

Comparison of the pediatric hospitalizations due to COVID-19 and H1N1pdm09 virus infections during the pandemic period

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Abstract

There are two major pandemics in the new millennium, including the pandemic of *swine influenza* and the COVID-19 pandemic. These two pandemics affected children as well as the adult population. In this case-control study, we compared children with COVID-19 infection and those with H1N1pdm09 virus infection. We also compared the demographic factors, underlying disease, and the requirement for intensive care admission between the hospitalized children with COVID-19 infection and children with H1N1pdm09 virus infection who were hospitalized during the 2009 H1N1 pandemic. In this study, we evaluated 103 patients with H1N1pdm09 virus infection and 392 patients with COVID-19 infection. The age was significantly higher in the COVID-19 patients' group compared to the pandemic influenza group ($p < 0.001$). The ratio of the children ≥ 12 years was 10.7% ($n = 11$) in the H1N1pdm09 virus infection and 36.2% ($n = 142$) in the COVID-19 group. The rate of underlying disease was significantly higher in the patients with H1N1pdm09 virus infections ($p = 0.02$). The prevalence of underlying disease in patients requiring PICU hospitalization was 69.2% ($n = 9/13$) compared to 25.7% ($n = 124/482$) in patients who did not require PICU hospitalization. The rate of underlying disease was significantly higher in the PICU group regardless of COVID-19 or H1N1pdm09 virus ($p = 0.002$). Our results suggest that older children were more hospitalized for COVID-19 infections compared to pandemic influenza. In addition, regardless of the type of pandemic infection, the underlying disease is an important factor for pediatric intensive care unit admission. This finding is important for developing strategies for the protection of children with the underlying disease in the upcoming pandemics.

KEYWORDS

COVID-19 infections, H1N1pdm09 virus infections, hospitalization, underlying disease

1 | INTRODUCTION

Humanity had to fight two major pandemics in the new millennium. One of them was the pandemic of *swine influenza*, caused by *H1N1 influenza* (H1N1pdm09) virus, which entered into our lives in 2009, and the other was the COVID-19 pandemic, which still affects all of us and entered our lives in 2019. These two pandemics, which were seen within a 10-year interval, affected children as well as the adult population. According to the Centers for Disease Control and Prevention (CDC), during the 2009 H1N1 pandemic, 358 flu-attributable deaths were reported at children in the United States from April 2009 to September 2010,¹ while the American Academy of Pediatrics reported the cumulative child deaths due to COVID-19 infection as 292, for a duration including April 2020 to August 2021.² These two pandemics, despite their differences in nature, have had an impact on the entire society and have put a huge strain on the health system.

In this case-control study, we compared the demographic factors, underlying disease, the requirement for intensive care admission, and the duration of hospitalization between the hospitalized children with COVID-19 infection and the children with H1N1pdm09 virus infection who were hospitalized during the 2009 H1N1 pandemic.

2 | MATERIALS AND METHODS

This case-control study was conducted in the University of Health Sciences Dr. Behçet Uz Children's Hospital in Izmir, Turkey. This current hospital is a 350-bed tertiary care hospital with an annual capacity of approximately 600 000 outpatients and 24 000 hospitalizations and is a reference center for contagious diseases in the Egean region.

All children between one month and 18 years old who were hospitalized only due to COVID-19 infection and H1N1pdm09 virus infection were included in the study. Newborns and cases whose data were not available were excluded from the study. The current case-control study included two groups, including children who were hospitalized with the diagnosis of COVID-19 infections and a second group who were hospitalized with the diagnosis of the 2009 H1N1 Pandemic. The study included the periods from March 11 through August 21, 2021, for the COVID-19 Pandemic, and the periods from July 21, 2009, through February 10, 2010, for the 2009 H1N1 pandemic. A diagnosis of H1N1pdm09 virus infection was confirmed by testing nasal aspirates or combined nasal and throat swabs using a real-time polymerase chain reaction (RT-PCR) assay at our National Influenza Reference Laboratory in the Istanbul Faculty of Medicine. The standard operating protocol as defined by the CDC was adhered to throughout this process.³ Diagnosis of COVID-19 was documented by quantitative real-time RT-PCR positivity. The protocol of RT-PCR was consistent with the recommendation of the World Health Organization.⁴

Demographic characteristics, pre-existing comorbidities on admission, and hospitalization at the pediatric intensive care unit (PICU) were collected from the electronic database of the hospital. Of the comorbid diseases, obesity was defined as a *body mass index* (BMI) at or above the 95th percentile for children and teens of the same age and sex.⁵

2.1 | Statistical analysis

Statistical analysis was performed using SPSS statistical software (version 22; SPSS). Categorical variables were analyzed using relative frequencies, whereas numerical variables were analyzed using median or mean values (depending on whether they had a normal distribution). Categorical variables were compared using Pearson χ^2 and Fisher's exact tests. Numerical variables were compared using the *t* test or the nonparametric Mann-Whitney *U* test. A $p < 0.05$ was considered to be statistically significant.

3 | RESULTS

3.1 | Patients' overview and comparison

In this study, we evaluated 103 patients with H1N1pdm09 virus infection and 392 patients with COVID-19 infection. The rate of males was 57.3% ($n = 59$) among the patients with H1N1pdm09 virus infection and 52.8% ($n = 207$) with COVID-19 infections, and no significant difference was present between these two groups ($p > 0.05$). The median age of the patients with H1N1pdm09 virus infection was 4 years (range 1 month–18 years) and the median age of the patients with COVID-19 infection was 7 years and 10 months (range 1 month–18 years), and the age was significantly higher in the COVID-19 patients' group compared to the pandemic influenza group ($p < 0.001$). The χ^2 independence test revealed an association between the type of pandemic virus and age group ($\chi^2(3) = 27.0$, $p < 0.001$). The rate of the children aged ≥ 12 years was 36.2% ($n = 142$) in the COVID-19 group and 10.7% ($n = 11$) in the H1N1pdm09 virus infection group, and significantly higher in the COVID-19 group ($p < 0.001$) (Figure 1).

Underlying disease was present in 37 (35.9%) of the patients in the influenza group and 96 (24.5%) of the patients in the patients with COVID-19 infections, and the rate of underlying disease was significantly higher in the patients with H1N1pdm09 virus infections ($p = 0.02$). The most common underlying diseases were pediatric hematologic malignancy (9 patients, 8.7%), cerebral palsy (8 patients, 7.7%), and epilepsy (8 patients, 7.7%) in the H1N1pdm09 virus infection group, whereas obesity (21 patients, 5.4%) and asthma (14 patients, 3.6%) were found in the COVID-19 group (Table 1).

FIGURE 1 Age distribution of the children with COVID-19 and H1N1pdm09 virus infections. *The rate of the children ≥ 12 years old was 36.2% ($n = 142$) in the COVID-19 group and 10.7% ($n = 11$) in the H1N1pdm09 virus infection group, and the difference was significantly higher in the COVID-19 group ($p < 0.001$)

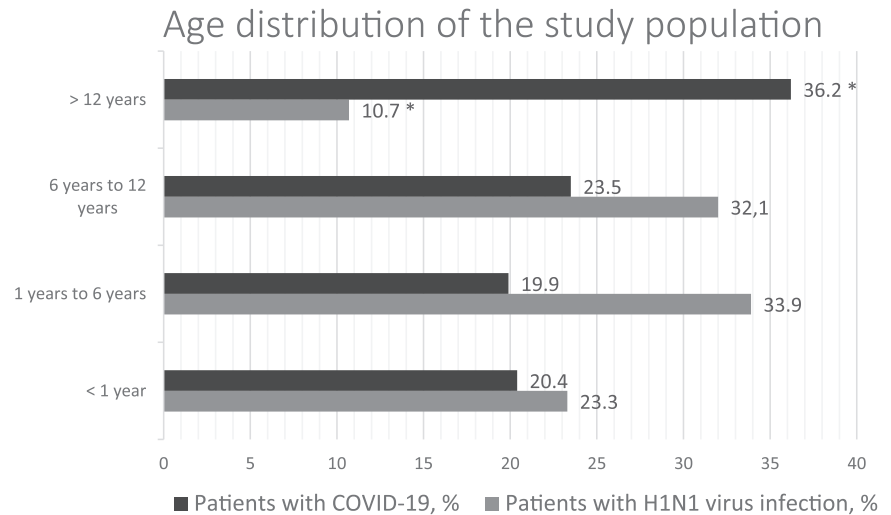


TABLE 1 Underlying chronic medical conditions of the patients with COVID-19 infections and H1N1pdm09 virus infections

Comorbidity	Number of patients with H1N1 virus infection (N = 103), n (%)	Number of patients with COVID-19 (N = 392), n (%)
Obesity	3 (2.9)	21 (5.4)
Bone marrow transplantation	null	3 (0.8)
Asthma	2 (1.9)	14 (3.6)
Malignity	10 (9.7)	11 (2.8)
Epilepsy	8 (7.8)	7 (1.8)
Cerebral palsy	8 (7.8)	14 (3.6)
Congenital heart disease	4 (3.9)	6 (1.5)
Rheumatologic disease	null	4 (1.0)
Down syndrome	null	3 (0.8)
Dilate cardiomyopathy	null	2 (0.5)
Diabetes mellitus	null	3 (0.8)
Primary immunodeficiency	null	3 (0.8)
Miscellaneous	2 (1.9)	5 (1.3)
Total	37 (35.9)	96 (24.5)

3.2 | The proportion of patients admitted to intensive care units and the duration of their hospital stay

Four of 103 children with influenza infections (3.9%) and nine of 392 (2.3%) children with COVID-19 infections required intensive care unit admission, and no significant difference was present between these two groups ($p > 0.05$). The prevalence of underlying disease in patients requiring PICU hospitalization was 69.2% ($n = 9/13$) compared to 25.7% ($n = 124/482$) in patients who did not require PICU

hospitalization. and was significantly higher in the PICU group regardless of COVID-19 or H1N1pdm09 virus ($p = 0.002$).

The median length of stay was 5 days (minimum 1 day–maximum 24 days) in the children with H1N1pdm09 virus infections group, and 4 days (minimum 1–maximum 56 days) in the children with COVID-19 infections, and significantly longer in the children with H1N1pdm09 virus infections ($p = 0.037$).

4 | DISCUSSION

In this study, we compared hospitalized children with COVID-19 infections and H1N1pdm09 virus infections in the two different pandemic periods. Each pandemic has its characteristics, such as disease burden, contagion rate, and exposure density. We set out to show that these factors can change the characteristics of hospitalized patients to compare these two viral infections by selecting patients from their respective periods: patients with H1N1pdm09 virus infections during the years 2009–2010 and patients with COVID-19 during 2021. The underlying diseases were significantly higher in the hospitalized patients in the influenza group, and the most common underlying diseases were pediatric hematologic cancers and cerebral palsy in the influenza patient group. Obesity and asthma were the most common underlying diseases in the COVID-19 infection group. The influenza patients were found to have a longer length of stay compared to the COVID-19 infection group.

Age is reported to be an important determinant factor for hospitalization in children with influenza infection. Hospitalization due to lower respiratory tract infections was reported to be highest in those younger than 5 years.^{6–8} In a recent study, Boncuoglu et al.⁹ reported that nearly half of the hospitalizations due to influenza infection were in the age group younger than 2 years of age. These studies mainly focused on influenza infections, including the period after the H1N1 2009 pandemic. In their report, Çiftçi et al.¹⁰ reported that 56.9% of the 821 children who were hospitalized due to pandemic H1N1

infection during the pandemic were younger than 5 years of age, which was 57.3 in our case. Furthermore, the rate of hospitalized children over the age of 12 in the COVID-19 group was higher compared to the influenza group. A multi-center study on children hospitalized for COVID-19 infection in Turkey discovered that the median age was 10.75 years old, with 43.4% of the children being older than 12 years old.¹¹ Another study of 177 children from the Children's National Hospital in Washington, DC reported that adolescents and young adults were more likely to have critical illness than younger children, supporting our study.¹²

In our study, the rate of underlying disease in the hospitalized patients was significantly higher in the H1N1pdm09 virus infection group compared to the COVID-19 infection group. In a multicentre study, the underlying disease or comorbidity was reported to be 45.8% in hospitalized children with H1N1pdm09 virus infection, and the most commonly reported underlying disease was chronic neurological diseases and malignancy, which supported our findings.¹⁰ On the other hand, obesity and bronchial asthma were significant underlying diseases for severity and mortality in adult patients with COVID-19 infections.¹² In a recent study, obesity was found to be remarkable comorbidity for severity, especially in older children.¹³ In a systematic review of published articles, only two reports described asthma bronchial as a risk factor for severe COVID-19 infections.¹⁴ In addition, a recent study from Spain reported no demographic differences between asthmatic children with and without probable COVID-19 infections.¹⁵ One study from our center reported asthma and obesity as risk factors, which was consistent with our findings.¹⁶ In addition, a study with a high case number reported the most frequent underlying medical condition like asthma, with a frequency of 10.2%.¹⁷ The newer pandemic virus, SARS-COV-2, differs from the H1N1pdm09 virus infection in this study. Nearly three of the four children who required hospitalization were previously healthy children. A recent report including 2708 hospitalized children with COVID-19 infection found that 62.9% of the children had the underlying disease.¹⁶ However, some of the medical conditions such as headaches and anxiety were not included in our study, which might result from the high number of healthy children. Compared with the pandemic influenza infections in our center, the predominance of previously healthy children in the hospitalized population revealed a major pitfall for COVID-19 infection.

During the H1N1 pandemic, Çiftçi et al.¹⁰ reported that 11.0% of children with H1N1pdm09 virus infection were hospitalized in the pediatric intensive care unit. On the other hand, one large series from the US reported that 29.6% of the hospitalized COVID-19 infections required intensive care unit admission,¹⁷ while different studies from Mexico City and the USA reported that 23.0% and 39% of the children required PICU admission.^{18,19} In our study, we didn't observe any significant difference regarding pediatric intensive care unit admission for both of the viral infections. Moreover, admission to the intensive care unit was associated with an underlying disease regardless of the type of pandemic. Previous studies reported the association of intensive care unit admission and the presence of

underlying disease in the COVID-19 infections^{11,17} and the H1N1pdm09 virus infections,¹⁰ supporting our finding.

In conclusion, comparing the two patient groups during two major pandemic eras, our results suggest that older children were more hospitalized for COVID-19 infection compared to pandemic influenza. In addition, regardless of the type of pandemic infection, the underlying disease is an important factor for pediatric intensive care unit admission. This finding is important for developing strategies for the protection of children with the underlying disease in the upcoming pandemics.

CONFLICT OF INTERESTS

The authors declare that there are no conflicts of interest.

ETHICS STATEMENT

Ethics approval was obtained from the Institutional Review Board of Dr. Behcet Uz Children's Training and Research Hospital. Informed consent was obtained from legal guardians of the participants included in the study. Consent for publication was obtained from the legal guardians of the participants included in the study.

AUTHOR CONTRIBUTIONS

İlker Devrim, Nuri Bayram, Elif Böncüoğlu, and Elif Kıymet performed the research. İlker Devrim, Nuri Bayram, and Hasan Ağın designed the research study. Aybüke Akaslan Kara, Miray Yılmaz Çelebi, Kamile Ötiken Arıkan, Şahika Şahinkaya, Fatma Devrim, Ela Cem contributed essential reagents or tools. İlker Devrim and Nuri Bayram analyzed the data. İlker Devrim and Nuri Bayram wrote the paper. All authors read and approved the final manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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