Characteristics of Children with Coronavirus Disease-2019 From The Pediatric Emergency Room

emel berksoy[1], Ali Kanik[2], Alper Çiçek[1], Şefika Bardak[1], Gülşah Demir[1], Pelin Elibol[1], Nisel Yılmaz[1], Tuğçe Çelik[1], Gamze Gökalp[2], and Dilek Yilmaz Çiftdoğan[2]

[1]Izmir Tepecik Training and Research Hospital
[2]Izmir Katip Celebi Universitesi

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Abstract

We describe the demographic, clinical, and laboratory characteristics of children with COVID 19 in comparison with those of not-laboratory-confirmed cases. We conducted a cross-sectional study on the epidemiological, clinical, radiological, and laboratory characteristics, and outcome of 422 children (aged 0–18 years) with suspected and confirmed COVID 19 admitted to the pediatric emergency department from March 23rd to July 23rd, 2020. Of the 422 children with suspected COVID-19 included in this study, COVID-19 was PCR-confirmed in 78 (18.4%). Fever (51.2%) and cough (43.5%) were the most prominent symptoms in children with confirmed cases. The clinical status of the patients with confirmed COVID-19 was significantly milder than that of those with suspected COVID-19. The proportion of COVID-19 pneumonia cases was 44.4%, 5.5%, 18.7%, and 8.5% for the age groups of [?] 1, 2–6, 7–12, and [?] 12 years, respectively. Of the 422 children, 128 (30.3%) underwent nasopharyngeal PCR testing for other respiratory viral pathogens; 21 (16.4%) were infected with viral pathogens other than severe acute respiratory syndrome-related coronavirus-2. Only one patient (4.7%) with confirmed COVID-19 had coinfection with respiratory syncytial virus and rhinovirus. The areas under the receiver-operating characteristics curves were 0.812 for WBCs, 0.752 for neutrophils, 0.717 for lactate dehydrogenase, and 0.708 for lymphocyte for predicting COVID-19 (p [?] 0.001). Fever and cough or other clinical symptoms or signs should not be considered hallmarks of COVID 19. In this study, the WBC, neutrophil, and lymphocyte counts were predictive of COVID-19 positivity.

Clinical and laboratory characteristics of children with coronavirus disease-2019 from the pediatric emergency room of a tertiary research hospital in turkey

Ass. Prof. MD, Emel BERKSOY[1], Ass.Prof. MD, Ali KANIK[2], MD, Alper ÇİÇEK[1], MD, Şefika BARDAK[1], MD,Pelin ELİBOL[1], MD,Gülşah ELİBOL[1], Ass.Prof. MD, Nisel YILMAZ[3], MD,Tuğçe NALBANT[1], MD, Gamze GÖKALP[1], Prof.Dr. MD, Dilek YILMAZ ÇİFTDOĞAN[4]

[1]Health Science University, Tepecik Education and Research Hospital, Pediatric Emergency Department, İzmir TURKEY

[2]İzmir Katip Çelebi Üniversity, Faculty of Medicine, Pediatrics A.D. TURKEY

[3]Health Science University, Tepecik Education and Research Hospital, Microbiology Department, İzmir TURKEY

[4]İzmir Katip Çelebi Üniversity, Faculty of Medicine, Pediatric İnfection Department, TURKEY

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Corresponding author:

Ass.Prof.Dr Emel Berksoy,

Health Science University,

Tepecik Education and Research Hospital,

Pediatric Emergency Department

GSM: 0905052520655,*emelberksoy@hotmail.com*

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Introduction

Coronavirus disease-2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), had affected more than 28 million people worldwide by September 9th, 2020 [1].

Although it is constitutively defined in adults, studies from China, Italy, and the United States revealed that it was also seen in the pediatric age group with a rate of 1.2% to 2% during the first peak of the pandemic [2,3]. The largest pediatric case series reported in the literature revealed that the majority of children and adolescents infected with SARS-CoV-2 had a milder disease course and a very low fatality rate, unlike infected adults. Accordingly, 5% of pediatric cases were severe and 0.6% of them had critical COVID-19 disease [4]. After the identification of the first pediatric COVID-19 case on January 20th, 2020, although single cases and case series were reported in the literature, the epidemiological and clinical features of COVID-19 in pediatric patients are still not fully defined [5].

Additionally, the differential diagnosis of COVID-19 disease is difficult, because the symptoms (cough, fever, respiratory distress) caused by SARS-CoV-2 are similar to those of infections caused by other respiratory pathogens in children [6]. Other viral respiratory pathogens and seasonal influenza may be present in the community and cause co-infections during the pandemic[7]. One fifth of patients with COVID-19 have co-infections [8]. Moreover, as the pandemic continues, the number of COVID-19–infected children is increasing

gradually. However, the main complaint in the majority of children admitted to emergency rooms is respiratory tract symptoms such as cough and fever. Therefore, clarifying the clinical spectrum and laboratory characteristics of COVID-19 in children can assist in evaluating potential COVID-19 patients in the absence of rapid antigen tests for SARS-CoV2.

We determined the demographic, clinical, and laboratory characteristics of suspected and confirmed COVID-19 pediatric patients who were admitted to the pediatric emergency room during the first 4 months of the pandemic. We also evaluated coinfection with other community-acquired respiratory tract pathogens.

Materials and Methods

Study population and data sources

From March 23rd to July 23rd, 2020, we conducted a cross-sectional study of the epidemiological, clinical, and laboratory characteristics of 422 children (aged 0–18 years) with suspected and confirmed COVID-19 admitted to the pediatric emergency room of Health Science University, Tepecik Training Hospital, Turkey.

We examined all patients with cough, fever, and respiratory distress at admission and for epidemiological purposes, and patients with a history of close contact with an infected individual or whose family member had fever and cough or respiratory distress for the last 14 days or a history of hospitalization for respiratory tract infection for the last 14 days. Any patient with lobar consolidation suggesting bacterial pneumonia was excluded.

Gender, age, epidemiologic history, symptoms, signs, clinical status, laboratory and radiologic findings, diagnosis (suspected or confirmed), other respiratory pathogens, comorbidities, and outcome data (follow-up at home, admission to wards or intensive care unit) were recorded using a standardized case report form. Laboratory examinations included complete blood count (CBC), C-reactive protein (CRP), procalcitonin (PCT), measurement of liver, muscle, myocardial, and renal functions, and coagulation parameters including the levels of D-dimer and fibrinogen.

The study population was subgrouped into the suspected and confirmed groups based on the result of a SARS-CoV-2 PCR test. One respiratory sample for COVID-19 was obtained from each patient. A second respiratory test sample was not obtained from patients with clinical and imaging findings that lead to suspicion of COVID-19. Such patients were included in the suspected (COVID-19 negative) group.

Case definitions and procedures

We followed the periodic updates of case definitions in the national guidelines of the T.C Ministry of Health. Respiratory samples were obtained from all suspected cases. The diagnosis of COVID-19 is routinely based on the identification of SARS-CoV2 RNA in respiratory secretions (such as nasal and pharyngeal swabs) by quantitative real-time reverse transcriptase-polymerase chain reaction (rRT-PCR) assay (Bio-Speedy, Turkey). During the study period we had no blood test for SARS-Cov-2. We performed PCR tests using nasopharyngeal swabs for other viral and bacterial respiratory pathogens (RSP) to detect concomitant infections. Influenza virus type A and B, respiratory syncytial virus type A/B, parainfluenza virus types 1–4, coronaviruses (229E, NL63, and OC43), metapneumovirus, rhinovirus, enterovirus, adenovirus, parechovirus, and bocavirus were detected by a multiplex PCR method (Respiratory Pathogens Panel Kit v. 4, Bosphore, Anatolia, Turkey) in nasopharyngeal swab samples from children.

During the study period, other RSP PCR tests were temporarily suspended to alleviate the workload of the laboratory. For this reason, we preserved the RSP swab samples at -80°C for 2 months.

The clinical status of COVID-19 comprised asymptomatic infection, upper respiratory tract infection (URTI), pneumonia, and critical cases. Asymptomatic infection was defined as the absence of clinical and radiologic signs and symptoms with a positive SARS-CoV-2 PCR test. Patients with URTI infection have running nose, fever, malaise, sneezing, cough, nausea, vomiting, and diarrhea but no auscultatory abnormalities. Clinical (frequently fever and cough, auscultatory findings such as wheezing, rhonchus, and crackles but no hypoxemia) and subclinical (no clinical signs and symptoms but radiological lung lesions) pneumonia

were included. Severe and critical cases were defined as respiratory failure requiring mechanical ventilation (ARDS), dyspnea with an oxygen saturation of less than 92%, septic shock, or multiple organ failure.

Chest computed tomography (CT) without contrast material was performed as necessary using a Siemens Go Up with a 1 mm slice thickness and 1 mm increments. If the chest X-ray was normal, chest CT was performed with a 2 mm slice thickness to reduce the risk of excessive radiation.

Statistical analysis

Means, standard deviations, medians, interquartile ranges (IQR), and percentiles were calculated for discrete and continuous variables. The homogeneity of the variances, a prerequisite of parametric tests, was checked by Levene test. The assumption of normality was tested by Shapiro–Wilk test. Student's t -test was used to compare two groups when the parametric test prerequisites were fulfilled; the Mann–Whitney U-test was used otherwise. A chi-squared test was used to determine the relationships between two discrete variables. The cut-off points for the parameters were evaluated by receiver operating characteristics (ROC) analysis. The area under the ROC curve (AUC), sensitivity, and specificity values were calculated. The data were analyzed using SPPS v. 25 (IBM Corp., Armonk, NY). A p-value of < 0.05 was taken as indicative of statistical significance.

Ethics

This study was approved by the T.C. Ministry of Health and Ethics Committee of the Tepecik Education and Training Hospital (2020/7-10). Written informed parental/patient consent was obtained from each patient before enrollment in the study.

Results

Demographic and epidemiological characteristics

A total of 422 children with suspected COVID-19 were recruited to the study. Of these, 78 (18.4%) patients were identified as laboratory confirmed COVID-19 cases. The median age of confirmed COVID-19 cases was 132.6 months (IQR, 136.1 months; age range, 1 day to 219 months) and the median age of the confirmed and COVID-19–negative groups differed significantly (51.9 [IQR, 17.3] months). Among the patients, 243 (57.6%) were boys and 179 (42.4%) were girls; the difference was not significant. Regarding age, nine (11.5%) patients were COVID-19 positive and 77 (22.4%) were COVID-19 negative among infants and 35 (45%) patients were COVID-19 positive and 77 (22.4%) were COVID-19 negative among children aged over 12 years ($p < 0.001$) (Table 1).

Regarding exposure history, 61 (81.4%) patients with confirmed COVID-19 were household contacts of adults and 88 (25.5%) COVID-19–negative cases had a history of contact with a COVID-19–positive adult at home. Among COVID-19 positive patients, 17 (18.6%) were sporadic (Table 1).

Clinical characteristics and outcome

Only three patients with confirmed COVID-19 had an underlying disease. Fever (51.2%) and cough (43.5%) were the most common symptoms in children with confirmed COVID-19. The less common symptoms included myalgia, weakness, headache (21.7%), sore throat (8.9%), nausea-vomiting (6.4), and diarrhea (6.4). Rhinorrhea (7.2%) was seen only in the COVID-19–negative group ($p = 0.0014$) (Table 1). The physical signs, clinical status, supporting management, and outcome measures of all patients are shown in Table 1. The frequency of pneumonia was 44.4%, 5.5%, 18.7%, and 8.5% in the age groups [?] 1, 2–6, 7–12, and [?] 12 years, respectively (Figure 1).

Radiological findings

The chest X-ray and chest CT findings of the patients are shown in Table 1.

Laboratory findings

Of the 422 children, 128 (30.3%) underwent nasopharyngeal PCR testing for RSP; 21 (16.4%) were infected with other RSPs—seven with rhinovirus, five with metapneumovirus, three with adenovirus, two with bocavirus, two with RSV, and two with both RSV and rhinovirus. In comparison, one (4.7%) patient with confirmed COVID-19 had coinfection with RSV and rhinovirus. The median values of laboratory parameters are shown in Table 2. The AUCs for COVID-19 positivity were 0.812 for WBCs, 0.752 for neutrophils, 0.717 for LDH, and 0.708 for lymphocytes (p [?] 0.001) (Figure 2). The sensitives, specificities, and cut-offs of these parameters are shown in Table 3.

Discussion

There are few data on pediatric patients with COVID-19. Clarifying the clinical, laboratory and radiographic characteristics of pediatric patients is important for differential diagnosis of COVID-19 from other respiratory viral respiratory pathogens, particularly in busy emergency departments. We report that some clinical and laboratory characteristics differed between suspected and confirmed COVID-19 in pediatric patients. The first COVID-19 case was reported in Turkey on March 13th, 2020. During the early months of the pandemic, we evaluated pediatric patients with suspicion of COVID-19 in the pediatric emergency room.

Among children with suspected COVID-19, 18.4% were confirmed to have COVID-19 by PCR test. This high rate is because children with a history of contact with COVID-19 were evaluated to confirm the diagnosis. Although the definition of suspected cases of COVID-19 has changed during the outbreak, children are typically infected by a sick or carrier parent or an adult family member. Of the 78 COVID-19–positive patients in this study, 81.4% had an adult household contact, similar to prior reports [9–11]. However, the route of transmission was not identified for 18.7% of the cases. We could not evaluate other transmission routes because schools were closed during the study period and none of the children had a history of hospitalization or foreign travel. Lu *et al* . [11]reported that the median age of 171 pediatric patients was 6.7 years (1 day to 15 years). Qin Wu *et al* . [12] reported that the median age of infected children was 6 years and almost half were aged 3–10 years. Dong [4] reported that the median age of patients with suspected and confirmed COVID-19 was 7 years. In this study, the median age of infected children was 11 years (1 day to 18 years), comparable with 2,572 COVID-19 cases in US children. Nearly half of the confirmed cases were more than 12 years of age, possibly because adolescents are more active and spend more time outside the home. The proportion of boys was slightly higher than that of girls, in agreement with previous epidemiological studies[4,11,12].

COVID-19 has a favorable clinical course and is typically mild in children. In this study, more than half of the confirmed cases were mild and one third were asymptomatic and admitted to the emergency room after a family member had been diagnosed with COVID-19. Of the 56 patients who presented with a family contact history and had no symptoms, 33 (58.6%) were COVID-19–negative by PCR. Almost half of the COVID-19 pneumonia cases were infants. Moreover, bronchopneumonia and severe illness were more frequent among PCR-negative patients.

Another issue to be considered is co-infection with other respiratory pathogens. Among the 422 patients, 21 (16.4%) of 128 children were infected with pathogens other than SARS-CoV-2; also, one (1.2%) of 78 children had coinfection with RSV and rhinovirus. That patient was 5 months of age and had a mild disease course without bronchopneumonia. These rates are lower than in prior reports [12–14]. This low co-infection rate may be because the sample sticks were stored at -80degC and examined later or because the incidence of other viral agents was low during the study period.

More patients in the suspected COVID-19 group had fever and cough than in the confirmed COVID-19 group. By contrast, the prevalence of fever and cough was high in all of the groups. Cough (43.5%) and fever (51%) were the most common symptoms in infected children. Briefly, our findings show that COVID-19 in children has a milder presentation than do other upper and lower respiratory tract diseases. This hampers the differential diagnosis of COVID-19 in practice. The most striking finding in terms of symptomatology is the absence of rhinorrhea in confirmed COVID-19 cases. This is not in agreement with the results of Lu [11], who reported nasal symptoms including rhinorrhea in 171 children with COVID-19. Larger studies are needed to clarify this important issue.

Most of the COVID–positive patients (89%) had normal chest radiography findings on admission. During the first months of the pandemic, we requested chest radiography for almost every patient with fever and cough. Only eight (10.9%) of the 73 PCR-positive patients who underwent chest x-ray had bilateral patchy infiltration. However, one third of the COVID-19–negative patients among those who underwent chest x-ray because of respiratory auscultation findings, fever, and cough had abnormal radiographic results. Of the 32 children who underwent chest CT, 93.7% did not have CT abnormalities or ground glass opacity. Only five (3.2%) of the 156 patients who underwent chest CT had abnormal findings compatible with COVID-19. Of them, three and two patients were negative and positive for SARS-CoV-2, respectively. Qin Wu *et al* .[12] reported that 12.6% of 37 cases showed ground-glass opacity on chest CT; by contrast, 28 cases showed nonspecific changes suggestive of pneumonia. The low rate of ground-glass opacity on CT may be because only 11 of the 78 infected patients had pneumonia. We performed radiographic examinations at admission to the emergency room. During the early stages of the disease, the chest X-ray findings may be normal [15]. Although unremarkable radiologic features of infected children have been reported by others, the role of chest CT in the diagnosis and management of children with COVID-19 needs to be clarified.

The laboratory findings of confirmed cases were different from those of suspected cases. The WBC, neutrophil, lymphocyte, and platelet counts were significantly lower in confirmed than in suspected cases. Viral respiratory infections can cause leucopenia, lymphopenia, and thrombocytopenia [16]. We found significant differences in all CBC parameters (WBC, neutrophil, lymphocyte, and platelet counts) and acute-phase reactants. Although we could not detect other respiratory agents in the suspected cohort, the respiratory disease and pneumonia were likely to have been caused by viral infection, because patients with lobar pneumonia or clinically suspicious for bacterial pneumonia were excluded. However, these findings may also be a result of the twofold higher frequency of bronchopneumonia in the suspected than in the confirmed COVID-19 cohort. The lymphocyte count is used to distinguish between patients with COVID-19 and other respiratory diseases and to evaluate clinical severity in adult patients[17,18]. Leukopenia and an increased serum CRP level have been reported in adult patients with COVID-19[5,19,20]. Prior reports have suggested considerable variance in the WBC counts in children [21–26]. Similarly conflicting results are extant for lymphocyte and platelet counts [26,27]. The LDH and CRP levels are high and positively correlated with COVID-19 severity in adult patients[28,29]. Similarly, elevations of muscle enzyme and d-dimer levels have been reported in severe pediatric cases[30]. In summary, the laboratory findings may be a result of the mild clinical course of our patients with confirmed COVID-19, none of whom were in critical condition. Finally, although the WBC, neutrophil, and lymphocyte counts were predictive of COVID-19 positivity, use of a WBC count threshold of [?] 6950 would mean that 30% of COVID-19–positive children would be missed.

Limitations

This study was limited by its focus on the pediatric emergency perspective, which prevented analysis of the treatment and follow-up of inpatients. We reviewed the clinical, laboratory, and radiological characteristics of the patients only at admission to the pediatric emergency room. Another limitation is that clinical and laboratory findings could not be compared between pneumonia cases in the suspected and confirmed cohorts because of the low rate of pneumonia in the COVID-19–positive group.

Conclusion

The clinical course of COVID-19 disease is similar but milder than that of other viral respiratory diseases. Considering the time needed for PCR diagnostic testing in the busy pediatric emergency room, especially during the influenza season, there is a need for differential diagnosis of COVID-19 in terms of clinical and laboratory features. Fever and cough or any other clinical symptoms or signs should not be considered a hallmark of COVID-19. Studies involving larger patient groups, including critical cases, are needed to identify laboratory parameters useful for the diagnosis, and predicting the severity, of COVID-19 in children.

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The English in this document has been checked by at least two professional editors, both native speakers of English.

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