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Clinical Characteristics and Associated Factors in Hospitalized Children with COVID-19: An Analysis of Over 19,000 Cases in Iran

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ABSTRACT

Introduction: The COVID-19 disease, caused by the novel coronavirus SARS-CoV-2, emerged in Wuhan, China, in late December 2019. It rapidly spread worldwide and declared a pandemic by the World Health Organization (WHO) shortly thereafter . The clinical spectrum of COVID-19 ranges from mild respiratory symptoms to severe cases leading to acute respiratory distress syndrome (ARDS). Research into the virus, its pathophysiology—particularly in the later stages—clinical manifestations, disease progression, laboratory findings, diagnostic methods, prevention strategies, and potential treatments is ongoing. To date, no definitive or specific treatment has been identified.

Materials and methods: This descriptive-analytical, cross-sectional study conducted over one year, from May 2019 to June 2021, during the initial phase of the COVID-19 pandemic. The study included all patients presenting with suspected COVID-19 infection who referred to infectious disease clinics in hospitals across the country. Patients were evaluated for respiratory symptoms (e.g., fever, runny nose, sore throat, dry cough), gastrointestinal symptoms (e.g., nausea, vomiting, abdominal pain, diarrhea), and general symptoms (e.g., muscle pain, weakness, headache, confusion, groaning). Those requiring hospitalization were included in the study. Patient selection performed continuously. A total of 19,438 patients meeting the inclusion criteria were enrolled in the study. Data from completed questionnaires recorded, organized into data tables, and subjected to detailed analysis.

Results: Among the 19,438 hospitalized children, 2,836 (14.5%) were admitted to the intensive care unit, and 5.88% required mechanical ventilation. Of the hospitalized patients, 85.5% were seriously ill, while 14.5% were in critical condition. The most common clinical symptoms observed in hospitalized children were fever and chills (75.86%) and dry cough (32.37%).Among the hospitalized children, 13.06% had an underlying condition. Of these, 1.83% had a respiratory disease, 2.08% had a cardiovascular disease, 1.92% had malignancy, 0.28% had diabetes, 1.69% had immune system deficiencies, and 7.8% had other underlying conditions. According to this investigation, the total number of confirmed COVID-19 cases in the country is 258,540, and 3,760 deaths have been reported. Additionally, 222,003 people have recovered from COVID-19 in Uruguay.

Conclusion: Despite numerous studies on COVID-19 infection in adults, there is a limited body of research focused on children. The prevalence and severity of the disease in children are significantly lower than in adults, and the prognosis is generally more favorable. However, in infants under one year of age, clinical symptoms tend to be more severe compared to older children. Children with humoral and cellular immune system deficiencies, as well as those with cancer, are at increased risk of contracting COVID-19 due to the need for prolonged hospitalization. In children, the disease typically follows a milder course with a more favorable prognosis.As the virus transmitted by asymptomatic carriers, children may contribute to household cluster transmission

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Introduction

COVID-19, caused by the novel coronavirus, originated in Wuhan, China, and spread globally in late December 2019, leading the World Health Organization (WHO) to declare it a pandemic (1). The disease presents a spectrum of severity, ranging from mild symptoms to acute respiratory failure, and no specific treatment has yet been identified.

In humans, coronaviruses primarily affect the respiratory and digestive systems. In children, COVID-19 generally follows a milder course with a more favorable prognosis. However, due to mild or asymptomatic presentations, many pediatric cases remain undiagnosed during the early stages.

Human-to-human transmission is one of the primary modes of spreading the virus, particularly through respiratory droplets or direct contact with contaminated surfaces, such as children's toys (5). Notably, 41% of COVID-19 cases have been associated with intra-hospital transmission (6). Furthermore, asymptomatic carriers significantly contribute to the virus's spread, heightening its pandemic potential in human societies (7, 8).

Since asymptomatic carriers can transmit the infection, children may contribute to cluster transmission within households (9, 10). Additionally, in infants and young children, where gastrointestinal symptoms often predominate, the virus can be shed in feces for several weeks after diagnosis. This prolonged shedding increases the risk of transmission in settings such as kindergartens or elementary schools (11).

Children and adults with cancer face an even higher risk of severe COVID-19 outcomes due to prolonged hospitalizations and underlying immune deficiencies caused by chemotherapy and radiation therapy, making them more vulnerable to hospitalization compared to the general population (12).

A study conducted on 2,143 children in China found that over 90% of confirmed COVID-19 cases were asymptomatic, mild, or moderate in severity. Approximately 5% of children experienced severe disease, while less than 1% developed a critical form of the illness. Severe disease defined as presenting with shortness of breath, central cyanosis, or arterial oxygen saturation levels below 92%. The critical form characterized by respiratory failure, acute respiratory distress, shock, and symptoms of multiple organ failure, such as encephalopathy, heart failure, coagulation disorders, or acute kidney failure. Notably, the study revealed that half of the critical cases occurred in infants under one year of age (13).

In a study conducted by Yang et al. involving 171 children in Wuhan, China, only three children with underlying conditions required special care. Epidemiological studies and evaluations of clinical symptoms and underlying factors are essential for aiding decision-makers and clinicians in taking proactive measures, reducing the disease burden, and controlling the pandemic. While numerous studies have reported epidemiological features of COVID-19, few have specifically examined these factors in the Iranian population (14, 15).

This study was therefore conducted to determine the clinical characteristics and associated factors in children aged 1–59 months with COVID-19 who were admitted to public and private hospitals across the country.

Materials and methods

This descriptive cross-sectional study conducted on 19,438 children aged 1–59 months who admitted to public and private hospitals in the country between May 2019 and June 2021 with clinical symptoms of COVID-19.

Children were categorized into three groups—mild to moderate, severe, and critical—based on the severity of their clinical symptoms, including dry cough, fever, and positive radiological findings. The study included children hospitalized due to severe or critical illness.

- **Dry cough**: Defined as a cough that is not accompanied by phlegm.
- **Fever**: Measured as a rectal temperature exceeding 38.4°C.
- **Mild to moderate disease**: Characterized by fever, respiratory symptoms, and radiological findings of pneumonia, treated on an outpatient basis.
- **Severe Disease**: Defined by the presence of any of the following symptoms: respiratory distress, a breathing rate exceeding 40 breaths per minute in children over 1 year old or 50 breaths per minute in children under 1 year old, blood oxygen saturation levels below 90% at rest in room air, or below 92% with supplemental oxygen. These cases required hospitalization in the COVID-19 ward.
- **Critical Illness**: Defined by the presence of severe disease symptoms alongside respiratory failure, the need for mechanical ventilation, blood oxygen

saturation levels below 90% even with supplemental oxygen, septic shock, or extra pulmonary organ failure. These cases required transfer to the COVID-19 special care unit.

Demographic data, clinical symptoms, and disease risk factors extracted from the national COVID-19 registration system. Data quality ensured by identifying and removing duplicate entries based on national identification codes or admission codes. In cases of multiple hospitalizations for a child, only data from the first admission were included.

The collected demographic and clinical data recorded in a research questionnaire and analyzed using statistical software developed by the Ministry of Health, Treatment, and Medical Education for COVID-19 information management.

Findings

This report presents data on 19,438 children aged 1 to 59 months who hospitalized in hospitals across Iran between May 2019 and June 2021. The highest relative frequency of cases observed in children aged 3 to 5 years.

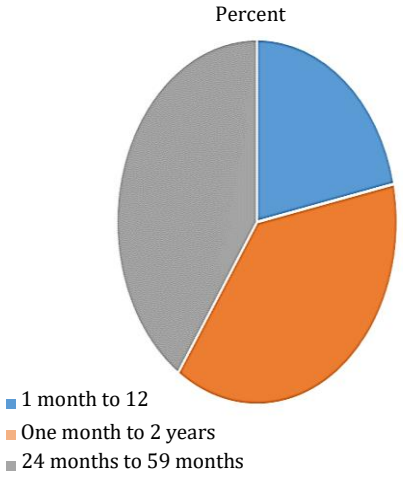

Chart 1. Age Distribution of Hospitalized Children by Relative Frequency

Among the hospitalized children, 56.91% were male, and 43.09% were female.

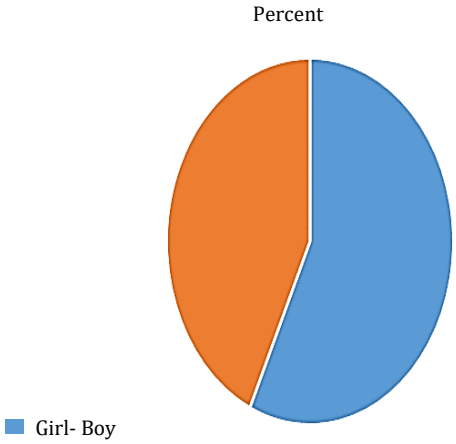

Chart 2. Distribution of Hospitalized Children by Gender

Among the 18,706 PCR tests performed, 22.66% of the children tested positive. Meanwhile, 34.42% of the children who died from COVID-19 had a negative test result.

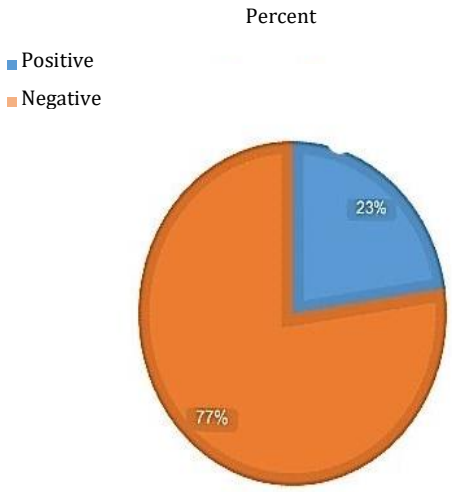

Chart 3. Distribution of Hospitalized Children by PCR Test Results Among the 19,438 hospitalized children, 2,836 (14.5%) were admitted to the intensive care unit (ICU).

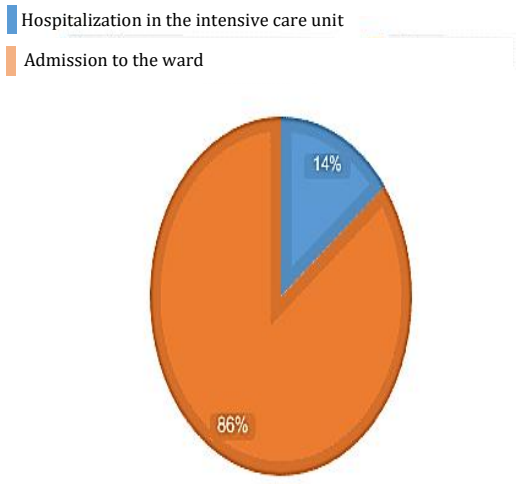

Chart 4. Distribution of Hospitalized Children in the Intensive Care Unit and General Ward

Among the 19,438 hospitalized children, 2,836 (14.5%) were admitted to the intensive care unit, and 5.88% required mechanical ventilation. Of the hospitalized patients, 85.5% were seriously ill, while 14.5% were in critical condition. The most common clinical symptoms observed in hospitalized children were fever and chills (75.86%) and dry cough (32.37%) (the frequency of clinical symptoms is shown in Chart 5).

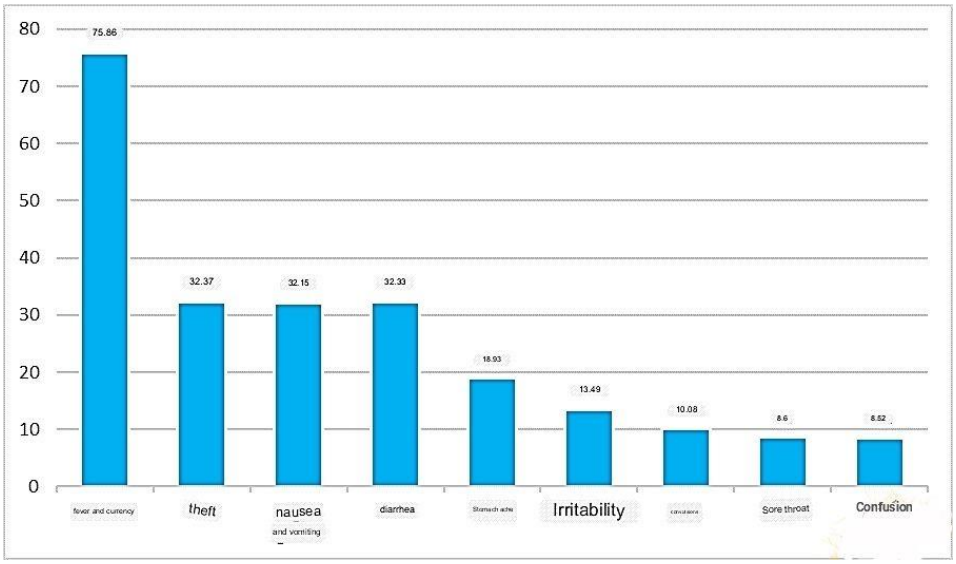

Chart 5. Frequency of Clinical Symptoms in Hospitalized Children with COVID-19

Among the hospitalized children, 13.06% had an underlying condition. Of these, 1.83% had a respiratory disease, 2.08% had a cardiovascular disease, 1.92% had malignancy, 0.28% had diabetes, 1.69% had immune system deficiencies, and 7.8% had other underlying conditions (see **Chart 6**).

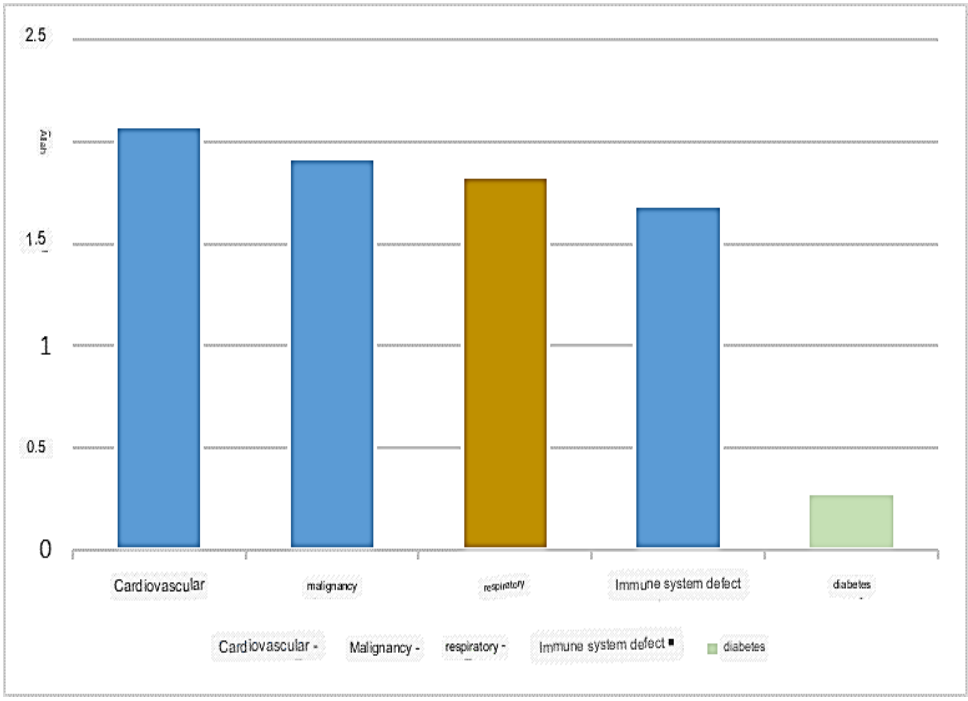

Chart 6. Frequency of Underlying Diseases in Hospitalized Children with COVID-19

Treatment Methods:

- 0.36% of children received antiviral treatment.
- 73.24% received antibiotic treatment.
- 10.23% received both antiviral and antibiotic treatments.
- 13.26% did not receive any medication.
- 2.90% neither received antiviral treatment nor antibiotic treatment, or the treatment status was unclear.

Consequences of COVID-19:

In a national survey, 0.94% of hospitalized children died due to COVID-19, and 2.23% died from other causes. Additionally, 7.69% were discharged against medical advice, while 86.07% were discharged following recovery. A total of 3.05% of the children were transferred to another hospital. Among the hospitalized children, 18.77% had a confirmed diagnosis of COVID-19, 12.72% had a probable diagnosis, and 68.49% had a suspected diagnosis.

Breathing Rate:

Of children under one year of age, 29.27% had respiratory rates between 30 and 50 breaths per minute, while the remaining children were outside this range. Among children over one year of age, 50.20% had respiratory rates between 30 and 40 breaths per minute, with the rest falling outside this range.

Discussion:

In a study conducted on 19,438 children aged 1 to 59 months who were hospitalized in Iranian hospitals between May 2019 and June 2021, 21.81% of the 18,806 PCR tests performed returned positive results. Among the hospitalized children, 2,836 (14.5%) were admitted to the intensive care unit (ICU), and 5.88% required mechanical ventilation.

According to the largest study conducted on 2,143 children in China, more than 90% of patients with confirmed COVID-19 had asymptomatic, mild, or moderate forms of the disease. Additionally, 5% of children experienced severe disease, and less than 1% had a critical form. Based on the classification used in Chinese studies, severe disease is defined by the presence of shortness of breath, central cyanosis, or arterial oxygen saturation levels below 92%. The critical form is characterized by respiratory failure, acute respiratory distress, shock, and symptoms of multiple organ failure, including encephalopathy, heart failure, coagulation disorders, or acute kidney failure. This study also found that half of the critical cases occurred in infants under one year of age (16,17).

In another study by Yang et al. on 171 children in Wuhan, China, only three children required special care, all of whom had underlying conditions. One child had hydronephrosis, another was undergoing chemotherapy, and the third had intestinal torsion (18,19).

The warning signs of COVID-19 in children are:

1. **Tachypnea**: One of the most important warning signs in children is tachypnea, which is defined as a respiratory rate greater than 50 breaths per minute in children under 1 year of age, and more than 40 breaths per minute in children over 1 year (Mana).
2. **Respiratory distress**: This includes symptoms such as chest retractions, cyanosis (bluish discoloration of the lips and tongue), grunting, nasal flaring, and tachypnea.
3. **Inability to drink or swallow**: Difficulty with feeding or swallowing liquids.
4. **Inability to communicate or extreme restlessness**: The child is unable to communicate during waking periods or shows signs of severe agitation.
5. **Excessive dryness of the oral mucosa**: Significant dryness or cracking in the mouth.
6. **Decreased urine output and shock**: Reduced urine production or signs of shock.
7. **High fever**: A fever exceeding 40°C (104°F) or a persistent high fever lasting more than three to five days.
8. **Return of symptoms**: The recurrence of symptoms after partial recovery (20,21).

Severe pneumonia is characterized by the following:

- **Temperature**: A fever greater than 38.5°C.
- **Moderate to severe respiratory distress**: Defined by a respiratory rate greater than 70 breaths per minute in infants under 12 months of age, and greater than 50 breaths per minute in older children.
- **Chest retractions**: Drawing in of the chest above the sternum, intercostal, and subcostal spaces.

- **Cyanosis**: Bluish discoloration of the lips and tongue, wheezing, nasal congestion, and apnea.
- **Arterial blood oxygen levels**: Below 93% when the patient is receiving oxygen, or below 90% in room air.
- **Drowsiness**: A significant level of drowsiness or lethargy.
- **Respiratory fatigue**: The patient may experience respiratory fatigue, with or without increased carbon dioxide concentration.

In a study conducted in the country, **75.86%** of hospitalized children presented with fever and chills, **32.37%** had a cough, **6.26%** had conjunctivitis, **32.15%** experienced nausea and vomiting, **10.08%** had seizures, **33.32%** had diarrhea, **18.93%** reported chest pain, **8.60%** had a sore throat, **8.52%** exhibited confusion, and **13.49%** showed signs of irritability.

Regarding underlying conditions, **13.06%** of the hospitalized children had an underlying disease. Specifically, **1.83%** had an underlying respiratory disease, **2.08%** had an underlying cardiovascular disease, **1.92%** had malignancy, **0.28%** had diabetes, and **1.69%** had an immune system deficiency.

The laboratory findings associated with COVID-19 are similar to those of other human coronaviruses. In children, the white blood cell count is typically normal or decreased. In some cases, there may be a reduction in peripheral blood neutrophils (neutropenia) or lymphocytes (lymphopenia). The definition of lymphopenia varies by age group: less than 3,000 lymphocytes per microliter for infants between one and twelve months, less than 2,000 per microliter for children aged one to five years, and less than 1,100 per microliter for children over five years. Mild thrombocytopenia may also occur; however, its presence can indicate a poor prognosis. In most cases, plasma C-reactive protein (CRP) and procalcitonin levels remain normal. In severe cases of the disease, an increase in liver enzymes, serum lactate dehydrogenase (LDH), coagulation disturbances, or an elevation in D-dimer levels may be observed (21, 24, 25). According to a study by Liu et al., laboratory findings during the course of COVID-19 are similar to those of influenza A or B viruses, and based solely on these findings, these two infections cannot be distinguished from one another (26).

In the early stages of COVID-19, simple chest X-rays in children typically show no abnormal findings. Therefore, chest radiography is not recommended for individuals without symptoms or risk factors in the early stages of the disease. A chest CT scan should be performed promptly for suspected cases. The most significant early finding is one or more limited ground-glass opacities, typically located under the pleura or near the bronchial blood vessels, particularly in the lower lobes. In severe cases, one- or two-sided lung consolidation is usually observed, with a ground-glass appearance (22,23).

In children, compared to adults, the density surrounding the "halo sign" is more commonly seen and is proposed as a typical and common feature in pediatric cases. Generally, the resolution of radiological lesions on CT scans occurs after the patient's symptoms have resolved and after negative nucleic acid testing. However, lesions may still be visible on the CT scan even after two consecutive negative nucleic acid tests.

It is important to differentiate COVID-19 findings on CT scans from those of other viral infections, such as influenza, parainfluenza, adenovirus, and respiratory syncytial virus (RSV). In adenovirus-induced pneumonia, the lesions are typically denser, with more prominent sub pleural involvement. In RSV or parainfluenza infections, lesions are more commonly distributed around the bronchi, and thickening of the bronchial walls is observed. Influenza virus infections typically present with a grid-like pattern on imaging (24,25).

In our study, 21.81% of the 18,806 PCR tests performed on children returned positive results. Additionally, 34.42% of the children who died from COVID-19 had a negative test result. For children strongly suspected of having COVID-19, sampling should be performed from the upper respiratory tract using a nasopharyngeal or oropharyngeal swab. All collected samples should be considered potentially infectious, and those collecting the samples must adhere to proper standards both during the sample collection and transfer to the laboratory. Personal protective equipment (PPE) such as goggles, masks, and gloves should be worn by those handling the samples.

Samples must be transported in a three-layer container, and in the laboratory, samples suspected of containing COVID-19 must be completely isolated from other samples. For sample collection, cotton swabs should not be used; only sterile Dacron or rayon swabs are acceptable. Samples taken from the tonsils or small tongue are not considered valid.

In children strongly suspected of having COVID-19, a negative test result does not rule out the disease. A

second sample should be collected from the upper respiratory tract or from the lower respiratory tract and sent for testing. Sputum induction is not recommended for sample collection. Additionally, bronchoscopy as a sample collection method carries a risk of transmitting the infection to others and should be avoided. Its use should be limited to clearing the airways of intubated patients with mucous plaques (26,27,28).

The RNA of the SARS-CoV-2 virus is detected using reverse transcription polymerase chain reaction (RT-PCR). Test results are generally available within a few hours to two days. A positive test result should be confirmed by a second RT-PCR test targeting a different SARS-CoV-2 gene (29).

Another diagnostic method involves measuring IgG and IgM antibodies produced in response to the virus in blood, serum, and plasma samples. This test utilizes a type of immune chromatography. The combined measurement of IgG and IgM antibodies offers higher sensitivity and specificity compared to testing each antibody individually. This method can be used for rapid screening of both symptomatic and asymptomatic individuals in hospitals and clinics (30).

To date, no specific treatment developed for COVID-19, making prevention the most effective approach. Given the virus's unique characteristics—such as non-specific symptoms, transmission during the latent period, its affinity for mucous membranes like the conjunctiva, the long duration of the disease, and the possibility of transmission even after recovery—preventing its spread remains highly challenging. Additionally, while vaccines developed, they are still in the experimental stage, and no definitive vaccine is available yet (31).

Treatment for COVID-19 involves two main components: supportive and specific treatments. Supportive care includes managing hydration and electrolytes, fluid administration, oxygenation, respiratory support, antipyretics, and pain relievers. Specific treatments involve the use of antiviral drugs, although there is currently no strong evidence supporting the efficacy of any particular antiviral for children (32).

In a national survey, 10.6% of children received antiviral treatment according to the country's COVID-19 protocol, while 83.47% treated with antibiotics, and 10.23% received both antiviral and antibiotic treatments based on clinical and laboratory findings.

Furthermore, recognizing the critical importance of prevention to control the COVID-19 epidemic and pandemic, recommendations and training on preventive measures provided to children, their parents, and caregivers prior to discharge. Infected individuals with COVID-19 are considered the primary source of transmission within the community. Given their condition, infected children should be isolated at home in a private room with a separate toilet and bathroom, or hospitalized in specialized departments under the supervision of medical staff in an isolated room.

To prevent the transmission of the virus through respiratory droplets, children should be taught to cover their mouths and noses with tissues when sneezing or coughing. Frequent hand washing should also be taught. To disinfect children's toys, methods such as heating to 56°C for 30 minutes, using 75% alcohol, disinfectant solutions containing chlorine, or ultraviolet (UV) rays can be effective. Additionally, children should wear a mask when entering crowded areas or spaces with poor ventilation.

Children with a history of contact with someone infected with or suspected of having COVID-19 should be closely monitored. Their body temperature should be checked regularly, and they should go to the hospital if any symptoms develop (32, 33). If the child requires respiratory support during hospitalization, they should be immediately transferred to an isolated room with negative pressure (34).

Family members of a child suspected of having COVID-19 must strictly adhere to health protocols and maintain a distance of at least one meter from the child. The surfaces of the toilet, bathroom, tables, beds, and any other areas frequently touched by the child should first be washed with soap and water, followed by disinfection using a 0.5% sodium hypochlorite bleach solution.

The nurse caring for the child must wear a surgical mask and avoid direct contact with respiratory or oral secretions, as well as the child's feces. In addition to frequent hand washing with soap, it recommended to use disposable plastic or latex gloves, if possible. The child's clothes, towels, and sheets should be kept in a separate nylon bag and washed with hot water (temperature between 60°C and 90°C). Gloves must be worn when handling these items (35).

Conclusion

Due to the absence of specific antiviral drugs and vaccines for COVID-19, the most effective approach remains adherence to strict health protocols.

Despite numerous studies on COVID-19 infection in adults, there is a limited body of research focused on children. The prevalence and severity of the disease in children are significantly lower than in adults, and the prognosis is generally more favorable. However, in infants under one year of age, clinical symptoms tend to be more severe compared to older children. Children with humoral and cellular immune system deficiencies, as well as those with cancer, are at increased risk of contracting COVID-19 due to the need for prolonged hospitalization.

As the prevalence of the disease rises in adults, it expected that more children will be infected with the virus. Furthermore, children are more likely to have co-infections with other respiratory viruses alongside COVID-19. The incubation period for COVID-19 ranges from one to fourteen days, with an average of five days. Common clinical symptoms during infection include fever, cough, sore throat, fatigue, muscle pain, and shortness of breath. Conjunctivitis reported in some patients.

Typically, the clinical symptoms of COVID-19 in children are similar to those of other respiratory infections, making them difficult to distinguish. In some cases, by the end of the first week, the disease can progress to pneumonia, respiratory failure, and even death. As the disease progresses, there is often a significant increase in inflammatory cytokines, such as interleukin 2, 7, and 10, as well as granulocyte colony-stimulating factor, tumor necrosis factor alpha, and macrophage inflammatory protein.

In infants and children, clinical symptoms are generally much milder compared to adults, though younger infants are more susceptible to COVID-19 infection. Among children with confirmed virological evidence of the disease, 13% are asymptomatic. Of those children hospitalized due to COVID-19, 14.5% experience shortness of breath or a drop in arterial oxygen saturation, requiring admission to the pediatric intensive care unit. This rate is significantly lower than that observed in adults.

In a small percentage of cases, COVID-19 can progress to acute respiratory distress syndrome (ARDS) or organ dysfunction. In infants and preschool-aged children, the clinical manifestations of the disease are typically more severe compared to older children. Additionally, underlying lung diseases and immune system deficiencies can lead to more severe clinical symptoms in children.

It is important to note that children can play a significant role in the transmission of the virus within the community. In some cases, the virus can continue to spread through feces for several weeks after diagnosis in children.

Other clinical manifestations in children include gastrointestinal symptoms such as abdominal pain, nausea, diarrhea, and vomiting, which occur more frequently than in adults. Some children may also exhibit wheezing or a runny nose.

Due to the lack of specific antiviral drugs and vaccines for COVID-19, the best approach remains adherence to strict health protocols.

The Ministry of Health of Brazil has reported that the number of COVID-19-related deaths has reached 446,309, with the total number of confirmed cases rising to 15,970,949. Brazil, the second most affected country in the world after the United States in terms of both cases and deaths, has also reported that 14,422,209 people have recovered from the virus.

In Mexico, the total number of COVID-19-related deaths has increased to 221,256, with the number of confirmed cases rising to 2,392,744. Additionally, 1,909,187 patients have recovered from COVID-19 in Mexico.

The Ministry of Health of Argentina has reported that the total number of COVID-19-related deaths has reached 73,391, while the number of confirmed cases has risen to 3,411,160. The number of recoveries in Argentina has also increased to 3,060,145. With a population of over 45 million, Argentina ranks 11th in the world in terms of total COVID-19 cases.

According to the latest data from the Ministry of Health of Colombia, the total number of COVID-19-related deaths in the country has reached 83,719, while the number of confirmed cases stands at 3,192,050. Additionally, 2,998,123 people have recovered from the virus in Colombia. With a population of approximately 50 million, Colombia ranks 12th globally in terms of total COVID-19 cases.

The Ministry of Health of Chile announced today that the total number of COVID-19-related deaths has reached 28,290, with 121 additional deaths reported in the past 24 hours. The number of confirmed cases has risen to 1,315,913. So far, 1,245,988 people have recovered from the virus in Chile.

Ecuador's Ministry of Health reported that the total number of COVID-19-related deaths has increased to 20,107, with 416,621 confirmed cases. A total of

354,499 people have recovered from COVID-19 in Ecuador.
In Paraguay, the number of COVID-19-related deaths has reached 8,115, and the total number of confirmed cases stands at 327,229. So far, 270,516 people have recovered from the virus in Paraguay.
In Honduras, the total number of confirmed COVID-19 cases is 231,560, with 6,133 deaths.
According to the Ministry of Health of Uruguay, the total number of confirmed COVID-19 cases in the country is 258,540, and 3,760 deaths have been reported. Additionally, 222,003 people have recovered from COVID-19 in Uruguay.

Declarations

Ethics approval and consent to participate

Do not need

Consent for publication

Not applicable. Included in the research study consent.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding authors on reasonable request.

Competing interests

The author declare that they have no competing interests.

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Authors' contributions

Writing original draft: Dr.Soheila Khazaei
Reviewing: Dr.Soheila Khazaei
Conceptualization: Dr.Soheila Khazaei
Figure design: Dr.Soheila Khazaei

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