

## Clinical research

# COVID-19 implications at the Clinical University Center in Kosovo – Department of Pediatrics

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## Abstract

**Introduction:** In late December 2019, the first pneumonia cases of unknown origin were identified in Wuhan, the capital city of Hubei province in central China. While the most data are available for adult patients with COVID-19, limited reports analyze pediatric patients infected with SARS-CoV-2. The aim of the study was to describe the epidemiological and clinical characteristics of coronavirus disease (COVID-19) in patients at the Pediatric Clinical Center of Kosovo.

**Material and methods:** This research is retrospective and includes data for the period from 8 July 2020 to 6 January 2021. In this study we obtained data from different documents and patients' records, providing information regarding gender, age, number of cases, most frequent diagnosis, critical patients, etc.

**Results:** Out of 69 pediatric patients hospitalized in the clinic during the seven months, 50 patients tested positive with COVID-19. The study sample represented an equal number of males and females (50/50), while the average age of the patients was 6 years. Based on the pediatric age groups, the study sample comprises 16 patients of the age groups of 1 month–2 years, 20 patients of the age group of 2–6 years; 4 patients of the age group of 6–12 years, and 10 patients of the age group of 12–18 years.

**Conclusions:** Data suggest that pediatric cases of COVID-19 in adolescents have more severe symptoms than in the other age groups; however, in general children tend to cope much more easily with the virus than adults.

**Key words:** COVID-19, multisystem inflammatory syndrome in children, pediatric patients.

## Introduction

The first pneumonia cases of unknown origin were identified in Wuhan in December 2019, the capital city of Hubei province in central China [1]. The causative pathogen was identified as a novel enveloped RNA  $\beta$ -coronavirus. In December 2019 the SARS-CoV-2 infection emerged. Very soon, SARS-CoV-2 spread across the globe and caused a pandemic situation, and thus SARS CoV-2 has become a major health concern [2, 3]. The WHO on June 1, 2020, reported a total of 17,057,853 cases worldwide with 690,166 deaths due to COVID-19 [4]. It is known that coronaviruses belong to the family of the *Coronaviridae*, and consist of

four genera, namely *Alphacoronavirus*, *Betacoronavirus*, *Gammacoronavirus* and *Deltacoronavirus*. SARS-CoV-2 is part of the *Betacoronavirus* genus [5]. Like all coronaviruses, SARS-CoV-2 appears to be a positive-strand, non-segmented RNA virus. The coronaviruses have the largest genome among all RNA viruses, 27–32 kDa [6]. Clinical features of SARS-CoV-2 infection are similar to SARS and MERS. The shape of SARS-CoV-2 is spherical and pleomorphic [7]. SARS-CoV-2 has a single-stranded, non-segmented, positive-sense RNA. Most of the genomic material constitutes gene replicase; the replicase codes 16 nonstructural proteins (nSPs) [3, 8]. Transmission [9] of SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) occurs via respiratory droplets from face-to-face contact, and to a lesser degree, via contaminated surfaces. It turned out that aerosol spread may occur, but the role of aerosol spread in humans remains unclear. It is known that 48% to 62% of transmission may occur via pre-symptomatic carriers.

The most common symptoms [10] in hospitalized patients include fever (70–90%), dry cough (60–86%), shortness of breath (53–80%), fatigue (38%), myalgias (15–44%), nausea/vomiting or diarrhea (15–39%), headaches, weakness (25%), and rhinorrhea (7%). Anosmia or ageusia may be the sole presenting symptom in approximately 3% of individuals with COVID-19. Common laboratory abnormalities [11] among hospitalized patients include lymphopenia (83%), elevated inflammatory markers (e.g., erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), ferritin, tumor necrosis factor- $\alpha$ , IL-1, IL-6), and abnormal coagulation parameters (e.g., prolonged prothrombin time, thrombocytopenia, elevated D-dimer (46% of patients), low fibrinogen).

The most common complications among hospitalized patients with COVID-19 include pneumonia (75%); acute respiratory distress syndrome (15%); acute liver injury, characterized by elevations in aspartate transaminase, alanine transaminase, and bilirubin (19%); cardiac injury, including troponin elevation (7–17%), acute heart failure, dysrhythmias, and myocarditis; prothrombotic coagulopathy resulting in venous and arterial thromboembolic events (10–25%); acute kidney injury (9%); neurologic manifestations, including impaired consciousness (8%) and acute cerebrovascular disease (3%), and shock (6%) [10, 12–16].

### Children infected with COVID-19

While data are available mostly for adult patients with COVID-19, limited reports analyze pediatric patients infected with SARS-CoV-2. In this context, we performed a systematic review, to our knowledge, of COVID-19 in children and ad-

olescents to evaluate clinical features, diagnostic tests, current therapeutic management, and prognosis at our University Clinical Center of Kosovo, the Pediatric Department.

In April 2020, during the peak of the coronavirus (COVID-19) pandemic in Europe, a cluster of children with hyperinflammatory shock with features similar to Kawasaki disease and toxic shock syndrome was reported in England [17]. The patients' signs and symptoms temporally were associated with COVID-19 but presumed to have developed 2–4 weeks after acute infection with COVID-19; all children had been tested by the serologic method and the evidence of infection with SARS-CoV-2, the virus that causes COVID-19, had been established. The clinical signs (symptoms) which were present in the first cluster included fever, rash, conjunctivitis, peripheral edema, gastrointestinal symptoms, shock, and elevated markers of inflammation and cardiac damage. At the beginning of May 2020, Centers for Disease Control and Prevention (CDC) published an online Health Advisory that summarized the manifestations of the reported multisystem inflammatory syndrome in children (MIS-C), outlined a case definition, and asked clinicians to report suspected U.S. cases to local and state health departments [18].

Multisystem inflammatory syndrome in children (MIS-C) is a new phenomenon that is reported worldwide with a temporal association with COVID-19. Multisystem inflammatory syndrome in children (MIS-C) is a very rare but severe condition, which has been reported approximately 2–4 weeks after the onset of COVID-19 in children and adolescents [18]. Distinguishing MIS-C from other severe diseases such as infectious or inflammatory conditions poses a challenge to clinicians caring for children and adolescents. The COVID-19 pandemic continues to expand in many ways; health care provider awareness of MIS-C will facilitate early recognition of infection, diagnosis, and treatment. Generally, children are known to have low immunity, and some exhibit a long incubation period after SARS-CoV-2 infection. Therefore, children should try to avoid contact with complex populations to avoid being infected by potential spreaders. COVID-19 is an acute, self-limiting disease; the mortality rate is 2%, and it has also been reported as critical for children [19]. This paper aims to describe the epidemiological and clinical characteristics of coronavirus disease (COVID-19) pediatric patients at the Pediatric Clinical Center of Kosovo.

### Material and methods

This is a retrospective study and includes data for the period from 8 July 2020 to 6 January 2021.

In this study, we obtained data from different documents and patients' records, providing us

with information regarding: gender, age, number of cases, most frequent diagnosis, critical patients, etc.

The data collected in this research were processed using the MS Excel program wherein different formulas such as arithmetic mean, minimum, maximum, histogram, circular diagram, distribution polygon, and other graphs are used to better summarize the results of the study.

**Results**

In this study, there were in total 69 patients hospitalized in the clinic during the 7-month period, of whom 50 patients have tested positive with COVID-19. For this study, only patients who had tested positive with COVID-19 were selected for further analysis. From the gender perspective, males and females were represented equally, 50/50, in the sample and the average age of the patients was 6 years (Figure 1).

Based on the pediatric age groups the study sample is composed of 16 patients of the age group of 1 month to 2 years, 20 patients of the age group of 2–6 years, 4 patients of the age group of 6–12 years, and 10 patients of the age group of 12–18 years. The average age of the patients was 6 years (Figure 2).

From this, we can see that the age groups of 2–6 years and 1 month to 2 years were more affected. The graph above shows the fluctuation of COVID-19 cases during the period from July 8 when the unit for COVID patients was established at our clinic, until January 2021. The study shows that the highest numbers of COVID-19 cases were recorded during October and November (Figure 3).

According to the data the most common diagnosis among the patients was bilateral bronchopneumonia and incipient pneumonia (24 cases), followed by Status febrilis (7 cases) and acute gastroenteritis (5 cases) (Table I, Figure 4).

The clinical state was defined according to the following classification: mild – uncomplicated upper respiratory tract viral infection (e.g., fever, cough, sore throat, malaise, headaches,

muscle pain); severe (e.g., pneumonia, hypoxia dyspnea, tachypnea requiring hospitalization), and multi-systemic inflammatory syndrome (e.g., severe pneumonia, acute respiratory distress syndrome, and/or multiple organ dysfunction requiring hospitalization in intensive care) (Figure 5).

Considering the clinical state in this study, we have focused on the sample of patients with critical conditions. Thus, four groups of patients will be described as follows.

The patients of the first group complained of having fever, cough, sore throat, and diarrhea. The laboratory examinations of this group were ESR 85 mm/h, leukocytes  $8.3 \times 10^3/\text{mm}^3$ , erythrocytes  $4.40 \times 10^6/\text{mm}^3$ , hemoglobin 12.4 g/dl, thrombocytes  $388 \times 10^3/\text{mm}^3$ , lymphocytes 27.2%, monocytes 3.7 l and granulocytes 69.1%. Level of urea 4.11 mmol/L (normal range: 1.70–8.30 mmol/l), creatinine 89.9 mg/dl (normal range: 53–115 mg/dl), aspartate transminase (AST) 59 IU/l (normal range: 2–37 IU/l), alanine transminase (ALT) 37.9 IU/l (normal levels: 3–4 IU/l), iron 33  $\mu\text{mol/l}$  (normal range: 11.6–31.3  $\mu\text{mol/l}$ ), D-dimer 898 mg/l (normal range is till 255 ng/ml), CRP 185 mg/l (normal range: 0–6 mg/l), estimated glomerular filtration rate (eGFR) 79.19 ml/min/1.73 m<sup>2</sup> (Table II). By further examination of the patients of this

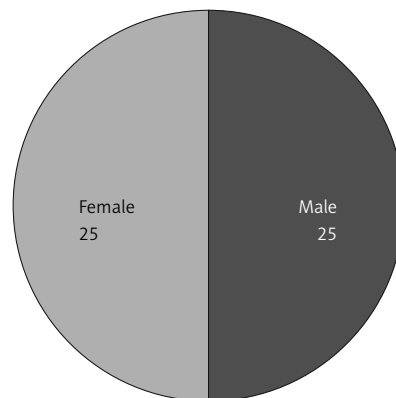


Figure 1. The patient ratio by gender

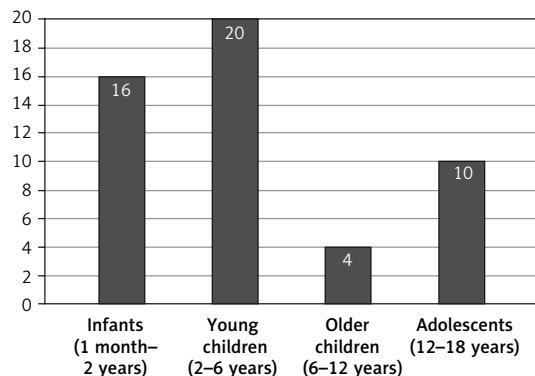


Figure 2. Pediatric group ages

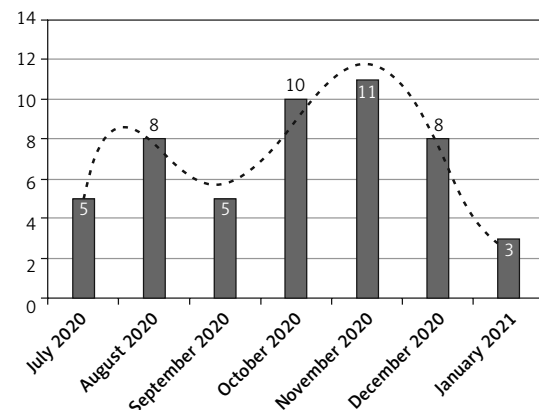
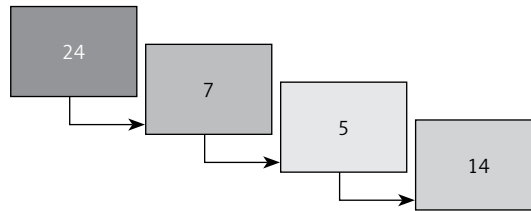


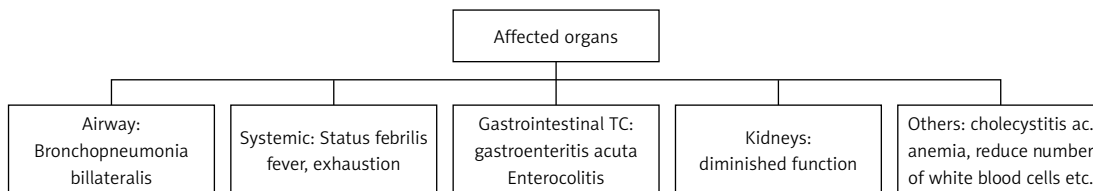
Figure 3. Number of cases from July 2020–January 2021

**Table I.** Most frequent diagnoses among patients

Clinical cases	No. of cases
Bronchopneumonia billateralis & pneumonia incipiens	24
Status febril	7
Gastroenteritis acuta	5
Other causes	14



**Figure 4.** Most frequent diagnosis among patients



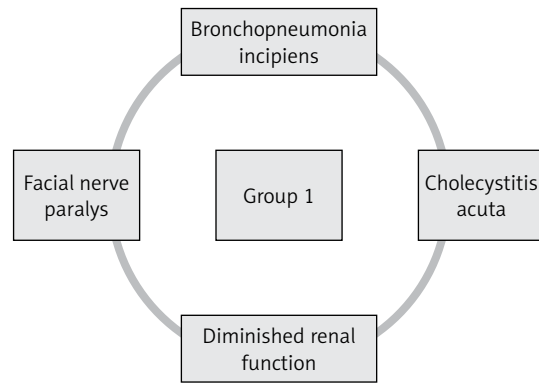
**Figure 5.** Cases with most the frequent symptoms

**Table II.** Average reported serum laboratory values for COVID-19 in four groups – Pediatric Clinical Center of Kosovo

Parameter	Group 1	Group 2	Group 3	Group 4	Normal value of biochemical and hematological analysis
ESR	85 mm/h	90 mm/h	100 mm/h	50 mm/h	M: 10 mm/h F: 15 mm/h
Leukocytes	$8.3 \times 10^{-3}/\text{mm}^3$	$10 \times 10^{-3}/\text{mm}^3$	$18.6 \times 10^{-3}/\text{mm}^3$	$10.01 \times 10^{-3}/\text{mm}^3$	$4.0\text{--}8.0 \times 10^9/\text{l}$
Erythrocytes	$4.40 \times 10^{-6}/\text{mm}^3$	$3.25 \times 10^{-6}/\text{mm}^3$	$4.32 \times 10^{-6}/\text{mm}^3$	$3.89 \times 10^{-6}/\text{mm}^3$	M: 4.5–5.8 g/l F: 3.8–4.9 g/l
Hemoglobin	12.4 g/dl	10.6 g/dl	10.9 g/dl	13.0 g/dl	M: 140–180 g/l F: 120–160 g/l
Thrombocytes	$388 \times 10^{-3} \text{ mm}^3$	$108 \times 10^{-3} \text{ mm}^3$	$183 \times 10^{-3} \text{ mm}^3$	$288 \times 10^{-3} \text{ mm}^3$	$140\text{--}310 \times 10^9/\text{l}$
Lymphocytes	27.2%	10.0%	9.1%	12.7%	25–33%
Monocytes	3.7	4.0 l	2.4 l	8.3 l	3–7%
Granulocytes	69.1%	86.0%	88.5%	79%	$1.5\text{--}8.5 \times 10^9/\text{l}$
Urea	4.11	8.5	4.62	4.62	2.5–8.2 mmol/l
Creatinine	89.9 (normal range: 53–115)	101 (normal range: 53–115)	113.9 (normal range: 53–115)	113.9 (normal range: 53–115)	M: 70–108 mmol/l F: 44–88 mmol/l
AST (aspartate transaminase)	59	48	39	39	42 U/l
ALT (alanine aminotransferase)	37.9	66	36	36	42 U/l
Iron	33 $\mu\text{mol/l}$	36 $\mu\text{mol/l}$	17 $\mu\text{mol/l}$	17 $\mu\text{mol/l}$	M: 10.667,79 28.3 mmol/l F: 6.6–26.0 mmol/l
D-dimer	898	336	156.9	156.9	Normal range 255
C-reactive protein	185 mg/l (normal range: 0–6)	156.8 mg/l (normal range: 0–6)	156.8 mg/l (normal range: 0–6)	113 mg/l (normal range: 0–6)	0–6 mg/l
Estimated glomerular filtration rate	79.19 ml/min/ 1.73 m <sup>2</sup>	65.92 ml/min/ 1.73 m <sup>2</sup>	43.19 ml/min/ 1.73 m <sup>2</sup>	67.79 ml/min/ 1.73 m <sup>2</sup>	100 ml/min/ 1.73 m <sup>2</sup>

group during hospitalization by chest radiography, we diagnosed incipient bronchopneumonia; by abdominal ultrasound: acute cholecystitis, in the meantime and also facial nerve paralysis and diminished renal function (Figure 6). The patient was treated with antibiotics (ceftriaxone 100 mg/kg mt for 24 h; amp. amikacin 15 mg/kg mt for 24 h; amp. dexamethasone), imipenem (imipenem 50 mg/kg me for 24 h for 10 days), corticosteroids (methylprednisolone for 2 mg/kg mt first day–day 10 16.4) and Fraxiparin, but when the general conditions deteriorated, a palliative care protocol was started (Table III).

The patients of the second group were children admitted for fever, blood in urine, dermatitis, and weakness. The laboratory examination findings of patients of this group were ESR 90 mm/h, leukocytes  $10 \times 10^3/mm^3$ , erythrocytes  $3.25 \times 10^6/mm^3$ , hemoglobin 10.6 g/dl, thrombocytes  $108 \times 10^3/mm^3$ , lymphocytes 10.0%, monocytes 4.0 l and granulocytes 86.0%. Level of urea 8.5 (normal range: 1.70–8.30), creatinine 101 (normal range: 53–115), AST 48 (normal range: 2–37), ALT 66 (normal levels: 3–41), iron 36  $\mu mol/l$  (normal range: 11.6–31.3), D-dimer 336 (normal range:

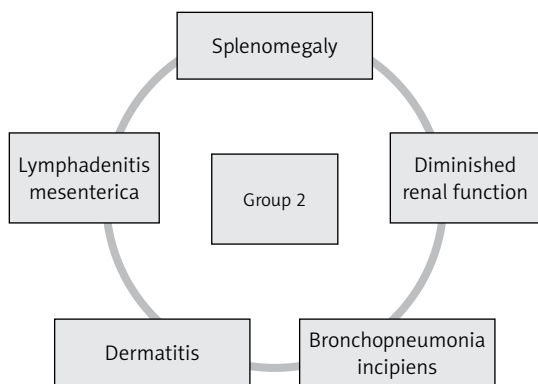


**Figure 6.** Patients of group one infected with virus SARS COVID-19 who have suffered from other diseases

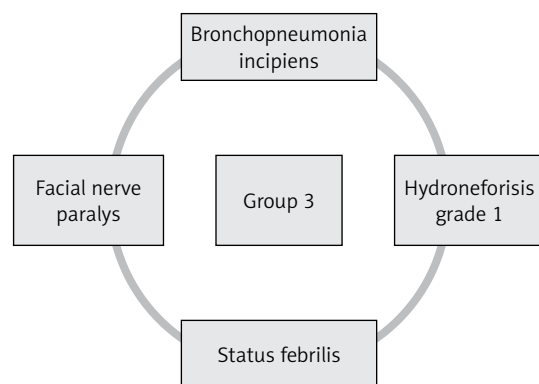
255), CRP 156.8 mg/l (normal range: 0–6), eGFR 65.92 ml/min/1.73 m<sup>2</sup> (Table II). By further examination of the patients of this group during hospitalization by chest radiography, we diagnosed incipient bronchopneumonia; by abdominal ultrasound: splenomegaly, mesenteric lymphadenitis, according to blood analysis he had diminished renal function (Figure 7). The patient was treated with antibiotics (ceftriaxone vancomycin, dexa-

**Table III.** Treatment of patients with COVID-19 in pediatric clinical center of Kosovo

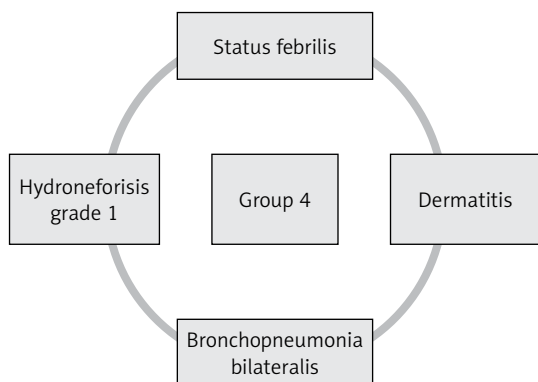
	Group 1	Group 2	Group 3	Group 4
Drugs used for patient treatment	Antibiotics (ceftriaxone 100 mg/kg mt for 24 h; amp. amikacin 15 mg/kg mt for 24 h; amp. dexamethasone), imipenem (imipenem 50 mg/kg me for 24 h for 10 days), corticosteroids (methylprednisolone for 2 mg/kg mt first day–day 10 16.4) Fraxiparin	Antibiotics (ceftriaxone vancomycin, dexamethasone – for 5 days) corticosteroids (methylprednisolone– for 5 other days), imipenem, Fraxiparin	Antibiotics (vancomycin, dexamethasone – for 3 days), corticosteroids (methylprednisolone), imipenem, Fraxiparin	Antibiotics (ceftriaxone from the first day), corticosteroids (methylprednisolone – from second day), imipenem, Fraxiparin



**Figure 7.** Patients of group two infected with the virus SARS COVID-19 who have also suffered from other diseases



**Figure 8.** Patients of group three infected with the virus SARS COVID-19 who have also suffered from other diseases. The patients of the third group were children complaining of headaches, vomiting and temperature



**Figure 9.** Patients of group four infected with the virus SARS COVID-19 who have also suffered from other diseases

methasone – for 5 days), corticosteroids (methylprednisolone – for 5 other days), imipenem, and Fraxiparin but when the general conditions deteriorated, a palliative care protocol was started (Table III).

The laboratory examination findings of patients from group three were ESR 100 mm/h, leukocytes  $18.6 \times 10^3/\text{mm}^3$ , erythrocytes  $4.32 \times 10^6/\text{mm}^3$ , hemoglobin 10.9 g/dl, thrombocytes  $183 \times 10^3/\text{mm}^3$ , lymphocytes 9.1%, monocytes 2.4 l, and granulocytes 88.5%. Level of urea 4.62 (normal range: 1.70–8.30), creatinine 113.9 (normal range: 53–115), AST 39 (normal range: 2–37), ALT 36 (normal levels: 3–41), iron 17  $\mu\text{mol/l}$  (normal range: 11.6–31.3), D-dimer 156.9 (normal range: 255), CRP 156.8 mg/l (normal range: 0–6), eGFR 43.19 ml/min/1.73 m<sup>2</sup> (Table II).

By further examination of the patients of group three during hospitalization by chest radiography we diagnosed bilateral bronchopneumonia; by abdominal ultrasound: hydronephrosis grade 1, they also had facial nerve paralysis and diminished renal function (Figure 8). The patient was treated with antibiotics (vancomycin, dexamethasone – for 3 days), corticosteroids (methylprednisolone), imipenem, and Fraxiparin but after the general conditions deteriorated, a palliative care protocol was started (Table III).

The last (fourth) group comprised children who suffered from dermatitis, temperature, and vomiting. The laboratory examination findings of patients of this group were ESR 50 mm/h, leukocytes  $10.01 \times 10^3/\text{mm}^3$ , erythrocytes  $3.89 \times 10^6/\text{mm}^3$ , hemoglobin 13.0 g/dl, thrombocytes  $288 \times 10^3/\text{mm}^3$ , lymphocytes 12.7%, monocytes 8.3 l, and granulocytes 79%. Level of urea 4.62 (normal range: 1.70–8.30), creatinine 113.9 (normal range: 53–115), AST 39 (normal range: 2–37), ALT 36 (normal levels: 3–41), iron 17  $\mu\text{mol/l}$  (normal range: 11.6–31.3), D-dimer 156.9 (normal range: 255), CRP 113 mg/l (normal range: 0–6), eGFR 67.79 ml/min/1.73 m<sup>2</sup> (Table II). By further examination

of the patients of this group during hospitalization by chest radiography, we diagnosed bilateral bronchopneumonia; by abdominal ultrasound: hydronephrosis grade 1 (Figure 9). The patient was treated with antibiotics (ceftriaxone from the first day), corticosteroids (methylprednisolone from the second day), imipenem, and Fraxiparin but when the general conditions deteriorated, a palliative care protocol was started (Table III).

## Discussion

Until April 2020, infection with SARS COVID-19 in children was asymptomatic or with mild symptoms. Herein we have reported about four groups of patients who were treated in our clinic. These patients had symptoms suggestive of a multi-system, hyper-inflammatory syndrome that are similar to some symptoms in inflammatory processes seen in children. The new symptoms have been called the multisystem inflammation syndrome in children related to COVID-19. The COVID-19 pandemic situation is continuing and the number of cases is the same or some days higher; health-care providers should continue to monitor the ill children and to identify children with COVID-19 symptoms, such as lung hyper-inflammation, shock, and cardiac problems [4, 10, 12–16]. All our patients from four groups were tested for SARS-COVID-19 and all were positive.

The sample represented males and females equally, 50/50, and the average age of the patients was 6 years. If we consider such results, there is no specific impact on a specific gender.

Patients of the first group (1 month to 2 years old) and the second group (2–6 years old) were most affected because they tend to be less aware of the virus; this is because their immature immune systems and smaller airways make them more likely to develop breathing issues with respiratory virus infections, even though their symptoms were less severe than those observed in other group ages.

As of January 2021, 69 patients were hospitalized in our clinic, whereas the highest numbers of cases were recorded during October and November. Such findings support the fact that during those months the schools were open and certain measures were lifted by the government of our country. According to the study the most common diagnoses among all age groups are bronchopneumonia, Status febrilis (7 cases), and acute gastroenteritis, so this shows that there is no significant presence in a specific age group.

Finally, based on the medical records of 4 patients who had multisystemic inflammatory syndrome, 3 adolescents and 1 child had bronchopneumonia, systemic problems with Status febrilis fever, exhaustion and kidney function insufficien-



cy, high levels of D-dimer, and other diagnoses. They were treated with antibiotics, imipenem, corticosteroids, and Fraxiparin. The patients had no record of any past diseases and after finishing the treatment for COVID-19 they were released home in a stable condition.

### Conflict of interest

The authors declare no conflict of interest.

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