

## The Frequency of COVID 19 in Children with Fever and/or Respiratory Symptoms in 2020-2021 Winter: Preliminary Report from Cyprus

Ateş ve/veya Solunum Sistemi Semptomları ile Başvuran Çocuk Hastalarda COVID 19 Enfeksiyonu Sıklığı: Kıbrıs 2020-2021 Kış Dönemi Raporu

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### ABSTRACT

**Objective.** The data regarding Covid-19 in children is still limited. Although the course of Covid-19 disease in children seems milder than adults, the co-morbid conditions that may cause severe infection or death have not been fully clarified and this creates anxiety. This study aims to evaluate the frequency of Covid-19 in children admitting to hospital with symptoms.

**Methods.** A retrospective study during 7 months of the pandemic period was conducted in two tertiary care academic hospitals in North Cyprus. All patients admitted into the pediatric outpatient clinics with fever and/or respiratory symptoms and tested for Covid-19 with real-time polymerase chain reaction (RT-PCR) were involved in the study. Clinical characteristics including symptoms, physical examination findings, laboratory results, hospitalization status, and diagnosis were all recorded from hospital database retrospectively, and the frequency of positive Covid-19 testing in children was evaluated.

**Results.** A total of 111 patients with fever and/or respiratory symptoms without a contact history with Covid-19 were assessed. The age of the children ranged from 2 -172 months, with a median age of 32 months, and 60.4% were male. A total of 19 (17.3%) were hospitalized and the Covid-19 positivity rate was 1.8%.

**Conclusion.** There is a certain need for guidelines to be followed for Covid-19 diagnosis in symptomatic children without a contact history. Test timing, the need for consecutive testing or isolation and recommendations for symptomatic child caregivers about how to protect themselves should be considered and seriously discussed.

**Keywords:** Childhood infections, children, Covid-19, MIS-C

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### ÖZET

**Amaç:** Çocuklarda Covid-19 enfeksiyon seyri ile ilgili bilgiler halen sınırlıdır. Hernekadar erişkinlerde olduğundan daha hafif seyirli hastalık yaptığı gösterilmiş olsa da Co-morbiditeler durumunda nasıl bir seyir izleyeceği konusu netleşmemiştir ve kaygı yaratmaya devam etmektedir. Bu çalışmanın amacı ateş ve solunum sistemi semptomları ile hastaneye başvuran çocuk hastalarda Covid-19 enfeksiyon sıklığını ortaya koymaktır.

**Yöntem:** Çalışma Kuzey Kıbrıs'ta iki üçüncü basamak üniversite hastanesinde pandemi dönemindeki 7 aylık sürede retrospektif olarak gerçekleştirilmiştir. Her iki hastanenin pediatri polikliniklerine ateş ve/veya solunum semptomları ile başvuran, Covid-19 temas öyküsü bulunmayan ve gerçek zamanlı polimeraz zincir reaksiyonu (RT-PCR) ile Covid-19 testi yapılan tüm hastalar çalışmaya dahil edilmiştir. Semptomlar, fizik muayene bulguları, laboratuvar sonuçları, hastanede yatış durumu ve tanı gibi klinik özellikler retrospektif olarak hastane veri tabanından elde edilmiştir.

**Bulgular:** Ateş yüksekliği ve/veya solunum semptomları olan toplam 111 hasta çalışmaya dahil edilmiştir. Çocukların yaşları 2-172 ay arasında değişmekte olup, ortanca yaşları 32 ay, %60,4'ü erkek olarak tesbit edilmiştir. 19 hasta (%17,3) hastaneye yatırılarak tedavi edilirken Covid-19 pozitiflik oranı %1,8 olarak saptanmıştır.

**Sonuç:** Temas öyküsü olmayan semptomatik çocuklarda Covid-19 tesbiti için izlenecek kılavuzlara belirgin ihtiyaç olduğu bilinmektedir. Test zamanlaması, ardışık test gerekliliği veya semptomatik çocuklara bakım verenler için izolasyon önerileri gibi konularda daha fazla çalışmaya ihtiyaç vardır.

**Anahtar Sözcükler:** Çocuk enfeksiyonları, Covid-19, MIS-C

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**INTRODUCTION**

Novel coronavirus disease (Covid-19) emerged in China in December 2019 and the World Health Organization declared the outbreak of the pandemic in March 2020 (1). The striking impact of the Covid-19 Pandemic is continuing and although mortality among the child population is low, the number of affected children is increasing daily. Children represent 2% of COVID-19 diagnosed cases in China (2), 1.2% of cases in Italy (3) and 5% of cases in the United States (4).

The data regarding Covid-19 in children is still limited. Although the course of Covid-19 disease in children seems milder than adults, the co-morbid conditions that may cause severe infection or death have not been fully clarified (5).

In terms of infectious diseases in childhood, the winter and spring months have an increased prevalence of intensively viral agents such as influenza, respiratory syncytial virus (RSV), adenovirus or rhinovirus. The impact of the pandemic on the frequency of common infectious diseases in the winter-spring season of 2020-2021 led to less infections and hospital admissions in pediatric practice (6). Although children do not seem to be a major vector of Covid-19 transmission, many pediatric cases have been reported in familial clusters (7). Fever and respiratory symptoms are the most common symptoms seen in pediatric cases with no typical and specific radiological signs or laboratory findings (5,7).

Due to the fact that pediatric SARS-COV-2 cannot be differentiated from other viral infections at first sight with clinical course of the disease, the pandemic has caused hesitation in the conventional approach to infections in children.

The variability of presentation poses a challenge for the early recognition of patients with suspected COVID-19 in pediatric routine, which is currently playing a role in disease control and prevention in pandemic (8).

The aim of this study is to evaluate the clinical features of infections during the pandemic winter-spring season and the frequency of Covid-19 cases in children in Cyprus.

**MATERIALS and METHODS**

We conducted a cross-sectional, observational retrospective study during 7 months of the pandemic period (between 1 October 2020 and 30 April 2021) in two outpatient clinics of tertiary care academic hospitals in Nicosia and Kyrenia, North Cyprus. The study protocol was approved by the Ethics Committee of Near East University with the number of 2021/94-1392. All patients admitted to the pediatric outpatient clinics with fever and/or respiratory symptoms and tested for Covid-19 with real-time polymerase chain reaction (PCR) on nasopharyngeal sampling were involved in the study. The decision to test the patients for Covid-19 was made by their physician based on clinical features according to the Covid-19 Pediatric Patient Management and Treatment Guideline of Republic of Turkey-Ministry of Health (9). Symptoms, physical examination findings, other laboratory results, hospitalization status, and diagnosis were all recorded from the hospital databases retrospectively. Any positive contact history with family members or others were excluded. The patients' clinical characteristics and frequency of positive Covid-19 testing in children with fever and/or respiratory symptoms were evaluated.

**Table 1.** Demographic and clinical characteristics of the study population.

Age (min-max, median, $\pm$ SD) (months)	2-172, 32, $\pm$ 36.2
Gender (M/F) (%)	67/44 (60.4/39.60)
Admission month n(%)	
October	2(1.8)
November	23(20.7)
December	13(11.7)
January	22(19.8)
February	11(9.9)
March	10(9)
April	30(27)
Symptom Onset (min-max, median, $\pm$ SD) (days)	1-7, 2, $\pm$ 1.27
Symptoms n (%)	
Fever only	4 (3.6)
Fever + respiratory symptom	78 (70.3)
Cough/wheezing	12 (10.8)
Cough + rhinorrhea	11 (9.9)
Vomiting / Diarrhea	5 (4.5)
Sore throat	1 (0.9)
Hospitalization status n (%)	
Hospitalized	19 (17.3)
Not hospitalized	91 (82.7)
COVID-19 Test results n (%)	
PCR positivity (n=111)	1 (0.9)
IgM seropositivity (n=12)	1 (8.3)
Test timing (min-max, median, $\pm$ SD) (days)	0-7, 2, $\pm$ 1.16
Final Diagnosis n(%)	
URTI	43 (38.7)
Tonsillitis	8 (7.2)
Bronchiolitis	21(18.9)
Pneumonia	11(9.9)
AOM	5(4.5)
Gastroenteritis	14 (12.6)
UTI	2 (1.8)
Croup	5 (4.5)
Infectious mononucleosis	1 (0.9)
Roseola infantum (6th Disease)	1(0.9)

(AOM: Acute otitis media, URTI: Upper respiratory tract infections, UTI: Urinary tract infections)

**RESULTS**

A total of 111 patients with fever and/or respiratory symptoms were all assessed and tested for Covid 19 by PCR tests on nasopharyngeal samples during the 7- month period. The age of the children ranged from 2 months to 172 months, with a median age of 32 months, and 60.4% were male. Of the 111 patients, 19 of them (17.3%) were hospitalized and the others were treated on an outpatient basis. SARS-COV-2 IgM detection from serum samples were made only on 12 patients additionally to PCR tests. One patient who was diagnosed with croup at the age of 18 months was detected to be positive by SARS-COV-2 IgM testing and another 14-month-old patient was detected to be positive for Covid-19 by PCR test. The median PCR test timing after symptom onset was 2 days, ranging from 1-7 days.

Both of the SARS-COV-2 patients had the disease at home with mild symptoms without any need for hospitalization. Distribution of symptoms and final diagnosis of 111 patients with other demographical and clinical characteristics of the study population are detailed in Table 1.

**DISCUSSION**

It is known that children infected with SARS-COV-2 have milder symptoms or are completely asymptomatic, unlike adults or elderly people. Several hypotheses have been proposed to explain these differences in the immune systems between children and adults (5). However, it is still uncertain whether children transmit the virus and may play a role as a reservoir for SARS-COV-2 or not. Laboratory findings and radiological signs do not show typical findings in pediatric patients as in adults. 83% of children cases had a positive contact history commonly with family members (5). Therefore, diagnosis in children can be difficult and complicated, especially when there is no positive contact history documented. The literature has thus far reported that nasopharyngeal swabs can be positive before the onset of symptoms (7,10,11), while on the other hand, false negative swab testing is also possible and not rare (10,12). Several studies have reported incubation periods varying between 2-25 days with mean of 7 days, median of 6 days and 11 days respectively (13-15). Some studies did conduct consecutive nasopharyngeal sampling in children and showed that it remains positive between 1-22 days (13,16) and can be even longer in stool samples (17). However, false negativities and the cases with no known contact history cause doubts in diagnosis in children.

This study revealed a Covid-19 positivity rate in children with fever and/or respiratory symptoms in a 7-month period of 2020-2021 in Northern Cyprus detected with nasopharyngeal PCR and serum IgM analysis. Since the study was conducted in a retrospective manner using the data of past illness, consecutive sampling was not performed. The benign nature of the disease in children suggests the need for consecutive testing for this population. On the other hand, the series from hospitalized children with moderate to severe SARS COV-2 infection reported that the first testing was negative in most patients (12). This complexity in diagnosis indicates the need for a consensus on the diagnostic approach in children during the COVID 19 pandemic.

Current study revealed the frequency in symptomatic Covid-19 positive children in North Cyprus 1.8%. This retrospective study utilized a hospital database to examine the final diagnoses of patients. The study focused on pediatric patients who primarily visited the hospital due to fever as their sole symptom. As a result, the final diagnoses of patients who presented with fever and underwent Covid-19 testing during their initial admission could vary significantly, including conditions such as sixth disease or urinary tract infections (UTIs).

In a similar study conducted in Italy between 1 March 2020-13 April 2020, 42 children admitted to Pediatric Emergency for acute problems were suspected and tested for Covid-19 and none of the patients were found to be positive for SARS-COV-2 infection (18).

In contrast to the disease in the adult population, SARS COV 2 in the pediatric group is not associated with underlying health conditions (19). Symptoms can change from mild upper respiratory tract infections to severe pneumonia, myocardial dysfunction or shock (20). In the field of pediatrics, the multisystem inflammatory syndrome in children (MIS-C) aspect of the Covid 19 pandemic should also be considered. In the past year, there have been increasing reports worldwide describing children and adolescents with Covid-19 associated with multisystem syndrome, similar to Kawasaki disease, which seems to develop after a while from the acute phase of SARS COV 2 infection in children (20, 21).

Therefore, the diagnosis of acute SARS-COV-2 in children is important, although it is very mild or asymptomatic. Early detection of Covid-19 cases in children is crucial for care providers who look after the infected child (13) and will also provide alertness for MIS-C that may develop later.

This study was conducted in Northern Cyprus during a period in which the R value was mostly less than 1 and 7 days and the cumulative cases per 100,000 population ranged between 6.54-123.5 (22). The primary and secondary schools in the country were completely closed during this time period due to pandemic restrictions imposed by the government. Therefore, the prevalence of Covid-19 cases in symptomatic children is expected to be higher in periods where the epidemic rate was higher or when restrictions were lifted. Further studies are needed to examine the prevalence of Covid-19 cases in symptomatic children without contact history in different circumstances.

This is the preliminary report of 2020-2021 winter in Cyprus and the frequency in next winter will be reassessed in changing circumstances such as vaccination of parents and the resumption of face-to-face education in schools.

**CONCLUSION**

Although SARS-COV-2 does not seem to be a disease that impacts children and the frequency in symptomatic children were 1.8% in Cyprus study, it may affect children more when restrictions are lifted and schools are opened. It seems that there is a certain need for guidelines that will determine the path to be followed for Covid-19 diagnosis in symptomatic children without a contact history. Test timing, the need for consecutive testing or isolation, and identification of recommendations for symptomatic child caregivers about how to protect themselves should be considered and seriously discussed.

**Conflict of interest**

No conflict of interest was declared by the authors.

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