



2019 Novel Coronavirus Infection in Children and Infants: Where We Are and What We Know?

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Abstract

Since the outbreak of coronavirus disease 2019 (COVID-19), in Wuhan, China, there were more than 10,021,401 confirmed infected cases. This infection has spread to almost all countries around the world with reported high mortality and morbidity. Infections in children and infants have been reported as well. The condition of the infected children was mostly mild. To date, there have been reported deaths in pediatrics testing positive for COVID-19 in countries such as China, Italy and America. The therapy strategy for the children who suffer coronavirus disease (COVID-19) has been based on the adult experience. The present review summarizes current knowledge of the etiology, epidemiology, clinical manifestations, transmission, diagnosis, treatment, and prevention of COVID-19 infection in children and infants.

Keywords: Children, Infants, COVID-19, SARS-CoV-2, 2019 Novel Coronavirus

1. Context

Patients who have dry cough, decreased to normal white blood cell counts, fever, initially identified as “fever of unknown origin with pneumonia”, had been steadily increasing in Wuhan, China, since December 2019 (1). The causative agent of this unexplained infected pneumonia, described as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is reported not only to cause severe pneumonia but characterized by strong human-to-human transmission (2, 3). The prevalence of coronavirus disease 2019 (COVID-19) is quickly increasing around the world, providing an important public health emergency with the possibility of an epidemic (4-7). By June 29, 2020, the COVID-19 outbreak has affected over 10,021,401 people globally with most of the cases being reported from United States of America, Brazil and Russian Federation. The absolute number of deaths has surpassed 499,913 worldwide and is expected to increase further along with the rapid spread of the disease (8, 9).

The number of reported child and neonate cases is limited, leastways in the early stages of this prevalence. In a recent investigation, out of 44,672 COVID-19 cases approved in China, only 2.1% were observed in the pediatric patients (at the age of 19 or less) (10). The reason for this is not

clear yet but it may be a combination of epidemiologic and biologic factors or even due to non-reported pediatric infected cases. It must be remembered that during the outbreaks of the Middle Eastern respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS), a limited number of cases with fewer hospitalizations, less mortality, and milder symptoms were found in children and adolescents in comparison to adults (11-14). Pediatric analysis of available epidemiological data can provide situational information about child health and provide a better understanding of the prevalence and effects of COVID-19 in these patients (15). Therefore, the present review is aimed to summarize current knowledge on etiology, epidemiology, clinical manifestations, transmission, diagnosis, treatment, and prevention of COVID-19 infection in children and infants in order to provide a better understanding of the disease in this population.

2. Etiology

The first identification of coronaviruses occurred in late 1960s and they have been known to cause a widespread colds and respiratory tract infections (16). The 2019-Novel Coronavirus (2019-nCoV) is an enveloped and positive-

sense single-stranded RNA virus that belongs to the subfamily Orthocoronavirinae, family Coronaviridae, and order Nidovirales. The subfamily Orthocoronavirinae is divided into four genera (alphacoronavirus, betacoronavirus, gammacoronavirus, and deltacoronavirus) and the 2019-novel coronavirus (2019-nCoV) belongs to the betacoronavirus genus (17). Although alphacoronaviruses and betacoronaviruses can only infect mammals, gamma and delta corona viruses mainly affect birds. 229E, NL63, OC43, HKU1, the Middle East respiratory syndrome related coronavirus (MERS-CoV), severe acute respiratory syndrome related coronavirus (SARS-CoV), and 2019-Novel Coronavirus (2019-nCoV) are coronaviruses that can infect human (18, 19).

Genome analyses have shown 88% sequence identity between 2019-nCoV and two bat-derived severe acute respiratory syndrome (SARS)-like coronaviruses (bat-SARS-like (SL)-ZC45 and bat- SL-ZXC21). 2019-nCoV also shares 79.5% genome sequence to SARS (17, 20). Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was the name chosen for 2019-nCoV by the Coronavirus Study Group (CSG) of the International Committee on Taxonomy of Viruses on February 11, 2020 (21). Later, the disease caused by SARS-CoV-2 was named Coronavirus Disease 2019 (COVID-19) by the World Health Organization (WHO) (22).

Patients infected with the virus at the beginning of the outbreak in Wuhan were linked to the Huanan seafood market, which is a wholesale market for seafood and wet animals (23, 24). According to current information, it is likely that the hosts were initially bats and then humans were infected by pangolins or other wild animals. The virus is now spreading via human-to-human transmission (25-27). Due to the high similarity in the sequence of the receptor-binding domain between the Guangdong pangolin coronaviruses and SARS-CoV-2, it has been suggested that pangolins may be intermediate host for this virus (25). However, a unique furin cleavage motif exists in the spike protein of SARS-CoV-2, which has not been seen in coronaviruses hosted by pangolins. Hence, it has also been suggested that pangolins may not be the direct source of SARS-CoV-2 (28).

SARS-CoV-2 revealed weak resistance to a temperature of 56°C for 30 min, 75% ethanol, peroxyacetic acid, chlorine containing disinfectants, peracetic acid and chloroform (2). Angiotensin-converting enzyme 2 (ACE2) is used by the SARS-CoV-2 as a receptor and enables the virus to enter the cell (29, 30).

3. Epidemiology

A novel type of coronavirus, called “2019-nCoV”, in December, 2019, emerged in Wuhan city of China (19). Ac-

cording to WHO updated information, by June 29, 2020, 10,021,401 confirmed cases of COVID-19 infection have been reported globally and 499,913 deaths among them; and its risk is assessed as very high and at the global level (8). Just a small proportion of the COVID-19 cases have been from children. Pediatric COVID-19 infected patients were infrequent in the first days of its outbreak, so it was thought that children (2 to 12 years) are not at risk of this disease. However, children infected by COVID-19 emerged parallel with the emergence of familial aggregation (31). Chinese Centers for Diseases Control and Prevention reported that there were 44672 COVID-19 cases confirmed until February 11, 2020, that 549 cases (1.2%) were 10 - 19 years old and 416 cases (0.9%) were 0 - 10 years old and among these children 134 cases had clinical records (10). There have been two reported deaths in pediatrics testing positive for COVID-19 in China (32). Yang et al. (33) declared that there had been 300 infected children diagnosed by February 19, 2020 and mentioned that children with cancer are more prone to this disease because of their poor immune system. Yang et al. (34) reported that on January 28, 2020, 8 days after the report of the first COVID-19 infected child patient in Shenzhen City, the first COVID-19 infected child patient in Wuhan, the main area of COVID-19 outbreak, was diagnosed. Subsequently, the number of pediatric COVID-19 cases increased. Most of the pediatric cases were determined by epidemiological screening and had history of exposure to familial clustering infection. Pediatric COVID-19 infected cases have mild symptoms in comparison with adults (34). The children's asymptomatic infection requires attention because it might turn into a potential source of spread (34). However, it is concluded that children are not greater transmitters than adults (35).

Chen et al. (18) and Shen et al. (19) determined the epidemiological history of infected pediatric patients i.e. children with history of residence or travel to regions with continuous local transmission e.g. Wuhan and adjacent areas during 14 days before the onset of disease, history of contact with patients with respiratory or fever symptoms who had contact with patients from regions with continuous local transmission during 14 days before the onset of disease, children who had close contact with COVID-19 cases, and newborns delivered by COVID-19 infected mothers. Shen et al. (34) declared that the principal way of transmission in children is close contact with COVID-19 infected patients.

Xia et al. (31) reported that among 20 studied pediatric cases (males:13 and females:7), 65% (13 cases) had a history of close contact with family members infected by COVID-19. According to a study by Wei et al. (36) between December 8, 2019, and February 6, 2020, nine COVID-19 infected infants (1 month to 2 years) were detected. All of them

were hospitalized and two cases of them were male. The oldest infant was 11 months and the youngest was 1 month old. Seven cases either lived in Wuhan or their family member(s) had visited Wuhan, one did not have any direct connection with Wuhan, and there was no information available for one infant. There was reported occurrence of family clustering for all nine infants. As 7 cases among the 9 infants were female, further studies are needed to understand if, among infants, females are more at risk of SARS-CoV-2 infection than males.

Wang et al. (37) conducted a study on 31 COVID-19 infected children and showed that 68% (21 cases) had history of contact with infected adults and 3% (1 case) had history of contact with asymptomatic individuals who had returned from Wuhan. 90% (28 cases) of these 31 children were cases of family cluster. Therefore, close contact with family members has been reported as the main cause of infection and having this history as a significant base of diagnosis. In a cohort study by Chen et al. (38), which followed 31 pediatric COVID-19 cases (18 females and 13 males) in Shenzhen, it has been reported that 93.5% (29 cases) of them were in family clusters, 29% (9 cases) had not had any history of being to Wuhan or Hubei recently, but 8 cases had family members with history of recently travel to the Hubei Province and 1 case had history of contact with an individual from Wuhan. It has also been reported that there were no immunocompromised patients among them and 6.5% (2 cases) of them had underlying diseases. There wasn't any gender preference indicated in these pediatric cases, while in a study by Chen et al. (39) male cases were significantly more than females among adult COVID-19 cases. Henry et al. (15) by combining data from pediatric cases reported by Sun et al. (39) and Xu et al. (40), analyzed 82 COVID-19 pediatric patients. 38 cases were from China and 44 were from other countries. They reported that 14 cases lived in Wuhan, 25 cases had history of traveling to Wuhan, there was no available data about the other 43 cases' travel history and 29 cases had a family member infected by COVID-19.

In one previous study, only 5% of the total 4226 COVID-19 detected cases in America were among children and adolescents (12 to < 19 years). This age group formed less than 1% of the total 508 hospitalizations and were not part of the 121 ICU admissions and those who died (41). Until now, the prevalence of SARS-CoV-2 infection among males is more than females in adolescents and in children (15).

4. Transmission

Wang et al. (42) and Lu et al. (2) reported that SARS-CoV-2 is transmitted by contacts, respiratory aspirates, droplets

and feces, and transmission through aerosols is also extremely possible. Contact with eye, oral and nasal mucous membranes are other common modes of spread. Viral shedding occurs from saliva, respiratory tract, urine and feces resulting in other sources of virus spread (43). Chen et al. tested samples of cord blood, neonatal throat swab, amniotic fluid and breastmilk from 6 newborns delivered by COVID-19 infected mothers for SARS-CoV-2 and all were negative (42). There is presently no evidence that COVID-19 could be transmitted from mother to the newborn transplacentally (2). Inter-person transmission is a possible way for spread of COVID-19 infection (44, 45); this kind of transmission happens mainly through direct physical contact between people or via spread of droplets from an infected patient (46).

5. Diagnosis

Diagnosis of COVID-19 depends on extensive laboratory tests (2). Samples include nasopharyngeal swab (which is the most common sample), blood, secretion of lower respiratory tract, feces and sputum. A lab confirms infection when the patient's sample tests positive for COVID-19 by quantitative real-time polymerase chain reaction (RT-PCR), or existence of viral genome profoundly similar to the reference sequence of COVID-19 by homemade PCR. The positive rate from nasopharyngeal swab is lower than 50%. Infection is confirmed in the presence of at least 2 positive test results (2, 15, 36).

Xia et al. (31) reported that at early stages the COVID-19 RNA detection test could produce a false negative. Plain chest X-ray could not detect pulmonary lesions because the condition in most pediatric patients was not severe. Chest CTs provide support information for management and diagnosis. Children chest CT findings were similar to adults, and most of the cases were mild. However, CT imaging alone is insufficient for the diagnosis of COVID-19, especially in cases with coinfection with other pathogens. Thus, in children corresponding pathogen detection combined with early chest CT screening and timely follow-up, is a suitable clinical protocol (31). Other methods being evaluated such as ultra-rapid, immunodiagnostic, and stool PCR tests in both pediatric and adult populations (47).

Kunling et al. (19) reported that Covid-19 specific diagnosis should be made to differentiate from human metapneumovirus, adenovirus, respiratory syncytial virus, influenza virus, parainfluenza virus, SARS coronavirus, rhinovirus and other viral infections, like bacterial pneumonia, mycoplasma pneumonia and chlamydia pneumonia. In diagnosis, the coinfection of CoVID-19 with other bacteria and/or viruses must be anticipated (19). These discrim-

inant tests are important and molecular methods help in accurate diagnosis.

Unlike in adults, a dependable pattern of laboratory derangements in children with COVID-19 is yet to be found. Clinicians are advised to monitor CRP and lymphocyte count as signs of severe infection and to monitor PCT for possible bacterial co-infection. IL-6 must be checked as a possible prognostic predictor in severe COVID-19 (48).

6. Clinical Manifestations

According to earlier studies, the incubation period of COVID-19 infections varies from 1 to 14 days, frequently in the range of 3 to 7 days (approximately 5.2 days) (19, 34, 46). Age of onset in children is estimated to range from 1.5 months to 17 years, with most cases having familial transmission (49). Accordingly 93.5% of infected children were reported in family clusters (38). At the onset of the disease, the most common symptoms are fever, fatigue, dry cough and diarrhea (28, 46, 50). Most of the pediatric cases represent low to moderate fever, and in some cases no fever (50). Other symptoms include headache, sputum production, dyspnea, lymphopenia, and hemoptysis (45, 51-53). Chest CT scans reveal clinical features presented as pneumonia, and in more severe cases, abnormal features such as acute respiratory distress syndrome (ARDS) (52). As the infection progresses, after about 1 week, dyspnea, cyanosis and other related symptoms can appear, and they can be accompanied by systemic toxic symptoms such as restlessness (malaise), loss of appetite and reduced activity (50). The disease progression in some children might be rapid and result in respiratory failure. In these severe cases, even, irreversible bleeding (and coagulation dysfunction), metabolic acidosis and septic shock are possible (50). Muscle ache, headache, confusion, rhinorrhea, sore throat, sputum production, nausea (and vomiting) and chest pain have been reported as symptoms of COVID-19 infection (28, 39, 52).

According to guidelines for diagnosis and treatments for COVID-19 published by the National Health Commission of China, based on the severity of symptoms, COVID-19 is classified to 4 levels (28):

6.1. Mild

Most of the pediatric cases show mild clinical manifestations (19). They only have mild symptoms without any radiographic features (28). Most of these patients recover in about 1 - 2 weeks after onset of the disease. Few may progress to lower respiratory infections (19). This group of patients consists of asymptomatic cases (54), patients with upper respiratory infection (URI) and patients with mild pneumonia (50).

6.2. Moderate

Patients with moderate symptoms may represent respiratory symptoms, radiographic features and fever (28).

6.3. Severe

Patients with severe symptoms may represent one of the following criteria (28):

- 1) Dyspnea, RR > 30 times/min (In children: RR $\geq$ 70/min (in children with younger than 1 year), RR $\geq$ 50/min (in children older than 1 year) (50));
- 2) Oxygen saturation < 93% in ambient air (< 90% in premature infants (50));
- 3) PaO₂/FiO₂ < 300 mmHg.

In another article, some other criteria have been attributed to this stage of disease (50), such as:

- 1) Intercostal, subcostal and suprasternal retractions, nasal flaring, apnea, cyanosis and etc.
- 2) Blood gases: PaCO₂ > 50 mmHg, PaO₂ < 60 mmHg.
- 3) Consciousness impairment: lethargy, restlessness, convulsion, coma, etc.
- 4) Nourishment problems: Poor appetite, poor feeding, and even dehydration.
- 5) Myocardial damage: Increased level of myocardial enzyme, cardiomegaly, electrocardiogram ST-T changes and even cardiac insufficiency in severe cases.

- 6) Other manifestations: coagulation disorders (prolonged prothrombin time (PT) and elevated level of d-dimer), gastrointestinal dysfunction, rhabdomyolysis and raised levels of liver enzymes.

6.4. Critical

Critical patients may exhibit one or more of the following conditions (28):

- 1) Respiratory failure (patients represent acute respiratory distress syndrome (ARDS) and refractory hypoxemia, which is irresponsible to conventional oxygen therapy, such as oxygen mask or nasal catheter (50));
- 2) Septic shock;
- 3) Multiple organ failure;

There have been a few reports about COVID-19 infection in newborns as well. According to Shen et al. (19) no newborns delivered from infected mothers have been shown to be COVID-19 positive (19). There were no infections among newborns until the publication of their work in until January 29th 2020. However, by March 1st, 2020, Lu et al. (2) reported three newborns with COVID-19 mainly as part of family cluster cases. A 17 days old newborn diagnosed with COVID-19 showed cough, fever and milk vomiting. His mother was infected as well (55). The second (birth to 1 month) presented with fever on 5th day after birth. In this case the mother was infected as well (45). The

third case whose mother was infected, was silent and diagnosed 30 hours after birth by the viral nucleic acid test (54). From these, we understand that milk vomiting, shortness of breath, fever and cough are symptoms of COVID-19 infection in neonates (birth to 1 month). The vital signs of these neonates were found to be stable. There have also not been any severe emergency cases (49, 55-57). On the other hand, maternal hypoxemia as a result of severe infection could cause premature delivery, intrauterine asphyxia and other further risks. Neonates, specifically preterm newborns, may represent non-specific symptoms, which requires careful observation (50).

It has been found that most pediatric cases show mild symptoms, without any sign of pneumonia or fever. They mostly have good prognosis and, within 1-2 weeks after disease onset, they recover fully (58). Only a few cases have presented infections in their lower respiratory tract (19). According to Shen et al. (19) despite the generally mild cases in children, the probable risk of death in pediatric population must not be ignored. During epidemics of Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS), ARDS and death happened among pediatric patients as well (12, 59-61). It is also important to know that the data from these studies have been conducted based on a limited number of patients, and therefore, continuous observation of further cases is recommended. (Table 1).

7. Infection Control and Treatment

Lu et al. (2) reported that early identification and isolation are necessary for control of COVID-19. With reference to MERS management, COVID-19 neonates must be placed in rooms with negative pressure or in rooms in which the room exhaust is filtered through high-efficiency particulate air (HEPA) filters. Visiting must not be allowed for COVID-19 neonates (2). Even if there are no clinical manifestation, children who are from families with clustered infections must be screened for COVID-19 to exclude potential sources of infection. To protect children with underlying diseases, early isolation must be performed. Enhancing protection during delivery and isolating the newborns immediately after delivery is imperative (62). According to the standard prevention protocol, good personal protection, environmental ventilation, ward management, hand hygiene, medical waste management, object surface disinfection and cleaning and other hospital infection control work, are necessary to reduce nosocomial infection (18). Medical personnel must wear caps, surgical mask, medical overalls and goggles or face shield for daily medical duties. Goggles or face shields must necessarily be worn when collecting respiratory samples; latex gloves must be

worn on activities that involve coming in contact with body fluid, secretions or excreta and blood. Face shield or goggles, surgical mask, latex gloves, respiratory hood and medical protective clothing must be worn when necessary, to prevent splash or aerosol during bronchoscopy, operations of endotracheal intubation, sputum suction and airway nursing. Patients and their family must wear surgical masks (18).

As with SARS-CoV and MERS-CoV, there is no specific drug treatment for COVID-19. The general treatments include resting, symptomatic and supportive treatments; including preservation of water acid-base balance and electrolyte and the supply of oxygen. Extracorporeal membrane lung (ECMO), high-dose pulmonary surfactant (PS), high-frequency oscillatory ventilation (HFOV) and inhaled nitric oxide (iNO) may be useful for newborns with severe acute respiratory distress syndrome. Moreover, three drug combinations (mercaptopurine plus melatonin, toremifene plus emodin and sirolimus plus dactinomycin) are candidate repurpose drugs. In addition, convalescent sera from COVID-19 recovered cases may be helpful for COVID-19 infection, because of a significant decrease in the death rate following this treatment (2, 18). Shen et al. (19) reported that IFN- α atomization is an alternative of treatment for COVID-19 pneumonia. The safety and the efficacy of interferon in the treatment of COVID-19 children must be confirmed (19). Lopinavir/ritonavir (LPVr) is mostly used to treat HIV. LPVr is recommended for treating COVID-19, centered on the clinical experience in MERS and SARS treatment. Chloroquine diphosphate (CD) is an optimized medication based on the composition of an antimalarial medicine named quinine that is mostly used for parenteral amoebiasis, malaria, etc. CD has demonstrated clear effectiveness in adult clinical trials for COVID-19 treatment. Until now, no CD dosage is recommended for children with COVID-19 (63). Ribavirin is an antiviral drug with a wide spectrum and inhibitory effects on DNA viruses and RNA viruses. In China and other nations, various age limits and dosage forms of ribavirin are being administered. For children with COVID-19, intravenous ribavirin has been recommended 2-3 times daily at a dosage of 10 mg/kg per time (maximum 500 mg per time) (64). Arbidol (umifenovir) is an antiviral compound with a wide spectrum, and has been recommended for influenza treatment and prophylaxis in China and Russia. Arbidol shows activities against various RNA and DNA viruses (65). Arbidol was seen to be efficient *in vitro* to SARS-CoV-2 (66). Until now, no dosage of arbidol has been recommended for children with COVID-19.

It has been reported that it is not advisable to combine three or more antiviral drugs at the same time (63). Cai et al. (67) have reported that no antivirals are necessary

Table 1. Current Available Data About the Clinical Manifestation of COVID-19 in Children

	Chen et al.	Henry et al.	Cai Jiehao et al.	Wei Xia et al.	Zheng et al. (58)
Fever, %	45.2	68.0	70.0	60.0	40.4
Cough, %	41.9	36.0	60.0	65.0	48.1
Nasal congestion, %	9.7		30.0		
Pharyngitis, %	6.5	12.0	40.0	5.0	5.8
Rhinorrhea, %	6.5	8.0	20.0	15.0	
Fatigue, %	6.5			5.0	9.6
Diarrhea, %		4.0		15.0	1.9

for non-severe self-limiting COVID. In consideration of the seasonal overlap between COVID and influenza, influenza virus screening is required to eliminate the possible coinfection of these agents (67). Appropriate antibiotics should be applied timely if there is sign of secondary bacterial infection (18). Yang et al. (62) stated that secondary infection may be caused by the premature use and extreme use of antibiotics and corticosteroids. Considering that symptoms of children with viral respiratory infection are mild and can be self-healed, antiviral agents must not be used, except for critical cases (62). During the treatment, children's vital signs, SpO₂, etc. must be monitored. Critical cases must be identified as soon as possible (18).

8. Are Children Less Susceptible to 2019-nCoV?

In a recent study, Henry et al. (15) reported that the reason behind the reduced susceptibility among pediatric patients is still unknown. The fewer pediatric cases may be a result of underreporting of children and infant cases as well as a combination of epidemiologic and biologic factors. Another study by Lee et al. (68) reported that fewer outdoor activities by children and less international travel, which translates to less contact with infected people could be possible reasons. Accordingly, the number of pediatric patients may increase in future; thus fewer pediatric cases at the beginning of such a pandemic does not necessarily mean that children and infants are less susceptible to COVID-19 infection. Furthermore, since children have not normally been exposed to as much air pollution and cigarette smoke as adults, they have fewer underlying disorders. Therefore more active innate immune response and healthier respiratory tracts are generally observed in children, which make them less susceptible to coronavirus disease (69). Moreover, the SARS virus, human coronavirus-NL63 (HCoV-NL63), and SARS-CoV-2 all use the same angiotensin-converting enzyme-2 (ACE2) as their cell receptor in humans (20, 58, 70). An experimental mouse model study has shown that ACE2 is involved in protective mechanisms in the lungs and additionally protect against severe lung injuries that result from respiratory virus in-

fections. Furthermore, its expression in rat lung has been found to dramatically decrease with age (71). ACE2 is also known to protect against severe acute lung injuries, which could be triggered by acid aspiration, sepsis, lethal avian influenza A H5N1, and SARS virus infection (72, 73). Additionally, difference between children and adults could be due to the condition of their blood vessels. In a recent study, SARS-CoV2 infected the endothelium and caused inflammation, as well as signs of clotting in the blood vessels. Since the endothelium is in a better condition in children than adults, their blood vessels might be better able to withstand SARS-CoV2 attack (74, 75). These findings may not be necessarily related with a lower susceptibility of children to 2019-nCoV, but can be regarded as a possible reason, which needs to be further investigated.

9. Home Confinement Impacts on Children During the 2019-nCoV Outbreak

Following the widespread COVID-19 outbreak, many schools around the world have been closed by the order of governments to stop the spread of the virus. This has caused millions of children and adolescents to stay at home. Although education has largely continued through media, such as television and the Internet, long-term school closures could have negative physical and psychological effects on children (76). Post-traumatic stress scores in children who had been quarantined have been shown to be four times higher than in children who hadn't been quarantined (77). Government, families, schools, and other elements of society must be aware of the adverse physical and psychological consequences of long-term stay at home and provide children and adolescents with appropriate training and education to help them maintain a healthy lifestyle, nutritious diet, regular sleep, and adequate physical activity (76). Parents' committees should work together to fulfil the needs of many students with the school requirements as well as to support children's rights for a healthy lifestyle. Accordingly, psychol-

ogists must provide online services to cope with anxiety from becoming infected, mental health disorders that usually result from domestic conflicts and probable tension with parents (78), COVID-19 is now a pandemic and all countries involved in this disease should consider the effects of quarantine on children and adolescents to prevent long-term harm to them (76). Since children do not have much power to express their basic needs, parents and governments must ensure that all mental and physical impacts of the 2019-nCoV pandemic on children are kept minimal.

10. Conclusions

The COVID-19 pandemic has spread from Wuhan, China to more than 120 countries around the world. This novel coronavirus is mainly transmitted via physical contacts, respiratory aspirates, droplets and feces, and transmission through aerosols is also possible. COVID-19 may be asymptomatic or lead to severe symptoms. However, it appears that the pediatric age group is less susceptible than adults to the 2019-nCoV infection but current findings show that children and infants can be infected by this virus. While the infected children may be asymptomatic or have milder symptoms than adults, they can be carriers of the virus and spread it to others. Some common symptoms among children include fever, cough, nasal congestion, pharyngitis, and rhinorrhea.

The diagnosis of disease mostly depends on extensive contact and laboratory tests such as RT-PCR. Chest CTs may also provide support information for management and diagnosis of the disease. To protect children with underlying diseases, early isolation must be practiced. Moreover since there is no specific drug treatment for COVID-19, general treatments include resting, symptomatic and supportive treatments. However, some antiviral treatments such as IFN- α , ribavirin, and lopinavir/ritonavir are used in the management of children infected with COVID-19. More clinical, epidemiological and virological data to manage and treat COVID-19 are required to help us understand the natural history of 2019-nCoV infection and clinical characteristics in children.

Footnotes

Authors' Contribution: Niloofar Deravi did study concept and design-Acquisition of data, drafting of the manuscript, and administrative support. Shirin Yaghoobpoor did analysis and interpretation of data and drafting of the manuscript. Mobina Fathi did drafting of the manuscript and acquisition of data. Kimia Vakili did drafting of the manuscript and critical revision of

the manuscript for important intellectual content. Elahe Ahsan did critical revision of the manuscript for important intellectual content and drafting of the manuscript. Melika Mokhtari did drafting of the manuscript, analysis, and interpretation of data. Maryam Vaezjalali did critical revision of the manuscript for important intellectual content-Study supervision.

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