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COVID-19

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Epidemiological, Clinical, Laboratory, and Imaging Features and Treatment of Children with COVID-19 in Kosovo

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Abstract

Background: This study aimed to identify the epidemiological, clinical, and laboratory features and treatment options of children with COVID-19 in Kosovo.

Methods and Results: This retrospective study analyzed the hospitalization records of all children at the Department of Pediatrics of the University Clinical Center of Kosovo diagnosed with COVID-19 between March 16 and December 31, 2022.

The diagnosis of SARS-CoV-2 infection was confirmed by PCR performed on nasopharyngeal or oropharyngeal swabs. The recorded case characteristics included age, sex, disease onset and diagnosis dates, and family and contact information. The collected clinical data comprised the duration and severity of symptoms and treatment. Laboratory parameters such as complete blood count, biochemical tests, chest X-ray, and chest computed tomography (CT) were also documented. One hundred and seventy-six pediatric COVID-19 cases were confirmed, with boys accounting for 59.65% (n = 105) and girls for 40.35% (n = 71). The median age was 62 months (1–210) for girls and 44.6 months (1-204) for boys. The most common symptoms were fever, cough, vomiting, diarrhea, and dyspnea. Twenty-six patients (14.77%) had underlying diseases among the total cases. Laboratory findings included elevated ESR in 39.77% of cases, high CRP level (38.63%), high WBC count (46.02%), and high AST level (56.25%). Chest X-rays were normal in the majority of patients. Pathological CT scans were found in 77.78% of cases. Antibiotics and rehydration were commonly used for treatment.

***Conclusion*:** This is one of the largest pediatric data sets about confirmed COVID-19 cases in Kosovo. Children of all ages appear to be susceptible to COVID-19. Based on available data, children have lower rates of hospitalization compared to adults with COVID-19, indicating that children may experience less severe illness than adults. However, research indicates that the incidence and frequency of cases have been progressively rising. **(International Journal of Biomedicine. 2024;14(3):417-422.)**

Keywords: SARS-CoV-2 • COVID-19 • pediatric patients

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Abbreviations

ADE, antibody-mediated enhancement; **CRP**, C-reactive protein; **CT**, computed tomography; **ESR**, erythrocyte sedimentation rate; **PCR**, polymerase chain reaction; **RBC**, red blood cells; **WBC**, white blood cells.

Introduction

On March 11, 2020, the World Health Organization (WHO) declared COVID-19 a global pandemic.[1] Since then, the severe acute respiratory syndrome coronavirus (SARS-CoV-2) has caused immense health, social, and economic upheaval worldwide. The research community has been actively generating a significant amount of data on COVID-19 pathogenesis, diagnosis, and management.

In the initial stages of the outbreak, it was observed that adults were more prone to the disease while children were relatively less vulnerable and made up a minor portion of the affected

population. This could be attributed to various factors such as a stronger innate immune response, healthier respiratory systems (as they are less exposed to cigarette smoke and air pollution than adults), virus-virus interaction and competition, age-related ACE-2 expression, ADE mechanism, and fewer underlying health conditions. However, as the outbreak progressed, the number of child infections increased significantly. [2,3]

The aim of this study was to identify the epidemiological, clinical, and laboratory features and treatment options of children with COVID-19 in Kosovo.

Materials and Methods

Data Acquisition

This retrospective study analyzed the hospitalization records of all children at the Department of Pediatrics of the University Clinical Center of Kosovo diagnosed with COVID-19 between March 16 and December 31, 2022. The diagnosis of SARS-CoV-2 infection was confirmed by PCR performed on nasopharyngeal or oropharyngeal swabs. Patient records and databases were used to extract clinical and laboratory data from the cases following their diagnosis. The recorded case characteristics included age, sex, disease onset and diagnosis dates, and family and contact information. The collected clinical data comprised the duration and severity of symptoms and treatment. Laboratory parameters such as complete blood count, biochemical tests, chest X-ray, and chest computed tomography (CT) were also documented.

Definitions

Determining disease severity was primarily based on clinical features and laboratory testing, with chest radiograph imaging being utilized if available. Disease severity was categorized into asymptomatic infection, mild, moderate, severe, or critical disease. The diagnostic criteria for each severity category were based on the classification proposed by the Society of Pediatrics of Chinese Medical Association:[4]

a) Asymptomatic infection: Patients did not exhibit any clinical signs or symptoms, but the 2019-nCoV nucleic acid test result was positive. Chest imaging results were normal. Patients from this group were not included in the study.

b) Mild: Patients showed symptoms of upper respiratory tract infection, with congestion of the pharynx, but no auscultator abnormalities during physical examination.

c) Moderate: Patients exhibited pneumonia, frequent fever, and cough, with some experiencing wheezing or rales. This group also included cases where chest computed tomography revealed subclinical lung lesions despite the absence of clinical signs and symptoms.

d) Severe/Critical: Patients in this category presented with obvious hypoxemia and required respiratory support (invasive or non-invasive), as well as intensive care.

Statistical analysis was performed using the statistical software package SPSS version 22.0 (SPSS Inc, Armonk, NY: IBM Corp). Baseline characteristics were summarized as frequencies and percentages. The one-way chi-squared test was used to test the statistical significance of differences in a one-way classification system. A probability value of $P<0.05$ was considered statistically significant.

Results

Demographics

One hundred and seventy-six pediatric COVID-19 cases were confirmed, with boys accounting for 59.65% (n=105) and girls for 40.35% (n=71). The median age was 62 months (1–210) for girls and 44.6 months (1-204) for boys. Among the cases, 38.93% (n=65) were under one year old, 13.65% (n=24) were between one and three years old, 20.45% (n=36) were between three and six years old, 15.34% (n=27) were between six and twelve years old, 5.11% (n=9) were between twelve and fifteen years old, and 8.52% (n=15) were older than fifteen years of age.

Clinical Findings

The most common symptom of the patients at the first visit was fever (n=115 [65.34%]) for a median of 2 days (1–3 days). The fever median was at 38.2°C (38.0–38.7 °C). The second most common symptom was cough (n=70 [39.77%]). The other common symptoms were vomiting (n=51 [28.97%]), diarrhea (n=39 [22.16%]), dyspnea (n=26 [14.77%]), febrile convulsions (n=16 [9.1%]), malaise (n=13 [7.38%]), chills (n=12 [6.82%]) and nasal discharge (n=10 [5.68%]). Less common symptoms were skin rush (n=6 [3.4%]) and sore throat (n=4 [2.27%]). Twenty-six patients (14.77%) cases had underlying diseases among the total cases. Nine (8.06%) cases with underlying conditions had asthma or obstructive lung disease (Table 1).

Table 1.

Epidemiological, clinical, and laboratory findings in children with COVID–19

Variable	Number	Percentage	χ^2- test *P*-value
Gender			
Boys	105	59.65	χ^2=6.56 *P*<0.05
Girls	71	40.35	
Total	176	100	
Age (years)			
0 – 1	65	36.93	χ^2=67.13 *P*<0.001
1 – 3	24	13.65	
3 – 6	36	20.45	
6 – 12	27	15.34	
12 – 15	9	5.11	
>15	15	8.52	
Total	176	100	
Clinical Findings			
Fever	121	68.8	χ^2=434.0 *P*<0.0001
Cough	70	39.8	
Vomiting	51	29.0	
Diarrhea	39	22.2	
Dyspnea	26	14.8	
Febrile convulsions	16	9.1	
Malaise	13	7.4	
Chills	12	6.8	

Table 1. (Continued)

Epidemiological, clinical, and laboratory findings in children with COVID–19

Variable	Number	Percentage	χ^2- test *P*-value
Nasal Discharge	10	5.7	
Skin rash	6	3.4	
Hypothermia	5	2.8	
Sore throat	4	2.3	
Laboratory Findings			
ESR *(*mm/hr)			
Normal ESR (0 – 10)	106	68.23	χ^2=7.36 *P*<0.01
High ESR (>10)	70	39.77	
Total	176	100	
WBC Count (× 10^3/μL)			
Low WBC (<4.5)	16	9.09	
Normal WBC (4.5–11)	79	44.89	χ^2=46.57 *P*<0.0001
High WBC (>11)	81	46.02	
Total	176	100	
Platelet count (× 10^3/μL)			
Low PLT (<150)	12	6.82	
Normal PLT (150-450)	154	87.5	χ^2=232.4 *P*<0.0001
High PLT (>450)	10	5.68	
Total	176	100	
CRP level (mg/L)			
Normal CRP (0.1 – 10)	108	61.37	χ^2=9.09 *P*<0.01
High CRP (>10)	68	38.63	
Total	176	100	
ALT level(U/L)			
Normal ALT (10-40)	137	77.84	χ^2=54.56 *P*<0.001
High ALT (>40)	39	22.16	
Total	176	100	
AST level(U/L)			
Normal AST (10-40)	77	43.75	χ^2=2.75 *P*>0.05
High AST (>40)	99	56.25	
Total	176	100	
D–dimer level (ng/mL)			
Normal (0 – 500)	133	75.57	χ^2=46.02 *P*<0.001
High (>500)	43	12.5	
Total	176	100	
X Ray			
Normal	120	75.95	χ^2=40.04 P<0.001
Pathological	38	24.05	
Total	158	100	
CT scan			
Normal	4	22.22	χ^{22}=65.00 *P*<0.001
Pathological	14	77.78	
Total	18	100	

Laboratory Findings

All patients tested positive on standard SARS-CoV2 PCR test performed on nasopharyngeal or oropharyngeal swabs. Laboratory data are presented in Table 1. Of 176 patients, 70 (39.77%) had an elevated ESR, with a mean value of 22.99 mm/hr (ranging from 0 to 110 mm/hr). High WBC count was found in 81 (46.02%) patients and low WBC count in 16 (9.09%) patients, with a mean value of 10.34 × 103/μL) (ranging from 0.6 to 32.9 × 103/μL) (*P*<0.0001). CRP level was elevated in 68 patients (38.63%), with a mean value of 17.96 mg/L (ranging from 0 to 188 mg/L). Patients who had symptoms showed higher CRP levels than those who were asymptomatic (*P*<0.078). Among the total cases, the ALT level was high in 39 (22%) patients. The AST level was elevated in 99 (56.25%) patients. Leukopenia and lymphopenia were observed more commonly in females without statistically significant differences (*P*=0.582). Thrombocytopenia was present in 12 (6.81%) patients, whereas thrombocytosis was present in 10 (5.68%). D-dimer value was elevated in 43 (24.43%) patients; a median value for all patients was 1194 ng/mL (ranging from 100 to 13.780 ng/mL).

Imaging

Chest X-ray was performed on 158 (89.77%) patients. Among these patients, 120 (75.94%) had normal results, whereas others (24.95%) had at least one pathologic finding. Chest CT was performed in 18 (10.22%) patients. Of these patients, 14 (77.78%) had pathological results with statistical significance (*P*<0.0001). The most common finding was one or more ground-glass opacities in 2 (50%) patients (Table 1).

Treatment and Outcome

Antibiotics were used to treat patients with COVID-19 in 159 (90.34%) cases (Table 2). Ceftriaxone was the most common antibiotic; it has been used in 123 patients (69.88%) as a single therapy.

Table 2.

Treatment modalities and length of stay.

Antibiotics therapy (alone or in combination) (n=159)		
Ceftriaxone	123	77.36%
Ceftriaxone with Amikacin	21	13.2%
Azithromycin	5	3.14%
Imipenem	4	2.52%
Erythromycin	2	1.26%
Ciprofloxacin	2	1.26%
Vancomycin	1	0.63%
Levofloxacin	1	0.63%
Total	159	100%
Rehydration		
Intravenous	167	94.9%
Oral	9	5.1%
Total	176	100.00%
Hospital stay, days		
Short stay (0 – 5)	113	64.20%
Medium length stay (6 – 10)	52	29.55%
Long stay (> 10)	11	6.25%
Total	176	100%

In 21 (11.93%) patients, ceftriaxone was combined with amikacin. Azithromycin (n=5, 2.84%), Imipenem (n=4 [2.27%]), Erythromycin (n=2 [1.14%]), Ciprofloxacin (n=2 [1.14%]), Vancomycin (n=1 [0.57%]) and Levofloxacin (n=1 [0.57%]) were used less frequently.

Intravenous rehydration was the most common mode employed in our patients (n=167 [94.9%]). Oral rehydration was used alone in 9 cases (5.11%) and in addition to intravenous rehydration in all other cases. All patients have successfully recuperated, except four, who unfortunately passed away. The majority of patients had short stays at the hospital (n=113 [64.20%]). Data on treatment modalities and length of hospital stay are presented in Table 2.

Discussion

As far as we are aware, this is the most extensive collection of pediatric data on COVID-19 in children in Kosovo that has been documented. Our study, with boys accounting for 59.65% (n=105) and girls for 40.35% (n=71) of the cases, corroborates the existing literature, which indicates that male cases slightly outweigh female cases. The results of the study revealed a noteworthy finding regarding the age of children infected with COVID-19. The highest number of confirmed cases was observed in children aged between 0 and 3 years, accounting for 52.56% of the total cases, with 38.93% being younger than one year. This finding conflicts with the outcome of Lu et al.'s study.[5] In a review by Ding et al.,[6] most pediatric COVID-19 patients were above 5 years of age. Karbuz et al.[7] found most cases between 6 and 12 years old. That being said, it is crucial to acknowledge that children of all ages are vulnerable to the virus, with cases reported from 1 day to 18 years old. There is insufficient data to elucidate the differences in susceptibility to COVID-19 among various age groups and genders. Therefore, it is imperative to conduct further studies to delve deeper into this subject matter.

Of all cases, 26(14.77%) patients had underlying conditions. Of those with underlying conditions, 9(8.06%) patients had asthma or obstructive lung disease. Several authors have discussed the relationship between underlying conditions such as chronic lung disease, cardiovascular disease, and COVID-19.[7-10] We were able to look at this relation regarding asthma. Our data does not conclude that asthma increases the risk of COVID-19, but it does draw attention to this issue and provide insights for future studies. Additionally, despite the rate of 8.6%, it is a new and significant finding in the literature that asthmatic patients tend to have symptomatic, but not severe, COVID-19.

In our study, 75.42% of the patients showed mild symptoms of COVID-19, whereas 22.72% had moderate symptoms and 2.27% had severe symptoms. According to Dong et al.,[11] 43.1% of the confirmed cases were asymptomatic, while 12.9% had mild symptoms. Similarly, Hoang et al.'s systematic review[8] revealed that 19.2% of cases were asymptomatic. A study by Lu et al.[5] showed that 15.8% of patients were asymptomatic, while 19.3% had mild symptoms. In a study by Karbuz et al.,[7] 74.8% had mild disease. Our findings are consistent with the general literature suggesting that children with COVID-19 tend to be asymptomatic or experience mild symptoms.

In our study, fever (65.34%) and cough (39.77%) were the most commonly reported symptoms among our patients, which is consistent with current literature.[5,6,11,12] Hoang et al.[8] also reported fever (60%) as the most common symptom in their study, while nasal congestion and rhinorrhea were the second most frequently reported symptoms (28%). In contrast, cough (24%) was not as prevalent in their study. Other commonly reported symptoms among our patients included vomiting (n=51 [28.97%]), diarrhea (n=39 [22.16%]), dyspnea (n=26 [10.77%]), febrile convulsions (n=16 [9.1%]), malaise (n=13 [7.38%]), chills (n=12 [6.82%]), and nasal discharge (n=10 [5.68%]). Less common symptoms included skin rash (n=6 [3.4%]) and sore throat (n=4 [2.27%]). Myalgia was reported in only 14% of our patients,which is inconsistent with current literature [15] and likely reflects the fact that the majority of our patients were under the age of three years.

Numerous reports have emerged on laboratory findings among pediatric COVID-19 patients. However, no classification by age group, sex, or disease severity has been provided.[5,13-16] A review of pediatric cases revealed that leukopenia and leukocytosis were present in 7.3% and 10.7% of cases, respectively. Another review found that the most common abnormal laboratory findings in pediatric patients were leukopenia/lymphopenia and increased creatine kinase. Lymphopenia and lymphocytosis were present in 21% and 5% of cases, respectively, while thrombocytopenia was observed in just 4% of cases. A review from Turkey[7] reported that leukopenia was observed in 5.7% of cases, and lymphopenia was observed in 10 20.5% of all cases. In our study, WBC count was elevated in 81 (46.02%) patients and diminished in 16 (9.09%) patients, with a mean value of $10.34\times10^3/\mu L$ (ranging from 0.6 to $32.9 \times 10^3/\mu L$). COVID-19 probably affects cytopenia, much like other viral infections, particularly in adolescents.

One hundred fifty-eight patients underwent chest X-rays, accounting for 89.77% of the study population. Of these patients, 75.94% showed normal results, while 24.95% had at least one pathologic finding. Chest CT was performed on 18 patients, constituting 10.22% of the study population. Of these patients, 22.22% showed normal results, while ground-glass opacities were the most common finding observed in 50%. The results of this study provide evidence that the utilization of CT scans in children can be less frequent compared to adults, owing to the milder nature of the disease in the pediatric population. It is, therefore, advisable to reserve the use of computerized tomography for patients with moderate to severe conditions to minimize radiation exposure in this vulnerable group.[15,16]

Adequate hydration and supportive care are the primary management priorities in these children. The predominant rehydration method in our patient population (n=167 [94.9%]) was intravenous administration. In a small fraction of cases (5.11%), oral rehydration was the exclusive mode used, while in all other cases, it was utilized 8 in conjunction with intravenous rehydration.

Antibiotics and antifungals are rational in all cases with bacterial or fungal co-infection, respectively. In our study, antibiotics were administered in 159 cases (90.34%). Among these patients, ceftriaxone was the most commonly used antibiotic, with 123 patients (77.36%) receiving it as a single therapy. In 21 cases (13.2%), ceftriaxone was combined with amikacin. Azithromycin (n=5 [3.14%]), Imipenem (n=4 [2.53%]), Erythromycin (n=2 [1.26%]), Ciprofloxacin (n=2 [1.26%]), Vancomycin (n=1 [0.63%]) and Levofloxacin (n=1 [0.63%]) were used less frequently for treatment purposes.

Oxygen therapy was provided only in severe cases and in patients admitted to the Intensive Care Unit. Antivirals were not given to our patients.

One of the constraints of this research is its retrospective design, which did not include outpatient patients. Furthermore, there were instances of incomplete data, particularly concerning symptoms and diagnostic tests, which presented challenges in standardizing the outcomes for the entire study cohort.

Conclusion

The actual prevalence of SARS-CoV-2 infection in children remains uncertain due to the limited availability of testing and the preference for testing adults and individuals with severe symptoms. Based on available data, children have lower rates of hospitalization compared to adults with COVID-19, indicating that children may experience less severe illness than adults. These arguments were initially attributed to their relatively lower exposure, particularly among those cared for at home. Furthermore, children typically experience more respiratory tract infections during winter and have antibody-mediated enhancement mechanisms than adults. However, research indicates that the incidence and frequency of cases have been progressively rising.

We have presented our experience with COVID-19 in children, aiming to contribute to the worldwide discussion on the disease's epidemiological, clinical-laboratory, and imaging features and its treatment.

Ethical Approval

The study protocol was reviewed and approved by the Ethics Committee of the Kosovo Medical Chamber (137/23).

Competing interests

The authors declare that they have no competing interests.

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