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ABSTRACT

A limited number of pediatric cases of coronavirus disease 2019 (COVID-19) have been reported since the emergence of the pandemic. The clinical characteristics of COVID-19 in children remain unclear. The aim of this review article is to describe the current knowledge of COVID-19 in children regarding its prevalence, signs, symptoms, severity and the role of children in disease transmission. This article is based on a comprehensive review of PubMed and Google Scholar for original articles, letters to editors, editorials, and case reports published from January to October 2020. It was concluded that Children of all age groups are susceptible to acquiring COVID-19 but will most likely be asymptomatic or with mild symptoms. Many explanations for this have been suggested, but the exact reason is not clear. Although children may show typical symptoms such as fever and cough, yet gastrointestinal involvement is much more common than in adults. Dry coughing is also lighter in children. There is no significant difference in prevalence between both sexes. Regarding transmission, it has not been confirmed whether COVID-19 is often transmitted from children to adults, but it is wise for families and their COVID-19 affected children to follow preventive measures to help stop COVID-19 from spreading.

Key words: COVID-19, Coronavirus, Children, Pediatric, Dentistry


INTRODUCTION

In December 2019, the Wuhan Municipal Health Commission in China reported that a cluster of pneumonia cases of unknown origin had emerged in the city of Wuhan, Hubei province, China [1,2]. The number of cases increased rapidly over the following days. On January 7, 2020, the World Health Organization (WHO) attributed the condition to a novel type of coronavirus and named it the 2019 novel coronavirus (2019-nCoV); on February 11, 2020, the WHO named the associated illness the novel coronavirus disease (COVID-19).

COVID-19 is a highly infectious disease transmitted from person to person via respiratory droplets, hand, saliva, and surface contacts. In March 2020, the WHO declared the COVID-19 outbreak a global pandemic [3]. The COVID-19 cases reported in the literature have mostly been of adults, and studies of the disease in children are limited [4, 5]. The term “children” is used to refer to those who are younger than 18 years old. Children with COVID-19 have mostly been reported to be asymptomatic or to have milder symptoms than adults. However, infants and younger children, especially those who are immune compromised or have pulmonary conditions, are reported to be more likely to suffer from a severe disease course. Apart from medical conditions, a child’s age is considered the most important factor in determining the potential severity of their disease [6]. A considerable amount of the existing literature is based on data from Chinese studies; however, a regional variation in the disease course among different populations has been reported [7].

The aim of this review article is to describe the current knowledge of COVID-19 in children concerning its prevalence, signs and symptoms, and severity, as well as the role of children in transmission.
METHODS

The terms “COVID-19,” “SARS-CoV-2,” and “children” were used as the keywords in this paper’s research. Additional terms included “epidemiology,” “transmission,” “signs and symptoms,” and “prognosis.” Medline (PubMed interface) and Google Scholar were searched for original articles, letters to the editor, editorials, and case reports. The search covered work published in peer-reviewed journals between January 2020 and October 2020. Only work published in the English language was included. The abstracts were evaluated for eligibility, duplicates were removed, and the data were then analyzed.

RESULTS

Prevalence

In the city of Wuhan, China, where COVID-19 was first detected, none of the first reported cases were children. The first case of COVID-19 in children was detected in the city of Xiaogan, China, on January 26, 2020 in a three-month-old infant with fever symptoms [8]. The second reported case of a COVID-19-infected child was in Wuhan on January 28, 2020. This could mean that either children were not infected with the disease before then or that children who were infected were asymptomatic [9,10]. The incidence of COVID-19 in children increased after the WHO declared the COVID-19 outbreak a global pandemic in March 2020. As of 20 December 2020, a total of 76,627,080 COVID-19 cases have been confirmed, 1,691,595 deaths reported, and 53,751,803 cases reported recovered. The number of active cases in December 2020 was 21,183,318, of which 99.5% were mild cases and 0.5% were serious or critical cases [11]. In the United States (US), a total of 1,639,728 COVID-19 cases in children have been reported so far. Children represent 12.2% of all US cases, and 0.2–4.4% of all COVID-19 cases in children resulted in hospitalization [12].

Concerning the ratio of COVID-19 cases among genders, the WHO reported that as of 6 May 2020, only 40% of 3,588,773 confirmed COVID-19 cases reported to WHO included age and sex details [13]. The analysis of this data showed no significant gender difference (51% males to 47% females), with some variations across age groups. However, there appears to be a higher number of deaths in men [13]. The results of a published systematic literature review and meta-analysis on the influence of gender on COVID-19 mortality, severity, and disease outcomes showed that the male to female ratio for cases was 1:0.9 [14]. A significant association was found between male sex and mortality, as well as a lower chance of recovery. Male patients were more likely to present with a severe form of COVID-19. The authors concluded that males are slightly more susceptible to COVID-19 infection, present with a more severe disease, and have a worse prognosis [14].

Ranabothu et al. reported the demographic data of COVID-19 cases in a sample size of 1353 infected children [15]. The gender ratio was 49% females to 51% males. The age distribution showed the highest percentage of cases in the age range of 11–18 years old (52%), followed by 1–5 years old (21%) and 6–10 years old (15.2%), and finally infants of less than one year old (11.4%). The most commonly affected race was White (34%), followed by Black or African American (16%), and then Asian (2%). However, 48% of the children were reported as being of unknown race. The mortality rate was less than 0.7%.

Signs and symptoms

COVID-19’s incubation period usually ranges from 2 to 14 days, after which clinical symptoms of the disease start to appear [16]. In adults, the main clinical symptoms are fever, dry cough, fatigue, severe headache, upper respiratory symptoms, and, occasionally, gastrointestinal (GI) symptoms, such as diarrhea, nausea, and vomiting [17]. However, the symptoms seem to be less severe in children than in adults, and in many of the reported cases, the affected children were asymptomatic [17,18]. Although children may show typical symptoms such as acute upper respiratory tract infection, GI involvement is much more common than in adults than in children, and dry coughing is lighter in children [5]. Upper respiratory symptoms like nasal congestion are fewer and milder in children and rarely progress to lower respiratory tract infections. Zhang et al. [19] reported in their study of 171 confirmed cases of COVID-19 in children that 32.1% had a fever ranging between 38.1°C and 39°C. Most studies on COVID-19 in
children suggest that their fever usually does not exceed 39°C [20], and symptoms in children are more atypical than in adults. Liang et al. [21] investigated the various clinical characteristics of COVID-19 in family members and their children. The results of their study showed that 59% of adults had a fever and 46% had a cough. Among the children, 50% experienced diarrhea, 3.6% had vomiting, 1% experienced nausea, and 2.2% had abdominal pain. Twenty-six percent of the children were asymptomatic. GI symptoms are two times more common in children than in adults [16,22,23].

Another study of 1117 COVID-19-positive children reported that the most prevalent symptom was fever (7.5% of the cases), followed by cough (41.5%), nasal symptoms including runny nose and nasal congestion (11.2%), diarrhea (8.1%), nausea/vomiting (7.1%), fatigue (5.0%), and respiratory distress (3.5%). The nasal symptoms described were runny nose and nasal congestion; the symptom of loss of smell was not described. One hundred forty-five (36.9%) children were diagnosed with pneumonia, and 43 (10.9%) upper airway infections were reported [24].

In late April 2020, some studies reported a similarity between the symptoms of COVID-19 in children and the symptoms of Kawasaki disease, which is also known as multisystem inflammatory syndrome (MIS-C). The results of this study by Feldstein et al. showed that 33% of the children diagnosed with COVID-19 and who had Kawasaki disease–like symptoms were younger than five years old [25]. Researchers have also reported cases in which Kawasaki disease manifested three to four weeks after the child recovered from COVID-19 infection and developed antibodies against the virus [26].

Severity

The severity of COVID-19 in children can be classified into five categories based on clinical features, laboratory testing, and chest imaging [18].

1. Asymptomatic infection: no signs or clinical symptoms, normal chest imaging results, but positive COVID-19 laboratory test result.
2. Mild: symptoms of acute upper respiratory tract infection, such as fever, fatigue, cough, sore throat, runny or congested nose, sneezing, and congestion of the pharynx with no auscultatory abnormalities. Some cases may complain of GI symptoms, such as nausea, vomiting, abdominal pain, and diarrhea.
3. Moderate: pneumonia, fever, and cough. No obvious hypoxemia, such as shortness of breath. Some cases may be asymptomatic, but chest computed tomography (CT) shows lungs with subclinical lesions.
4. Severe: early respiratory symptoms may be accompanied by GI symptoms. A characteristic feature of this stage is the development of dyspnea with central cyanosis. The oxygen saturation drops to around 92% with other hypoxia manifestations.
5. Critical: rapid deterioration of the child’s condition and development of acute respiratory distress syndrome, respiratory failure, heart failure, coagulation dysfunction, shock, and acute kidney injury. The organ dysfunction stage is life-threatening.

The data published globally regarding COVID-19 in children suggest that most children do not exhibit severe disease and that a large number of COVID-19 cases in children are asymptomatic. Tiago de Souza et al. reported that of a total of 1117 COVID-19-positive children, 159 cases (14.2%) were asymptomatic, 406 (36.3%) were mild, 514 (46.0%) were moderate, 25 (2.1%) were severe, and 13 (1.2%) were critical [24].

In China, the largest nationwide case series of its type so far involving 2143 COVID-19 cases in children who were clinically diagnosed, or laboratory verified showed that 94 (4.4%) cases were asymptomatic, 1088 (51.0%) mild, and 826 (38.7%) moderate, accounting for 94.2% of all cases. Only 5.2% of cases were severe and 0.6% were critical cases [18], and most of the children hospitalized due to COVID-19 recovered and were discharged within one to two weeks [27,19].

In addition, children with underlying conditions, such as obesity, diabetes, asthma, congenital heart disease, genetic conditions, or conditions affecting the nervous system, are at higher risk of serious illness and hospitalization for COVID-19. Overall, the prognosis of COVID-19 is good in children with a fatality rate of less than 0.7%.
lower than that of Severe Acute Respiratory Syndrome (about 10%) and Middle East respiratory Syndrome (approximately 34%) [28] but higher than that of seasonal influenza (0.01% to 0.17%) [29].

It is not clearly understood why children are less severely affected than adults by COVID-19. However, the research published so far has attributed this to several reasons. First, young children usually have a more active innate immune response and healthier respiratory system [30,31]. Second, children have less of a tendency toward immune dysregulation. Third, pro-inflammatory response markers, such as C-reactive proteins, which reduce the inflammatory response to infection, are unknown in children. Finally, angiotensin converting enzyme 2 (ACE2) receptors are immature in children. ACE2 receptors were discovered to be COVID-19 receptors, necessary for COVID-19 binding, the entry of host cells, and subsequent viral replication [32]. Their immaturity reduces the chance of COVID-19 infection in children [17,33]. It is worth mentioning that men have more ACE2 in their alveolar cells than women. This may also explain the higher infection rate among men [33]. Literature review has shown that the most commonly reported reasons for age-related differences in COVID-19 infection are the differences in the distribution, maturation, and function of viral receptors between children and adults [31].

Role of children in COVID-19 transmission

Very few studies have reported the effect of COVID-19 on pregnancies and neonates, so no clear conclusion can be drawn on whether babies can become infected in utero. The results of a case series study involving 31 COVID-19-positive pregnant women showed that none of their babies or placentas were positive when screened for COVID-19 [34]. One case of a COVID-19-positive newborn delivered by cesarean section was reported [34].

The role of children in spreading COVID-19 has raised many concerns since the beginning of the pandemic. These concerns can be attributed to the playful and talkative nature of children, as children tend to express themselves without restraint.

However, a recent literature review revealed some studies on the household transmission of COVID-19, most of which reported that children were less susceptible to COVID-19 than adults and not likely to be responsible for transmitting the disease to adults [35-37].

The collected evidence points to the limited spread of COVID-19 between children and from children to adults. Danies et al. [38] reported on a cluster of COVID-19 in the French Alps, including the case of a nine-year-old boy who attended three schools while symptomatic with COVID-19; none of his 112 school contacts acquired the disease.

Another incident involved nine high school students and nine staff members in New South Wales, Australia, who were confirmed to be COVID-19 positive. These 18 individuals had contact with 735 students and 128 staff members. Only two children contracted COVID-19, while none of the staff were affected [39,40].

A study done by Kim et al. [41] investigated children's role in the household transmission of COVID-19 in South Korea. A total of 107 children and 248 adult family members were observed. The study's findings showed that the rate of COVID-19 transmission was 2.6%. They concluded that children are not efficient transmitters of COVID-19.

Moreover, a study by Murno et al. [42], who investigated the infection patterns and transmission methods of COVID-19 among different populations, found that the rate of infection transmission between children is low. This means that children do not transmit the virus between themselves at rates as high as adults [43].

Recommendations for pediatric dentists

The Royal College of Surgeons of England, as well as many other international and national legislation authorities, have published guidelines and protocols for the dental treatment of children during the COVID-19 pandemic [44-46]. Dental care providers, including dentists, hygienists, and dental assistants, are highly advised to stay updated about and strictly adhere to local recommendations. They should take extra care and follow strict precautional measures. Full personal protective equipment (PPE), including a protective disposable over-gown, surgical mask, and protective face shield or goggles, should be
worn to minimize the possibility of exposure to or spread of infection. Surgical masks that do not seal around the nose and mouth are not adequate to completely protect against aerosol-borne disease transmission. N95 masks with a positive seal around the nose and mouth, in combination with a full face shield, should be worn when treating patients [44].

All guidelines emphasize the importance of screening patients prior to dental appointments [44-46]. This screening is intended to identify patients with possible COVID-19 infections and minimize the risk of spreading the infection to dental care providers, staff, and other patients.

It is mandatory to establish a pre-appointment triage zone where each patient's temperature can be measured. Patients with fever, meaning a body temperature of 37.7°C or above, should be registered and referred to designated hospitals. Triage zone staff should obtain adequate medical history from patients, including whether they have experienced symptoms such as fever, cough, or upper respiratory symptoms. They should also check patients' travel history to any affected countries during the past 14 days as well as their history of contact with people diagnosed with or suspected to have COVID-19. The patient's condition and their suitability for treatment in the dental clinic can thus be determined.

During the COVID-19 pandemic, it is advisable to eliminate or minimize aerosol-generating procedures, such as the use of a three-way syringe or high-speed handpiece. The use of rubber dams and high-volume suction is recommended to reduce the production of droplets and control the spread of infection. Also, procedures that provoke coughing should be avoided as much as possible. For example, extraoral dental radiographies, such as panoramic radiography and cone beam computed tomography should be used as alternatives to intraoral radiographs. No routine dentistry should be provided for children during this pandemic [47]. Dental treatment should be provided in emergency cases only, and routine dentistry should be deferred to minimize risks to patients, staff, and the public.

**CONCLUSION**

COVID-19 is found to cause low-risk infection that is asymptomatic or has mild clinical manifestations in children compared to adults. Several explanations have been suggested by researchers, but the exact reason is not yet clear. Children of all ages may acquire COVID-19 infection, but young children, particularly infants, are more vulnerable. There is no significant difference in the prevalence of COVID-19 between the two sexes. The distribution of children's COVID-19 cases varies with time and place. Although it is not confirmed whether children often transmit COVID-19 to adults, it is wise for families and their COVID-19 affected children to take action and follow preventive measures to help stop COVID-19 from spreading. Pediatric dentists should regularly review any updates to policies and guidelines, and these guidelines should be followed strictly.

**CONFLICT OF INTEREST**

The author declares no conflict of interest.

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