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RESEARCH ARTICLE

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Influenza is more severe than our newest enemy (COVID-19) in hospitalized children: Experience from a tertiary center

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Abstract

Understanding differences in terms of clinical phenotypes and outcomes of coronavirus disease 2019 (COVID-19) compared with influenza is vital to optimizing the management of patients and planning healthcare. Herein, we aimed to investigate the clinical differences and outcomes in hospitalized patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and influenza. We performed a retrospective study of hospitalized children who were positive for SARS-CoV-2 between March 2020 and March 2021 and for influenza between January 2016 and February 2020 in respiratory samples. The primary outcome of this study was pediatric intensive care unit (PICU) admission, and the secondary outcome was the need for respiratory support. A total of 74 patients with influenza and 71 who were positive for SARS-CoV-2 were included. The distribution among the sexes was similar, but patients with COVID-19 were older than patients with influenza (96 vs. 12, $p < 0.001$). In terms of underlying chronic diseases, the frequency was 26.7% in the COVID-19 group and 54% in the influenza group ($p = 0.001$). The comparison of symptoms revealed that fatigue, headache, nausea, vomiting, and abdominal pain occurred more frequently with COVID-19 (for all $p < 0.05$) and runny nose with influenza ($p = 0.002$). The frequency of admission to the PICU was relatively higher (18.9%) in the influenza group than with COVID-19 (2.8%) with a significant ratio ($p = 0.001$), secondary bacterial infections were observed more frequently in the influenza group (20.2% vs. 4.2%, $p = 0.003$). Some 88.7% of patients with COVID-19 did not need respiratory support, whereas 59.4% of patients with influenza did require respiratory support ($p < 0.001$). This study noted that influenza caused more frequent admissions to the PICU and a greater need for respiratory support in hospitalized pediatric patients than COVID-19.

KEYWORDS

children, COVID-19, hospitalized, influenza, outcome

1 | INTRODUCTION

The emergence of coronavirus disease 2019 (COVID-19) was first recognized in January 2020, and the disease rapidly spread worldwide, being declared a global pandemic by the World Health Organization (WHO) in March 2020.[1] Although COVID-19 occurs in all age groups, epidemiologic evidence has consistently shown that children typically have the less severe disease than adults.[2] Given the significant health consequences of severe COVID-19, including hospitalization, the need for respiratory support, and death, several studies have evaluated the predictive ability of various factors for poor outcomes. A multicentre study involving 582 children and adolescents infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) determined that 13% of the patients received respiratory support, 8% were admitted to the pediatric intensive care unit (PICU), and 4% needed mechanical ventilation.[3] Understanding the clinical features and determinants of disease severity due to SARS-CoV-2 virus infection is crucial for both the identification and clinical management of high-risk cases.

Influenza virus infection is common in children. Every year, seasonal influenza viruses are estimated to cause >100 million illnesses and 870 000 hospitalizations globally for acute lower respiratory infection among children aged under 5 years.[4] However, because seasonal flu outbreaks infect millions of children worldwide each year, the detailed risk and prognostic factors for severe complicated flu in children remain clear. Although all children younger than 5 years are considered at higher risk of severe flu complications.[5,6] The risk of complications such as pneumonia and hospitalization is higher in children aged under 2 years and those, especially with underlying conditions.[7]

It is essential for physicians to accurately identify these two respiratory tract infections through their various clinical manifestations because of their different treatment approaches and prognoses. To date, identification of the SARS-CoV2 and influenza infections in children has mainly been limited to clinical research studies, and differences have not yet to become put forth. Therefore, to provide guidance, the current study aimed to compare the different clinical presentations and outcomes between patients infected with COVID-19 and influenza.

2 | MATERIALS AND METHODS

This study was performed by the Department of the Pediatric Infectious Diseases, Health Sciences University, Izmir Tepecik Training and Research Hospital, in Izmir, Turkey. The study was approved by the Medical Ethical Committee of our hospital (approval number: 2021/02-52).

2.1 | Patient selection

This study included pediatric patients who were diagnosed as having laboratory-confirmed COVID-19 and who were hospitalized between March 2020 and March 2021, and from January 2016 to February 2020 for influenza. The study included pediatric patients admitted to our center who need hospitalization.

Patients with the multisystem inflammatory syndrome in children (MIS-C) who tested positive for COVID-19 were excluded from the study. Patients with concomitant viral infections with influenza and missing details were also excluded from both groups. No patients in this cohort were hospitalized with a coinfection of both COVID-19 and seasonal influenza.

A broad definition of acute respiratory illness was used to identify patients who had potentially contracted influenza: the presence of two or more signs or symptoms (temperature ≥37.8°C, cough, headache, sore throat, myalgia, congestion, and rhinorrhea) with a duration of 1 or more days during follow-up, as defined in previous studies.[8] The surveillance definition for influenza-like illness recommended by the Centers for Disease Control and Prevention (temperature ≥37.8°C plus cough or sore throat) was also used.

Diagnosis of COVID-19 was documented by quantitative real-time polymerase chain reaction (RT-PCR) positivity. The protocol of RT-PCR was consistent with the recommendation of the WHO. Samples were taken from patients with COVID-19 symptoms and/or contact with COVID-19 cases.

Combined nasopharyngeal and oropharyngeal swab samples were taken from children with suspected COVID-19 and only nasopharyngeal swab samples for influenza were sent to the medical microbiology laboratory. SARS-CoV-2 was detected using RT-PCR (Bio-Speedy SARS CoV-2 double Gene RT-qPCR Kit). Specifically, two target genes, including open reading frame 1ab and nucleocapsid protein (N), were tested using RT-PCR assays. Influenza types A and B were detected using multiplex PCR assays (Bosphore Respiratory Pathogens Panel Kit v4) from nasopharyngeal swabs.

2.2 | Study protocol

Hospital records and laboratory results from both the COVID-19 and the influenza groups were retrieved and analyzed. Demographics, clinical symptoms, underlying diseases, length of hospital stay, need for oxygen and mechanical ventilation, development of systemic inflammatory response syndrome (SIRS)/sepsis, and laboratory tests were compared between the groups.

Laboratory data were collected in patients with COVID-19 on admission. Because firstly we tested for COVID-19 and then hospitalized but in the influenza group, some of the patients tested during the hospitalization period so we analyzed when we diagnosed influenza. Influenza testing was performed all year round but PCR positivity was determined during influenza season in all patients.

The primary outcome of this study was PICU admission, and the secondary outcome was the need for respiratory support.

2.3 | Definitions

Lymphopenia, neutropenia, and creatinine levels by age were classified according to the data in *Nelson Pediatrics Textbook*.[9,10] The American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference guidelines were used for the definitions of SIRS and sepsis.[11]

The WHO defines pneumonia primarily as cough or difficult breathing and age-adjusted tachypnea: (age 2–11 months, ≥50/min; 1–5 years, ≥40/min; and ≥5 years, >20 breaths/min).[12]

Most hospitalized patients infected with respiratory viruses require some form of respiratory support. This is usually due to hypoxemia or respiratory failure or both. The support offered ranges from oxygen therapy with a face mask, to noninvasive techniques such as continuous positive airway pressure, and full ventilation support with endotracheal intubation.

The patients were divided into four groups those who did not receive oxygen support, received oxygen with a nasal cannula, needed noninvasive mechanical ventilation, and needed mechanical ventilation. Respiratory support needs of patients were determined according to the following parameters: moderate to severe dyspnea unresponsive to supplemental oxygen or other treatments, persistent tachypnea caused by respiratory diseases, hypoxemia, and respiratory acidosis.[13]

2.4 | Statistical analysis

Statistical analyses were performed using the SPSS software (version 24.0; IBM Corp). Descriptive statistics were used to summarize the patients' baseline characteristics, depending on the normality of distribution, values for continuous variables were provided either as means ± standard deviations or as medians (minimum–maximum [min–max]). Frequencies of nominal variables were presented as percentages. Comparisons between groups for categorical variables were made using the χ^2 test. For two-group comparisons of independent variables, Student's *t*-test was used as a parametric test, and the Mann–Whitney *U* test was the preferred nonparametric test. Statistical significance was defined as $p < 0.05$.

3 | RESULTS

During the study period, 808 children with symptoms of COVID-19 were admitted to our outpatient clinic. Of these, 71 patients who were symptomatic were hospitalized and followed up. All hospitalized patients had COVID-19 symptoms and 20 of them had underlying diseases.

From January 2016 to February 2020, 2607 samples were studied throughout all seasons to detect viral respiratory pathogens. Influenza virus was detected in 299 of them, 74 patients had influenza without any co-infection. Influenza A was detected in 48 (64.8%) of these patients and influenza B was detected in 26 (35.2%) patients. In the influenza group ($n = 74$), 51 (68.9%) of them were hospitalized due to only influenza-related disease, while 23 (31.1%) were hospitalized for another reason, and concomitantly influenza was detected.

The distribution of sex of patients was not statistically significantly different between the two groups (male; 40.8% vs. 56.7%, $p = 0.055$). Significant differences were found in the median age between patients with COVID-19 and influenza (96 vs. 12 months, $p < 0.001$). Among substantiated COVID-19 cases, 19 (26.7%) patients had an underlying disease, while the number of children with the underlying disease was 40 (54%) in the influenza group and the difference was statistically significant ($p = 0.001$).

In both groups, fever was the most commonly reported symptom at the time of diagnosis, followed by a cough. The proportions of weakness (14%), headache (5.6%), and abdominal pain (12.6%) in patients with COVID-19 were more frequent than those of patients with influenza (1.3%, $p = 0.004$; 0%, $p = 0.038$; and 0%, $p = 0.002$, respectively). The rate of having a runny nose was significantly higher in the influenza group than that of patients with COVID-19 (24.3% vs. 5.6%, $p = 0.002$). Demographic characteristics and clinical symptoms are depicted in Table 1.

Thirty-two (45.1%) patients with COVID-19 had lymphocytopenia compared with 48 (64.9%) patients with influenza ($p = 0.017$). The median level of creatinine was higher in patients with influenza than in those with COVID-19 ($p < 0.001$); high creatinine levels according to age groups were more common in influenza than in COVID-19 (35.2% vs. 17.1%, $p = 0.015$). The influenza group demonstrated higher median levels of lactate dehydrogenase (LDH) than those in the COVID-19 group ($p < 0.001$). When D-dimer results were compared between both groups, the median value was 1275 μg/L fibrinogen equivalent unit (FEU) in the influenza group and 535 μg/L FEU in the COVID-19 group, and the difference was statistically different ($p = 0.041$). The median procalcitonin value was 0.6 μg/L in the COVID-19 group and 0.26 μg/L in the influenza group, which was statistically significantly different ($p < 0.001$). However, the median C-reactive protein (CRP) value was similar between the groups ($p = 0.928$). Laboratory findings of the patients are summarized in Table 2.

According to the disease course, all patients were hospitalized, the median hospitalization time was 10 (min–max: 1–78) days in the influenza group and 5 (min–max: 1–16) days in the COVID-19 group ($p < 0.001$). Only two (2.8%) patients were admitted to the PICU in the COVID-19 group, whereas 14 (18.9%) patients were admitted in the influenza group ($p = 0.002$). The length of hospital stay in the PICU was a median of 3 (min–max: 1–5) days for patients with COVID-19, whereas for patients with influenza, it was 12 (min–max: 1–50) days ($p = 0.001$). When determined according to the WHO, 29.1% of influenza patients and 33.8% of COVID-19 patients were followed up and treated for pneumonia. Eight (11.2%) patients in the COVID-19 group required respiratory support, and this number was significantly higher with 44 (59.4%) in the influenza group ($p < 0.001$). In the COVID-19 group, two (2.8%) patients received oxygen by nasal cannula, five (7%) patients received oxygen with a high flow nasal

TABLE 1 Demographical characteristics and clinical symptoms of patients with COVID-19 and influenza.

Characteristics	COVID-19 (*n* = 71)	Influenza (*n* = 74)	*p*
Male[a]	29 (40.8)	42 (56.7)	0.055
Age (months)[b]	96 (2–204)	12 (1.5–204)	**<0.001**
Underlying medical conditions[a]	19 (26.7)	40 (54)	**0.001**
Prematurity	1 (5.2)	6 (15)	
Neurometabolic problems	9 (47.3)	14 (35)	
Hematological diseases	2 (10.5)	1 (2.5)	
Cardiological diseases	1 (5.2)	6 (15)	
Nephrological diseases	0	7 (17.5)	
Respiratory diseases	3 (15.7)	2(5)	
Endocrinological diseases	3 (15.7)	0	
Malignancies	0	4 (10)	
Weakness	10 (14)	1 (1.3)	**0.004**
Headache	4 (5.6)	0	**0.038**
Chest pain	1 (1.4)	0	0.306
Vomitting – nausea	14 (19.7)	5 (6.7)	**0.021**
Diarrhea	12 (16.9)	10 (13.5)	0.570
Abdominal pain	9 (12.6)	0	**0.002**
Rash	1 (1.4)	1 (1.3)	0.976
Conjunctivitis	0	1 (1.3)	0.326
Dysgeusia- anosmia	2 (2.8)	0	0.146
Convulsions	5 (7)	6 (8.1)	0.827

Note: Significant *p* values are indicated in bold.

Abbreviation: COVID-19, coronavirus disease 2019.

[a]*n*, %.

[b]Median (min–max).

cannula, none of the patients needed a noninvasive mechanical ventilator, and one (1.4%) patient needed mechanical ventilation. In the influenza group, 18 (24.3%) patients received oxygen by nasal cannula, 15 (20.2%) patients received oxygen with a high flow nasal cannula, 2 (2.7%) of the patient needed a noninvasive mechanical ventilator, and 9 (12.1%) patients needed mechanical ventilation. SIRS/sepsis developed in two (2.8%) children with COVID-19 and 12 (16.2%) with influenza ($p = 0.006$). Secondary infection developed in three (4.2%) children diagnosed with COVID-19 and 15 (20.2%) children with influenza ($p = 0.003$). No mortality was reported in the COVID-19 group, but four (5.4%) children died in the influenza group. Patients who died in the influenza group were children with underlying diseases. One patient had acute lymphoblastic leukemia, two patients had neurodevelopmental problems, and one patient had Down syndrome accompanied by cardiac pathology. A common feature of all of them was that FLU A was detected. When the follow-up and treatment of the patients are evaluated, deaths can be attributed to influenza. Hospitalization characteristics are depicted in Table 3.

4 | DISCUSSION

SARS-CoV-2 and influenza viruses share similarities, such as clinical features, outcomes, and laboratory findings, yet both have differences. There were no striking differences in the distribution of patient sexes in terms of both virus types in our study, but patients with COVID-19 were older than those with influenza. This supports the notion that influenza primarily causes severe diseases in infants, whereas SARS-CoV-2 severely affects adolescents. Most of the patients were aged over 5 years, as supported by many studies.[14–16] Song et al.[17] observed in the community-based study that COVID-19 occurred especially in children aged higher than 5 years of age (62.9%). Additionally, an influenza virus was detected in 44% of patients higher than 5 years in the seasonal influenza group. Interestingly the distribution of patients under 1 year is similar (24% vs. 20%) between groups, but the median age was statistically significant (9.7 vs. 4.2 years).[17] In our study, the median age was found that 96 versus 12 months, it was very remarkable that the number of our patients in the influenza group in the infant period was higher than in other studies.[16–18]

Patients with COVID-19 had fewer comorbidities compared with the influenza group, which corresponds to previous observations.[16,19] According to a meta-analysis, 6.1% of children with COVID-19 had an underlying disease.[20] In pediatric studies, different rates were observed in patients with COVID-19 and influenza regarding underlying medical conditions.[17,21] In our research, patients with influenza had more underlying diseases. According to other studies in the literature, the disease severity predictors were the presence of underlying disease and being an infant.[22,23] In this situation, the severity of the disease is known to increase with these conditions; children with underlying diseases and/or infants (age >6 months) need to have the influenza vaccine regularly every year.

This study supports the literature that fever and cough were the most widespread symptoms for both groups.[14,17,20,24,25] The present study shows that it may not be possible to distinguish between influenza viruses and COVID-19 based on symptoms alone, since both pathogens evaluated have the potential to cause a febrile illness in affected children. Among them, the influenza group exhibited a much higher portion of patients that experienced runny noses. Noticeably, both viral infections affected the gastrointestinal system, and COVID-19 induced more abdominal pain, vomiting, and nausea, as well as weakness and headache. The detected statistical difference in the frequency of abdominal pain and headache may be attributable to the age distribution of the groups. In one study, fever, diarrhea or vomiting, headache, body ache or myalgia, and chest pain were more common in COVID-19 compared with seasonal influenza.[17] In another study assessing patients with COVID-19 and H1N1 found

TABLE 2 Laboratory features of patients with COVID-19 and influenza.

Laboratory tests	COVID-19 (*n* = 71)	Influenza (*n* = 74)	*p*
WBC (4.2–10.6 10^3/μl)[a]	7700 (2700–28 000)	10 200 (0–34 500)	0.098
ANC (2–6.9 10^3/μl)[a]	4400 (900–17 600)	5300 (0–20 400)	0.256
ALC (0.6–3.4 10^3/μl)[a]	2100 (400–12 900)	2600 (0–11 700)	0.194
Neutropenia[b]	7 (9.8)	8 (10.8)	0.547
Lymphopenia[b]	32 (45.1)	48 (64.9)	**0.017**
Monocyte (0–0.9 10^3/μl)[a]	900 (200–2800)	800 (0–5100)	0.495
Platelets (140–400 10^3/μl)[a]	250 000 (6000–974 000)	302 000 (15 000–602 000)	0.403
Hemoglobin (12.2–16.2 g/dl)[c]	12.28 ± 1.7	10.49 ± 1.98	0.294
CRP (0–5 mg/L)[a]	7.5 (0.1–210)	9.75 (0.1–260)	0.928
Procalsitonin (0.04–0.1 μg/L)[a]	0.6 (0.01–75)	0.26 (0.01–71.8)	**<0.001**
ESR (0–20 mm/h)[a]	23 (11–104)	30 (4–82)	0.884
AST (15–60 U/L)[c]	38 ± 34	52 ± 38	0.058
ALT (13–45 U/L)[a]	17 (8–368)	17 (6–121)	0.639
LDH (110–295 U/L)[a]	301 (140–1476)	342 (171–1794)	**<0.001**
BUN (8.4–25.8 mg/dl)[a]	21 (8–66)	17 (3–183)	0.050
Creatinine (0.4–0.7 mg/dl)[a]	0.6 (0.3–1.3)	0.5 (0.2–2.9)	**<0.001**
CK (0–171 U/L)[a]	92 (30–736)	104 (13–1481)	0.591
D-dimer (0–440 μg/L FEU)[a]	535 (190–7550)	1275 (394–3734)	**0.041**

Note: Significant *p* values are indicated in bold.

Abbreviations: ALC, absolute lymphocyte count; ALT, alanine aminotransferase; ANC, absolute neutrophil count; AST, aspartate aminotransferase; BUN, blood urea nitrogen; CK, creatinine kinase; COVID-19, coronavirus disease 2019; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; FEU, fibrinogen equivalent unit; LDH, lactate dehydrogenase; WBC, white blood cell.

[a]Median (min–max).

[b]*n*, %.

[c]Mean ± SD.[d]

TABLE 3 Hospitalization characteristics.

Variables	COVID-19 (*n* = 71)	Influenza (*n* = 74)	*p*
Hospitalization length (day)[a]	5 (1–16)	10 (1–78)	**<0.001**
Patients requiring stay in PICU[b]	2 (2.8)	14 (18.9)	**0.002**
PICU length of stay (day)[a]	3 (1–5)	12 (1–50)	**0.001**
Patients requiring respiratory support[b]	8 (11.2)	44 (59.4)	**<0.001**
Patients developing SIRS/sepsis[b]	2 (2.8)	12 (16.2)	**0.006**
Patients developing secondary infection[b]	3 (4.2)	15 (20.2)	**0.003**
Death[b]	0	4 (5.4)	0.120

Note: Significant *p* values are indicated in bold.

Abbreviations: COVID-19, coronavirus disease 2019; PICU, pediatric intensive care unit; SIRS, systemic inflammatory response syndrome.

[a]Median (min–max).

[b]*n*, %.[c]

that symptoms, including dry cough, shortness of breath, and runny nose, were observed in a higher percentage of influenza patients than COVID-19.[21] The conclusion shared by different studies is that on its own, clinical presentation should not be considered a reliable indicator of influenza or COVID-19. A limitation of this study is that anosmia and dysgeusia were not routinely questioned in the early phase of the pandemic. Faury et al.[24] reported that these symptoms might be beneficial in distinguishing COVID-19 from other illnesses.

In our research, the anosmia and dysgeusia rate was only 2.8%, which may be related to the fact anosmia and dysgeusia were more common in patients with mild disease.

Both COVID-19 and influenza infections caused abnormalities in blood cell counts, resulting in neutropenia, lymphocytopenia, elevations of acute-phase reactants (CRP, procalcitonin, and erythrocyte sedimentation rate) in a prominent part of patients. In a study comparing adult patients, white blood cell and procalcitonin levels were found to be higher in patients with influenza. In contrast, no difference was found between the groups in terms of lymphocyte counts.[26] According to another study that compared COVID-19 and H1N1, CRP levels were not statistically significantly different between the groups.[21] In a study examining the hematologic parameters of patients with COVID-19 and influenza, it was found that the absolute neutrophil count was higher in patients with influenza, and LDH and CRP values were higher in patients with COVID-19.[18] Our findings showed that patients with influenza had a higher frequency of lymphocytopenia, but lower procalcitonin levels. We determined that serum LDH and creatinine levels were different between the groups.

Interestingly, D-dimer levels were significantly higher in patients with influenza. In a study conducted to determine the prognostic markers of influenza, D-dimer levels were found to be significantly different between the group with respiratory failure and the group without respiratory failure.[27] In a comparative study conducted in children aged under 5 years with pneumonia, D-dimer levels were found to be higher in the influenza group than in the COVID-19 group, similar to our study.[28] A systematic review showed that underlying disease might trigger an increase in D-dimer levels in patients with COVID-19.[29] In the COVID-19 pandemic, D-dimer levels were generally used to support the diagnosis, but our results showed that D-dimer was not a specific marker for COVID-19, it could be increased in other medical conditions. Also, the higher LDH, creatinine, and D-dimer levels may be attributable to the high frequency of secondary infections in the influenza group.

The risk of severe septic shock was also higher in the influenza group, inconsistent with reports of septic shock in patients with COVID-19.[30] In a study conducted on pediatric patients with COVID-19 in our country, it was found that a secondary infection developed in 18.2% of patients.[31] In a multicenter cohort study that included 55 270 patients with COVID-19, it was reported that the rate of sepsis ranged from 2% to 9.4%.[32] In a study involving 17 534 COVID-19 patients in India, secondary bacterial or fungal infection was detected at a rate of 3.6%.[33] In our study, secondary bacterial infections were found to be significantly lower at 4.2% compared with patients with influenza. Although the distinction between secondary bacterial infections in COVID-19 has not yet been clarified, it can be thought that the underlying diseases in the influenza group predispose to secondary infections. In addition, the evaluation of the development of secondary bacterial infections in patients was mostly made on the basis of bloodstream infections, secondary bacterial pneumonia may not have been demonstrated due to the difficulty of sampling.

In a study from the United States of America (USA), a comparison between children with COVID-19 and seasonal influenza showed no differences in hospitalization rates, PICU admission rates, and mechanical ventilator use. In the same study, the duration of hospitalization due to COVID-19 ranged from 1 to 45 days, whereas it ranged from 1 to 100 days in patients with influenza.[17] In another study, the need for mechanical ventilation in patients with COVID-19 was found to be higher than in the influenza group. In the same study, hospitalization of patients aged under 5 years in the PICU was also more frequent in patients with COVID-19 than in those with influenza. However, there was no difference in mortality between the two groups.[15] In a comparative study of patients hospitalized for acute respiratory distress syndrome in China, no difference was observed in terms of mechanical ventilator need, whereas patients with influenza required more nasal cannula oxygen compared with patients with COVID-19.[16] In a multicenter study conducted on children with COVID-19 in Europe, 13% needed respiratory support, 8% of patients were admitted to the PICU, and 4% were followed up with a mechanical ventilator.[3] In our study, both PICU admission rates and duration of hospitalization were higher in patients with influenza than in COVID-19. These differences in hospitalization, PICU admission, and requirement of mechanical ventilation rates could be attributed to variations in age, seasonality, racial factors, environmental factors, socioeconomic status, and perhaps SARS-CoV2 variants.[17,34] There was no study in the literature comparing outcomes between influenza and SARS-CoV2 variants.

In a cohort of 1227 patients with COVID-19, in-hospital mortality was higher in the COVID-19 group, mortality was more common between the ages of 11–17 years, and this increased rate was attributed to MIS-C. In the same study, although the need for intensive care was more common in the COVID-19 group among patients aged under 5 years, no difference was found between the influenza group and mortality.[15] On the contrary, while two children died due to influenza, no child died in the COVID-19 group in one study from the USA.[17] Like our results, four patients died in the influenza group, and no patients died in the COVID-19 group. Another similar result was that patients who died in both studies were due to influenza A.

Our study has several limitations. Owing to the retrospective study design, patients' symptoms were not systematically collected. There may be some little variations in management as the study period includes different years. During the study period, our hospital adhered to a similar protocol where treatment was offered upon suspicion of influenza infection. Respiratory support treatments have been applied in our hospital since 2016 according to current guidelines. The treatment of COVID-19 has been updated periodically during the pandemic, and our management has been given to our patients in accordance with these protocols. These minor differences may have caused some different clinical outcomes in the study. Another limitation is that clinical findings of influenza may vary from year to year through differences in subtypes.

5 | CONCLUSION

From our results, it may be speculated that influenza may result in more severe outcomes and more frequent complications in children. Although it was thought that our newest enemy (COVID-19) would cause more serious consequences than other respiratory tract viruses at the beginning of the pandemic, current studies have once again revealed that influenza is not such an innocent virus for children.

AUTHOR CONTRIBUTIONS

Dilek Yilmaz-Ciftdogan: Conceptualization, writing, and critically revising the manuscript. **Eda Karadag-Oncel**: Statistical analysis and writing the manuscript. **Selin Tasar**: Data collection. **Aysegul Elvan-Tuz**: Data collection. **Aslihan Sahin**: Data collection. **Nisel Yılmaz**: Measurements. **Ahu Kara-Aksay**: Conceptualization, writing, and critically revising the manuscript. **Muhammet A. Kanık**: Conceptualization, writing, and critically revising the manuscript. **Yildiz Ekemen-Keles**: Conceptualization, writing, and critically revising the manuscript. **Gulnihan Ustundag**: Conceptualization, writing, and critically revising the manuscript. The manuscript was written by Dr. Selin Tasar. All authors have made substantive contributions to the manuscript, and all authors endorse the data and conclusions. All the named authors have seen and agreed to the submitted version of the paper.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

ETHICS STATEMENT

This study was approved by the Health Sciences University, Izmir Tepecik Training and Research Hospital Ethical Committee in accordance with the Helsinki Declaration (Decision Number: 2021/02-52).

DATA AVAILABILITY STATEMENT

Not applicable.

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