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Review Article

An In-depth Look at COVID-19 for Children and Newborns in a Few Minutes. An Analysis of the Literature

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Abstract

As of March 11, 2020, the human coronavirus disease 2019 pandemic had begun. The most typical signs of a lower respiratory infection include fever, cough, and dyspnea. One or more organs may fail, leading to the development of the acute respiratory distress syndrome (ARDS). SARS-CoV-2 is capable of infecting humans of all ages, including infants as little as one day old. Of the 72,314 cases that were documented in China, just 2% included a child who was under the age of 19. Among the United States, Covid-19 is more prevalent in the 12- to 17-year-old age range. Since 2003, more than 1,100,000 illnesses and 62,784 deaths have been attributed to COVID-19. In the initial published study, just 0.39 percent of children were diagnosed with the disease. As of 2021, 18 children between the ages of 10 and 19 have died as a result of the disease. S1 has the most common mutation, which increases the virus' affinity for the ACE2 receptor by replacing D614G (Asp 614Gly). SARS-CoV-2 infection in children results in far fewer neurological complications than in adults. A probable case of COVID-19 is indicated by the presence of clinical signs and symptoms in a suitable epidemiological environment. Virus detection laboratory tests might be used to confirm the diagnosis. The incubation period of 2-14 days is critical in determining the time of infection. Coughing, tiredness, and exhaustion were the most common post-acute symptoms. At the most recent review in March 2021, all 151 children were confirmed to be healthy and free of these symptoms. Changes in innate and adaptive immunity, more frequent recurrences and concomitant infections, and pre-existing immunity to coronaviruses are all possible safeguards for children. Over the course of the months of December 2019 and February 2020, nine infants in China were diagnosed with SARS-CoV-2 infection. Approximately 1-2 weeks following the onset of symptoms, most of the paediatric patients had fully recovered. Babies who were infected by a member of their families were more likely to get infected themselves.

Keywords: Children; Infants; Corona Virus; Pandemic; Biomarkers

Introduction

The human coronavirus disease 2019 (COVID-19) pandemic, which began on March 11, 2020, was caused by the SARS-CoV-2 (severe acute respiratory syndrome coronavirus-2) virus (Cucinotta and Vanelli, 2020). COVID-19 infection had been linked to 50,539,082 confirmed cases and 1,258,321 deaths as of the date of this report's writing (November 9th, 2020). (COVID-19 Map, 2020). Fever, cough, and dyspnea are the most common symptoms of infection in the lower respiratory tract, but gastrointestinal (GI) symptoms can also occur (Huang., *et al*. 2020; Shi., *et al*. 2020). Acute respiratory distress syndrome (ARDS) and multiple organ failure can develop in severe COVID-19 infection, despite the fact that the infection is usually non-fatal (Huang., *et al*. 2020; Zhou., *et al*. 2020) [1].

It is the third time in this century that the world has been confronted with a new and highly contagious virus strain that has spread across the globe and killed many people. The coronavirus that triggered the 2002 pandemic known as severe acute respiratory syndrome (SARS) was the primary culprit (SARS-CoV).

The outbreak began in China's Guangdong province. Middle Eastern Respiratory Syndrome Virus (MERS-CoV) was the cause of a second outbreak that occurred in 2012, which began in the Middle East and expanded throughout the globe. Coronavirus 2 (SARS-CoV2) is the third wave of coronavirus infection presently sweeping the globe (SARS-CoV-2).

Smaller numbers, milder symptoms, and lower mortality rates (approximately 0-0.2 percent) make juvenile patients more likely to survive than adults, and they have a better outlook [2].

The prevalence of COVID-19's most prevalent symptoms was low in children infected with the virus. Some 59% had a fever, 55% a cough, and 20% had a runny nose among them; in adults, the percentages were 84% and 84%, respectively [3]. CoVs are divided into Alphacoronaviruses, Betacoronaviruses, and Gammacoronaviruses and Deltacoronaviruses, which are typically found in mammals such as bats, rats, civets, and humans (which are mainly found in birds). People are infected with four types of CoVs: HCoV2-229E, -HKU1, -NL63, and -OC43. These four types of CoVs are the most commonly seen in humans. 15,16 They are thought to have originated from bats (NL63, 229E), dromedary camels (229E) and cattle (NL63).(OC43) [4].

HKU1's origins remain a mystery. Bats are the primary reservoir for a number of CoVs, although they have not been linked to human infection.[4] When evidence-based medicine is prevalent in modern medicine, we have a challenging position in which the requisite data is inadequate; while extensive studies exist for adults, the evidence is extremely restricted for paediatric populations. SARS-CoV-2 can infect people of all ages [5].

There have been a modest number of instances among youngsters that have been confirmed so far. It has been estimated that 2.2 percent of youngsters in China are affected, while in the United States this figure is only 1.7 percent. Therefore, guidelines established thus far are more suited for adults rather then kids. Numerous simple meta-analyses of systematic reviews have been published, but these have primarily focused on the clinical characteristics of paediatric COVID-19, and data on the transmissibility, rate of viral coinfections, and therapies of paediatric COVID-19 remain scarce [6].

Epidemiology

The literature on paediatric COVID-19 uses a variety of different case definitions. Only 2% of the 72,314 cases reported to the Chinese Centers for Disease Control and Prevention involved children under the age of 19 years. The number of children with COVID-19 infection has increased from 9 percent to 12 percent, according to more current statistics from the United States (in general, 90 percent of children positive for SARS-CoV-2 are asymptomatic or have mild to moderate symptoms) [2]. There will be more than a million paediatric cases of COVID-19 by the middle of November 2020, according to the CDC. Covid-19 is more common in the 12- to 17-year-old age group in the United States than the 5- to 11-year age group. COVID-19 can infect children of all ages, starting with newborns. SARS-CoV-2-positive adults in the household are the primary source of infection for children, according to the available data. A good way to keep children safe from illness is to promptly isolate adults who have a history of exposure to an infectious agent in the household. Children are less prone than adults to spread SARS-CoV-2,and have a longer incubation period and longer viral excretion time in faeces than adults. Infection rates from viruses may fall as a result of fewer children participating in outdoor activities and overseas travel. According to the World Health Organization (WHO), SARS-CoV-2 has caused a large number of illnesses [3].

According to WHO, there have been 1,133,758 confirmed cases and 62,784 fatalities as a result. Many research have been done on the paediatric population and have yielded significant information. Only 0.39 percent of children were diagnosed with the condition in the first published investigation. According to a later Chinese research of 72,314 patients of various ages, the virus had been found in 1% of the children included. COVID-19 was found in 4.8 percent of children in a large-scale testing investigation in Korea that included youngsters from 18 percent of the country's population. Prior to more broad testing, Lu and colleagues conducted a series of studies. There was an increase in the number of confirmed COVID-19 among children, with a mean age of 6.7 years, in a recent study conducted in China. An extensive Chinese research by Dong., *et al*. examined 2143 children with COVID-19 (34.1 percent of cases were confirmed by laboratory testing and 65.9 percent were clinically diagnosed). These children were, on average, 6.7 years old. There was no discernible variation in the percentage.

However, other studies have found that adult males had a slightly higher incidence than adult females [5].

Diversity in COVID 19's ethnic composition

Spanish children have a low mortality rate for COVID-19

There have been eight deaths from COVID-19 in children under the age of nine, and there have been 18 deaths in children between the ages of 10 and 19 as of Feb. 10, 2021, according to the letter. That's why we wanted to explain how and why this happened to The Lancet Child and Adolescent Health readers.

According to the primary source cited by Bhopal and colleagues, the data were tentative and unconsolidated. Children with the COVID-19 pandemic have been documented in clinical registries at more than 75 Spanish hospitals since the outbreak began [7].

Cohort study spanning multiple countries and locations across Europe

SARS-CoV-2 infection cases that had been managed at or remotely by a haematology or infectious disease unit in one of the 128 European paediatric health-care institutions that belong to the Paediatric Tuberculosis Network European Trials Group (ptbnet) were invited to participate in this cohort study, which included 304 clinicians and researchers from 31 European countries [8].

The mutation of the new coronavirus (Types of Mutations)

Studies have revealed that over time, the SARS-COV-2 produces mutations, and with the accumulation of the number of mutations, eventually certain mutational features would dominate, allowing mutational viral epidemics. So far, there are 4 worldwide recognized variants: Alpha or pedigree B.1.1.7 (UK), Beta or pedigree B.1.351 (South Africa), Gamma or pedigree P.1 (Japan/Brazil), and Delta or pedigree B.1.351 (South Africa) pedigree B.1.617.2 (India) (India). The S protein has two subunits: S1, which contains the receptor binding domain (RBD), and S2, which mediates virus-host cell fusion. The most prevalent mutation in the viral genome is the replacement of D614G (Asp 614→Gly) in S1, which improves the affinity of the virus to the ACE2 receptor, leading to enhanced host vulnerability and higher transmission [3].

Clinical characteristics of COVID-19 in children

Clinical manifestations

Mild or asymptomatic infection is the major clinical manifestation in pediatric patients, mainly presented as fever, sore throat, shortness of breath and pneumonia. Compared with adults, vomiting and diarrhea are more common in pediatric patients, but the prevalence of fever and pulmonary symptoms is lower, and anosmia and taste are less common. Children with cancer, children undergoing hematopoietic cell transplantation, children undergoing solid organ transplantation and other children taking immunosuppressive agents mostly present with asymptomatic or mild gastrointestinal symptoms due to low immune function and weak immune response after infection with COVID-19,32,74 with a low risk of death.

The prevalence of dyspnea and mortality in immunocompromised persons hospitalized may be attributable to their incidence of comorbidities (such as hypertension, cardiovascular disease and diabetes) (such as hypertension, cardiovascular disease and diabetes). Children have considerably less neurological sequelae after infection with SARS- CoV-2 compared with adults. Neurological symptoms are largely non-specific symptoms such as headaches, and the prevalence of severe symptoms and particular consequences is only approximately 1 percent. This also causes respiratory Children with modest symptoms are readily misdiagnosed and overlooked. Children with severe infections may develop acute respiratory distress syndrome, septic shock, metabolic acidosis and coagulopathy. Some children

with progressing illness may have significant consequences MIS-C. The consequences are significant in cardiovascular lesions with clinical presentations similar to macrophage activation syndrome, symptoms of staphylococcal and streptococcal TSS, sepsis [3].

Diagnosis

The presence of clinical signs and symptoms in a relevant epidemiological context (i.e., an endemic area) indicates a suspected case of COVID-19, especially if contact with a confirmed COVID-19 case is known. The diagnosis can be confirmed by virus detection laboratory tests. It is vital to identify the timing of the commencement of infection, based on the incubation period of 2-14 days with a mean of 3-7 days There may be suspicion of a case of COVID-19 in a kid if at least one of the following exists:

- Fever, particular respiratory symptoms, stomach issues, or exhaustion
- Suggestive biological findings: normal leukocyte level, leukopenia, and increased C reactive protein (CRP) and procalcitonin (PCT) levels
- Specific imaging results (based on chest X-ray [CXR] and CT scans) (based on chest X-ray [CXR] and CT scans)

In a suspected case, the confirmation necessitates laboratory confirmation, although some clinicians would propose that in the presence of clinical signs and symptoms and contact with a COVID-19 case, a diagnosis can be made [5].

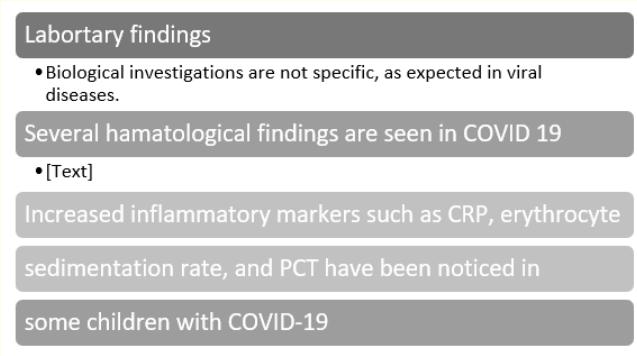

Figure a

Diagnosis of COVID patients

Figure b

Management of Covid Patients

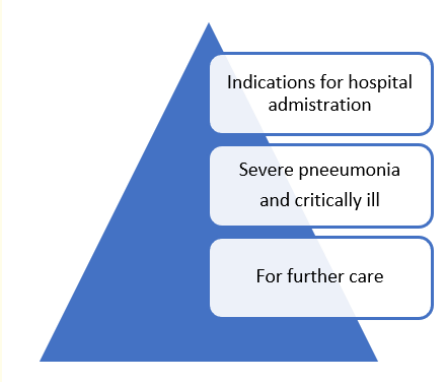

Figure c

Indications for admission to hospital

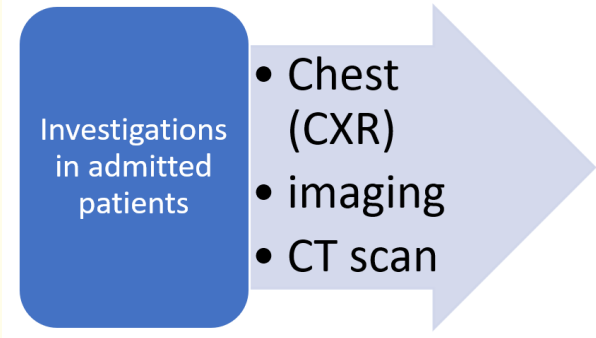

Figure d

Management of Covid Patients with chest investigations

Figure e

Management of hospitalized cases

Figure f

Management of Covid Patients during ICU admission [9].

A little bit of vaccines

Complex and time-consuming, the creation of a vaccine varies from the development of conventional medications in many ways. Vaccines often take 12 to 15 years to develop. Vaccines, in contrast to conventional medicine, are meant to be administered to people who have not yet shown any signs of illness in order to prevent disease from occurring. Since long-term human studies are extremely rare (especially when measured in decades), clinical trials to prove the efficacy of a vaccine must enrol a greater number of people than in traditional drug studies in order to demonstrate the vaccine's ability to prevent disease with minimal short-term adverse reactions.

A huge volume of viruses or bacteria, which might live for months, is required for traditional vaccine development methods to tackle highly contagious illnesses such as measles. Those bacteria, known as antigens, serve as the basis for a vaccination that alerts the human immune system to the presence of alien organisms. Antigen-presenting cells (APCs) in the immune system are given the information they need to recognise and respond to pathogens like bacteria and viruses. Antigens (a different molecular pattern) are used in traditional vaccinations.

Inactivated or half-active bacteria or attenuated viruses are used to create markers) that are then injected into the body. While these antigens may not cause the disease, they might nonetheless activate the body's immune system, resulting in the production of antibodies. Because of the vaccination, the immune system is already primed to respond quickly if the patient comes into touch with the native pathogen and the body's antibodies are activated [10].

Post-acute COVID-19 outcomes in children with mild and asymptomatic illness

The most prevalent post-acute COVID-19 symptoms were mild post-viral cough [4 percent] of 151 children), fatigue [2 percent] children) or both post-viral cough and exhaustion [1 percent] kid) [1 percent] child). The length of post-viral cough ranged from 3 weeks to 8 weeks and of post-viral fatigue ranged from 6 weeks to 8 weeks from the time of symptom onset. At the most recent review in March, 2021, all 151 children had restored to their baseline health condition and post-acute COVID-19 symptoms were resolved. Follow-up data for 20 children were not available; seven (35 percent) of these children had asymptomatic COVID-19.

These findings contrast those of investigations of COVID-19 in adults, which have revealed multisystem problems and a higher prevalence and severity of persistent symptoms [11].

Why is COVID-19 less severe in children?

Factors postulated to explain the difference in severity of COVID-19 in children and adults include those that put adults at higher risk and those that protect children. The former include: (1) age-related increase in endothelial damage and alterations in clotting function; (2) higher density, increased affinity and different distribution of angiotensin converting enzyme II receptors and

transmembrane serine protease. (3) pre-existing coronavirus antibodies (including antibody-dependent enhancement) and T cells; (4) immunosenescence and inflammaging, including the effects of chronic cytomegalovirus infection; (5) a higher prevalence of comorbidities associated with severe COVID-19 and (6) lower levels of vitamin D. Factors that might protect children include: (1) changes in innate and adaptive immunity; (2) more frequent recurring and concurrent infections; (3) pre-existing immunity to coronaviruses; (4) differences in microbiota; (5) greater levels of melatonin; (6) protective off-target effects of live vaccinations and (7) decreased intensity of exposure to SARS-CoV-2 [3].

Variations among different groups in childhood

Clinical symptoms of SARS-CoV-2 in children

Children with COVID-19 infection may be asymptomatic or have fever, dry cough, and lethargy, with a few upper respiratory symptoms, including nasal congestion and runny nose some patients suffer gastrointestinal problems, include abdominal discomfort, nausea, vomiting, stomach pain, and diarrhoea. Most afflicted children have minor clinical signs, and the prognosis is excellent. Most of the paediatric patients had recovered within 2 weeks after onset.

Clinical features of babies and infants with SARS-CoV-2 infection

Although COVID-19 instances were rare in babies and neonates, nine hospitalised newborns identified with COVID-19 in China from December 8, 2019, to February 6, 2020, were recorded. The minimum age was 1 month and the maximum 11 months. Of the nine infants, four developed fever, two mild upper respiratory symptoms, one asymptomatic, and two no information about symptoms. The time between admittance and diagnosis was 1to 3 days. All nine newborns had at least one infected family member, and the baby's infection usually occurred following the family member's sickness. All nine infants did not require acute care or mechanical ventilation and had no serious complications [12].

Potential role of biomarkers in covid-19

A biomarker is described as a "characteristic that can be objectively assessed and evaluated as an indicator of normal biological and pathological processes, or pharmaceutical responses to a therapeutic intervention". Biomarkers in COVID 19 can be useful in the following areas:

- Recognizing illness symptoms early.
- Indication of the degree of disease severity, confirmation, and classification
- Requirements for being admitted to a hospital identification of the high-risk group
- framing ICU admission criteria
- Therapy rationalization
- Assessing a patient's response to treatment Predicting the outcome
- Discharging patients from the ICU and/or establishing criteria for doing so serious issues at the hospital [13].

Conclusion

Among the United States, Covid-19 is more prevalent in the 12- to 17-year-old age range. In the initial published study, just 0.39 percent of children were diagnosed with the disease. COVID-19 infection had been linked to 50,539,082 confirmed cases and 1,258,321 deaths as of the date of this report's writing (November 9th, 2020). Coronavirus 2 (SARS-CoV2) is the third wave of coronavirus infection presently sweeping the globe (SARS-CoV-2). The prevalence of COVID-19's most prevalent symptoms was low in children infected with the virus. Bats are the primary reservoir for a number of CoVs, although they have not been linked to human infection.

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