Novel Coronavirus disease 2019 (COVID-19) in Newborns and Children

Yenidoğanlarda ve Çocuklarda Yeni Koronavirus Hastalığı 2019 (COVID-19)

Melis Deniz, Hasan Tezer

Department of Pediatric Infectious Diseases, Faculty of Medicine, MD, Gazi University, Ankara, Turkey

ABSTRACT

In December 2019, the coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus (SARS CoV- 2) in Wuhan, China, was the first coronavirus to be declared as a pandemic by the World Health Organization. It was observed that the majority of affected adult patients developed serious life-threatening complications, whereas the disease was milder in children. Despite the increasing number of affected children and newborns, there is still limited information on treatment options and disease management. In this article, the literature on COVID - 19 in newborns and children is reviewed and the findings are summarized and it is aimed to present up-to-date information about pediatric and neonatal COVID-19 management, epidemiological, clinical, laboratory and treatment options.

Key Words: Pediatric, COVID-19, novel coronavirus, neonatal, SARS CoV-2

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ÖZET

Aralık 2019'da Çin'in Wuhan kentinde şiddetli akut solunum yolu sendromu koronavirusunden (SARS CoV 2) kaynaklanan koronavirus hastalığı 2019 (COVID-19) büyük salgınlarla tüm dünyaya etkilemiş ve Dünya Sağlık Örgütü tarafından pandemik ilan edilen ilk koronavirus olmuştur. Etkilenen erişkin hastaların büyük bir kısmında ciddi hayatı tehdit eden komplikasyonlar geliştiği, öte yandan, çocuklarda hastalığın daha hafif seyirli olduğu gözlenmiştir. Etkilenen çocuk ve yenidoğan hasta sayısı giderek artmasına rağmen, bu yaş grubunda tedavi seçenekleri ve hastalığın yönetimi ile ilgili halen kısıtlı bilgi mevcuttur. Bu makalede, yenidoğan ve çocuklarda COVID - 19 hakkındaki literatür taranarak bulgular özetlenmiş ve pediatrik ve neonatal COVID-19 yönetimi, epidemiyolojik, klinik, laboratuvar ve tedavi seçenekleri ile ilgili güncel bilgileri sunmak amaçlanmıştır.

Anahtar Sözcükler: Pediatrik, COVID-19, yeni koronavirus, neonatal, SARS CoV-2

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ORCID IDs: M.D. 0000-0002-9740-4196, H.T. 0000-0001-6871-4112

Address for Correspondence / Yazışma Adresi: Melis Deniz,MD Department of Pediatric Infectious Diseases, Faculty of Medicine, MD, Gazi University, Ankara, Turkey. E-mail: mlsdnz@gmail.com

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INTRODUCTION

The new coronavirus (2019-nCoV) infection causing epidemics worldwide has been declared as a pandemic by the World Health Organization (WHO) and has been referred as 'Coronavirus Disease 2019 (COVID-19) (1). In this epidemic, which had a low number of cases in children while it was initially more common in adults, the incidence of children with COVID-19 has increased dramatically in recent days due to the fact that children could not wear masks and could not take other protection control (2,3). Because of the growing spread of COVID-19 all over the world the information regarding this issue is updated frequently, yet there is still inadequate evidence on how the approach towards pediatric patients and newborns will be, the effect of COVID-19 on the fetus, and the safety of breastfeeding, and clinical studies are still proceeding (4,5). In this review, it was aimed to summarize the management of children and newborns with COVID 19, diagnosis, clinical findings and current treatments by using of the limited scientific evidence in the literature.

Etiology and virology

Coronaviruses, which can cause zoonotic epidemics and have potential for interspecies transition , are enveloped, single stranded, with positive polarity, composed of zoonotic RNA viruses and contain four genera (alpha-, beta-, gamma- and delta- coronavirus). SARS-CoV and MERS-CoV belong to the beta-coronavirus genus, and are the factors causing severe pneumonia epidemics in humans in past years. SARS-CoV-2 is a new β-CoV; it is a zoonotic pathogen which is the cause of the disease that is called COVID-19 and declared a global pandemic (6).

The structure of the receptor binding gene region is very similar to that of the SARS coronavirus and has been shown by Chinese scientists that SARS CoV -2 uses the same receptor, angiotensin converting enzyme 2 (ACE2) for cell entry. Dipeptidyl peptidase 4 (DPP4, also known as CD26) is a functional receptor for MERS-CoV, and MERS-CoV can bind to more than one species with DPP4, causing infection to humans and other species and causing multiple types of infections. Coronavirus S protein is important for virus entry into host cells and binds to the spike glycoprotein cellular receptor on its surface, SARS-CoV and ACE2 for SARS-CoV-2. The introduction of SARS-CoV into cells is initially accomplished by direct membrane fusion between the virus and the plasma membrane. Once the virus enters the cells, the viral RNA genome is released into the cytoplasm and translated into two polyproteins and structural protein, after which the viral genome begins to multiply. The newly formed envelope glycoproteins are placed in the endoplasmic reticulum or golgi. Nucleocapsid is created by a combination of genomic RNA and nucleocapsid protein. Eventually, vesicles containing virus particles then fuse with the plasma membrane to release the virus. As the virus enters the cells, its antigen is delivered to the antigen presenting cells (APC). Antigenic peptides, are presented by MHC; or in humans by (HLA) and then recognized by virus-specific cytotoxic T lymphocytes (CTLs). There is no clear report on the antigen presentation of SARS CoV 2, the available information is based on previous research on SARS-CoV and MERS-CoV. Antigen presentation then stimulates the body's virus-specific B and T cells mediated humoral and cellular immunity. Similar to common acute viral infections, IgM and IgG antibodies are produced against the SARS-CoV virus (7).

Pathogenesis

Acute respiratory distress syndrome (ARDS) is a common immunopathological event in SARS-CoV-2, SARS-CoV and MERS-CoV infections. In SARS-CoV infection, there is a fatal uncontrolled systemic inflammatory response resulting from the release of large amounts of proinflammatory cytokines (IFN-a, IFN-γ, IL-1, IL-6, IL- 12, IL-18, IL-33, TNF-α) and chemokines (CCL2, CCL3, CCL5, CXCL8, CXCL9, CXCL10, etc.).

Severe pneumonia caused by human coronaviruses (HCoV) is associated with hypercytokinemia resulting in uncontrolled overproduction of inflammatory cytokines which is called cytokine storm, leading to acute lung injury and ARDS in immunocompetent individuals (8). A fatal condition leading to immunopathogenic damage to the tissues and organs progressing with hyperactivation and rapid proliferation of T cells, macrophage and NK cells is observed. In a patient who died of SARS CoV-2 infection, indications of damage caused by T cell hyperactivation with increased concentration of proinflammatory CCR4 +, CCR6 +, Th17 +, CD4 T have been observed (7). In post-mortem examinations in patients, cellular fibromixoid exudates along with bilateral diffuse alveolar damage, SARS and MERS-like pathological findings, hyaline membrane formation signalling ARDS was observed (9).

Epidemiology

When compared to adults, the number of pediatric cases diagnosed is small and the rate of mortality is lower. In China, in Zhonghua Liu Xing Bing Xue Za Zhi journal , it is reported that in a study in which 44672 cases diagnosed with COVID-19 , 1022 deaths (2.3%) among 43.707 patients older than 20 years old, and only one death among 549 patients aged 10-19 years (% 0.2), and no death among 416 patients between the ages of 0-9 (0%) were observed (10). Korea Center for Disease Control and Prevention stated that 6.3% of all cases tested positive for COVID-19 by March 20 were children under 19, but China Disease Control and Prevention Center reported that after examination of 72,314 cases, less than 1% of the cases were children under the age of 10 (3, 11). Data published in Italy on March 18, 2020 reported that only 1.2% of 22,512 COVID-19 Italian cases were children, and there was no death in children. 5% of 4,226 COVID-19 cases diagnosed in the USA until March 16, are children. Children accounted for less than 1% of all COVID-19 hospitalizations in the USA (12). Consequently, it can be said for COVID-19 that it is an infection with a better prognosis in children in the light of current limited scientific evidence (10). This infection affecting all age groups had an average of 7 in the Chinese pediatric case series (with 2143 cases), while 171 children reported from the Wuhan pediatric hospital had an average age of 6.7 (12). Nine infants with COVID-19 diagnosed with COVID-19 in China from December 8, 2019 to February 6, 2020 and minimum age was 1 month (13). Data published in Turkey reported that only 1% of 11535 COVID-19 cases were children by 30.03.20. There were 3 neonatal cases (14).

Why do children with COVID-19 have better prognosis than adults?

Several different hypotheses have been suggested for this issue. There is a correlation between the amount of viral load and the severity of COVID-19 disease. It can be interpreted by the fact that healthcare professionals are exposed to more viral loads and have more severe infections (11). That the presence of other concomitant viruses in the lower respiratory mucosa in children can limit the viremia of SARS-CoV 2 by causing competition because of direct virus-virus interactions is one of the hypotheses put forth about this issue. The SARS CoV- 2 S protein is bound to the angiotensin converting enzyme 2 (ACE 2) receptor. Since this enzyme is immature at young ages, children might be protected from SARS CoV-2 in this way (12). Another probable theory for mild COVID-19 infections in children is about the differences in the expression of the ACE 2 receptor. Treatment with ACE inhibitor or angiotensin receptor blocker drugs induces ACE 2 receptor expression. Whereas both treatments are commonly used in adults with hypertension, it is a rare treatment in children. This illustrates the severity of SARS-Cov2 in adults with high ACE2 expression. However, there is inadequate evidence about the mild course of the disease in most children with COVID-19 (11).

Transmission

SARS-CoV-2 can be transmitted rather quickly and transmission is thought to take place mainly through respiratory droplets. Most often, it is transmitted through close contact with the infected person adn the droplets from coughing or sneezing of the infected person (15).

Even though viable virus is detected in fecal samples from very few cases, the role of fecal-oral transmission in COVID-19 spread is still unclear (16). It was observed that after the virus was negative in oropharyngeal samples taken from adults diagnosed with COVID-19, virus excretion continued in fecal samples (7 days on average) (17).

There is very little evidence in the literature for the transmission of SARS-CoV 2 vertical transmission. No vertical transmission was shown in a case series in which 9 pregnant women were observed in China (18).

Yet, in another case report, the presence of high level of SARS CoV-2 lgM in the postnatal 2. hour in the baby which was born 23 days after the mother's diagnosis of COVID-19 gave rise to the thought that the baby might be affected in utero period.(16) However, vertical transmission was evaluated as suspicious because in the polymerase chain reaction (PCR) SARS CoV-2 virus was not seen in the nasopharyngeal sample taken 5 times intermittently from the baby and due to the prediction that because of placental decollement or the deterioration of placental barrier with maternal-fetal hemorrhage, virus and IgM antibodies may enter the fetal circulation (20). For vertical transmission diagnosis, samples must be taken soon after birth and if these samples are negative for SARS-CoV-2 RNA while the IgM and IgG antibodies are positive in the newborn, long term IgG antibody monitoring is required for the baby.

If IgG antibodies in the baby become negative in six months time, the possibility of intrauterine infection can be excluded. If these antibodies, though, continue until the age of eighteen months or older, the diagnosis of congenital infection can be verified, but it should be shown that during this period, it experienced no infection in the infant period(21).

The transmission of SARS CoV 2 by the environmental settings is also important as transmission from the contaminated environmental setting can also take place by inoculation of the virus into the nasal, mouth and eye mucosa. While the coronavirus remains infectious for hours in the aerosol, it can remain infectious for days on inanimate surfaces. In the study researching for how long SARS-CoV-2 remains infective in aerosols and surfaces, it has been revealed that SARS-CoV-2 can remain viable in aerosols for up to 3 hours and up to 72 hours on plastic surfaces (22).

Clinical signs and symptoms

COVID-19 incubation period is 14 days, but most cases occur about four to five days following exposure (13). In children, the COVID-19 spectrum manifested itself as influenza-like symptoms, pneumonia, fever, and upper respiratory tract infection findings (rhinorrhea, cough, sore throat, nasal congestion, sneezing) (12) Yet, nonspecific findings are observed in newborns, especifically in premature babies (10). In newborns, irregular body temperature, tachypnea, nasal flaring, breathing effort, apnea, cough or tachycardia may develop. Other findings are lethargy, diarrhea, vomiting, and abdominal discomfort (23).

The first critical childhood infection reported in Wuhan, China, started with gastrointestinal symptoms and proceeded to acute respiratory distress syndrome. In a published study, while the most common reported complaint of 134 children diagnosed was fever (n = 89), fever was mostly 1-2 days, the longest time 8 days (2). Another report that collected data from nine children in China showed that three children had fever (22.2%) or cough (11.2%) symptoms and six (66.7%) children had no symptom (24).

In a study carried out in Wuhan's children hospital, the most common symptoms in 171 diagnosed children were respectively, cough (48.5%), pharyngeal erythema (46.2%) and (41.5%) fever (12).

Diagnosis

In diagnosis of SARS-CoV-2, RT-PCR (real-time polymerase chain reaction) is regarded as the gold standard (20). SARS-CoV-2 can be identified in the upper respiratory tract (nasopharyngeal and oropharyngeal), lower respiratory tract (endotracheal aspirate or bronchoalveolar lavage), blood and stools (20). It is crucial in the diagnosis that RT- PCR COVID 19 is positive for nucleic acid or COVID -19 IgM and IgG serology are positive, and COVID specific Ig G illustrate titre increase 4 times in the recovery phase in comparison to the acute phase (25). Clinical diagnosis is based on the existence of at least 2 symptoms in China (fever, respiratory symptom, GIS symptom or malaise), combination of laboratory tests (normal or low leukocyte count and increased crp) and abnormal chest radiography (12).

Clinical classification

Mild COVID-19 cases are regarded as clinical symptoms are mild and there is no evidence of pneumonia on radiography. Moderate Illness is defined as the patients with fever and respiratory symptoms including pneumonia findings in radiologic imaging. Severe illness is defined as tachypnea according to age (without fever or crying), oxygen saturation ≤ 92 , difficulty in respiratory effort (nasal, retraction, cyanosis, intermittent apnea), lethargy and convulsions and dehydration. Critical COVID -19 cases are regarded as being accompanied by respiratory failure with mechanical ventilation, other organ failure requiring intensive care unit follow-up and treatment and shock (25).

Underlying medical conditions that may increase risk of COVID-19 related morbidity and mortality

Studies have revealed that younger age can not be a risk factor for severe COVID-19 alone. Although there is not sufficient study that immunocompromised children are at higher risk for severe COVID-19, it was observed that mortality was higher in adults with malignancy in adult studies. Though information on SARS CoV-2 and immunocompromised pediatric patients is insufficient, in other virus studies (RSV, parainfluenza, seasonal coronavirus) immune deficiency has been found to be a risk factor for severe lower respiratory tract infection. Similarly, COVID -19 related morbidity and mortality ascended in adults with underlying cardiovascular, pulmonary disease and hypertension.

Although there is not sufficient data on children, coronaviruses other than COVID-19 , influenza, parainfluenza infections have been proven to be more severe in children with chronic cardiac and pulmonary disease. Obesity can cause negative respiratory results, creating a risk factor for severe COVID. In adult studies, it has been observed that diabetes mellitus (DM) is a risk factor in the progression towards severe disease and causes death. However, in most of these reported adult cases, there was a comorbid disease accompanying DM. It is suggested that diabetes and accompanying comorbidities should be taken into consideration during the treatment decision in children as well.

Existence of cardiomyopathy for any reason, Ross classification 2 -4 patients with heart failure, children with untreated cyanotic heart disease and children who need oxygen by noninvasive mechanical ventilation because of pulmonary hypertension, cardiac or pulmonary disease (cystic fibrosis, bronchopulmonary dysplasia, bronchiectasis) and history of hospitalization 3 and over 3 in the last 12 months, severe neuromuscular diseases (duchenne muscular dystrophy..etc), and severe persistent asthma are among the other diseases that should be taken into consideration in the COVID-19 antiviral treatment decision (26).

Laboratory Findings

Laboratory findings are nonspecific. The number of leukocyte is reduced or normal in the early stage of the disease. In some patients, aspartate aminotransferase (AST), alanine aminotransferase (ALT) , lactate dehydrogenase (LDH) , creatine kinase (CK) and myoglobin increased. Troponin also increased in severe patients. Lymphocytopenia, elevation of D-dimer, crp and sedim is also observed. Other tests must be considered to exclude other infectious etiologies (influenza, respiratory syncytial virus, bacteria, etc.) (13, 23). As a result of the study conducted on 66 children, normal leukocyte number was observed in 69.2% of the children. Lymphocytopenia was found only in 2 children (3%) , C-Reactive Protein (CRP) increase was seen in 13.6% of patients and procalcitonin increased in 10.6% of patients (12).

Imaging profile of COVID -19: Radiologic Findings

Chest radiograph: When the reported cases regarding the newborn were examined, similar findings in imaging were observed with the children. However, due to lack of data on the subject, the radiographic features of newborns with lower respiratory tract infections related to SARS-CoV-2 have not been able to be identified adequately (20). In another recent study, typical findings of pneumonia were detected on chest radiography of 3 newborns diagnosed with early neonatal COVID -19 (27). The sensitivity of chest radiography is low in children. In the early stages, chest graphy may be normal and do not show ground-glass lesions, but in severe cases advance to bilateral multifocal consolidation may be observed (25).

Thorax computed tomography (CT) scan: As regards the latest evidence, the CT scan findings of COVID-19 pneumonia manifest themselves from the appearance of multifocal, unilateral or ground glass opacification often to peripheral localized mixed ground- glass opacification and consolidation (28). In a study in China in which 5 children diagnosed with PCR were examined, while the thorax CT was normal in two children with verified COVID-19 infection, the other 3 patients had irregular ground glass opacification (29). Lymphadenopathy is not generally seen, and pleural effusion is rare (30).

In a study in which 171 patients with COVID 19 were examined, 1/3 of children were found to have ground glass opacification, but in the same study, no pneumonia clinical or radiological findings were observed in 15.8% of the children (12).

In a study involving 20 child patients, unilateral pulmonary infiltration (6/20, 30%) in 6 patients, bilateral pulmonary infiltration (10/20, 50%) in 10 patients were observed and thoracic CT in 4 patients were not abnormal (4/20, 20%) (28).

Recently, bedside lung ultrasound is advised instead of thorax CT as a COVID-19 imaging device for children. It enables patients to reduce exposure to radiation.It is possible to be performed at the bedside, thus reducing the movement of the patient in the hospital and prevents the in-hospital transmission of Sars-CoV. However, further studies are needed on this issue. (31).

Treatment

Treatment is basically arranged by making use of clinical experience with adult patients. COVID -19 does not have any specific medication treatment in childhood. Symptomatic and supportive therapy, oxygen therapy and fluid-electrolyte support are recommended.(13).

For newborns, high-dose pulmonary surfactant, inhaled nitric oxide, HFO (high frequency oscillation) treatment and ECMO (extracorporeal membrane oxygenation) can be useful (18). Oxygen therapy and mechanical ventilator support must be given to patients with respiratory distress and severe acute respiratory disease (SARI) (hypoxemia and shock) with oxygen therapy saturation at a level above 94%. Nasal cannula is recommended in children (20).

Antivirals can be considered in the context of clinical studies on a case basis. All antiviral use should be considered experimentally, due to the absence of antivirals that have proven efficacy for treatment and should be tested in clinical trials to ensure efficacy and safety. Hydroxychloroquine and chloroquine, which inhibit SARS CoV-2 in vitro (inhibit entrance to cells) are FDA approved and widely used for the treatment and prophylaxis of the malaria when it is not complicated.

Hydroxychloroquine is also FDA approved for discoid lupus erythematosus, systemic lupus erythematosus and rheumatoid arthritis. There is not adequate evidence of its use in the treatment of pediatric COVID-19, but it has pediatric clinical experience owing to its acceptable side effect profile and other indications. So, although it seems to be advantageous, the combination of azithromycin is not recommended because of the fact that it increases cardiac side effects. Infant and child dosage is 13 mg / kg/dose (maximum: 800 mg/dose) po followed by 6.5 mg / kg/dose (maximum: 400 mg/dose) po to be taken 6, 24 and 48 hours after the initial dose. Given that acute malaria has 3-day treatment period, it is recommended not to be given longer than 5 days in COVID-19 in the context of clinical trials (26).

Remdesivir is a nucleotide analogue prodrug that inhibits viral RNA polymerase. It has been found to be effective in SARS CoV-2 in in vitro studies (32). It is recommended using remdesivir as part of the clinical trial (26).

Favipiravir (FPV) is another drug which is currently undergoing clinical research for the treatment of COVID -19 but there is not any evidence for pediatric patients with severe COVID-19 (14). This drug is an RNA-dependent RNA polymerase inhibitör and it has found effective in Ebola outbreak (33). It is contraindicated in children younger than 1 year (34).

The combination of Lopinavir / Ritonavir (LPV/RTV) which is a protease inhibitor used in HIV infection, has a very low role in the treatment of SARS-CoV-2 infection, and it has been observed in previous studies that it has some activity against SARS CoV and MERS-CoV (26). The use of LPV/RTV which is the only tablet form that can be used safely in HIV-infected pregnant women, is open to debate when it comes to newborns and children. Antiviral drugs recommended in SARS-CoV-2 infection can be considered in the treatment of newborns and children after the risk-benefit ratio is carefully evaluated in context of clinical trials (35).

The issue of iatrogenic suppression of immunity due to cytokine storm in COVID -19 has been negotiated; it is not recommended to give corticosteroids especially in the light of current limited scientific evidence due to the lower immune response in children compared to adults (36).

If there is evidence of secondary bacterial infection, the relevant antibiotics ought to be used and the logical use of antibiotics must be provided (23).Interferon α2b nebulization applied in MERS-CoV and SARS-CoV can also be used in the treatment of SARS-CoV-2 (18).

Children who have a considerably increased risk of thrombosis and can be treated with low molecular weight heparin in early stages ; and anticoagulant therapy can be administered if necessary. Convalescent plasma therapy can be used in children whose clinical condition deteriorates rapidly and who have serious and critical diseases (37).

Neonatal Management Recommendations

Delivery

The delivery is mainly determined by obstetric indications. Careful approach is necessary while choosing anesthesia when delivery by cesarean is required. In two published reports including a total of 18 pregnant women with COVID-19 from China, all but two were delivered by caesarean section and none of the newborns were infected with SARS-COV-2. As there is no evidence of the virus for vaginal transmission, vaginal delivery can be considered in stable patients (38).

Newborn Management in the Delivery Room

The designated operating room must have sufficient equipment approved by the American Academy of Pediatrics (AAP) and Neonatal Resuscitation Program (NRP), including radiant heater, face mask, endotracheal tube, laryngeal airway, positive pressure apparatus, oxygen, etc. If the procedure for neonatal stabilization is to be performed, the procedure must be performed by the neonatal team with appropriate personal protective equipment (N95 mask, face shield, gown, glasses, double gloves, etc.). All newborns with COVID-19 must be admitted to neonatal intensive care unit (NICU) for close monitoring and necessary interventions (20). Newborns with COVID - 19 must be isolated in one room and if possible, placed in negative pressure rooms. The follow up of the patients must be performed by a newborn team wearing appropriate personal protective equipment (PPE) (25). Newborn babies must be washed as soon as possible in order to eliminate the virus potentially present on their skin after birth. Regardless of the gestational age, the newborn must be transported in a closed incubator and kept there for post-resuscitation care (20). In a study where 9 pregnant women with COVID-19 were assessed no neonatal depression / asphyxia was reported. However, it is not known whether maternal infection is the risk factor. The baby born from the mother with respiratory distress of COVID -19 may be born depressed as a result of general anesthesia or mother's respiratory failure, and it must be remembered that there may be a need for resuscitation and preparation must be made accordingly (39).If the mother is SARS CoV-2 positive, the baby should be tested at the postnatal 24 h or later, taking separate samples from the nasopharynx, oropharynx, and rectum (20).

Umbilical cord management

The Chinese expert opinion advises immediate cord clamping to babies born from mothers of COVID -19 with possible or definitive diagnosis due to the risk of transplacental transmission. However, there are no cases of vertical transmission from mother to baby validated with viral RNA. Current limited scientific evidence indicates that the possibility of vertical transmission is quite low and further evidence is required (20).

Breastfeeding considerations

WHO suggests that the mother with possible or definitive diagnosis of COVID -19 should stay in contact with the skin of the baby after birth, especially during breastfeeding (20). In a recent study from Italy there was no detected virus in the breast milk analysis of two diagnosed mothers of COVID-19. This study has also revealed that transmission from mother to newborn may occur via infected droplets rather than the milk (18, 40). WHO recommends breastfeeding since the benefits of breastfeeding outweigh, but at this critical time, it is advised that the mother should adhere to protective measures; wash her hands before touching the baby and wear a mask while feeding the baby, and regularly clean the surfaces the mother touches (41). AAP recommends that the mother and baby should remain separated until it is observed that the mother has no fever for 72 hours without using antipyretic, the symptoms of respiratory improvement, and at least two consecutive SARS-CoV-2 nasopharyngeal swab tests that have become negative at ≥24 hours apart (39). In a review published recently, urgent inclusion of nursing mothers and pregnant women in clinical studies of COVID-19 was called for, as there was no information about the safety of drugs used in the treatment of COVID -19 (42). In the light of limited scientific evidence, due to the potential for adverse reactions of experimental drugs in the treatment of COVID- 19, these drugs should be used carefully during breastfeeding. During COVID -19 pandemics, due to the lack of scientific evidence, long-term follow-up might be necessary for babies exposed to drugs via breast milk. Further studies are required to research the effect of COVID -19 specific treatments on pregnancy and breastfeeding.

CONCLUSION

Clinical experience of children and newborns with COVID - 19 is gradually increasing, and the approaches outlined here are based on available evidence. Although the findings are milder in pediatric patients compared to adult patients in the COVID-19 pandemic, it should be considered during the treatment selection that children with accompanying cardiac and pulmonary disease may progress severe based on clinical experience from other viral infections.

It should be remembered that all newborns diagnosed with COVID-19 should be admitted to NICU to be able to monitor them and to perform close interventions and make necessary interventions as the disease may progress with nonspecific findings and develop respiratory distress rapidly. Concerns remain due to COVID -19 mother-to-baby vertical transmission and lack of evidence on potential fetal outcomes, further studies are required.

Conflict of interest

No conflict of interest was declared by the authors.

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