Pediatric infected with 2019 coronavirus: A referral center study on 21 pediatrics in north of Iran

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Abstract

Background: COVID-19, a novel pneumonia associated with the 2019 coronavirus infected pneumonia suddenly broke out in the world. The aim of this study is to analyze and summarize the clinical characteristics of pediatric patients with COVID-19. Patients and method: Twenty-one patients confirmed by clinical and laboratory findings from 20 February to 19 April, 2020 in North of Iran were included. Demography information, clinical, laboratory and radiological findings, and treatment strategies of patients were evaluated. All statistical analyses were performed using SPSS version 13.0 software. Results: Body temperature was [?]38ºC in 11(52.4%) patients. Eleven (52/3%) patients had tachypnea and 4(19%) of them developed tachycardia. Six (30%) of patients suffered from a decrease in white blood cells. Also a decrease in creatine phosphokinase level was seen in 1(33%) of patients. Nine CT scans (42.85%) demonstrated a halo sign. Seven patients' (33.33%) CT scans showed a patchy infiltration. Nine (42.85%) CT scans had bilateral crazy-paving pattern. 38.1% of patients were treated with chloroquine and oseltamivir. Four (19.04%) patients died and 17(80.95%) patients were discharged from the hospital. One of the patients who died suffered from acute respiratory distress syndrome. Conclusion: We found out that pediatrics, especially boys are more susceptible to COVID-19 and it is more common in school-age and toddlers. Manifestations are milder than adults and severe cases associated with underlying disease. The effectiveness of medications used in the treatment of this disease need further study.

Title page

Pediatric infected with 2019 coronavirus: A referral center study on 21 pediatrics in north of Iran

Running title: Pediatric and COVID-19 infection

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ABSTRACT

Background : COVID-19, a novel pneumonia associated with the 2019 coronavirus infected pneumonia suddenly broke out in the world. The aim of this study is to analyze and summarize the clinical characteristics of pediatric patients with COVID-19. **Patients and method:** Twenty-one patients confirmed by clinical and laboratory findings from 20 February to 19 April, 2020 in North of Iran were included. Demography information, clinical, laboratory and radiological findings, and treatment strategies of patients were evaluated. All statistical analyses were performed using SPSS version 13.0 software.**Results** : Body temperature was [?]38^{o}C in 11(52.4%) patients. Eleven (52/3%) patients had tachypnea and 4(19%) of them developed tachycardia. Six (30%) of patients suffered from a decrease in white blood cells. Also a decrease in creatine phosphokinase level was seen in 1(33%) of patients. Nine CT scans (42.85%) demonstrated a halo sign. Seven patients' (33.33%) CT scans showed a patchy infiltration. Nine (42.85%) CT scans had bilateral crazy-paving pattern. 38.1% of patients were treated with chloroquine and oseltamivir. Four (19.04%) patients died and 17(80.95%) patients were discharged from the hospital. One of the patients who died suffered from acute respiratory distress syndrome. **Conclusion** : We found out that pediatrics, especially boys are more susceptible to COVID-19 and it is more common in school-age and toddlers. Manifestations are milder than adults and severe cases associated with underlying disease. The effectiveness of medications used in the treatment of this disease need further study.

INTRODUCTION

COVID-19 (novel 2019 coronavirus) is currently causing a global pandemic[1]. In humans, COVID-19 mostly causes respiratory and gastrointestinal symptoms[2] and its clinical manifestations range from a common cold to more severe diseases such as bronchitis, pneumonia, severe acute respiratory distress syndrome, multiorgan failure, and even death [2]. COVID-19 has fewer symptoms and is less likely to affect children, and is less severe in compared with adults [3]. COVID-19 is also associated with much lower mortality rates in children compared with adults. The evidence shows that children who suffered from COVID-19 are less likely to be symptomatic or develop severe symptoms. Compared with adults, children more often have gastrointestinal symptoms, and most children with COVID-19 had fever [4]. The majority of children infected by COVID-19 documented household contact. Neonates who were born to mothers with COVID-19 infection also were in danger[4]. In this prospective study, we collected the demography information, clinical, laboratory, and radiological findings, as well as treatment strategies with a focus on infections in pediatrics

2. PATIENTS AND METHODS

Twenty-one pediatric patients with COVID-19 infection confirmed by clinical and laboratory findings from 20 February to 19 April, 2020 in Children's Hospital (Rasht/Iran) were included in this study. All the patients are in accordance to the "Diagnosis and Treatment Protocol for COVID-19 (Fifth Revised Edition)" distributed by the National Health Commission[5]. The protocol for this retrospective study was approved by the Ethics Committee of Guilan University of Medical Sciences (IR.GUMS.REC.1399.028). Then, demography information, clinical, laboratory and radiological findings, and treatment strategies of pediatrics patients with COVID-19 were evaluated. The demography information include contact history, previous history, travel history over the last 2 weeks, contact history with the suspected person, contact history with definite positive person, hospital visits or hospitalizations history over the last month, influenza vaccine history, routine vaccination history, underlying disease, using corticosteroid over the last month, chemotherapy or immunosuppressive drugs over the last 3 months, antibiotic consumption over the past two weeks, types of antibiotics before administration. The hospital stays were updated to 20 June 2020. The chest computed tomography (CTs) was obtained from majority of subjects. Two experienced pediatric radiologists reviewed

the CT images as some ground-glass opacities, consolidations with surrounding halo sign, nodules, fine mesh shadow, pleural effusion, lymphadenopathy, unilateral or bilateral, subpleural/non-subpleural, and residual fiber strips. To confirm the existence of COVID-19 RNA, pharyngeal and nasopharyngeal swab samples of the subjects were collected and identified by a reverse transcription, polymerase chain reaction. All statistical analyses were performed using SPSS (Statistical Package for the Social Sciences) version 13.0 software (SPSS Inc). Categorical variables were described as frequency rates and percentages, and continuous variables were described using median and interquartile range (IQR) values. Normally distributed continuous variables were presented as means with standard deviations (SD). Comparison of the differences between the two groups was conducted using the t -test or Chi-square test. Variables with a two-tailed$P$ -value<0.05 were considered statistically significant.

RESULTS

Demography information

Out of 21 pediatric participants with COVID-19, 12 patients were young males 12(57.1%) and nine patients were young girls 9(42.9%) (Table 1). The mean age of pediatric patients with COVID-19 was 91.5+-68.38 months (Table 1). Four pediatric patients 4(19.4%) had an identified history of close contact with suspected COVID-19-diagnosed family members. Five pediatric patients 5(23.8%) had had a history of hospital visits or hospitalizations over the last month. We demonstrated two pediatric patients 2(9.5%) who had asthma and two pediatric patients 2(9.5%) who had malignancy (Table 1).

clinical finding Regarding complications (Table 2), 11(52/3%) pediatric patients with COVID-19 presented with tachypnea. Among all patients 4(19%) of them developed tachycardia. However, two (9%) of them had bradycardia. About, 2 (9.5%) of pediatric patients with COVID-19 suffered from fatigue. Out of 21 pediatric patients, 8(38.1%) and 4(19%) patients suffered from dry and wet cough, respectively. None of the patients complained about sputum during coughing. Four out of 21(19%) patients complained about diarrhea and nausea during the disease. This study also showed that vomiting existed in 8 (38.1%) pediatric patients with COVID-19 (Table 2). Most common symptoms in pediatric patients with COVID-19 were fever 11(52.4%), cough 7(33.3%), weakness 5(23.8%), and discomfort in breathing 5(23.8%) (Table 2). On the comorbidity, most patients suffered from the acute respiratory distress syndrome (ARDS) and the acute kidney injury (AKI) as the ARDS was shown in 3(14.3%) of pediatric patients with COVID-19 (Table 2).

Laboratory finding

The RT-PCR test was performed on 18 patients, which RT-PCR test results was shown positive for 17 patients (81%) (Table 3). The mean value of laboratory findings was estimated as follows; white-blood-cells (WBC) count was 8460+-6438x109/L (Table 3). Six (30%) of patients suffered from a decrease in white blood cells (Table 3). This study shows lymphocytes and polymorph nuclear leukocytes (PMN) count were 28±1963 ($\times 10^{9}$/L), and 64±19.31 ($\times$109/L), respectively. In this study, platelets count of pediatric patients with COVID-19 was 152290±78030.48 ($\times$109/L). The hemoglobin serum levels of pediatric patients with COVID-19 was 12.33±5.54 (g/L). In addition, the mean value of blood urea nitrogen (BUN) was 24±4796 (mg/dL). The creatinine levels of serum were 0.97±0.99 (mg/dL). In addition, the serum electrolytes levels including potassium (K), sodium (Na) and calcium (Ca) were 4.57±1.14 (mmol/L), 131.84±30.53 (mmol/L) and 8.55±1.56 (mg/dL), respectively (Table 3). This study shows that coagulation screening tests values were 14.55±1.46 (s) for prothrombin time (PT), and 37.5±9 (s) for partial thromboplastin time (PTT). The findings revealed that the mean international normalized ratio (INR) was 1.26±0.21 pediatric patients with COVID-19. Serum bilirubin levels were 0.9±0.84 (mg/dl) (direct bilirubin), and 1.65±0.77 (µmol/L) (total bilirubin). Two (100) of patients suffered from direct bilirubin >0.2 (Table 3). Alanine aminotransferase (ALT) and aspartate transaminase (AST) were 28.08±21.1 (U/L) and 46.33±24.21 (U/L), respectively (Table 3). The creatine phosphokinase (CPK) was 190.67±162.58 (units/L), and the lactate dehydrogenase (LDH) was 698.71±336.18 (U/L) in pediatric patients with COVID-19. In this study a decrease in CPK level was seen in 1(33%) of patients (Table 3). Also 3 (42%) of patients had high levels of LDH (Table 3). Regarding with arterial blood gas (ABG), statue was exactly measured and recorded in pediatric patients with COVID-

19. Based on ABG findings; PH of pediatric patients with COVID-19 was 7.32±0.11, $PaCo_2$ of patients was 38.91±8.57, PaO_2 was 72.80±28.92, and finally $HCO_3$of patients was 20.52±5.17 (Table 3).

Radiology findings

Chest X-Ray

Chest x-ray (CXR) of five pediatric patients with COVID-19 (23.81%) out of 21 patients who were included in this study showed peripheral-airspace opacities (Table 4). The study showed that the CXR in five pediatric patients with COVID-19 (23.81%) revealed ground-glass opacity characterized by hazy-increased attenuation that did not obscure bronchial and vascular margins of the lung (Table 4). As we showed in Table 4, 7(33.33%) five pediatric patients with COVID-19 had lung consolidations. A few of pleural effusions appeared in six (28.57%) pediatric patients with COVID-19. This study also demonstrated that 4(19.05%) of the pediatric patients with COVID-19 had patchy infiltrations. Meanwhile, cavitation was observed in four (19.05%) of pediatric patients with COVID-19. In addition, 3(14.28%) of the pediatric patients with COVID-19 showed extensive peripheral lymphadenopathy (Table 4).

Lung CT scans

The most prevalent findings in lung CT scans were ground-glass opacity and cavitations (66.66%) (Table 4). Whereas, nine CT scans (42.85%) demonstrated a halo sign (Table 4). More than half of these patients (57.14%) had peripheral-airspace opacities in lung CT scans. Ten patients' CT scans revealed pleural effusion (47.62%) (Table 4). Seven patients' CT scans (33.33%) revealed patchy infiltrations and bilateral crazy paving pattern was revealed in nine CT scans (42.85%)(Table 4). Eight CT scans (38.09%) showed peripheral lymphadenopathy White lung appearance. Centro lobular nodule were observed in six patients. (28.57%). Lung consolidation and revers halo sign appearance were less common with the incidence of 28.7% and 14.28% respectively (Table 4).

Treatment strategies This study showed that nine pediatric patients 9(57.1%) had a history of antibiotics consumption over the past two weeks (Table 5). In the treatment of pediatric patients with COVID-19, chloroquine, oseltamivir and Kaletra (Lopinavir / Ritonavir) were used in 8(38.1%), 8(38.1%) and 6(28.6%), respectively (Table 5). This study shows that 95.2% of pediatric patients with COVID-19 took antibiotics repeatedly. During the treatment of pediatric patients with COVID-19, 2(9.5), 5(23.8), 3(14.33), 1(4.8) and 1(4.8) of patients consumed azithromycin ceftriaxone, vancomycin, ceftriaxone, clindamycin, ceftriaxone, vancomycin, ceftriaxone and azithromycin, respectively (Table 5). Based on the results of our study, 6(28.6%), 2(9.5%) and 2(9.5%) of pediatric patients with COVID-19 were treated by oxygen with mask, oxygen with hood and intubation, respectively (Table 5). In current study, 4(19.04%) pediatric patients with COVID-19 died and 17(80.95%) patients were discharged from the hospital. One of the patients who died suffered from acute respiratory distress syndrome (ARDS).

Discussion

COVID-19 viral pneumonia is an acute respiratory infectious disease caused by the novel coronavirus (SARS-CoV-2). The onset of the COVID-19 could be asymptomatic (4%), but often as a mild-upper respiratory viral illness (51%), with a lower incidence of pneumonia (39%) and rarely severe cases such as hypoxia, respiratory distress (5%), occurs as ARDS or multi-organ involvement (<1%)[6]. Because the clinical presentation of pediatric patients with COVID-19 is vague or similar to some respiratory infections, it is essential for pediatricians to have more information and also consider COVID-19[7]. In this study, with the mentioned aim, demographic, clinical, para clinical and imaging information, treatment and its results in hospitalized children with definite and probable diagnosis of COVID-19 were reviewed.

As we found out in this study, the COVID-19 was more common in school-age infants and toddlers (Table 1). We realized that the COVID-19 was also more common in young males, which may indicate that young males at school are more exposed to the COVID-19 and are more likely to be infected with COVID-19. We believe that the age of the pediatrics plays an important role in the incidence of COVID-19. This means that older pediatrics have more social contact with other people and are more likely to develop COVID-19. Huan

Wu and colleagues found that common large gender of pediatric patients with COVID-19 (59.5 %) were of the young girls[8]. Ansel Hoang and colleagues came to realize that 55.6% of COVID-19 children were males [9]. Remarkably, out of 21 patients 12 had a previous history of contact with COVID-19 infection. In other words, about 50% of pediatric patients with COVID-19 had no previous contact history, which may indicate that pediatric patients with no history of contact may be susceptible to COVID-19 infection. Ansel Hoang and colleagues found that 75.6% of pediatric patients with COVID-19 exposure were infected via family members[9]. In addition, eight out of 21 patients had a previous history of congenital or acquired diseases, which may indicate that pediatrics with underlying diseases such as asthma and malignancy may be more prone to more severe COVID-19 infection. Ansel Hoang and colleagues found that immunocompromised pediatrics (30.5 %) or pediatrics with respiratory (21.0 %), cardiac disease (13.7%) comprised the largest subset of COVID-19 pediatrics with underlying disease[9]. This study showed that fever, dyspnea or rapid breathing, cough and nausea and vomiting were the most common and the main complaints of pediatric patients with COVID-19. Our study focused on the more severe COVID-19 of hospitalized patients. This study is not comparable to asymptomatic or milder cases of COVID-19, because asymptomatic or milder patients are not hospitalized. The most common symptoms in pediatric patients with COVID-19 were fever (40.5%), dry cough (44.6%), vomiting or diarrhea (21.6%), and headache (3.4%)[8]. Ansel Hoang and colleagues found that fever (71.4%), cough (57.1%), and dyspnea (28.6%) comprised the largest clinical characteristics among children with COVID-19 disease[9]. Also, this study showed that fever, cough, dyspnea and weakness were the most common symptoms in pediatric patients with COVID-19. Ansel Hoang and colleagues found that the most common symptoms in pediatric patients with COVID-19 were asymptomatic (19.3%), fever (59.1%), cough (55.9%), myalgia, fatigue (18.7%), sore throat (18.2%), shortness of breath, dyspnea (11.7%), abdominal pain, diarrhea (6.5%), and rhinorrhea, nasal congestion (20.0%)[9]. The most common clinical signs on examination were fever 11(52.4%), cough 7(33.3%), weakness and lethargy 5(23.8%), and discomfort in breathing 5(23.8%). At present, there is no certain antiviral drug for covid19 virus treatment in children. However, some antiviral and anti-inflammatory agents may have clinically useful effects in reducing the manifestations of covid19 virus due to overresponse of immune system through interleukins and other inflammatory agents releasing[10,11]. Chloroquine as a potential pharmacologic agent against covid19 has immunomodulatory effects by inflammatory cytokines inhibition [12] In this study, 38.1% of pediatric patients with COVID-19 were treated by chloroquine. Combination Ritonavir with Lopinavir improved patients' symptoms and reduced the need for intensive care unit in severe cases[13].28.6% were treated by Kaletra:Lopinavir /Ritonavir, and 38.1% were treated by oseltamivir. There is no exact evidence for efficacy of these drugs above. In this study, 14.33%of pediatric patients with COVID-19 received vancomycin and ceftriaxone during treatment. 23.8% recieved ceftriaxone. 14.33% of pediatric patients with COVID-19 received vancomycin and ceftriaxone. Oxygen with masks was used in 28.6% of pediatric patients with COVID-19. 4.8% of pediatric patients with COVID-19 also used oxygen with hood intubation. In current study, 4(19.04%) pediatric patients with COVID-19 died and 17(80.95%) patients were discharged from the hospital. One of the patients who died suffered from ARDS.

Conclusion

We found out that pediatrics, especially boys are more susceptible to COVID-19 and it is more common in school-age and toddlers. Manifestations are milder than adults and severe cases associated with underlying disease. The effectiveness of drugs in the treatment of this disease needs further study.

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Conflicting interests

The authors have declared that no competing interests exist.

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Informed consent

Written informed consent was obtained for the anonymized information to be published.

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