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Review - Derleme

REVIEW OF EARLY STAGE EFFECTS OF CORONAVIRUS DISEASE 2019 (COVID-19) IN PEDIATRIC PATIENTS

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ABSTRACT

Objective: The outbreak of coronavirus disease 2019 (COVID-19) first appeared in December 2019. This virus has affected hundreds of thousands of people so far, causing deaths in tens of thousands. It is known that most of the studies are related to adults. Data on the nature of symptoms and the general process of the disease in children were not sufficient.

Methods: A systematic literature review was carried out to identify papers on COVID-19, which is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), using PubMed, ScienceDirect databases between 1 January-27 March 2020. The review was searched for relevant terms related to "SARS-CoV-2", "coronavirus", "COVID-19", "child".

Results: In the study, 45 scientific articles, COVID-19 prevention plan and guideline were determined. The results of the investigation showed that COVID-19 cases detected in children constitute 1-5% of all cases, child patients had a mild disease process than adults and deaths were rare. It was determined that children admitted to the hospital with high fever and respiratory diseases similar to adults. It has been observed that hemodynamic parameters can be stabilized with oxygen, inhalation and nutritional support for treatment in children, thereby protecting the fluid-electrolyte and acid-base balance of the body and thereby correcting inflammatory reactions.

Conclusion: Further studies are needed to explain why children infected with COVID-19 have a milder disease process than adult patients.

Key Words: Child, Coronavirus, COVID-19, SARS-CoV-2

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ÇOCUK HASTALARDA KORONAVIRÜS HASTALIĞININ (COVID-19) ERKEN DÖNEM ETKİLERİNİN İNCELENMESİ

ÖZ

Amaç: Koronavirus hastalığı 2019 (COVID-19) salgını, ilk kez 2019 yılı Aralık ayında ortaya çıkmıştır. Bu virüs şimdiye kadar yüz binlerce insanı etkilemiş, on binlercesinde ölüme neden olmuştur. Yapılan çalışmaların çoğunun yetişkinlerle ilgili olduğu bilinmektedir. Çocuklarda semptomların niteliği ve hastalığın genel sürecine ilişkin verilerin yeterli olmadığı görülmüştür.

Yöntem: İnceleme için 1 Ocak-27 Mart 2020 tarihleri arasında PubMed, Science Direct üzerinden açık erişime sunulan ve çocuklarda "SARS-CoV-2", "koronavirüs", "COVID-19", "çocuk" anahtar terimleri yardımıyla sistematik bir literatür taraması yapılmıştır.

Bulgular: Araştırmada 45 bilimsel makale, COVID-19 önleme planı ve kılavuz olduğu tespit edilmiştir. İnceleme sonuçları çocuklarda tespit edilen COVID-19 vakalarının tüm vakaların %1-5'ini oluşturduğunu, hasta çocukların yetişkinlerden daha hafif bir hastalık süreci geçirdiğini ve ölümlerin nadir olduğunu göstermiştir. Çocukların yetişkinlere benzer şekilde yüksek ateş ve solunum rahatsızlıkları ile hastaneye başvurduğu belirlenmiştir. Çocuklarda tedavi için oksijen, inhalasyon ve beslenme desteği ile hemodinamik parametrelerinin stabilize edilebildiği bu sayede vücudun sıvı-elektrolit ve asit-baz dengesinin korunarak iltihabi reaksiyonların düzeltilebileceği görülmüştür.

Sonuç: COVID-19 ile enfekte çocukların erişkin hastalara oranla neden daha hafif bir hastalık süreci geçirdiklerini açıklayabilmek için daha ileri çalışmalar yapılmasına ihtiyaç olduğu düşünülmektedir.

Anahtar Kelimeler: Çocuk, Koronavirüs, COVID-19, SARS-CoV-2

INTRODUCTION

SARS-CoV-2 related severe acute respiratory syndrome 2 (COVID-19), caused a serious pandemic and continues to spread rapidly (Dashraath et al., 2020). COVID-19, which is the first appeared in Wuhan province of China in December 2019, caused global effects all over the world and this virus was reported to be transmitted to more than 70.000 people (Z. Li et al., 2020). It was determined that 2-3 more people could be affected by an infected patient and the disease could spread. Chinese government officials have tried to control the outbreak, provide necessary medical support, take active and effective measures to prevent the rapid spread of COVID-19. However, it was observed that sufficient results could not be achieved for a certain period of time to reduce mortality and prevent contamination to other individuals (Caselli & Aricò, 2020).

Due to the rapid spread of the disease, the World Health Organization (WHO) classified coronavirus disease 2019 (COVID-19) as a pandemic on March 11, 2020 (Guan et al., 2020; Ludvigsson, 2020). According to "Coronavirus Disease 2019 (COVID-19) Situation Report-69-92" published by the World Health Organization (WHO) between 18-21 April, it reported that COVID-19 cases were the first time in five new countries from Africa, America and the Eastern Mediterranean Region (World Health Organization, 2020a). With the newly added countries, the number of COVID-19 cases have exceeded 2.3 million world-wide (Table 1) (H. Cai, 2020; World Health Organization, 2020b, 2020c, 2020d, 2020e).

Table 1. Data On Total (New) Cases and Deaths in The Last 24 Hours as of 18-21 April, 10.00

	18 April 2020	**19 April 2020**	**20 April 2020**	**21 April 2020**
Globally	2160207 confirmed 146088 deaths	2241778 confirmed 152551 deaths	2314621 confirmed 157847 deaths	2397217 confirmed 162956 deaths
European Region	1086889 confirmed 97201 deaths	1122189 confirmed 100938 deaths	1149071 confirmed 103586 deaths	1187184 confirmed 106342 deaths
Region of the Americas	784272 confirmed 35742 deaths	821860 confirmed 38258 deaths	858631 confirmed 40615 deaths	839119 confirmed 42686 deaths
Western Pacific Region	129256 confirmed 5598 deaths	131115 confirmed 5621 deaths	132438 confirmed 5648 deaths	134507 confirmed 5685 deaths
Eastern Mediterranean Region	120683 confirmed 5784 deaths	124691 confirmed 5908 deaths	129433 confirmed 6048 deaths	134470 confirmed 6185 deaths
South-East Asia Region	25291 confirmed 1134 deaths	27319 confirmed 1185 deaths	29576 confirmed 1275 deaths	31670 confirmed 1341 deaths
African Region	13104 confirmed 616 deaths	13892 confirmed 628 deaths	14760 confirmed 662 deaths	15555 confirmed 704 deaths
WHO Risk Assessment	Very high	Very high	Very high	Very high

Although many studies conducted with the adult population reviewed the symptoms and features of patients with COVID-19, it was observed that these studies did not contain much statistical data on children.

This article was carried out to summarize the findings of a literature review on current information about COVID-19 in children.

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METHOD

Search Process

The review was carried out with the keywords of "SARS-CoV-2", "coronavirus", "COVID-19", "child", which are openly accessible on PubMed and Science Direct. In the study, between January 1 and March 27, 2020, 76 publications accessed via PubMed and 62 publications via ScienceDirect were found. Duplicate results were removed and COVID-19 prevention plans and guides published by specific centers were included in these studies. 45 of these were accepted to this systematic review and analyzed in detail (Figure 1).

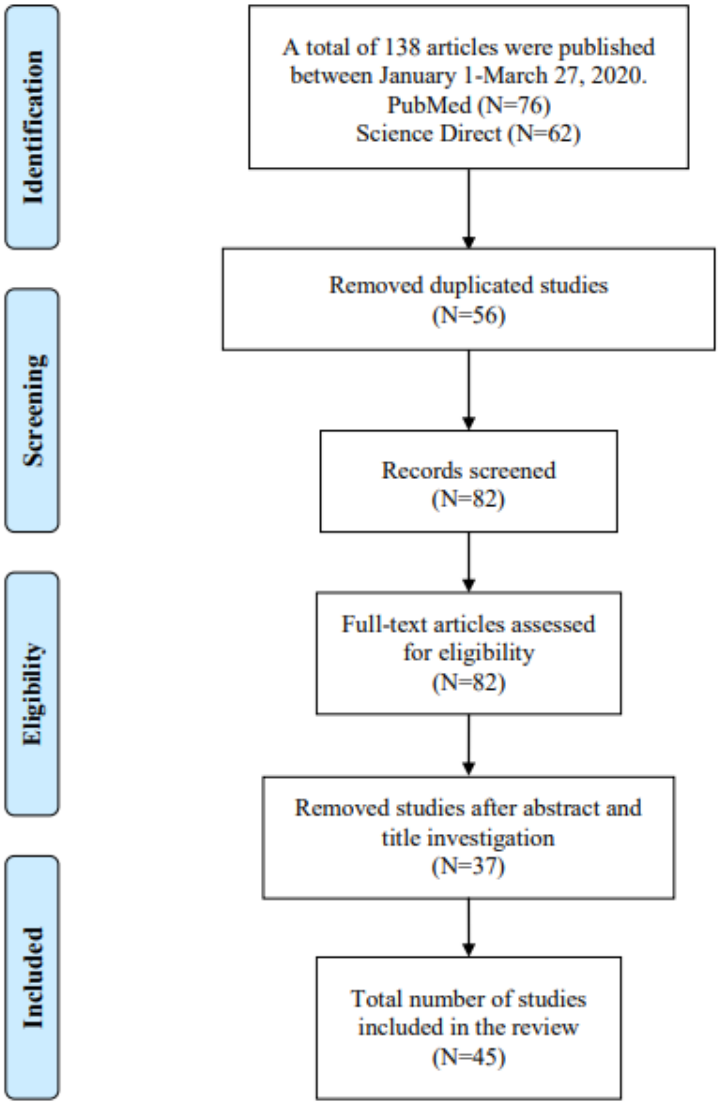

Figure 1. *Flow diagram of the studies included in the review*

It was determined that most of the studies consisted of publications originating from China. Despite the fact that a significant number of COVID-19 patients were diagnosed and died in Italy, Iran and South Korea following the outbreak, few reports were declared about pediatric patients. COVID-19 is characterized as a condition caused by the severe acute respiratory syndrome 2 (SARS-CoV-2) virus. However, there is no definitive information that children will not get this infection in any way (Brodin, 2020).

RESULTS

Background

The review with the largest number of positive COVID-19 cases was China, the United States, and Italy (Aricò & Maurizio, 2020; Qiu et al., 2020; Zheng et al., 2020). In the early stages of the epidemic, many children with COVID-19 were part of family clusters with the disease. The review with the largest number of positive COVID-19 cases was a Chinese paper by the Chinese Novel Coronavirus Pneumonia Emergency Response Epidemiology Team with 72,314 subjects, and this found that about 2% of the 44,672 confirmed cases of COVID-19 were children aged 0-19 years (Adhikari et al., 2020).

Incubation Process and Symptoms

It was reported that 6.3% of all cases where the COVID-19 test was positive during the period up to 20th of March was composed of children under the age of 19 (Kam et al., 2020).

Based on available epidemiological data, it is stated that the incubation period of COVID-19 varies between 1-14 days, mostly between 3-7 days. Reported data revealed that the onset age of the disease ranged from 1.5 months to 17 years of age in individuals with a history of close contact with most infected cases (Pediatric Branch of Hubei Medical Association Pediatric Branch of Wuhan Medical Association Pediatric Medical Quality Control Center of Hubei, 2020). It was observed that the important issue emphasized by the publications about COVID-19 are symptoms and signs. Pediatric patients can often appear asymptomatic. It has been reported that symptoms that may occur are fever, dry cough and fatigue (Chan et al., 2020).

Other studies have also produced similar evidence (J. H. Cai et al., 2020; Cao, Chen, Chen, & Chiu, 2020; F. Chen et al., 2020; Qiu et al., 2020; D. Wang et al., 2020). It has been expressed that in most of the reported cases, a fever with good prognosis can be observed or there are no pneumonia symptoms. It was found that recovery occurs in children 1-2 weeks after

the onset of the disease. It has been reported that clinical findings should be defined in pediatric patients after more pediatric case data are collected (Shen et al., 2020).

A retrospective study was carried out by Liu et al. in Tongji Hospital to determine the symptoms and characteristics of respiratory tract infections in children receiving inpatient treatment between 7-15 January 2020. The most common pathogens among 366 children were ranked according to their incidence. Accordingly, it was detected influenza A virus in 23 patients (6.3%), influenza B virus in 20 patients (5.5%), and SARS-CoV-2 related COVID-19 in 6 patients (1.6%). In the same study, the age characteristics of the patients were also listed, and the mean age of six patients was reported to be 3. It is stated that the most common clinical features of the patients mentioned are high fever (>39°C), cough and vomiting. Only one of these patients was admitted to the pediatric intensive care unit (PICU) and immune globulin treatment was started immediately. It was determined that all patients recovered in 5-13 days (average 7.5 days) after hospitalization (W. Liu et al., 2020). Tang et al. has stated that SARS-CoV-2 infections may not yet be reported at the desired level in children and other vulnerable patients (Tang, Tambyah, & Hui, 2020).

In an article referred to this fact quoted by Yang et al., when the cases were identified with diagnostic methods, it was reported that 134 cases in 416 children in China could reflect on clinical records. In this study, it was stated that fever (76.1%), viral pneumonia-like changes (70.4%), cough, vomiting, diarrhea and other gastrointestinal system symptoms were found similar to the case features of previous studies. Although it was shared that there were no newborn cases until an article published by Yang et al., It was reported that infection cases were observed in the neonatal period with the detection of new patients. Besides, in this study, it was reported that a patient was diagnosed with a pharyngeal swab 24 hours after birth, although there were no symptoms and fever was low (Yang, Liu, Li, & Zhao, 2020).

Age

Undoubtedly, the most affected in the first phase of the epidemic was Wuhan province of China and it was reported that many deaths occurred. As of January 22, 2020, the results of a study that reported the characteristics of the first 425 cases observed in Wuhan were found to be important in terms of reflecting the situation in children with all its reality in a short period of time. Some statistical data related to the study are shown in Table 2 in detail.

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Table 2. Age Characteristics of Patients Infected with Coronavirus in Wuhan as of January 22, 2020

Some characteristic features	Before January 1 (N=47)	Between 1-11 January (N=248)	Between 12-22 January (N=130)
Age Mean	56 (26-82)	60 (21-89)	61 (15-89)
Age Groups			
<15 ages	0/47	0/248	0/130
15–44 ages	12/47 (26)	39/248 (16)	33/130 (25)
45–64 ages	24/47 (51)	106/248 (43)	49/130 (38)
≥65 ages	11/47 (23)	103/248 (42)	48/130 (37)

* Reduced denominators indicate missing data. Percentages may not total 100 because of rounding.

When the table and study results are examined, the average age of the patients were 59 (15-89 age range) and 240 (56%) were male. In the same study, it was stated that there were no cases in children under 15 years of age. In this study, very few of the first cases were described as the occurrence in children. It was explained that the possibility of children to be less likely to infected or to show milder symptoms if they were infected (Table 2) (Q. Li et al., 2020).

It was stated that this study has a significant limitation especially in the earliest stage. Little is known about any aspect of the outbreak. Initial investigations of infections due to a lack of diagnostic kits may not be healthy for commenting (Table 2).

Mortality

As the cases approved after the diagnosis kits were made available in Wuhan on January 11, it was explained that the application results made in the previous period could not be predicted clearly, so the first focus of the case detection could be made on patients with pneumonia. In this study, it was stated that due to some patients with gastrointestinal symptoms admitted to healthcare centers and reported as an asymptomatic infection. It makes difficult to make a clear definition for cases (Q. Li et al., 2020). In an article by Caselli and Aricò, severe acute respiratory syndrome (SARS) was observed in Hong Kong and then world-wide from March to June 2003. More than 1700 individuals infected. Mortality rate has been reported to be 0% in cases under 18 years of age (Caselli & Aricò, 2020). It has also been reported by Stockman et al. that pediatric patients aged 12 and under had a milder course, and pediatric patients admitted to the intensive care unit received additional oxygen supplements or were more likely to be treated with methylprednisolone. No deaths have been reported among children or adolescents with SARS (Stockman et al., 2007).

Chan et al. published a study in China's Hubei province that they assessed the general features and outcomes of COVID-19-associated pneumonia epidemic. Accordingly,

phylogenetic analysis of genetic sequences was made to members of a family who showed unexplained pneumonia complaints after a visit to Wuhan province, where the outbreak was first seen. Five of the six family members traveled to Wuhan were diagnosed as infected with the new coronavirus. In the detailed examination, it was stated that only one of the family members became infected after contact with the other four individuals.

Radiologic Signs

It has been expressed that the ages of the five family members who admitted to hospital for fever, respiratory tract symptoms and diarrhea ranged between 36-66. After radiological examination of a 10-year-old child with asymptomatic features revealed glass opacities in the lung. In a study in which the clinical radiographs of 5 children were examined retrospectively, it was reported that glass-opacities findings were observed in the imaging findings of children infected with COVID-19 (Feng et al., 2020). It was pointed that the findings of the study are remarkable in terms of showing that there may be contamination from person to person in hospital and family environments. Therefore, it was mentioned that control measures will be of vital importance in the early stage of the outbreak (Chan et al., 2020). In a multicentre, cross-sectional study in ten hospitals, it was stated that the clinical features of pediatric cases were rarely identified despite the rapidly increasing number of cases. In addition, the average age of the pediatric patients was three, and the symptoms generally have respiratory characteristics (Zheng et al., 2020).

Infection Path Type

Different theories have been introduced in this event, whose spread and global impact is extremely fast compared to other coronaviruses. Peiris et al. revealed that coronaviruses may be a possible cause of severe acute respiratory syndrome. This study found evidence that SARS, a virus in the coronavirus family, as a factor associated with severe illness, can be a causative agent. It was stated that the disease is likely to be acquired through home contact, and that infected people can have the ability to transmit the disease agent to healthy people through social contact (Peiris et al., 2003). Recent study results have indicated that isolation measures can be of vital importance. It's stated that the main route of transmission of new coronavirus pneumonia is droplets in the respiratory tract and close contact with the sick individuals (S. J. Cai et al., 2020).

Studies after the spread of the outbreak and causing global pandemics have shown that it produces worse results in adults, especially older people (Chan et al., 2020; Q. Li et al., 2020). The reason why children suffer less than adults has not been clarified yet. And It was explained

by the fact that the innate immune system plays a crucial role in protecting infants and young children against external pathogens. It is a known fact that it is one of the leading causes of mortality in children under five, especially when respiratory tract infections are evaluated (L. Liu et al., 2015; Walker et al., 2013).

No evidence of oral-faecal transmission occurred in studies performed so far (Z. Li et al., 2020). Ma et al. evaluated the contamination issue from a different perspective, and stated that SARS-CoV-2 can also be found in the faeces of patients in recovery process. In particular, it was stated that children have the potential to spread this factor in their faeces for a longer time than adults. In-depth analysis conducted in order to better interpret the results of the study, the reasons why children are positive for a longer time than adults are explained as follows:

- Children generally have worse hand hygiene practices and may cause contamination of the gastrointestinal tract by repeated contact to virus or virus fragments by their hands,
- When SARS broke out in 2003, angiotensin converting enzyme 2 (ACE2) was confirmed to be a functional receptor for SARS-CoV. New findings have shown that 2019-nCoV uses ACE2 as the input receptor. It is believed that the amount of ACE2 in children's intestines may differ from adults; this difference could explain that children have a longer viral shedding time than adults,
- Children often cough poorly; but they are more prone to aspiration. Therefore, viruses in sputum or saliva can enter the gastrointestinal tract by swallowing. This may explain the reason why children have viruses in their feces.

For this reason, it was suggested that feces sample should be included in the discharge criteria in pediatric patients who want to be discharged because their respiratory functions are improved (Ma et al., 2020; Tang et al., 2020).

Child and Baby with COVID-19

The immune responses of babies are sensitive to incoming pathogens. This is thought to trigger a reaction set in the response to the infection agent (Lambert & Culley, 2017). Thanks to the innate immune response, pathogens are recognized by the associated molecules in the body systems. In this way, RNA viruses in the lungs are perceived as foreign substances that are pathogenic by the innate immune system, and infected cells begin to be surrounded by numerous interferons that create an antiviral condition. This effectively inhibits the further spread of infection and often helps remove the virus from the infected person (Davis & Gack, 2015). It is not very likely that the immunity caused by the factors coming from the mother continues to be a protective feature during childhood. Many questions come to mind at this

stage and the studies conducted cannot provide sufficient clarification to this subject (Caselli & Aricò, 2020).

- Do children provide cross protection when infected with other coronaviruses?
- Is there an innate immune response against RNA viruses due to conditions occurring in the respiratory system and other systems?

Prognosis

While these questions are still waiting for answers, new research results on new cases of childhood continue to be published and somehow it is explained that children's recovery processes are better than adults and older individuals (Britton & Marais, 2020). In the isolation clinic of a primary care children's hospital affiliated to Zhengzhou University, the symptoms caused by COVID-19 in three children has brought us new information about the process.

It was reported that two out of the three children that were treated in the clinic, were sisters who were aged between 6 and 8. The other child was a six-month old boy. It was observed that all three children had at least one infected relative and the infection in the children occurred after their parents showed signs of the disease. It was determined that the two sisters had family members who visited Wuhan. It was stated that the other child did not have a direct connection with Wuhan. It was reported that all three patients were admitted with high fever complaints and two had symptoms of fatigue, diarrhea, headache associated with nasal obstruction and rhinitis (Chan et al., 2020).

These results are similar to other study data (Yang et al., 2020). It was pointed that the 6-year-old girl had a somewhat more severe course. And there was a process that mostly continued with cough attacks, but none of the children accompanied the symptoms of dyspnea or cyanosis. In this line, there were no process like in adults. Similarly, it was reported that none of the children needed intensive care treatment or mechanical ventilation conditions and no serious complications occurred. In the shared information about the disease processes of children; It was expressed that the fever process improved within 3 days and the closely monitored sisters displayed significant improvements within a week after nebulized interferon treatment was given twice a day for seven days.

It was stated that the patients were discharged safely within ten days due to the complete recovery in the incoming cases and they were provided with psychological support by the nurses (Lou, Shi, Zhou, & Tian, 2020). However, in a recent study analyzing 44.672 laboratory-approved cases from China on February 11, 2020, only 416 cases (0.9%) were reported to be under the age of ten. In the same study, it was explained that 549 (1.2%) patients

between the ages of 10-20 were identified, and an increase was observed in the number of pediatric infections while increase in the number of contacts with infected adult individuals. Despite the increase in the number of cases diagnosed day by day, it has been reported that the infection has a mild course in children and young adults (Y. Zhang, Liu, & Li, 2020).

Both symptomatic and asymptomatic children with known contact with people who have confirmed or suspected SARS-CoV-2 infection. A study conducted with children under the age of 16 in Wuhan in order to contribute to limited data on the epidemiological and clinical features of infected children were evaluated. In this study, clinical results in the period up to 8 March 2020 were followed. For the study, the data of 1391 children who were treated at Wuhan Children's Hospital from January 28 to February 26, 2020 were evaluated. It was determined that 171 of the children (12.3%) had SARS-CoV-2 infection. It was stated that the average age of infected children was 6.7, and fever occurred in 41.5% of children during the disease or at any stage of the ongoing process. Although cough and pharyngeal erythema were among the most common signs and symptoms of the disease, 27 patients (15.8%) were found to have no signs of infection or pneumonia as well as radiological findings necessary for diagnosis. 12 patients had pneumonia related radiological features, no infection symptoms were reported. It was declared that three patients needed intensive care and invasive mechanical ventilation during hospitalization. On March 8, 2020, a 10-month-old child died four weeks after hospitalization after multiple organ failure, and a total of 21 patients were reported to be stable and 149 patients were discharged from the hospital (Lu et al., 2020).

Another study, which shared important data explaining the clinical course of coronavirus infection in regions other than Wuhan, where the outbreak occurred, was conducted with 10 patients. It was stated that the disease is usually mild in children, and even cases where pneumonia is mild or asymptomatic require close observation (J. Cai et al., 2020). In the study, in which the characteristics of the first baby COVID-19 case in Vietnam was emphasized that the patient admitted only with complaints of runny nose and congestion. It has been reported that it has not shown symptoms such as cough, fever, vomiting, diarrhea, wheezing, and was asymptomatic despite being diagnosed with COVID-19. Therefore, it has been expressed that the patient may need detailed examination in order to better understand the transmission of SARS-CoV-2 and to make a correct diagnosis in pediatric patients (Le et al., 2020).

Many infectious diseases affect children differently from adults, and understanding these differences can provide important information about the pathogenesis of the disease and shape the management of the disease. This will probably be the case for COVID-19, as in previous communicable diseases.

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Pregnant Women with COVID-19

There are very limited data on the effects of this disease on pregnant women and so on children. In another study that can clarify this issue. It was aimed to evaluate the effects of COVID-19's pneumonia symptoms on pregnant women in general pregnancy process. Laboratory results and chest scans of nine pregnant women with laboratory-approved COVID-19 pneumonia were retrospectively reviewed. Seven of the nine patients examined, who admitted to the hospital with a fever. Four patients had severe symptoms such as severe cough, and two had sore throat and weakness. It was observed that there were serious fetal problems in two cases. Although vertical transmission has not yet been reported, most babies born surgically due to mothers are infected with COVID-19. In fact, many infectious diseases seriously affect pregnant women. Therefore, respiratory problems in pregnant women infected with COVID-19 may cause fetal outcomes with negative course (H. Chen et al., 2020).

Although different technological methods were used in detecting the disease, it was emphasized that in some cases the results cannot be obtained as mentioned above and the detection of the disease can be difficult. The clinical process characteristics and Computed Tomography (CT) results of 55 patients diagnosed with COVID-19 between 27 January-14 February 2020 were analyzed. The results of the study showed that the clinical findings of pregnant women with COVID-19 pneumonia are atypical and cause difficulties in early detection. It was stated that in cases with clinical features, early diagnosis will be more useful for screening in children (H. Liu et al., 2020).

A new study aimed at identifying the effects of the disease in younger age groups was published on February 11, 2020. In this study, on January 26, 2020, the prognosis of a three-month-old baby who admitted to the hospital, lasted 4 hours of fever was discussed. In the shared information about this patient who was hospitalized and treated; It was determined that the number of white blood cells was not high and thickened right lung skin was seen on chest radiography. With the coronovirus disease 2019 test (2019-nCoV) results, the patient was diagnosed with COVID-19 infection. The patient's mother had asymptomatic features; however, the 2019-nCoV test was found to be positive. In addition, it was found that the symptoms of fever and respiratory system were not evident in the mother. This atypical prognosis complicated the clinical diagnosis of the case.

Prevention

One aspect of care, especially in families with children, was listed as the need to take effective personal protection measures. It has been suggested that the use of masks, long sleeved

clothing and hand hygiene should be provided to prevent infections caused by close contact (Y. H. Zhang et al., 2020). In a study on a similar case, the general course of a seven-year-old child who admitted to Fudan University Children's Hospital with a complaint of 3 hours of cough and high fever on 19 January 2020 was explained. It was reported that the maximum body temperature of this child is 38.3°C, after a clinical course with mild cough, runny nose and decreased appetite; nausea, vomiting, diarrhea, abdominal pain, headache and fatigue occured. It was determined that the child shows normal growth and development characteristics, does not have any underlying disease and childhood vaccines are completed.

It was emphasized that special protective measures would be necessary, especially since babies under one year cannot wear masks. And It was recommended that the parents who give care to baby should wear a mask, pay attention to washing hands before close contact with the babies and regularly sterilize babies' toys and dinner sets (Wei et al., 2020).

This has been explained in relation to the activation of humoral immunity and then the production of antibodies to inactivate the virus in children with acute infection. The immune system of children in the acute stage is over-activated (Caselli & Aricò, 2020). With the help of treatment given in the early stages, the hemodynamic parameters of children can be stabilized, the fluid-electrolyte and acid-base balance of the body is maintained, at the same time, inflammatory reactions are effectively eliminated (F. Chen et al., 2020).

Management and Treatment

An important part of the researchs is related to the application of prevention methods and how to arrange treatment options in children. An important part of the research is related to the application of prevention methods and how to arrange treatment options in children. It was expressed that due to the inactivation of most of the routine viral vaccines, it stimulates the secretion of many different cytokines such as interferon gamma and interleukin-2 (IL-2) and improves the cytotoxicity of natural cells that destroy them by recognizing viruses (Baskar et al., 1998).

Measles, mumps, rubella (MMR) are already been used to induce cross reactivity immunity against other virus strains. For this purpose, it was suggested using one or combined vaccination of MMR to either protect or treat the emerging epidemic of COVID-19 (Salman et al., 2019). Although the clinical course is not as severe as in adults, some treatments are requested to alleviate the effects occurring in infected cases and shorten the time of discharge. Currently, only antiviral drugs are used in the treatment of COVID-19 world-wide (Y. Wang & Zhu, 2020). In a study to develop pharmaceutical care recommendations for antiviral treatments

for children with coronavirus disease; It was suggested that the advantages and disadvantages of children should be thoroughly determined while using this type of medication.

It was suggested that low dose IFN-a nebulization can be used for children with mild symptoms, and Ribavirin is generally recommended as a combined drug. Simultaneous combination of three or more antiviral drugs is not recommended during the treatment process (Y. Wang & Zhu, 2020). A study by Xie suggests similar evidence. It was stated that lopinavir/ritonavir treatment is not recommended for children with mild symptoms in the mentioned study (Xie, 2020).

Some authors point that if the effectiveness of antiviral drugs is uncertain in children, high dose pulmonary surfactant, nitric oxide inhalation and high frequency ventilation should be applied in newborns if there is a respiratory distress (J. Wang & Shi, 2020). It was reported that intravenous administration of glucocorticoids or immunoglobulins may be considered in treatment in critical neonates (Hong, Wang, Chung, & Chen, 2020). Respiratory support was proposed to be implemented according to an internationally regulated approach (Luca, 2020).

DISCUSSION

COVID-19 has rarely been reported in children. This can be explained by their being asymptomatic (Chan et al., 2020; Feng et al., 2020; Le et al., 2020; Q. Li et al., 2020). It is thought that there may be undiagnosed (undocumented) cases. This systematic review aimed to identify available evidence on COVID-19 in children. Although there is not much data on children, but it can be seen that vertical intrauterine transmission may occur from pregnant mothers to newborn babies. In addition, there are studies in which mothers with positive tests have positive babies (H. Chen et al., 2020). Until now, COVID-19 contamination has not been reported in neonatal intensive care units (Ludvigsson, 2020). Although children show fewer symptoms than adult patients, newborns may experience respiratory distress and the disease may progress (Lou et al., 2020; Ludvigsson, 2020). The strength of this study was that the studies published until March 27, 2020 have been extensively examined in the databases. The main limitation was that we had only researched English abstracts from Chinese studies and rely on citing Chinese publications.

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CONCLUSION

In summary, many questions as source of the SARS-CoV-2 infection, the route of transmission, pathogenic mechanism and prognosis of infected patients, including the humoral and cellular immune responses, clinical features, high-risk populations are still awaiting answers. With these uncertainties and evidence, it was seen that understanding the role of the child population in the transmission traffic of the epidemic is very important. Because children can become an important host during the spread of the epidemic. Possible causes of lower SARS-CoV-2 infections in children are summarized as follows:

- Children are less likely to be exposed to the virus due to their daily activities,
- The congenital immune system plays a crucial role in protecting infants and children from external pathogens, causing less symptoms (Lee, Hu, Chen, Huang, & Hsueh, 2020),
- Pediatric patients may not have been subjected to laboratory tests because they show mild symptoms. This can lead to less diagnosed cases in the laboratory.

Of course, more observations are needed to test these hypotheses that we mentioned above. It is clear that further studies are needed to explain why pediatric patients have a milder disease process than adult patients. In order to prevent and control this epidemic, the solution suggestions that are thought to be useful if they are applied adequately after patient admission are listed below:

- Patients with high fever should be regularly controlled,
- Suspicious cases or confirmed cases should be chest radiographed and chest examined as soon as possible (Kelvin & Halperin, 2020),
- Children infected with coronavirus should be isolated at home, depending on their medical condition, or admitted to hospitals designated by healthcare professionals, depending on the severity of their medical condition,
- Critical cases should be referred to the intensive care unit as soon as possible,
- Among the general treatment strategies should be bed rest, providing adequate calorie and liquid intake. In addition, it should be maintaining water electrolyte balance and homeostasis, monitoring vital signs and oxygen saturation (F. Chen et al., 2020),
- When hypoxia occurs, effective oxygen treatment with nasal catheter and mask should be given immediately,
- Mothers infected with COVID-19 should not breastfeed their babies until they are healed, these mothers should strictly apply hand hygiene and disinfect the environment,

- Balanced nutrition, oral health, adequate exercise, avoiding excessive fatigue and enhancing immunity, maintain emotional stability and mental health are powerful measures to prevent infection (Shen et al., 2020),
- Quick advice guides on children should be prepared internationally. This guide can guide politicians. It can help healthcare professionals and parents get better health care for their children.
- Patients should not be discharged unless the fever is within normal limits for more than three days, respiratory symptoms and chest radiography show signs of significant improvement, 24-hourly nasopharyngeal swabs and COVID-19 tests in the sputum are not negative twice (F. Li, Feng, & Shi, 2020),
- It is thought that there is an urgent need to increase the number of immunotherapy studies and to develop protective vaccines.

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