronavirüs hastalığı (COVID-19) hastalarında ekstrakorporeal teknikleri değerlendirmemiştir. Bu yazıda, çocuk yoğun bakım ünitemizde (ÇYBÜ) terapötik plazma değişimi (TPD) ve sürekli renal replasman tedavisi (SRRT) ile tedavi edilen dört COVID-19 çocuğun klinik özelliklerini, tedavilerini ve sonuçlarını tanımlamayı amaçladık.

Materyal ve Metot: 23 Mart ve 6 Mayıs 2020 itibaren ÇYBÜ'ne kabul edilen COVID-19 pnömonisi olan çocuklar toplandı. Demografik veriler ve hastaneye yatış nedeni kaydedildi. Ekstrakorporeal tedavi uygulanan çocuklarda yaşamsal ve laboratuvar bulguları incelendi.

Bulgular: Noninvaziv mekanik ventilasyon, antiviral ve antibakteriyel tedavi, destekleyici antioksidan tedaviler 11 çocuğa uygulandı. Diğer hastalara göre dört hastada solunum yetmezliği ve vital bulguları daha ciddiydi. Bu nedenle ekstrakorporeal destek tedavileri, TPD ve SRRT uyguladık. Hastalar bu tedavilere hızlı bir klinik yanıt gösterdi.

Sonuç: TPD ve SRRT, çocuklarda diğer destekleyici ve tıbbi tedaviler alan ağır COVID-19 enfeksiyonu için kullanılabilir.

Anahtar Kelimeler: COVID-19, hemodiyafiltrasyon, plazmaferez

ABSTRACT

Objective: Few cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection have been reported in children compared with the total number of cases in the general population. No pediatric studies (or cases) have evaluated extracorporeal techniques in severe coronavirus disease 2019 (COVID-19) patients. In this article, we aimed to describe the clinical features, treatments, and outcomes of four children with COVID-19 who were treated with therapeutic plasma exchange (TPE) and continuous renal replacement therapy (CRRT) in our pediatric intensive care unit (PICU).

Materials and Methods: The children with COVID 19 pneumonia admitted to the PICUs from March 23, and May 6, 2020 were collected. Demographic data and reason for hospitalization were recorded. Vital and laboratory findings were examined in children with extracorporeal treatments.

Results: Noninvasive mechanical ventilation, antiviral and antibacterial therapy, supportive antioxidant treatments were administered for 11 children. Respiratory failure and vital signs were more serious in four patients than in other patients. Therefore, we performed extracorporeal support treatments, TPE and CRRT. The patients showed a rapid clinical response to these treatments.

Conclusion: TPE and CRRT can use for severe COVID-19 infection receiving other supportive and medical treatments in children.

Keywords: COVID-19, hemodiafiltration, plasmapheresis

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INTRODUCTION

In December 2019, coronavirus disease 2019 (COVID-19) emerged unexpectedly in Wuhan, Hubei Province, China, and has rapidly spread from Wuhan to other areas in China and all over the world.[1] The disease has affected more than 1,600,000 people and caused 95,000 deaths worldwide, but the epidemiologic characteristics, clinical manifestations, and treatment of COVID-19 among children remain largely unclear.[2] Few cases of COVID-19 caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection have been reported in children compared with the total number of cases in the general population. In addition, there are limited data from critically ill children.[1-5]

The predominant signs and symptoms of COVID-19 reported to date among all patients are similar to those of other viral respiratory infections. The most common symptoms in COVID-19 patients are cough, fever, and difficulty breathing. Abdominal pain, diarrhea, nausea, and vomiting were reported to have been present in nine hospitalized infants in China.[3-4] Most infected children were asymptomatic or had mild acute upper respiratory tract infection symptoms and recovered within 1–2 weeks of onset.[3-5] In addition, it is very uncommon for children to progress to severe or critical disease.[3]

Therapeutic plasma exchange (TPE) and continuous renal replacement therapy (CRRT) are extracorporeal procedures that can improve organ function in patients with sepsis and septic shock.[6] COVID-19 and plasmapheresis in children have not been adequately studied. In addition, no pediatric studies (or cases) have simultaneously evaluated the extracorporeal techniques, CRRT and TPE, in severe COVID-19 patients. Therefore, in this article, we aimed to describe the clinical features, treatments, and outcomes of 11 children with severe COVID-19 in the pediatric intensive care unit (PICU).

MATERIALS AND METHODS

Study Design: Healthcare provision for children aged from 1 month to 18 years is provided in our PICU, which is equipped with 25 beds, 19 ventilators (2 high frequency oscillatory ventilators), 4 Prismaflex™ hemofiltration machines (Baxter, USA), 1 extracorporeal membrane oxygenatory (ECMO) machine (Getinge, Gothenburg, Sweden), and 11 isolation rooms. We recorded all materials, data, computer codes, and protocols associated with the publication for readers. The study was approved by the Istanbul University, Cerrahpasa Clinical Research Ethics Committee (Date: 29/04/2020, decision no: 57698).

Patient Population and Data Collection: Demographic data and reason for hospitalization were recorded. The patients' sex, age, mechanical ventilation requirement, duration of hospitalization in the PICU, underlying diseases, symptoms, vital signs, family source of exposure, mortality, the pediatric risk of mortality (PRISM) score, and were recorded. In addition, haemogram parameters, biochemistry results, electrocardiography, and radiological findings were recorded at admission.

Continuous Renal Replacement Therapy Protocol: The patients received sedation and analgesia prior to catheterization. The aseptic method was used during catheterization. The catheters were attached using the Seldinger technique and fixed to the skin with silk sutures. Surgical catheters were not attached (cut-down, etc.).

CRRT was performed in continuous venovenous hemodiafiltration (CVVHDF) using the Prismaflex® (Baxter, USA) hemofiltration system. Three patients used oXiris® adsorbing membranes (Baxter, USA). The blood flow rate was 100 mL/kg/min. The dialysate rate, replacement fluid rate, and ultrafiltration rate were adjusted on the basis of the patients' diagnoses. The dialysate flow rates were set to 2000 mL/1.73m2/h. Multibic® (Fresenius Medical Care, AG Co., Germany) was used as dialysate solution.

Therapeutic Plasma Exchange: We performed plasma exchange using a filter membrane-based apparatus. Prismaflex® (Baxter, USA) TPE 2000 sets were used. The amount of plasma was calculated as follows: estimated plasma volume (L) = 0.07 × weight (kg) × (1 -hematocrit). We used fresh frozen plasma for the replacement fluid. Saline 0.9% was used to prime the TPE circuit. Heparin bolus was administered at the start, and 5-25 U/kg was administered hourly. During the TPE procedures, blood flow was adjusted to 100mL/min. Vital signs were thoroughly monitored during TPE procedures. Control blood samples were taken immediately before and after TPE.

Ventilation Strategy and Protocol: We used Maquet Servo-i® (Maquet Critical Care, Solna, Sweden) and Carespace-R860® (GE, Wisconsin, US) ventilators. Full face reusable noninvasive mechanical ventilation (NIV) masks (Philips-Respironics®, New York, US) were used during NIV. We used NIV-pressure

support and control as the two modes of mechanical ventilation. We did not use NIV-continuous positive airway pressure in these patients. NIV parameters were readjusted according to SpO2, blood gases, ventilator parameters (tidal volume and respiratory rate), and patients' clinic finds, after connecting NIV. The patients were administered respiratory physiotherapy and facial pressure points massage every two hours. Patients were reconnected to the NIV after aspirating the mouth and nose, followed by the acquisition of blood gas samples in the second hour of NIV. Salbutamol and ipratropium bromide were given to all patients by micro-pump nebulizer devices (Aerogen, Dangan, Ireland).

Statistical Analysis: Statistical analysis was performed using the IBM SPSS statistics for Windows version 20.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as means ± standard deviations and categorical variables as frequencies (percentages). Student's t-test was used for continuous variables with a normal distribution. Pearson's Chi-square test and analysis of variance were used for the comparison of the categorical data between the groups. Univariate and multivariate binary logistic regression models were employed to calculate the odds ratios (ORs) with 95% confidence intervals (CIs) for prognosis. P <0.05 was considered statistically significant.

RESULTS

Demographics: Between March 23, and May 6, 2020 11 patients were treated for COVID-19 related pneumonia in our PICU. Eight patients (72.7%) were male. The median age was 14 years 8 months old (2 years and 2 months - 17 years). Seven children were related with the family cluster outbreak and they didn't have any underlying disease. Other four children had pre-existing disease. A patient was Hodgkin lymphoma on maintenance chemotherapy and the other was diabetes mellitus. The other two patients had neurological disease, tuberous sclerosis and cerebral palsy. The median time from onset of symptoms to hospital admission was 2 days (range 1-10 days). The median duration of intensive care unit stay was 6.0 (from 4 to 12) days.

Common clinical symptoms were fever, cough and dyspnea. Laboratory investigations showed that C-reactive protein levels were elevated in 8 cases and elevated D-Dimer levels were found in 8 cases. Ten of the eleven patients assessed radiographically with computerized tomography. In these patients, there were showed bilateral ground glass opacities and multifocal consolidative opacities (Figure 1 and Figure 2).

ECGs of all patients were taken and the QTc value was calculated. Only one patient had an upper limit of QTc and electrolytes support was given. There was no rhythm problem during stay the PICU. Echocardiography was performed in 7 of 11 patients and heart failure was detected in a patient with tuberous sclerosis (ejection fraction was 45%).

Ventilatory Treatment: All 11 patients had hypoxemia on admission and median saturation was 84% (63-94) without O2 support. Two patients were intubated and a patient with pneumothorax didn't need NIV. Other 8 patients were treated only by NIV. NIV-PCV was used for patients who were younger than others. Six patients were sedated with midazolam or ketamine infusion when they connected NIV. Expiratory positive airway pressure (EPAP) was started between 6 to 15 cmH2O (median: 12.0) and inspiratory positive airway pressure (IPAP) was started between 12 to 30 cmH2O (median: 24.0). Median NIV duration was 120.0 hours (68–220). Vital signs; SpO2/FiO2 (SF) ratio, heart rate (HR), and respiratory rate (RR) were improved while NIV usage. The six patients' SF ratios were <100 and three of them were used >12 EPAP. In the NIV treatment, four patient's FiO2 requirement didn't decrease below 60% during in first 24 hours in the PICU.

Medical Treatments: All patients were treated in the isolation rooms. They received antiviral treatment, including oseltamivir (all of the patients) and favipiravir (three patients) tablets. Eight patients were given chloroquine. Four patients were given antibiotic treatments for secondary bacterial infection. The antibiotics used generally covered common pathogens. Four patients used anti-fungal treatment. Also, all the patients were given routinely azithromycin, ascorbic acid, n-acetyl cysteine, magnesium sulfate, and steroid. Low molecular weight heparin prophylaxis was given to 6 adolescent patients during the PICU stay (Table 1). None of the patients were given biological agents.

Continuous Renal Replacement Therapy and Therapeutic Plasma Exchange Treatments: In our study, CVVHDF and plasmapheresis were used considering the same indications for four patients; severe hypoxemia. First patient was diabetes mellitus and his first ferritin count was 13,500 ng/ml. TPE was performed and then CVVHDF was started with a cytokine-removing filter. Eight times of plasma exchange and 90 hours of CVVHDF were applied in

total. The other patient was a 17-year-old girl who was healthy before COVID-19 pneumonia. In this patient, three times TPE and 84 hours CVVHDF (with cytokine-removing filter) were performed. Third patient was cerebral palsy and COVID-19 treatment was started three days ago before the PICU admission. However, he occurred severe respiratory failure and he was intubated. Two times TPE were performed. Fourth patient was tuberous sclerosis and he had seconder bacterial infection. Seven times plasmapheresis and 156 hours CVVHDF (with cytokine-removing filter) were performed. After the first TPE treatments, HR, RR, and circulation improved significantly in the patients (Table 2).

DISCUSSION AND CONCLUSION

This study has shown that SARS-CoV-2 infection can cause severe pneumonia in childhood, especially in those without an underlying chronic disease. In the treatment of these patients, we used a higher EPAP with full face masks. In addition to antiviral and antibacterial therapy, supportive antioxidant treatments were administered. Respiratory failure and vital signs were more serious in four patients than in other patients. Therefore, we performed extracorporeal support treatments, TPE and CVVHDF. The patients showed clinical response to these treatments.

Children are typically more susceptible to viral infections; however, they have experienced lower than expected rates of COVID-19 disease and deaths in children appear to be rare. In more than 72,000 total cases from China,[7] only 2% of confirmed cases were children. In addition, very few patients needed PICU -based treatment. Three children, all of whom had underlying diseases, have been reported to require treatment in PICU. Only one child has died.[4]

The most common symptoms among children were fever and respiratory tract symptoms, similar to adult patients.[4] In our patients, the most frequent symptoms were fever (100%) and cough (100%). Gastrointestinal symptoms, such as abdominal pain, nausea, and diarrhea, were present in six patients. These patients were administered proton pump inhibitors and granisetron. Gastrointestinal symptoms improved after the second day.

According to the current approach, real-time reverse transcription polymerase chain reaction (RT-PCR) plays an important role in the diagnosis of COVID-19. However, its lack of sensitivity, insufficient stability, sampling method, and relatively long processing time should be considered.[8] ICU practitioners should be more suspicious of any patient with severe acute respiratory infection, considering the increasing number of local community transmission worldwide and the risk of missing cases in the early epidemic. Patients might have a false negative upper respiratory tract sample. Patients with a high clinical suspicion of COVID-19 may require repeated sampling, even if the initial tests are negative.[9] The COVID-19 RT-PCR test was positive in only five of our patients. However, in other patients, suspicious contact and clinical and radiological findings were compatible with COVID-19 pneumonia.

In a case series from Wuhan Children's Hospital,[10] all severe pediatric patients had abnormalities on chest CT or radiography. Seven patients had multiple patch-like shadows, six patients had ground glass opacity, one patient had pleural effusion and one patient had "white-lung-like" changes. Our patient had signs of pneumonia on chest radiography. However, eight patients' CT showed patch-like shadows and ground glass opacity. A 15-year-old girl's CT showed pneumothorax and pneumomediastinum. Her first symptom was chest pain before the admission.

The treatment of pediatric patients with COVID-19 remains unclear. Many clinical trials are in progress to evaluate specific treatments; however, very few of these studies involve children. Most studies recommend symptomatic and supportive treatment.[2-3] In our patients, oseltamivir and macrolide were routinely administered for five days. Hydroxychloroquine was administered to eight patients. In addition, favipiravir was administered to three patients who were worsening clinically under azithromycin, hydroxychloroquine, and oseltamivir therapy. Favipiravir treatment has not been previously reported in paediatric patients. We started this treatment with special permission. During the 5 days' favipiravir treatment, the 17-year-old patient's serum bilirubin and liver enzymes were elevated mildly. This disorder recovered after treatment completion. We did not observe any serious side effects during favipiravir treatment.

The data available thus far seem to indicate that SARS-CoV-2 infection is capable of producing an excessive immune reaction in the host. This reaction is characterized by a dysregulated immune response to infections that involves complex interactions between endothelial cells, platelets, leukocytes, the coagulation system, and multiple inflammatory mediators. In some cases,[11] a reaction takes place,

which as a whole is labelled a 'cytokine storm'. It has been suggested that CRRT and TPE can be used in patients with sepsis to reduce cytokine storm.[6,11-13] However, TPE treatment in children with COVID-19 has not been reported in the literature. In 2009, Patel et al.[12] reported that three pediatric patients with severe H1N1 influenza pneumonia and ARDS fully recovered after TPE treatment. These patients had similar findings to those seen in fulminant COVID-19 patients. In our study, four children had secondary bacterial infection, severe sepsis, and ARDS. We used TPE and CRRT treatment for these patients who worsened despite supportive and medical treatment. Even after the first treatment session, vital signs and respiratory values improved in these patients. After TPE treatment, we used CVVHDF with high-volume hemofiltration and a standard dialysate rate to reduce the severity of the cytokine storm using the cytokine-removing filter, oXiris®. High-volume hemofiltration can effectively correct lactic acidosis, improve inflammation-damaged organ function, and improve oxygenation in patients with acute respiratory failure.[13-14]

An allergic reaction occurred in a patient during the second TPE procedure. An antihistamine drug was administered. We did not observe any other serious complications during TPE treatment. Intravenous immunoglobulin was administered to patients after the final TPE treatment because of rebound cytokine release. Biological agents such as tocilizumab were not administered. We believe that TPE is a better immunomodulatory agent than biologic agents for severe infections.

Our study had some limitations. This was a retrospective observational study with a limited number of patients. These findings need to be confirmed in a prospective study with larger sample size. However, a major strength of our study is that no studies have examined TPE and CRRT in children with severe COVID-19 pneumonia.

In conclusion, plasmapheresis and CVVHDF can affect the prognosis of COVID-19 patients receiving other supportive and medical treatments. In these patients, TPE and CVVHDF showed promise. We believe that there is a need for large-scale prospective studies in pediatric COVID-19 patients to support this idea.

Ethics Committee Approval: Our study was approved by the Istanbul University, Cerrahpasa Clinical Research Ethics Committee (Date: 29/04/2020, decision no: 57698).

Conflict of Interest: No conflict of interest was declared by the author.

Author Contributions: Concept - FA; Supervision - FA, PO, HC; Materials - FA, FDA.; Data Collection and Processing - FA, CD, AAK; Analysis and Interpretation- FA; Writing - FA, CD.

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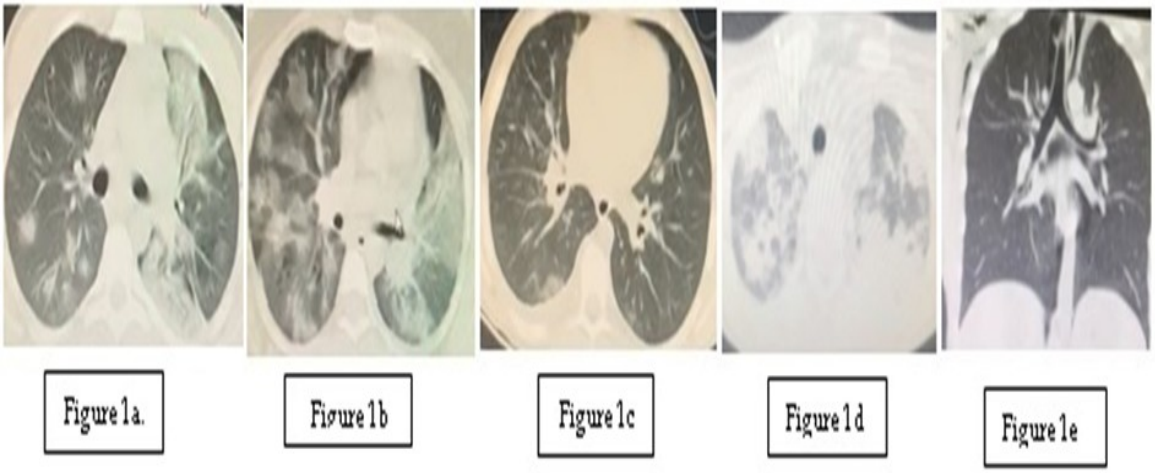

Figure 1. Our COVID-19 patients' computerized tomography findings before the PICU admission.
a. Widespread bilateral confluent GGO with multifocal patchy consolidations, ground-glass shadows, and bronchiectasis b. Widespread multifocal patchy consolidations and ground-glass shadows on the 17 years old patient's lung in computerized tomography c. Infiltration findings of the pleural region at CT before 3 days at the PICU admission. d. Diffuse consolidation and airspace opacities seen in patient no:11. e. Pneumomediastinum and pneumothorax were seen in our patients no:8.

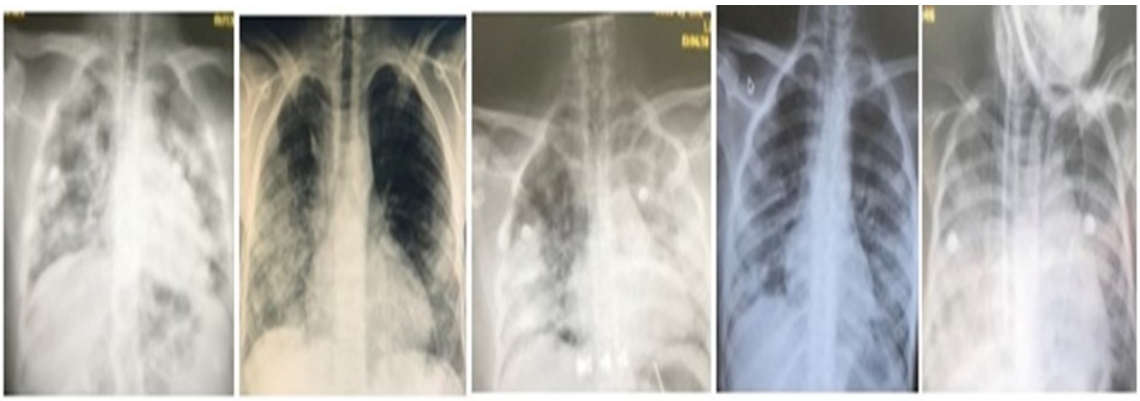

Figure 2. Our COVID-19 patients' X-ray findings at PICU admission.

Table 1. Characteristics of the COVID-19 patients.

Patients No	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**
Age (years)	15.8	17	15.3	14.7	6.4	4.2	2.2	15	4.6	8.4	9
Sex	Male	Female	Male	Female	Male	Male	Male	Female	Male	Male	Male
Comorbid disease	No	No	DM	HL	No	No	No	No	No	CP	TS
Exposure history	Yes	Yes	No	No	No	No	No	Yes	No	No	Yes
Family source of exposure	Yes	Yes	No	No	No	No	No	Yes	No	No	Yes
Time between onset symptoms and PICU admission	7	7	3	2	2	2	1	1	1	10	5
COVID-19 PCR Test Positive	+	+	+	-	-	-	-	+	-	-	+
Symptoms at onset											
Fever	+	+	+	+	+	+	+	-	-	+	+
Cough	+	+	+	+	+	+	+	-	-	+	+
Shortness of breath	+	+	+	+	+	+	+	-	-	+	+
Muscle ache	+	+	+	+	-	-	-	-	-	-	+
Sore throat	+	+	+	-	-	-	-	-	-	-	-
Chest pain	+	+	-	-	-	-	-	+	-	-	-
Diarrhea	-	-	+	-	-	-	-	-	-	-	-
Nausea and vomiting	+	+	+	+	-	+	-	-	-	-	-
Duration of stay in the PICU (days)	6	6	7	8	4	4	4	5	5	13	12
Duratiın of IMV (hours)	-	-	-	-	-	-	-	-	12	84	-
Duration of NIV (hours)	144	168	122	118	72	76	68	-	2	36	220
Maximum PEEP (cmH_2O)	12	14	14	14	6	8	6	-	6	8	15
Maximum PIP (cmH2O)	24	26	25	27	22	24	18	-	24	22	30
Computerized Tomography	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Plasmapheresis	No	Yes	Yes	No	No	No	No	No	No	Yes	Yes
Continuous venovenous hemodiafiltration	No	Yes	Yes	No	No	No	No	No	No	No	Yes
Secondary bacterial infection at PICU admission	Yes	Yes	Yes	Yes	No	No	No	No	No	Yes	Yes
Inotropic drug usage	No	Yes	Yes	No	No	No	No	-	-	Yes	Yes
Medical Treatment for COVID-19											
Hydroxychloroquine,	Yes	Yes	Yes	No	Yes	Yes	No	Yes	No	Yes	Yes
Macrolid	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Oseltamavir	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Faviripavir	Yes	Yes	No	No	No	No	No	No	No	No	Yes
Intravenous immunoglobulin	No	Yes	Yes	No	No	No	No	No	No	No	Yes
White blood cell count (5.2-12.4 10x3/µL)	4.8	7.2	13.3	14.7	8.2	14.8	10.8	3.4	9.5	14.3	12.4
Lymphocyte count (0.9-5.210x3/µL)	0.8	0.7	1.4	1.6	0.9	1.4	1.1	1.2	1.2	2.2	0.94
C-creative protein (<5 mg/L)	53.08	100.38	284.99	17	19.1	3.63	14.2	6.38	0.18	1.24	181
Lactate dehydrogenase (<615 U/L)	399	482	683	409	251	302	237	229	269	941	268
Prokalsitonin (ng/mL)	0.642	0.183	7.15	0.03	0.214	0.085	0.081	<0.02	0.047	41.56	3.62
D-Dimer (0-0.5 mg/L)	3.21	2.71	11.13	1.73	0.7	0.63	0.24	0.21	0.31	3.29	1.87
Ferritin (15-150 ng/ml)	468.2	277.4	13500	143.2	149.6	19.71	45.3	26.9		922.1	549

Table 2. Clinical and laboratory variables of the patients who were treated CRRT and plasmapheresis during stay the PICU.

Patient No:	2					3					10					11				
Time (day)	0	1	2	3	4	0	1	2	3	4	0	1	2	3	4	0	1	2	3	4
pH	7.45	7.44	7.41	7.38	7.39	7.47	7.45	7.46	7.41	7.40	7.39	7.43	7.48	7.42	7.45	7.40	7.32	7.38	7.42	7.40
PCO_2 (mmHg)	33.5	41.5	47	48.5	4.7	37.7	44.6	48.5	37.3	48.7	40.3	44.4	40.5	48	38.1	48	57.3	50.8	46.6	41
sO_2 (spontaneous)	85	87	88	92	94	89	88	90	92	95	80	91	99	99	100	68	73	85	82	77
SpO2/FiO2 (SF) ratio	141	174	176	230	235	111	125	150	153	190	133	182	247	247	250	92	158	192	198	160
HCO_3 (mmol/L)	24.4	27.1	27.7	26.3	27.3	27.8	30	32.7	24.1	28.6	23.4	28.5	30.1	29.6	26.7	28.6	29.5	28.0	28.0	27.7
Lactate (mmol/L)	1.5	1.2	1.7	1.8	1.7	1.6	1,1	2,2	1.4	1	2.1	3.1	4.7	3.2	2.8	1.9	0.8	1.4	2.3	1.5
PEEP/EPAP (cmH_2O)	14	14	12	12	10	14	14	14	12	12	8	6	6	6	8	15	15	15	14	14
PIP/IPAP (cmH_2O)	24	25	24	22	20	24	24	24	24	20	22	20	16	16	14	30	28	25	22	28
FiO_2(%)	60	50	50	40	40	80	70	60	60	50	60	50	40	40	40	100	60	50	60	60
Tidal volume (ml)	250	280	325	350	380	200	220	270	300	320	168	174	180	175	182	210	240	280	270	230
Respiratory rate (/min)	52	30	22	24	23	50	38	32	24	22	30	28	30	25	24	49	30	33	43	40
Heart rate (/min)	106	90	75	57	72	170	142	100	105	118	135	130	140	142	122	178	144	160	145	170
Tension (mm/hg)	114/70	119/74	106/55	125/75	103/53	120/66	122/64	124/70	126/76	114/67	58/34	109/80	105/75	112/94	108/67	117/65	115/76	121/65	134/76	112/67
Temperature (°C)	38.5	37.2	37	36.2	36.3	38.1	36.8	38	37.2	37	38	36.2	36.4	37	36.5	37.8	37.0	37.4	37.3	38.3
CRP (mg/L)	100.38	127.95	81	14.3	8.36	284.99	128.6	173	81	69.4	1.24	2.45	-	3.61	-	181	188	147	31.9	78.7
Procalcitonin (ng/dl)	0.183	0.48	0.335	0.201	0.1	7.15	4.38	3.1	1.91	1.44	41.56	10.98	-	3.65	-	3.7	2.2	1.47	0.03	12.6
Hemoglobin (g/dL)	11.9	11.1	11.1	9.7	10	10.2	9.1	10.3	9.9	9	10.6	10.7	14	12.1	10	8.9	7.5	9.6	10.1	9.9
RBC transfusion	No	No	No	No	No	No	Yes	No	No	No	No	Yes	No	No	No	No	Yes	No	No	No
Ferritin (ng/ml)	-	277.1	-	-	-	-	135000	9545	4987	-	922	-	-	-	-	582	-	-	345	-
QTc (s) interval	-	0.44	0.43	0.43	0.42	-	-	0.38	-	-	0.36	-	-	-	-	0.37	0.35	0.36	0.33	0.38
TPE	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	Yes	Yes	Yes	No	Yes
CRRT	No	No	No	No	No	Yes	Yes	Yes	Yes	No	No	Yes	No	No	No	Yes	Yes	Yes	Yes	Yes