Developing Nursing Knowledge on COVID-19 in Children and Adolescents: An Integrative Review

Janet Green, Julia Petty, Lynette Staff, Patricia Bromley, Fiona Orr, Nicola Brown, Larissa Smart, Karen Walker, and Linda Jones

The novel coronavirus COVID-19 is a threat to the health and well-being of millions of people around the world. People with weakened immune systems (Centers for Disease Control and Prevention [CDC], 2021) and the elderly are more likely to become critically ill (Mueller et al., 2020), and a significant proportion of adults require hospitalization, some developing severe life-threatening complications (Abate et al., 2020). COVID-19 infection has been reported in all age groups, including infants, children, and young adults. Although children can carry and transmit the virus, they typically do not develop severe disease, and the nature and presentation is different from adults (De Rose et al., 2020). Surprisingly, with an air-borne viral disease such as COVID-19, the number of children diagnosed is small; Hedrich (2020) reported that 2.1% of the 42,672 cases in China were children and adolescents, with a low disease associated mortality. On a wider scale, current statistics consistently indicate that children under 18

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Aim. To review and discuss recent literature on the specific nature of COVID-19 in children and adolescents compared to the adult population.

Background. The COVID-19 pandemic is a threat to the health and well-being of all people around the world. A significant proportion of adults require hospitalization, some developing severe life-threatening complications. However, although children can carry and transmit the virus, they typically do not develop severe disease, and the incidence is lower compared to adults.

Design. An integrative literature review, prepared using the PRISMA-ScR reporting checklist.

Methods. Using Arksey and O'Malley's framework, relevant databases were searched for articles published in English since the pandemic onset in March 2020 through August 2020. Inclusion and exclusion criteria were applied, and selected articles were thematically analyzed.

Results. Four themes were identified and discussed relating to the potential care implications for children and adolescents: 1) the differing immune system in children, 2) the presentation of COVID-19 in children and adolescents, 3) vascular disease as a response to COVID-19, and 4) global policy changes relevant to COVID-19 in children and adolescents.

Conclusion. The incidence, severity, and presentation of COVID-19 in young children differs to that of adults. Less is known about the disease pattern in adolescence. A new condition named as multisystem inflammatory syndrome in children (MIS-C) has emerged, about which we are still learning globally. Although perhaps not affected severely, children may still be vulnerable to the secondary consequences of policy changes (e.g., school closures, social distancing).

Relevance to clinical practice. It is vital to address the significant global issues and contribute a pediatric and adolescent nursing perspective to the rapidly emerging body of evidence during the COVID-19 pandemic. Knowledge and understanding of the disease impact in children and adolescents are essential to offering optimum support and care to this patient group.

Key Words: COVID-19, pandemic, children, adolescents, specific features, impact, well-being, multisystem inflammatory syndrome in children (MIS-C).

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years of age constitute around 2% of total cases worldwide (Royal College of Paediatrics and Child Health [RCPCH], 2021). Unlike other viral respiratory infections where children are key transmitters, children do not seem to be a major vector of COVID-19 (Isaacs et al., 2020). Children are usually infected by symptomatic or pre-symptomatic adults. Posfay Barbe and colleagues (2020) found that most pediatric cases occurred inside familial clusters with adult transmission.

The pathophysiology of the virus and how it impacts the human body is now known. Corona viruses are enclosed viruses with spikes, which attack host cells and infect them with the virus (Abdulamir & Hafidh, 2020). When the host cell is infected, the viral nucleic acid (RNA) replicates in the cytoplasm of the cell. Budding enables the offspring virions to be released from the infected cell. COVID-19 infects and hijacks host cells but does not destruct infected cells. The damage to lung tissue, severe pneumonia, and respiratory failure seen in adults who become very ill is due to severe inflammation rather than a direct damaging effect of the virus (Abdulamir & Hafidh, 2020). This is often termed the cytokine storm, an exaggerated immunopathic response (Sinha et al., 2020). The immune system is responsible for this cytokine storm, which leads to a destructive 'attack' on the infected cells. Alveoli are the final location before the virus invades the systemic system and blood. At alveoli level, the immune system increases its aggression. Usually, alveoli are protected by alveolar lymphocytes and macrophages, as well as airway epithelial cells. When the virus enters the alveoli, however, cell-mediated immunity begins its extensive response with a surge in local and systemic cytokines, resulting in severe alveolar and interstitial inflammation, damaging lung tissue, filling the alveoli with inflammatory exudates, and leading to hypoxia and respiratory failure (Abdulamir & Hafidh, 2020; Mehta et al, 2020).

The COVID-19 virus directly infects cells via the angiotensin-converting enzyme 2 (ACE-2) receptor (Sriram et al., 2020). This receptor for this enzyme is expressed in various organs, including the lungs. Cells in children's lungs express this receptor less than those in adult lungs, which may be why the infection affects children less severely (Cristiani et al., 2020). Zhu and colleagues (2020) agreed that the virus uses the ACE 2 receptor to invade cells and mainly spreads via the respiratory tract. These receptors are present on many immune cells, such as monocytes, lymphocytes, and neutrophils. The ACE-2 in children is considered to be less developed, resulting in a decreased ability of the virus to bind to receptors in children (Waltuch et al., 2020). ACE-2 is the entry point for epithelial cell infection, but additionally controls pulmonary inflammation and repair. Variable ACE-2 expression patterns may impact disease susceptibility and progression in children. Understanding this pathophysiology is an important starting point for comparing the situation in the younger age group, the focus of this paper. This review provides an overview of the current knowledge on COVID-19 specific to children and adolescents and the related implications for care.

Aim

The aim of this review was to select recent literature published since the advent of the COVID-19 pandemic in March 2020 through August 2020 to address the following question: What are the specific features of COVID-19 presentation in children and adolescents that are different from the adult population? The key objectives of the paper are 1) to collate and analyze key literature on the nature, incidence, and care implications of COVID-19 in children and adolescents, 2) to draw on key themes from the literature to inform child and adolescent nursing practice, and 3) to contribute a child and adolescent nursing perspective to the emerging body of evidence, which is largely medical in nature, in this unparalleled time of the COVID-19 pandemic.

Methods

Design

An integrative review methodology was used because it enables a broad review and facilitates a comprehensive understanding and knowledge summary of a topic, in this case, COVID-19 infection in children and adolescents. An integrative review generates new knowledge and perspectives about the chosen topic (Torraco, 2016). Arksey and O'Malley's five step framework (cited in Levac et al., 2010 was the approach used to gather and manage the literature for this review) (see Table 1).

Search Strategy

COVID-19 has presented an opportunity for researchers because publishers have made unprecedented free, full-text access to their peer-reviewed publications about COVID-19. Recent and relevant literature was easily sourced because COVID-19 has, in the main, only been seen in 2020; therefore, the timeframe for the literature search was narrow. PubMed, EMBASE (Excerpta Medica Database), Cochrane Library, PubMed Central (PMC), UpToDate and Google Scholar

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Table 1:
Arksey and O'Malley's Methodological Framework for Conducting a Literature Review

Stage	Description
1: Identifying the research question	This stage provides the direction for subsequent stages. Research questions are broad in nature as they seek to provide breadth of coverage.
2: Identifying relevant studies	This stage involves identifying the relevant studies and developing a decision plan for where to search, terms (see Table 2) and sources to use, time span, and language. Sources include electronic databases, reference lists, hand searching of key journals, and organizations and conferences. Practicalities of the search also need considering (e.g., time, budget), and other resources are potential limiting factors and decisions need to be made upfront about how these will impact the search.
3: Study selection	This stage involves inclusion and exclusion criteria (see Table 2) based on the specifics of the research question and on new familiarity with the subject matter through reading the studies.
4: Charting the data	A data-charting form is developed and used to extract data from each study (see Table 3). A 'narrative review' or 'descriptive analytical' method is used to extract contextual or process-oriented information from each study.
5: Collating, summarizing, and reporting results	An analytic framework or thematic construction is used to provide an overview of the breadth of the literature but not a synthesis. A numerical analysis of the extent and nature of studies using tables and charts is presented. A thematic analysis is then presented.

Source: Adapted from Levac et al., 2010.

were the databases chosen, using the search terms highlighted in Table 2.

An overwhelming amount of literature was found. In fact, the research on COVID-19 grows every day. This is referred to as 'Big Data,' a variety of data that arrives in increasing volumes with an ever-expanding velocity. Big data has value, and if it is trustworthy, also has veracity (Oracle Australia and the United Kingdom, 2020). For example, typing "COVID-19" into Google Scholar at the start of this paper yielded 960,543 results. The same search four weeks later just before article submission yielded 1,300,000 results. Therefore, this big data is growing exponentially over time.

Following the search, pragmatic decisions related to article selection were required to arrive at a manageable number that illustrated the main issues and areas of essential knowledge and was appropriate for the scope, time, and resources available. Firstly, specific papers were discounted after applying the exclusion criteria in Table 2. Secondly, four broad themes were named by identifying the key areas of interest and knowledge emerging from the selected body of literature paper and categorizing them: 1) the differing immune system in children, 2) the presentation of

Table 2.
Search Terms, Inclusion and Exclusion Criteria

Search Terms Used
• COVID-19 in children AND outcomes (608,000) • COVID-19 in adolescents AND outcomes (196,000) • Boolean operators used to combine these with the terms below*.
Inclusion Criteria
The search was then limited to: • Full text in English • Published March to August 2020 • Peer-reviewed research studies / reviews and / or literature reviews only • Case reports of COVID-19 in children and adolescents (29,700) • *Coagulopathy (*Multi-inflammatory system disease (MIDS) and COVID-19 in adolescents (2,410) • *Inflammatory vessel disease (*Kawasaki-like illness) and COVID-19 in children (10,300) • *Mental health in children and COVID-19 (46,100) • *School opening/closing and COVID-19 (157,000) • *Social distancing measures (5,200)
Exclusion Criteria
• Non-English text/papers • Non-peer reviewed papers/reviews • Blogs and news articles • Editorials • Opinion papers and commentaries
Final number of selected papers for thematic review = 32.

Table 3.
Summary of Selected Papers

Theme	Authors (All Are 2020)	Type of Paper/Study	Country of Origin
The differing immune system in children	Abdulami & Hafidh Hedrich Mehta et al. Sriram et al. Waltuch et al. Zhu et al.	Review paper Review paper Review paper Review paper Case series Review paper	Iraq United Kingdom United Kingdom United States United States China
The presentation of COVID-19 in children and adolescents	Balasubramanian et al. De Rose et al. Dong et al. Green et al. Ludvigsson et al. She et al. Swann et al. Viner, Mytton et al. Zhang et al. Zimmerman & Curtis	Review paper Review paper Case series Literature review Systematic review Review paper Observational cohort study Systematic review and meta-analysis Meta-analysis Review paper	India and United Kingdom Italy China Australia and United Kingdom Sweden China United Kingdom United Kingdom, Netherlands, and Australia Brazil Switzerland and Australia
Vascular disease as a response to COVID-19	Alsaied et al. Belot et al. Centers for Disease Control and Prevention (2020a) Feldstein et al. Levin Riphagen et al. Singh-Grewal et al. Toubiana et al. Wu & McGoogan	Review paper Epidemiological study Government guidance Epidemiological study Review paper Case cluster report Review paper Prospective observational study Case series	United States France United States United States United Kingdom United Kingdom Australia France China
Global policy changes relevant to COVID-19 in children and adolescents.	Bahn Clemens et al. Giannini et al. United Nations Viner. Russell et al. Wang et al. World Health Organization (2020e)	Literature review Discussion paper Global guidance Global guidance Systematic review Discussion paper Global guidance	Korea Various – Europe Various – Global Various – Global United Kingdom and Australia China Various – Global

COVID-19 in children and adolescents, 3) vascular disease as a response to COVID-19, and 4) global policy changes relevant to COVID-19 in children and adolescents.

The most recent 6 to 10 papers were selected for each theme. These themes and details of the chosen papers are outlined in Table 3. It was important to ensure that the selected papers represented a global view, so literature from a range of continents was included. Literature from other continents was not included if there was no primary research or if literature from those regions was limited to opinion reviews or editorials, in line with the inclusion/exclusion criteria.

The Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) checklist was used for the preparation of the final review. PRISMA is an evidence-based minimum set of items for reporting in systematic reviews and meta-analyses (PRISMA, 2015). Although primarily used for scoping reviews, PRISMA is also appropriate for integrative reviews (Tricco et al., 2018) to ensure transparency and a comprehensive process.

Results

The outcome of the selection of literature, after inclusion and exclusion criteria were applied, revealed mostly medical papers with one only from a nursing perspective. Most were review papers rather than primary research. Countries were represented within Europe, Asia, Middle East, Australasia, and the Americas, with none from Africa, for reasons given above. The four themes identified are discussed relating to the specific, unique differences in children followed by the potential care implications.

The Immune System of Children and Adolescents in Relation to COVID-19

In relation to the cytokine storm that occurs in adults, an unexpected

benefit for children is they are less capable to mount a destructive and vigorous cell-mediated attack on alveoli and interstitial tissue of the lung, possibly due to the lack of adult-like memory cells specific to other circulating coronaviruses (Abdulamir & Hafidh, 2020). However, adolescents have a more mature immune system and are not afforded the same immune protection against the disease and are more likely to develop the 'cytokine storm.' The increased levels of cytokines in adolescents causes damage to the lung tissue, recruitment of neutrophils to tissues, and other pro-inflammatory effects. This damage can lead to acute respiratory distress syndrome (Mehta et al., 2020).

Currently, it is unknown why children usually develop mild or moderate COVID-19 disease. It is believed that the different immune response in children when compared to adults contributes to effective virus containment, clearance, and reduced secondary lymphocyte-mediated inflammation (Hedrich, 2020). Children have immune priming to coronavirus infections and cross-immunity from other viral infections as a result of frequent exposure, which might explain the different response of their immune system and why they overcome SARS-CoV2 more effectively (Hedrich, 2020; Waltuch et al., 2020).

By adulthood, most people have become immune to coronavirus strains that commonly circulate. Children are predisposed to infection with common coronaviruses due to lack of immunity to most of these circulating coronaviruses. This has a positive impact on children because they lack sufficient memory cells to a repertoire of coronaviruses, including some COVID-19-crossreactive antigens, leading to milder immune and inflammation responses (Abdulamir & Hafidh, 2020).

Some exceptions to this favorable picture require consideration. Children with chronic diseases that affect their blood vessels may be at a greater risk of COVID-19 infection than their peers. Pathogen clearance by T cells leads to gradual progression of inflammation. Pathogen clearance may be reduced in adults, particularly in individuals with co-morbidities (e.g., heart disease, diabetes) that place them at greater risk of COVID-19. Although children have fewer comorbidities, Zhu and colleagues (2020) found that children with either very high ACE-2 levels (as seen in diabetes and cardiovascular disease) or very low levels (animal models of hypertension) could have an increased immune response and subsequently increased pulmonary inflammation.

Overall, specific and unique features of the pediatric immune system mean that children have a decreased risk of severe COVID-19 disease. Related to this is presentation of the disease.

The Presentation of COVID-19 in Children and Adolescents

COVID-19 infections in the pediatric population are often unrecognized or underestimated because children can remain asymptomatic or manifest with mild, nonspecific symptoms (e.g., headache, nasal congestion, cough, runny nose, expectoration, hypo reactivity) (Cavallo et al., 2020). Reportedly, children have only moderate to low grade fever, or even none. Knowledge of the mode of transmission of COVID-19 is important, particularly in child and adolescent care. The major transmission routes are through droplets, but can also be via skin contact, fecal-oral transmission, and ocular surface contact (De Rose et al., 2020).

Green and colleagues (2020) summarized the available evidence in relation to COVID-19 in neonates, and reiterates the finding that the immaturity of the neonatal immune system may provide protection against the 'cytokine storm' experienced by adults. Although more data are emerging related to COVID-19 infection, there remains a dearth of literature related to infants less than one year of age. Dong and colleagues (2020) undertook the largest (N = 2135) examination of this population at the time of this writing. Their retrospective study of the epidemiological characteristics of COVID-19 in the pediatric population (defined as less than 18 years of age) in mainland China identified that infants (less than 1 year) (n = 376) appeared particularly vulnerable to COVID-19 (Dong et al., 2020). A more recent systematic review by Ludvigsson (2020) suggested that globally, the clinical manifestations of COVID-19 in children may be less severe than those found in adult patients. However, the review also revealed that infants less than 1 year of age had a greater incidence of severe and critical disease when compared to older children (Ludvigsson, 2020). Nevertheless, case fatality rate in children is much lower, with two deaths in children with COVID-19 identified up to March 18, 2020 (Ludvigsson, 2020).

Additionally, these earlier studies have some inconsistencies. Dong and colleagues (2020) found that children with suspected COVID-19 appeared to have more severe symptoms than children with a positive COVID-19 diagnosis. Ludvigsson (2020) suggested that children identified in these studies with suspected COVID-19 disease may have been infected by other viruses. As such, it is too early to conclude that young children with COVID-19 have a more severe disease than older children.

Ludvigsson (2020) concluded that the disease progression in pediatric COVID-19 was milder than in adults, that children had better outcomes, and that death was extremely rare. It is unclear why children experience a milder disease than adults. As previously discussed, Dong and colleagues (2020) offered several possibilities. This could be due to the immaturity of ACE-2 in children; children are often infected with the respiratory syncytial virus (RSV) in winter months, resulting in higher levels of antibody against virus than adults; and children's immune systems are immature and may not respond to the infection with the same virulence as an adult.

Although it is clear that children can transmit COVID-19, albeit at a reduced rate, than adults (Isaacs et al. 2020), there are implications for asymptomatic or mildly symptomatic children because they may not be tested for the virus as frequently as adults, and therefore, may transmit the disease more easily (Dong et al., 2020). However, She and colleagues (2020) and Zimmerman and colleagues (2020) have identified that all children infected with COVID-19 in their respective reviews were part of a family cluster. This, therefore, needs to be considered with infected adults to ensure COVID-19 exposed children are similarly isolated with family. Ludvigsson's (2020) systematic review identified 45 relevant studies; however, most data originated from China and possibly reflect country-specific factors that impact children that are different from other countries.

Vascular Disease in Children and Adolescents as a Response to COVID-19

For adults with COVID-19, the severe complication most likely to occur is acute respiratory failure, which may also include other organ involvement, including heart. For children, however, the clinical picture of severe COVID-19 related illness is emerging and seems to be different from adults. As the COVID-19 pandemic has progressed, so too has the evolution of prolonged and associated health conditions in children and adolescents. COVID-19 has infrequently been evaluated in the adolescent population, often combining descriptions of disease and associated health conditions with infants and children. This may be attributed to low cases of diagnosed COVID-19 in this age group. A Chinese study (*N* = 72,314) reported 1% of all COVID-19 patients were in the adolescent age range (Wu & McGoogan, 2020). Although diagnosed cases of COVID-19 in adolescents remains low, the number of adolescent patients reported to have ongoing health concerns post-diagnosis is increasing. Internationally published case studies describe febrile illnesses, toxic shock syndrome, acute abdominal conditions, encephalopathy, elevated inflammatory markers, and multisystem involvement (Levin 2020). Although in younger patients, these symptoms are associated with a diagnosis of Kawasaki disease, the reporting of symptoms in older children and adolescents identifies post-COVID-19 symptoms associated with extensive vascular involvement and ongoing health concerns. It now appears that the consistent reporting of these clinical abnormalities in older children and adolescents is a new childhood disorder.

As the pandemic progressed through Europe and then the United States during the first quarter of 2020, concerns emerged regarding children developing a severe inflammatory syndrome, similar to Kawasaki disease and toxic shock syndrome (World Health Organization [WHO], 2020c). In April 2020, a cluster of eight seriously unwell children aged 4 to 14 years were identified in the United Kingdom with symptoms including high fever, rash, conjunctivitis edema, pain, vomiting, and diarrhea (Riphagen et al., 2020). All children exhibited symptoms of cardiovascular shock required inotropic support. Seven children required mechanical ventilation. All children were previously well with no prior comorbidity; however, most of the children were above the 75th centile for weight and were of Afro-Caribbean or Asian descent (Riphagen et al., 2020). Since this initial cluster report from the United Kingdom, similar clusters have been described elsewhere (Cheung et al., 2020; Dove et al., 2021; Toubiana et al., 2020). These clusters raised concerns, and as a result, surveillance and monitoring have been established to report similar cases as they occur.

In May 2020, the WHO (2020e) and CDC (2020a) published preliminary case definitions for this syndrome. The condition is now known as multisystem inflammatory syndrome in children (MIS-C) or as pediatric inflammatory multisystem syndrome temporarily associated with SARS-CoV-2 (PIMS-TS). Both definitions require evidence of COVID-19 infection or exposure, which may limit diagnosis because asymptomatic COVID-19 infection is believed to be more common in children (Levin, 2020). To date, the published studies suggest that children with MIS-C are more likely to be older and from non-Caucasian background (Belot et al., 2020; Feldstein et al., 2020).

Data reported from the case studies suggest that patients diagnosed with MIS-C are aged between 5 to 21 years and have high rates of cardiac involvement, coronary-artery aneurysms, and myocardial injury (Whittaker et al., 2020). There have been reports of MIS-C throughout Europe, the United States, and Middle East. At the time of this review, around 1000 cases had been reported internationally, with fewer than 10 reported deaths (Levin, 2020; Singh-Grewal et al. 2020). As with adult patients, older children and adolescents with pre-existing or predisposed to cardiac conditions are at higher risk of COVID-19 complications than the general population (Alsaied et al., 2020).

Surveillance data from the United States were used to evaluate the severity of cardiovascular involvement in children (*N* = 186) diagnosed with MIS-C (Feldstein et al., 2020). Cardiovascular involvement was common in 149 children (80%), with almost half of the population receiving support to maintain appropriate blood pressure, and one in 12 children diagnosed with coronary artery aneurysms (Feldstein et al., 2020). Whittaker and colleagues (2020) reported similar findings in their United Kingdom-based case series (*N* = 58); eight children (14%) had clinical findings of coronary artery aneurysms or dilation when diagnosed with MIS-C.

Data regarding cardiovascular involvement in older children and adolescents are advancing daily, with both scientifically reported information and anecdotal evidence from treating clinicians. Current thought is that cardiovascular symptoms and cardiac injury are occurring in this age group due to 1) cardiac cell injury because of a cytokine storm inflammatory response, and 2) invasion of viral cells in the cardiac tissue resulting in cellular damage and ischemic injury due to severe hypoxia as a result of acute lung injury (Alsaied et al., 2020). The pathophysiology of these symptoms has been reported, but little to no data exist regarding early detection of MIS-C or treatment options beyond supportive care of symptoms.

Although available data provide a beginning understanding of the incidence and pathophysiology of MIS-C and the associated cardiovascular involvement in older children and adolescents, further research is needed. Areas should include identification of cardiovascular involvement in older children and adolescents to facilitate early detection and discovery of treatment options.

Treatment for COVID-19

Supportive treatment is the mainstay for the pediatric population, including fluid and calorie requirements and oxygen therapy, if required. The aim is to prevent acute respiratory distress syndrome, organ failure, and opportunistic infections. Antibiotics are only used in confirmed bacterial infections (Zimmermann & Curtis, 2020).

Although currently there is no cure for COVID-19, research from the University of Oxford (2020) has shown promising results on the use of dexamethasone in COVID-19 infections. Dexamethasone is a steroid drug commonly used in respiratory conditions where there is an inflammatory response. It is effective in suppressing the cytokine storm, which, as seen, is a key influencer in the severity of COVID-19 infections. The RECOVERY (Randomised Evaluation of COVID-19 thERapY) trial enrolled over 11,500 patients in a randomized

controlled trial (RCT) in over 175 National Health Service (NHS) hospitals in the United Kingdom. The trial randomized 2104 patients to receive dexamethasone 6 mg in one daily dose for 10 days and compared that with 4321 patients who received usual care that did not include dexamethasone. Results showed the dexamethasone 6 mg significantly reduced mortality by one-third in ventilated patients and by one-fifth in patients receiving oxygen therapy.

Corticosteroid therapy has recently proven effective in severe COVID-19 infections in the adult population (Royal College of Paediatrics and Child Health [RCPCH], 2020). However, at the time of this review, there were no studies in the pediatric population. Belhadjer and colleagues (2020) investigated 35 pediatric febrile patients with acute heart failure, potentially associated with COVID-19 infection and MIS-C, with inflammatory markers indicative of the cytokine storm. They reported that early diagnosis and traditional therapies led to favorable outcomes. All pediatric patients received intravenous immune globulin, with one-third having adjunctive steroid therapy. Rapid recovery with immune globulin and steroids was observed, even in severe cases requiring mechanical circulatory and ventilatory assistance. Ludvigsson's (2020) systematic review recognized that glucocorticoids are used as part of the recommended treatment, emphasizing however that this therapy in the pediatric population is not yet properly supported by the literature.

Global Policy Changes Relevant to COVID-19 in Children and Adolescents

The WHO continually reviews and updates its advice for countries regarding best practice in the treatment of children and adolescents, and provides technical guidance on a range of topics related to COVID-19. Topics include evolving clinical issues, such as MIS-C in children and adolescents temporally related to COVID-19, and guidance for schools and communities.

School Closure

A key issue of much discussion and debate concerns school closures, with most countries shutting schools temporarily. The WHO lists recommendations for schools that emphasize the importance of having the required resources, policies, and infrastructure to ensure the safety of all attending the school; deciding to completely close, partially close, or reopen schools should be a decision guided by a risk management approach to maximize the educational, well-being, and health benefit for students, teachers, staff, and the wider community. Of concern is a recent report from the WHO/UNICEF Joint Monitoring Programme, which states that prior to the pandemic, "43 per cent of schools around the world lacked access to basic handwashing with soap and water in 2019" (WHO, 2020a), which is important for schools to be able to open safely. This adds to the many challenges for countries and individual schools.

The Use of Face Masks

Although limited evidence exists on the use of face masks in children in preventing COVID-19 transmission, in August 2020, the WHO published advice on the use of masks for children based on current data. The four key criteria for those making decisions are as follows: 1) children less than 5 years should not wear masks, 2) a risk-based approach should be used regarding recommending mask use in children from 6 to 11 years, 3) children and adolescents 12 years and over should follow WHO guidelines and national guidelines for adults, 4) mask use for immunocompromised children is recommended but in consultation with their medical practitioner and individually assessed for children with developmental disabilities (WHO, 2020b). The use of masks in schools, therefore, depends on the level of risk to staff and students and is recommended to be in line with national/regional guidelines. Studies are ongoing to understand the transmission of the virus and the utility of masks in children; however, is clearly stated that masks are only one part of the strategy to prevent transmission.

Vaccination Programs

The immediate consequences of the pandemic are evident. However, there are many long-term impacts to consider. One of the most concerning consequences of this pandemic is the impact on the uptake of routine childhood vaccinations and vaccination programs, with many programs stopped completely. At present, globally, over 13 million children are still not vaccinated, with many millions more not completely vaccinated. Although there has been great progress over the last decade in increasing coverage and programs, the impact of the pandemic on these programs has the potential to adversely affect the gains that have been made and the likelihood of more deadly outbreaks of diseases, such as polio and measles. In 2019, measles was already reported as the cause of death for 6000 people in the Democratic Republic of Congo. Therefore, the WHO (2020d) recommended that "Immunization is a core health service that should be prioritized for the prevention of communicable diseases and safeguarded for continuity during the COVID-19 pandemic, where feasible." In March 2020, the WHO stated that mass vaccination should be suspended temporarily because of social distancing and COVID-19 transmission but with regular re-evaluation and consideration of outbreaks of vaccine preventable diseases (WHO, 2020d).

In Ethiopia in July 2020, the Ethiopian Ministry of Health supported by WHO, UNICEF, Gavi, and the CDC held a 10-day vaccination campaign, initially scheduled for April. The campaign had a target of reaching 15 million children ages 9 to 59 months and achieved 96% (14.4 million). Prior training on COVID-19 precautions for health care workers, the availability of personal protective equipment (PPE), and the use of physical distancing by holding the clinics in open areas demonstrated it was possible to continue essential vaccination services with appropriate planning (CDC, 2020b).

Economic Challenges and Poverty

Although it appears children do not seem to be as affected by the virus itself, the impact on the health and well-being of children and adolescents is formidable and falls into three main categories: 1) infection with the virus, 2) socioeconomic effects, and 3) the impact on the delay in achieving the sustainable development goals. In 2019, an estimated 386 million children were living in extreme poverty; the United Nations (UN) now estimates up to 66 million more children in this category because of the pandemic. In addition, mortality rates

will increase due to economic challenges, disruption to services, and increasing malnutrition. The WHO continually updates recommendations on all aspects of the pandemic on its website and through their webinars. As new knowledge and evidence become apparent, recommendations and guidelines for countries will continually evolve.

Discussion

COVID-19 infection is less frequent and severe in the young. However, associated policies developed to prevent community transmission have led to significant considerations specific to child and adolescent health.

Impact of School Closures and Social Distancing

School closure is an effort to stem the spread of the virus despite children and adolescents experiencing very mild symptoms. Other individuals working in the school setting may become very ill, if they are older, or have existing co-morbidities (Bahn, 2020; Zhang et al., 2020). School closure changes almost every aspect of day-to-day life for a child or adolescent considering how much actual time is connected directly or indirectly to attending school. There are 120 hours in an average school week (Monday to Friday x 24 hours), depending on the individual country. Of these, one-quarter of the total hours of a school week (30 hours) is spent directly attending lessons. Additional time is expended on activities related to school (e.g., sport, extracurricular activities) and further time with school peers occurs outside of school hours (e.g., study groups, library time). Furthermore, the social interaction time adolescent students spend before and after school has been radically changed by school closure, quarantining, and physical distancing. Fundamentally, the whole way that a day 'happens' for a child or adolescent attending school has been altered, resulting in significant disruption to their academic and social world at a time of significant and accelerated neurophysical development (Bahn, 2020; Giannini et al., 2020; Van Lancker & Parolin, 2020; Wang et al., 2020). The short and long-term impacts of school closures and physical and social isolation are only recently beginning to become apparent.

The potential impact is illustrated by a closer discussion of adolescence. Adolescence is a critical period for brain development, and the experiences an individual has during adolescence are central in continuing to shape the adult brain. Although an adolescent's brain growth is almost complete in terms of size, extensive development and remodeling continues through adolescence and into the mid to late 20s. The three main processes responsible are 1) cell proliferation in response to genetic, hormonal and environmental stimuli; 2) pruning, or 'de-cluttering' of nerve fibers not 'used' frequently enough to develop permanent neural pathways; and 3) myelination or insulation of brain fibers that increases their conductivity capability and speeds up electrical impulse travel along nerve pathways (Arain et al., 2013).

In addition to these processes, the brain also develops connectivity between its regions in a posterior to anterior sequence. Arain and colleagues (2013) note that the first areas to develop and connect are the hindbrain, including the cerebellum (responsible for physical coordination, rudimentary senses, and early thought processes) and the amygdala (the seat of fear and rage). Next, the mid-brain (basal ganglia responsible for priority setting and fine motor skill perfection) and the corpus callosum (the seat of problem solving and decision-making) further develop and connect to the hindbrain. Finally, and last to fully develop and become connected to all other areas of the brain, is the forebrain. The pre-frontal cortex is where higher order thinking skills develop – those of rationalization, organization, the ability to think things through, the weighing of consequences, assumption of responsibility, and interpretation of emotions and emotional responses all take place here (Blakemore, 2012, cited in Arain et al., 2013). Thus, we know the risk-taking behavior of teens is largely due to the not-yet fully developed moderating influence of the frontal lobe due to incomplete cortical myelination. Further, during adolescence, the cortex is highly 'plastic' in nature, enabling the brain to rearrange and modify its neural connections in response to environmental stimuli and experiences.

Understanding the impacts that the developing adolescent brain has on behaviors, responses, and decision-making is essential when considering governmental and community actions to mitigate the rapid spread and adversity of the COVID-19 outbreak. Understanding the impact these decisions have on children and adolescents, including school closures and physical distancing, is imperative. Although adults can make decisions based on life experience to adverse situations, children or adolescents do not yet have that experience or knowledge relative to a particular serious and threatening life event they might face, such as COVID-19, to enable them to cope. They may have an impaired ability to make decisions about other significant aspects of their life, for example, health decisions and consequences of their behaviors in the longer term. This renders them vulnerable in several ways (Jiehao et al., 2020, cited in Balasubramanian et al., 2020). They may not fully understand the seriousness of contracting COVID-19, and because they feel well, may not realize they can still be infected with COVID-19, and can transmit it to others who may become very ill or die as a consequence.

Coupled with this vulnerability, the pressures placed on them as they are forced to remain home with school closures and physical and social distancing may cause stress-related physical and mental illness. Heavy stress may precipitate risk-taking behaviors in an attempt to escape the situation (Arain et al., 2013) due to the lack of insight, lack of empathy, and of feeling invincible, the consequences of which leave them exposed and susceptible.

Although adverse events can have serious consequences for the health and development of an individual, we also know many children and adolescents still thrive despite this. This ability to thrive in the face of adversity is known as resilience, and broadly defined, encompasses those skills, attributes, and abilities possessed by a person that enables them to adapt to hardships, difficulties, and challenges (Van Lancker & Parolin, 2020). In today's COVID-19 world, supporting and promoting resilience is vital for the world's children and adolescents, more than ever. Given the continuing uncertainty and long-term implications of this pandemic, it is imperative for our children, adolescents, and young adults to overcome these extreme circumstances and experiences and grow up to become confi-

dent, competent, and well-adjusted adults (Van Lancker & Parolin, 2020).

Importantly, although schools have re-opened in many countries, the emergence of a significant surge in cases of COVID-19 may result in a recurrence of further closures. Current evidence of infection patterns, morbidity, and mortality in children and adolescents is still emerging, which means that much more is yet to be discovered (Bahn, 2020; Balasubramanian et al., 2020; Clemens et al., 2020; Van Lancker & Parolin, 2020; Zhang et al., 2020). Thus, the benefits or potential adverse outcomes that may be associated with school closures also remain unclear, despite known adverse sequelae for students from school closures (Giannini et al., 2020).

Impact on the Mental Health Effects of Children and Adolescents

The mental health effects of the COVID-19 pandemic for children and adolescents are varied, related to exposure to stress, school closures and subsequent isolation, and access to support and therapies. The long-term mental health outcomes are yet unknown (Lee, 2020), and as mental disorders can develop during childhood and adolescence, prevention and early intervention are vital (Golberstein et al., 2020), and supporting parents and families is key.

Information about COVID-19 is pervasive in the media and wider society. Children witness the fear and stress adults experience as a reaction to the pandemic (Dalton et al., 2020). Children's fears of the infection, separation from school and friends, restricted living spaces, and negative feelings are further stressors they face (Wang et al., 2020). If predictions of increased numbers of adult mental health conditions, substance use, and family violence (Galea et al., 2020) are borne out, there could be adverse mental health outcomes for the children of affected parents. The resultant anxiety can manifest as behavioral changes, including expressions of anger and other emotions, not typically recognized by adults as indicators of anxiety, subsequently affecting access to mental health support (Dalton et al., 2020).

The pandemic has necessitated worldwide closures of schools, and although closures have decreased the spread of the infection through physical isolation, there are potential negative effects for child and adolescent mental health. School is their usual experience, and school closure disrupts routines, reduces contact with friends and teachers, limits access to learning resources and supports, and impacts learning (Golberstein et al., 2020; Lee, 2020; Wang et al., 2020). Online, home-based learning is not accessible to all children and adolescents, particularly those from less advantaged families without computers and the Internet (Galea et al., 2020; Van Lancker & Parolin, 2020).

For children and adolescents with existing mental health problems, the interaction of social isolation and the economic recession may exacerbate their situation (Golberstein et al., 2020). Due to closures, school-based mental health resources are unavailable (Lee, 2020). School-based health professionals might be their sole source of support and intervention, with 13% of adolescents in the United States receiving mental health services from their school (Golberstein et al., 2020). Although telehealth can be an effective mode of mental health care delivery, the technology available in schools and family homes determines its accessibility, and not all adolescents have a private space at home to engage with a health professional (Golberstein et al., 2020).

Given the stress associated with the pandemic and its effects on children's mental health, parents have a central role in providing psychological and emotional support. Genuine and honest conversations with children about their feelings and concerns and normalizing them can reduce fear and anxiety (Dalton et al., 2020; Pfefferbaum & North, 2020; Wang et al., 2020). Maintaining routines where possible and facilitating socialization, home-based learning, and regular exercise are other ways to enhance their children's health and well-being (Galea et al., 2020; Wang et al., 2020). It is imperative that nurses and other health professionals who care for children, adolescents, and their families are mindful of these potential effects and work with parents, families, and carers, along with the children and adolescents themselves to mitigate any potential lasting negative impacts of the pandemic.

Impact on Parents

For the small number of children who are admitted into the hospital for COVID-19 infection, providing information to parents is crucial. Alleviating anxiety should be a component of the management. If the mother is still breastfeeding, this should be continued. Children might be separated from parents due to COVID-19 infection, which causes added risk of mental health issues, potentially having long-term adverse effects on mental health. The age of the child at separation is relevant, with children in the first two years being more susceptible to poorer mental health outcomes (Liu et al., 2020).

Because parents fear infection and potentially lack full awareness of the risk and benefits, a great impact from COVID-19 on children is the delay in presentation of childhood illness. Further, parents may be unemployed or attempting to work remotely from home, while at the same time, caring for their children and supporting them through home schooling. Home schooling requires various levels of parent interaction and support that can affect parents' ability to undertake their own work. Children need to be kept occupied and safe within the home. If the family is living under lockdown, there are restrictions about going outside, and playgrounds might be closed. Economic uncertainty has increased parental stress and anxiety, and social distancing also is accompanied by increases in anxiety, depression, and substance abuse.

Evidence indicates that violence and vulnerability increase during periods when schools are closed (UN, 2020; WHO, 2020c). Increased media coverage, uncertainty, and an economic impact of loss or threat of loss of income all add to parental stress and anxiety. With raised stress levels, parents are more likely to engage in harsh parenting (Beckerman et al., 2017). This, in turn, can result in increased risk of child maltreatment, which can predispose parents to increased family violence and abuse of children (Galea et al., 2020).

Effective strategies are needed to help strengthen families to respond, care, and protect children. One helpful strategy is developing and implementing routines in the home, particularly for children (Galea et al., 2020). A mechanism is also needed to monitor, report, and intervene when mental health issues and family violence are apparent. Social isolation makes

assessment difficult for health care practitioners (e.g., maternal and child health nurses) who are conducting virtual visits rather than face-to-face.

Not all impacts of the pandemic are negative, however. Some families have reported stronger family relationships because everybody is home and having more time together (such as for meals). Parents may become more resilient, which can happen after emerging from such a stressful situation (Beckerman et al., 2020).

Strengths and Limitations

This article has summarized a selection of key literature and drawn upon key areas of interest on the topic of COVID-19 in children and adolescents specifically. Given the scarcity of nursing papers among the substantial quantity of medical publications, such knowledge is essential, not only to expand our knowledge base for application to nursing practice, but also to make meaningful sense of this new, vast, and rapidly expanding body of evidence. The literature review method explores what has been written and studied previously, building on previous work, for a thorough synopsis of what is known and what still needs to be addressed, particularly important given the novel nature of this condition and its impact. This review has collated key papers and vital messages to inform and educate nurses and other health care professionals caring for children and young people in such unprecedented times.

However, as with any research including literature reviews, the limitations must also be acknowledged. Traditional literature reviews often lack thoroughness and rigor due to not following a systematic methodology (Grant & Booth, 2009). Questions can, therefore, arise about quality and trustworthiness, especially if a review is deemed not to fully analyze data collected. Any conclusions authors reach may be therefore open to bias from a potential to inadvertently omit significant areas of the literature or by not questioning the validity of conclusions drawn. Additionally, authors may only select literature that supports their own stance or view, giving undue credence to a preferred perspective. With this critique in mind, it was essential that an approved framework was used and adhered to (Arksey & O'Malley, cited in Levac et al., 2010) in line with a specific question, congruent with this approach.

Relevance to Clinical Practice

Regardless of the differences relating to lower incidence and severity identified in this paper, children and adolescents may still be adversely affected, particularly regarding the effects on mental health and well-being bought about by social distancing, prevention of socialization, and anxieties about school and educational progression. Those working with and/or caring for children and adolescents must have an up-to-date body of new knowledge to understand the nuances of the disease in younger people and for care to be delivered to mitigate against any negative consequences. In addition, understanding the specific needs relating to children will help ensure that nurses and other health care professionals are empathic and sensitive to this specific population and able to offer appropriate support.

Conclusion

Health care around the world is faced with a continuously evolving clinical situation. The number of confirmed cases of COVID-19 has increased globally since the advent of the pandemic and continues to do so. More definitive evidence is required regarding COVID-19 in children and adolescents. COVID-19 must be taken seriously in view of its potential relating to the ramifications of mode of transmission, school closures, social distancing, and other policies that impact children, young people, families, and health care professionals. In light of the current lack of literature on COVID-19 in the nursing field, high-level research is needed that addresses these significant global issues and contributes a pediatric and adolescent nursing perspective to the rapidly emerging body of evidence during this pandemic. Nurses play a core, essential role in caring for patients globally. It is vital nurses are equipped with knowledge and understanding of COVID-19 and its implications to enable them to optimize support and care for young people and their families.

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