



Relationship with Domestic Spread and Progression of COVID-19 in Children

Çocuklarda COVID-19'un Seyri ve Aile İçi Yayılım İlişkisi

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Abstract

Objective: SARS-CoV-2 infection in children is usually mild, so the real positivity rate and the effect on children's virus spread are not exactly known. The purpose of this study is to investigate the effect of children on the spread of COVID-19.

Material and Methods: Children who were followed up and treated with a pre-diagnosis of COVID-19 between April and June 2020 were included in this study. The protocol for this retrospective study was approved by the Ministry of Health, Turkey, and the ethics committee of a university medical school. Data were collected retrospectively from the hospital medical system. Data analysis was done with IBM SPSS v21.0 statistical program. Categorical variables were expressed as n and %, while numerical variables were expressed as mean \pm std and median (min-max). The conformity of the data to the normal distribution was analyzed with the Kolmogorov Smirnov test. Chi-square test and Fisher's exact test were used in the analysis of categorical variables. In comparisons between groups, Independent-t and Mann-Whitney U tests were used. For correlation between continuous variables, Pearson and Spearman correlation coefficients were used. $p < 0.05$ was accepted for statistical significance.

Results: A total of 205 children were hospitalized in a three-month period with a suspected COVID-19 disease. SARS-CoV-2 RT-PCR was positive in 72.7% of the participants from 86 different families. As the number of siblings and households increased, SARS-CoV-2 RT-PCR positive cases also increased and were found to be statistically significant ($p < 0.05$). The presence of another SARS-CoV-2 RT-PCR confirmed case in the household under the age of 18 increases the clustering of cases within the family ($p < 0.001$). There was domestic contact in 74% of the participants;

Öz

Giriş: Çocuklarda SARS-CoV-2 enfeksiyonu genellikle hafif seyirlidir, bu nedenle gerçek pozitiflik oranı ve çocukların virüs yayılımı üzerindeki etkisi tam olarak bilinmemektedir. Bu çalışmanın amacı, çocukların COVID-19 enfeksiyonunun yayılması üzerindeki etkisini araştırmaktır.

Gereç ve Yöntemler: Bu çalışmaya Nisan 2020-Haziran 2020 tarihleri arasında COVID-19 ön tanısı ile takip ve tedavisi yapılan çocuklar dahil edildi. Çalışmanın Türkiye Sağlık Bakanlığı izni ve etik kurul izni alındı. Hasta verileri geriye dönük hastane medikal sisteminden toplandı. Veri analizi IBM SPSS v21.0 istatistik programı ile yapılmıştır. Kategorik değişkenler n ve % olarak, sayısal değişkenler ortalama \pm std ve medyan (min-maks) olarak ifade edildi. Verilerin normal dağılıma uygunluğu Kolmogorov Smirnov testi ile analiz edildi. Kategorik değişkenlerin analizinde ki-kare testi ve Fisher'in kesin testi kullanıldı. Gruplar arası karşılaştırmalarda Independent-t ve Mann-Whitney U testleri kullanıldı. Sürekli değişkenler arasındaki korelasyon için Pearson ve Spearman korelasyon katsayıları kullanıldı. İstatistiksel anlamlılık için $p < 0.05$ kabul edildi.

Bulgular: Üç aylık dönemde toplam 205 çocuk COVID-19 hastalığı şüphesiyle hastaneye yatırıldı. Seksen altı farklı aileden katılımcıların %72.7'sinde SARS-CoV-2 RT-PCR pozitif bulundu. Kardeş sayısı ve hane içi kişi sayısı arttıkça, kesin vaka sayısının artışı istatistiksel olarak anlamlı bulundu ($p < 0.05$). Ev içinde 18 yaş altı SARS-CoV-2 RT-PCR pozitif başka bir vakanın bulunması aile içi vaka kümelenmesini arttırmaktadır. ($p < 0.001$). Katılımcıların %74'ünde ev içi temas mevcuttu; bu oran pozitif vakalar için %91.9 ve olası vakalar için %26.8'dir ve istatistiksel olarak anlamlıdır ($p < 0.001$). Pozitif vakaların WBC, nötrofil, trombosit ve CRP parametreleri olası vakalardan daha düşüktür.

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this rate is 91.9% for positive cases and 26.8% for probable cases, which is statistically significant ($p < 0.001$). WBC, neutrophil, platelet and CRP parameters of positive cases are lower than probable cases.

Conclusion: COVID-19 infection in children appears to be asymptomatic or mildly symptomatic. Although the role of children in the spread of COVID-19 infection is unclear, the domestic clustering rate of COVID-19 infection is high in families with many children. Therefore, in order to reduce the spread of the disease, family clustering should be determined and quarantine measures should be taken.

Keywords: Family cluster, domestic spread, COVID-19, child

Introduction

Coronavirus disease 2019 (COVID-19) has a trend of global spread and has been declared as an international public health concern (1). After COVID-19 was first identified in China in December/2019, it was announced to cause a pandemic by WHO in March/2020. SARS-CoV-2 is a novel enveloped RNA beta-coronavirus and has been shown to cause severe acute respiratory syndrome (2,3). COVID-19 disease is thought to be linked to the Huanan seafood market (4). The transition from person to person was first shown in January, 2020 (5).

COVID-19 has caused severe upper respiratory tract infection in humans severe as well as lower respiratory tract infection, organ failure and death. Clinical findings in childhood were generally associated with the respiratory system and with gastrointestinal involvement symptoms, for example diarrhea. Overall, COVID-19 appears to be a less severe disease in children than adults. COVID-19 is mainly transmitted by droplet. In addition, contact with droplets scattered in the environment by coughing, sneezing is also effective in transmission. Incubation of COVID-19 is not exactly known. Infectiousness generally thought that it starts 1-2 days before the symptomatic period and ends with the disappearance of the symptoms. However viral load in asymptomatic carriers is known to be similar to symptomatic patients (6).

The numbers of cases are reported more in households where close contact is more intense than others. Family case clusters of COVID-19 have also been reported in previous publications (5,7,8). The predominance of with many children traditional lifestyle may cause increased domestic clustering. Therefore, during this period, various control measures were taken for children, with some restrictions, and travel bans were imposed except when necessary (9).

Contact screening and isolation of children is important in epidemic control, due to the detection of asymptomatic SARS-CoV-2 reverse transcription polymerase chain reaction (RT-PCR) positive children and increasing rate of domestic positivity. In this study; we aimed to investigate the epidemi-

Sonuç: Çocuklarda COVID-19 enfeksiyonu asemptomatik/hafif semptomatik görülmektedir. Çocukların COVID-19 enfeksiyonunun yayılmasındaki rolü belirsiz olsa da, çok çocuklu ailelerde COVID-19 enfeksiyonunun aile içi kümelenme oranı yüksektir. Bu nedenle hastalığın yayılımını azaltmak için aile içi kümelenme belirlenmeli ve karantina önlemleri alınmalıdır.

Anahtar Kelimeler: Aile içi kümelenme, aile içi yayılım, COVID-19, çocuk

ological, clinical and sociodemographic variables and family case clustering status of children hospitalized with COVID-19 pre-diagnosis in the COVID-19 pandemic.

Materials and Methods

Patients who were followed up and treated with a pre-diagnosis of COVID-19 between April and June 2020 were included in this study. Patient data were collected retrospectively from the hospital medical system. Cases in the study were defined as confirmed-probable cases according to the COVID-19 guideline published by the Ministry of Health. According to this guideline, in the presence of epidemiological and clinical findings, SARS-CoV-2 RNA RT-PCR positive cases were accepted as confirmed cases, and SARS-CoV-2 RT-PCR negative cases were accepted probable cases (10).

Epidemiological and clinical findings of the participants were evaluated. Close contact with the confirmed case, number of family members, presence of a family case, clinical, laboratory and radiological findings were recorded. Family members of people who were found to be positive for COVID-19 were screened with SARS-CoV-2 RT-PCR. SARS-CoV-2 RT-PCR positive cases were followed in the hospital. Asymptomatic patients with domestic contact and negative for SARS-CoV-2 RT-PCR were quarantined at home. Patients, that have symptoms of lower and upper respiratory tract diseases or that have RT-PCR positive and asymptomatic, were included in the study. Swab sample from nasopharynx and pharynx from all patients and endotracheal aspirate samples from patients that monitored on a mechanical ventilator and tested with SARS-CoV-2 RT-PCR were taken. A second sample was taken from patients whose first samples were negative.

The protocol for this retrospective study was approved by the Ministry of Health, Turkey, and the Ethics Committee of a university medical school (Date: June, 2020, No: 76244175-050.04.04). Informed consent was obtained from all of the participants. The data of the research was not used beyond scientific purposes. The procedures were carried out following the Declaration of Helsinki.

Statistical Analysis

Data analysis was done with IBM SPSS v21.0 statistical program. The normality of the variables were evaluated using Kruskal Wallis-Shapiro-Wilk tests, histogram, scatter plot, and Skewness-Kurtosis values. Categorical variables were expressed as n and %, while numerical variables were expressed as mean ± std and median (min-max). The conformity of the data to the normal distribution was analyzed with the Kolmogorov Smirnov test. Chi-square test and Fisher's exact test were used in the analysis of categorical variables. In comparisons between groups, Independent-t and Mann-Whitney U tests were used. For correlation between continuous variables, Pearson and Spearman correlation coefficients were used. p< 0.05 was accepted for statistical significance.

Results

A total of 205 children were hospitalized in a three-month period with a suspected COVID-19 disease. SARS-CoV-2 RT-PCR was positive in 72.7% patients. 96.6% of patients were citizens of Turkey, others were Syrian citizens. The mean age of the patients was 9.16 ± 5.67 (min-max, one month-17 years). 51.2% of the patients were male. Thirteen of patients had the chronic disease. Eight of this patients were probable cases. 51.0% of confirmed cases had least one clinic symptom. The most common clinical symptoms were cough (46.3%) and fever (42.6%). Less frequent symptoms were throat ache, abdominal pain and mild gastrointestinal symptoms, myalgia, and shortness of breath.

The sociodemographic variables of COVID-19 confirmed and probable cases were displayed in Table 1. In this study, participants from 86 different families has been included. As number of siblings and member number of household increase, ratio of confirmed cases has increased and these are significant statistically (p< 0.05).

The number of siblings and the number of household members were significantly associated with confirmed cases of COVID-19. Presence of another confirmed case at home and another confirmed case under the age of 18 were statistically associated with an increase in the number of confirmed cases (p< 0.001). In addition, having another COVID-19 patient under the age of 18 at home seems to be related to the number of siblings and household members (Table 2).

In addition, 74.0% of the participants had domestic contact; this rate was 91.9% for confirmed cases and 26.8% for probable cases, and this difference was statistically significant (p< 0.001).

95.6% of patients were observed in the pediatric pandemic department. Other patients were hospitalized pediatric intensive care unit (PICU). Patients, who were hospitalized PICU, were probable cases except for one patient who underwent allogeneic hematopoietic stem cell transplantation. 5 (8.9%) of probable cases who were followed up in PICU died. All of them SARS-CoV-2 PT-PCR had negative. Some statistical significant different between confirmed and probable cases were available (Table 3). Probable cases had more symptoms and pathologic X-ray findings than confirmed cases. Also, confirmed cases required less intensive care and intubation than probable cases.

Table 1. Sociodemographic variables of confirmed and probable cases

Sociodemographic variables n (%)	Confirmed case n= 149	Probable case n= 56	p
Boy, n (%)	74 (49.7)	31 (55.4)	0.18
Age (Mean)	8.9 ± 5.6	9.9 ± 5.9	
Age group, n (%)			0.21
≤1	21 (14.1)	9 (16.1)	
2-5	27 (18.1)	6 (10.7)	
6-11	45 (30.2)	11 (19.6)	
12-14	23 (15.4)	14 (25.0)	
15-17	33 (22.1)	16 (28.6)	
Underlying disease, n (%)	5 (3.4)	8 (14.3)	0.004
Number of siblings, n (%)			0.005
≤2	35 (23.5)	14 (25.0)	
3-5	85 (57.0)	41 (73.2)	
≥6	29 (19.5)	1 (1.8)	
Person number of household, n (%)			0.004
≤4	27 (18.1)	14 (25.0)	
5-7	92 (61.7)	41 (73.2)	
≥8	30 (20.1)	1 (1.8)	
Another confirmed case in the home, n (%)	136 (91.9)	15 (26.8)	<0.001
Another confirmed case under the age of 18 in the home, n (%)	86 (58.9)	15 (26.7)	<0.001

Table 2. Relations between another COVID-19 patient under the age of 18 in the home with number of siblings and person number of household

	Another COVID-19 patient under the age of 18 in the home		p
	Yes, n (%)	No, n (%)	
Number of siblings			<0.001
≤2	10 (10.6)	39 (41.5)	
3	31 (33.0)	25 (26.6)	
4	16 (17.0)	15 (16.0)	
5	12 (12.8)	10 (10.6)	
≥6	25 (26.6)	5 (5.3)	
Person number of household			<0.001
≤3	1 (1.1)	8 (8.5)	
4	5 (5.3)	27 (28.7)	
5	35 (37.2)	26 (27.7)	
6	16 (17.0)	18 (19.1)	
7	12 (12.8)	9 (9.6)	
≥8	25 (26.6)	6 (6.4)	

Table 3. Clinic and laboratory variables of confirmed and probable cases

	Confirmed case (n= 149)	Probable case (n= 56)	p
Clinical symptoma (least one symptom) n, (%)	80 (53.6)	48 (85.7)	<0.001
Chest X-ray Pathological n, (%)	6 (4)	26 (46.4)	<0.001
PICU Admission n, (%)	1 (0.67)	8 (14.2)	<0.001
Intubation n, (%)	-	7 (12.5)	<0.001
Ex n, (%)	-	5 (8.9)	0.001
WBC/mm ³	6.61 ± 2.51	10.22 ± 4.84	<0.001
Neutrophil/mm ³	2.77 ± 1.37	6.10 ± 4.05	<0.001
Lymphocyte/mm ³	2.96 ± 2.04	3.36 ± 2.50	0.24
Hemoglobin (g/dL)	12.47 ± 1.32	11.90 ± 2.05	0.06
Thrombocyte/mm ³	279436 ± 77444.9	310660 ± 10786.4	0.05
Total Protein (g/L)	7.25 ± 0.72	7.27 ± 1.07	0.88
Albumin (g/L)	4.50 ± 0.39	4.31 ± 0.61	0.03
CRP (mg/L)	5.32 ± 23.39	18.84 ± 30.24	<0.001

^aLeast one of cough, nasal flow throat ache, myalgia, colic, diarrhea and dyspnea.
PICU: Pediatric intensive care unit, WBC: White blood cell, CRP: C-reactive protein.

In Table 3 is it shown some laboratory findings differences between confirmed and probable cases. WBC, neutrophil, thrombocyte and CRP parameters of confirmed cases are less than probable cases (p< 0.05).

Discussion

Data of 86 family and 205 children were included this study. One hundred forty nine of this patients are confirmed case and 56 of them are probable case. At April, May and June, 2020, when pandemic had started new in Turkey, for local pandemic measures all persons, who have domestic contacts with COVID-19 were scanned with SARS-CoV-2 RT-PCR test; after that, positive cases were hospitalized to provide isolation and to follow clinical status of them. SARS-CoV-2 RT-PCR positive cases were followed in hospital for 3-5 days, then asymptomatic or mildly symptomatic cases were quarantined out-

side the hospital. Most of the children confirmed cases were asymptomatic or mild symptomatic cases as other studies in literature (11-13).

When COVID-19 cluster cases are examined in the literature, domestic contacts, hospital infections, clustering in shopping centers, clustering in meetings or clustering in tourist groups have been reported. The most common of these is the domestic cluster (14-17).

When the studies on clustering within the family are examined, it is seen that the first case is an adult (11,18). In our study, in which family clustering was examined, it was determined that the first case was an adult in all households. But, it should not forgotten that because usually children are asymptomatic or mild symptomatic, COVID-19 RT-PCR tests are performed more adults than children.

In family cluster has found association with frequency and duration of near contact. In literature, there are studies reporting that the in family attack rate of SARS-CoV-2 infection varies from 40% to 100%. Additionally, it is determined that viral load of asymptomatic or mild symptomatic child cases also elevated (11-13,18,19). The number of siblings and household members is high in this geography. Based on this data, in our study, it was shown that the number of COVID-19 cases in the family increased as the number of siblings and the number of people in the household increased. These results were statistically significant ($p < 0.001$). In addition, households with COVID-19 positive cases under the age of 18 have a higher rate of clustering within the family. These results show that children have a significant share in the spread of COVID-19 infection, even if they are asymptomatic.

In probable cases, domestic contact was 26.8% and this ratio was less than in confirmed cases. Additionally, when the contact history of possible cases was questioned, it was determined that 25.0% lived in a village quarantined due to COVID-19. Probable cases had more frequent clinical symptoms (mostly fever and cough) than others, while acute phase reactants were higher and pathological radiological findings were more frequent. Presence of underlying chronic disease, severe respiratory distress symptoms, intubation rate, frequency and duration of intensive care unit stay, and death were statistically higher in probable cases than in confirmed cases. At least two PCR results were negative in probable cases. In literature data, the rate of PICU stay, hospital stay, and intubation rate in pediatric patients with acute COVID-19 infection are similar to this study (13,20,21). In short, COVID-19 manifestations are generally milder in children with confirmed COVID-19 infection.

There are some limitations in this study. For example, other respiratory pathogens have not been investigated due to the pandemic. Therefore, other pathogenic factors that may cause respiratory tract symptoms could not be detected, especially in probable cases.

To reduce spread of disease with determination of case clusters and early quarantine has a great importance in the pandemic that affects all world. This study results support that spread rate of COVID-19 infection is higher in families with many children. Increase in the number of individuals under the age of 18 in the household increases also frequency of COVID-19 infection. The importance of children in transmitting COVID-19 is still unclear, as many children are asymptomatic and only positive for COVID-19 PCR on family screening. More research is needed in this area.

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Ethics Committee Approval: The protocol for this retrospective study was approved by the Ministry of Health, Turkey, and the Ethics Committee of a university medical school (Date: June, 2020, No: 76244175-050.04.04).

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