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Title: How COVID-19 affects children: a review article

Running title: How COVID-19 affects children

Type: Review article

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Abstract

COVID-19 has affected 550,369 confirmed cases, with 8,856 fatalities. COVID-19 was more common in adults over 15 during the early outbreak, and the proportion of confirmed cases among youngsters was relatively low. In addition, children with COVID-19 are asymptomatic or have mild clinical symptoms compared to adults. The present study reviewed the clinical features, signs, symptoms, and effect of COVID-19 in children. This review was performed through an electronic literature search for relevant studies identified using keywords on the MEDLINE database between 2020 and 2021, inclusive: COVID-19, COVID-19 in children, Coronavirus, novel Coronavirus in children, COVID-19 symptoms in children, COVID-19 effect in children. Similar keywords were used to peruse and identify relevant articles on Google Scholar. The articles were chosen based on defined inclusion criteria. The current review included papers published between 2020 and 2021. The review was written under specific titles in the discussion part. This review concluded that children of all ages are susceptible to getting COVID-19 due to human-to-human transmission. COVID-19 has a milder clinical course, quicker recovery, and a better prognosis in children than adults. Infants less than one year and children with underlying chronic disorders were at higher risk of having severe forms of COVID-19. Septic shock, toxic encephalopathy, multiple organ failure syndromes, disseminated intravascular coagulation, and status epilepticus were the most common consequences identified in children with severe forms of COVID-19. Infection prevention by isolation of diseased children is critical, as is thorough surveillance, early diagnosis of illness complications, and the ability to treat patients on time while preventing secondary dissemination.
1. Introduction

A series of acute atypical respiratory diseases occurred in Wuhan, China, in December 2019. This quickly spread from Wuhan to neighbouring cities. It was quickly revealed that a new coronavirus was the cause. The new Coronavirus was called SARS-CoV-2 because of its high similarity to SARS-CoV, which caused acute respiratory distress syndrome (ARDS) and significant mortality between 2002–2003. The SARS-CoV-2 outbreak was thought to have begun due to a zoonotic transmission linked to the seafood market in Wuhan, China. However, it was later discovered that human-to-human transmission had a significant part in the ensuing pandemic [1]. The condition caused by this virus was termed Coronavirus disease 19 (COVID-19), and a pandemic was proclaimed by the World Health Organization (WHO). COVID-19 has affected many individuals globally, with reports over 200 nations and territories [2].

A Saudi person travelling from Iran to Bahrain tested positive for COVID-19 on March 2. The case was immediately isolated and declared the first in Saudi Arabia by the Ministry of Health. [3] Mecca, Medina, and Riyadh were placed under lockdown on March 23, with travel restrictions imposed throughout the country, and the curfew was extended to 24 hours over the next ten days [4]. There have been 550,369 confirmed cases so far, with 8,856 fatalities [5]. COVID-19 was more frequent in adults over the age of 15 in the early phases of the outbreak, and the proportion of confirmed cases among children was comparatively low. However, more regions have launched pathogen detection campaigns since then. Because younger children cannot wear masks and have not taken other special preventive and control measures, the number of child infection cases has increased significantly, particularly in younger age groups, and should be given special attention [6].

China released a notification on "doing a good job in the prevention and management of pneumonia epidemics in children and pregnant women with novel coronavirus infection" on February 2, 2020, stating unequivocally that children are vulnerable to SARS-CoV-2 owing to the immaturity of their immune systems. The most recent recommendations also confidently state that everyone, including children, is susceptible to SARS-CoV-2. Furthermore, children display specific characteristics and cannot adequately articulate their health state or contact history, contributing to the difficulty of safeguarding, diagnosing, and treating this population [7].
The SARS-CoV-2 virus typically affects the respiratory system, while it also affects other organ systems. The earliest case series from Wuhan, China, reported lower respiratory tract infection-related symptoms such as fever, dry cough, and dyspnea. Headache, dizziness, widespread weakness, vomiting, and diarrhoea were also reported. It is now commonly acknowledged that COVID-19 respiratory symptoms vary, ranging from mild to severe hypoxia [8]. Children with COVID-19 have been asymptomatic or have modest clinical signs compared to adults. There have recently been more reports of older school-aged children and adolescents presenting with prolonged fever, shock, abdominal pain, and cardiac dysfunction following SARS-CoV-2 infections that overlapped with Kawasaki disease (KD), manifesting as a hyper-inflammatory syndrome and multi-organ involvement [9]. The present study reviewed the clinical features, signs, symptoms, and effects of Covid-19 in children.

2. Literature Search

Scientific researches involved in this review were obtained through scientific websites (Google scholar and Pubmed) using various keywords (COVID-19, COVID-19 in children, Coronavirus, novel Coronavirus in children, COVID-19 symptoms in children, COVID-19 effect in children) to obtain all possible articles related to the current subject. The articles were chosen based on defined inclusion criteria. First, each article's main titles and abstracts were reviewed, and then we excluded duplicate articles, non-full text articles, and irrelevant articles. The included articles in the current review were published between 2020 and 2021.

3. Results

The present study included studies on COVID-19 in children published between 2020 and 2021. Therefore, in the discussion section, the review was written under distinct subjects such as COVID-19, COVID-19 in children, Coronavirus, novel Coronavirus in children, COVID-19 symptoms in children, and COVID-19 effect in children.
4. Discussion

COVID-19 transmission is from human to human, with intra-family and intra-community spread. However, it is suspected that it originated in bats with an animal intermediary host. The virus is expelled through the respiratory and digestive systems. Contamination occurs by respiratory droplets (made by coughing, sneezing, and talking) or from contact with infected surfaces, with feces also being contaminated. Because it is exceedingly difficult to get children (particularly toddlers) to observe sanitary procedures (depending on their age), it is believed that children carriers will quickly transfer the virus [10].

4.1 Epidemiological data of COVID-19 in children

The data about COVID-19 in children is increasing. According to a comprehensive analysis of 45 scientific studies, children account for 1% to 5% of all confirmed COVID-19 cases [11]. According to an early report from the Centers for Disease Control and Prevention in the United States, 10% of children with COVID-19 required hospitalization, compared to around 25% of adults, and less than 2% of children required intensive care unit (ICU) admission. Infants under one year old were at a higher risk for hospitalization. In contrast, children with underlying chronic disorders, particularly chronic lung diseases, were at a higher risk for ICU admission. However; detailed data regarding COVID-19 among children from Saudi Arabia are limited [12]. Children have poor immunity, and some have an extended incubation period following SARS-CoV-2 infection. As a result, children should avoid interaction with complex communities to prevent getting infected by possible spreaders. COVID-19 is a self-limiting, acute condition; nonetheless, individuals can die, with a 2% mortality rate, and it has also been observed in severely sick children [13].

4.2 A potential explanation for the difference between children and adults in COVID-19

Infants and younger children are at a higher risk of hospitalization due to respiratory tract infections caused by respiratory syncytial and influenza viruses. In comparison to older patients, young COVID-19 patients generally have milder symptoms. The cause for this disparity between children and adults is yet unknown. Because a recent study found a link between the severity of COVID-19 and the number of viral loads (or the duration of the virus-shedding period), children may have lower viral loads even if they get COVID-19. A couple of theories can be examined
along this line. The first possibility is that the level of ACE2 expression differs between adults and children. ACE2 was shown to be more abundantly expressed in well-differentiated ciliated epithelial cells in a recent study. Following birth, human lung and epithelial cells continue to grow [14]. The second explanation is that children react differently to the SARS-CoV-2 virus than adults. Continuous antigen stimulation and thymic involution cause a change in T cell subset distribution from naïve T cells to central memory T cells, effector T cells, and effector memory T cells as people become older. The third hypothesis is that other viruses in the mucosa lungs and airways, frequent in young children, might allow the SARS-CoV-2 virus to compete with them and limit its growth. Currently, no research examining multiple viruses in addition to SARS-CoV-2 is available to assess this potential. Instead, these factors might account for pediatric and adult COVID-19 phenotypes [15].

4.3 Symptoms of COVID-19 in children

The symptoms of COVID-19 appear to be milder in children than in adults. Dong et al. conducted research in which 2143 children were selected by laboratory testing based on clinical signs and exposure history. 34.1% of them had a laboratory-confirmed COVID-19, while the rest had clinically suspected disease. Fever, cough, sore throat, sneezing, myalgia, and lethargy were all indications of an acute respiratory infection. Additionally, several children were wheezing [16]. Another research from Wuhan Children's Hospital assessed 171 children with proven illness and provided more comprehensive symptoms. Cough, pharyngeal erythema, and a fever of at least 37.5°C were the most prevalent symptoms. The results indicated that 32.1% of the children had a fever above 38°C, with the majority between 38.1°C-39.0°C. Other symptoms included diarrhea, lethargy, rhinorrhea, and vomiting. Four of the children had hypoxia. On hospital admission, many children had tachypnoea (28.7%) and tachycardia (42.1%) [17].

4.4 Diagnosis of COVID-19 in children

For SARS-CoV-2, the preferred diagnostic technique is reverse transcriptase-polymerase chain reaction (RT-PCR). For epidemiological and scientific objectives, next-generation sequencing is used to detect SARS-CoV-2 strains and mutations. Rapid serology tests may not be positive during the first 7–10 days of infection but may remain positive for several weeks after infection. For SARS-CoV-2, the preferred diagnostic technique is reverse transcriptase-polymerase chain reaction (RT-PCR). For epidemiological and scientific objectives, next-generation sequencing is
used to detect SARS-CoV-2 strains and mutations. Rapid serology tests may not be positive during the first 7–10 days of infection but may remain positive for several weeks after infection [18].

Upper respiratory tract samples (nasopharyngeal and oropharyngeal swabs) are preferred for children not undergoing mechanical ventilation and should be delivered on ice in a viral transport medium. Bronchoalveolar lavage or endotracheal aspirate would be the chosen specimen in mechanically ventilated children. These must be combined with the viral transport medium before being delivered on ice. Because of the possibility of aerosol production, sputum induction should be avoided [19].

The laboratory markers data in children with COVID-19 were few. The exception was researched by Henry et al., which compiled data from 12 separate investigations on 66 children. The findings revealed that 69.2% of the children had average leukocyte counts and that neutrophilia (4.6%) and neutropenia (6.0%) were uncommon. Only 3% had lymphocytopenia. C-reactive protein and procalcitonin levels were elevated in 13.6% and 10.6% of patients [20].

4.5 Outcomes and Prognosis in Children

COVID-19 has a milder clinical course, quicker recovery, and a better prognosis in children than in adults, according to various research. [21] However, recent research found that children with similar severe types of COVID-19 had satisfactory outcomes. The causes of these peculiarities are currently being researched. Some researchers think that lung epithelial cells in children express less or perhaps differently shaped ACE2 proteins, resulting in a decreased morbidity rate, but further studies are needed to understand the mechanisms of COVID-19's various presentations in children [22].

Children of all ages are vulnerable to getting COVID-19 due to human-to-human transmission. Although the prognosis in children is substantially better than in adults, asymptomatic carrier transmission is more frequent in the pediatric population. Nonetheless, as the epidemic progresses, the number of cases in children may alter in the future [23].

4.6 Risk Factors of COVID-19 in Children

The majority of research indicates that the same risk factors in adults also exist in children, including comorbidities such as diabetes, chronic lung illness, and heart pathology. Adults with comorbidities such as hypertension, diabetes, renal illness, immunosuppression (drug-induced immunosuppression and HIV), and chronic obstructive pulmonary disease have a greater risk of poor outcomes (including asthma) [24].

Given the disease's progression, prompt detection is critical, with ARDS potentially happening one week after symptom start. Septic shock, toxic
encephalopathy, multiple organ failure syndromes, disseminated intravascular coagulation, and status epilepticus were the most common consequences identified in children with severe forms of COVID-19 [25]. Fortunately, just one kid (aged 14 years) died in a study of 2173 children. However, severe and critical cases were 10.6 % among infected newborns and reduced to 3.0% among infected 16–18-year-olds. [13] More severe forms were more common in children aged three years (10.6 %) than children aged 16–18 years (3 %) infected with the virus, implying that younger children are more at risk of having severe forms than older children. Still, the study did not report if any children had underlying diseases [26]. According to another research, a 10-month-old infant died due to intestinal blockage. In the research, the comorbidities related to severe cases were leukemia (chemotherapy), intestinal obstruction, and hydronephrosis [17].

4.7 Disease severity in children

A study included 2,143 children, more than 90% of the identified patients with laboratory-verified or clinically confirmed COVID-19 had an asymptomatic, mild, or moderate illness in the most extensive child case series to date, according to research. The prevalence of severe and critical disease was 10.6 % in children aged one at diagnosis, 7.3 % in children aged one to five years, 4.2% in children aged six to ten years, 4.1 % in children aged eleven to fifteen years, and 4.1 % in children aged sixteen to seventeen years. Half of the children with critical COVID-19 were younger than one year old [26]. Another investigation found a significant frequency of severe illness in very young children. 1.8% of the 171 children treated at Wuhan Children's Hospital required critical care, and all of them had underlying disorders. One child had hydronephrosis, another had leukemia treatment, and another had intussusception [17].

4.8 Deaths in children

In a study, 965 fatalities of 44 672 confirmed COVID-19 cases (including adults and children). One kid died between the ages of 10 and 19, while no children between 0 and 9 died. No more information was provided regarding the kid who died or if the COVID-19 test was conducted before or after death [15]. A 10-month-old boy died of intussusception and multi-organ failure, according to Lu et al. [28]. So far, none of the 123 children in the United States with COVID-19 has died [26].

4.9 Management and treatment
Considering the asymptomatic nature of children with COVID-19, most cases need supportive home therapy. Instances must be segregated, and they require enough hydration and calorie intake. Paracetamol is indicated for fever treatment. Some investigators postulated a link between ibuprofen usage and a more aggressive course of SARS-CoV-2 infection; however, these findings were not verified [29]. In severe pathology cases, when pharmacological or respiratory assistance is required, hospitalization is essential. Hospitalized children must have their vital signs checked and enough hydration and calorie intake to maintain hydro-electrolytic equilibrium. Additionally, bed rest and keeping the upper airways free are advised. In the case of hypoxia (SpO2 95 per cent) without evidence of respiratory distress, oxygen supply by nasal cannulae or mask is adequate. Still, vigilant monitoring of vital indicators and attention to changes in the acid-base balance may suggest clinical deterioration [29]. Simple oxygen supply is insufficient in cases of respiratory distress caused by hypoxemia. High-flow nasal oxygen (HFNO) or non-invasive ventilation, such as continuous positive airway pressure (CPAP), should be employed in these circumstances [30]. There is limited credible evidence for the efficacy of medications in treating COVID-19 pneumonia in juvenile populations, and the only data known to date are from adult populations. As a result, pharmaceutical treatment is discouraged in lower COVID-19 forms but encouraged in more extreme versions; such judgments should always be taken on an individual basis. There is currently no anti-SARS-CoV-2 medication that has been demonstrated to be effective. Antiviral medication treatment appears to be helpful when started prior to clinical deterioration. The most widely utilized medicine is interferon-alpha via nebulization, which has been demonstrated to suppress viral replication, resulting in improved symptoms and a shorter duration of the condition [30].

5. Conclusion

Children of all ages are susceptible to getting COVID-19 due to human-to-human transmission. COVID-19 has a milder clinical course, quicker recovery, and a better prognosis in children than adults. Among the most common symptoms observed were fever, cough, sore throat, sneezing, myalgia, and lethargy were all indications of an acute respiratory infection. The majority of research indicates that the same risk factors in adults also exist in children, including comorbidities such as diabetes, chronic lung illness, and heart pathology. Infants under one year old and children
with underlying chronic disorders were at a higher risk for having severe forms of COVID-19. Septic shock, toxic encephalopathy, multiple organ failure syndromes, disseminated intravascular coagulation, and status epilepticus were the most common consequences identified in children with severe forms of COVID-19. More high-quality data is needed to understand COVID-19 in children fully and to establish the best effective case management options. Infection prevention by isolation of diseased children is critical, as is thorough surveillance, early diagnosis of illness complications, and the ability to treat patients on time while preventing secondary dissemination.

**List of Abbreviations:**

ARDS acute respiratory distress syndrome  
CPAP Continuous positive airway pressure  
COVID 19 Coronavirus disease 2019  
HFNO High-flow nasal oxygen  
KWS Kawasaki disease

**Conflict of interest:**

The authors declare that there is no conflict of interest regarding the publication of this article.

**Funding:** None.

**Consent for publication:** Not applicable

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13


