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Children in the Shadow of Viruses: Comparative Clinical Outcomes of COVID-19 and Influenza - A Single-center Retrospective Cohort Study

Virüslerin Gölgesinde Çocuklar: COVID-19 ve İnfluenzanın Karşılaştırmalı Klinik Sonuçları - Tek Merkezli Geriye Dönük Kohort Çalışması

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Abstract

Introduction: Respiratory viruses are the most common cause of morbidity and mortality in children around the world. Unlike other viral respiratory diseases, recommendations for coronavirus disease-2019 (COVID-19) in children are mainly derived from adult data, and it has been difficult to differentiate COVID-19 from influenza by clinical manifestations that are earlier than viral identification. The study aims to compare clinical and laboratory characteristics that will enable healthcare workers to differentiate COVID-19 from influenza.

Methods: This retrospective cohort study, conducted at a tertiary academic hospital's pediatric emergency department from January 1, 2019 to December 31, 2021 focused on children with confirmed COVID-19 or influenza. We compared demographics, clinical features, laboratory/radiological findings, reatments, pediatric intensive care unit admissions, length of stay, mortality, and clinical outcomes between COVID-19 and influenza in pediatric populations, providing valuable insights into the two diseases during the specified period.

Results: Six hundred and sixty-one children with COVID-19 and 499 children with influenza infection were included. In the vital signs at triage, significantly higher fever, tachypnea, and tachycardia were found in patients with influenza (p=0.001). In terms of chest X-ray (CXR) characteristics, 82.2% of the children in the COVID-19 group had normal CXR (p=0.001) while the children in the influenza group had more patchy involvement (p=0.003) and consolidation (p=0.001). Platelet counts in the COVID-19 group were significantly higher than those in the influenza group (p=0.001). Regarding infection-related biomarkers, the C-reactive protein level in the influenza cohort was significantly higher than in the COVID-19 cohort (4.92 mg/L vs. 0.94 mg/L, p=0.001).

Öz

Giriş: Solunum yolu virüsleri, dünya genelinde çocuklarda morbidite ve mortalitenin en yaygın nedenidir. Diğer viral solunum yolu hastalıklarından farklı olarak, çocuklarda koronavirüs hastalığı-2019 (COVID-19) yönelik öneriler ağırlıklı olarak yetişkin verilerinden elde edilmiştir. Ayrıca, COVID-19'un influenza ile erken dönemde, viral tanı konulmadan önce, klinik belirtilerle ayırt edilmesi zor olmuştur. Bu çalışma, sağlık çalışanlarının COVID-19 ile influenzayı ayırt etmelerini sağlayacak klinik ve laboratuvar özellikleri karşılaştırmayı amaçlamaktadır.

Yöntemler: Bu geriye dönük kohort çalışması, 1 Ocak 2019-31 Aralık 2021, tarihleri arasında üçüncü basamak bir akademik hastanenin çocuk acil servisinde yürütülmüştür. Çalışmaya, COVID-19 veya influenza tanısı kesinleşmiş çocuklar dahil edilmiştir. COVID-19 ve influenza tanısı alan çocuk hastalar arasında demografik veriler, klinik özellikler, laboratuvar ve radyolojik bulgular, uygulanan tedaviler, çocuk yoğun bakım ihtiyacı, hastanede kalış süresi, mortalite ve klinik sonuçlar karşılaştırılmış, belirlenen dönemde iki hastalığa dair önemli veriler sunulmuştur.

Bulgular: Çalışmaya 661 COVID-19'lu ve 499 influenza enfeksiyonlu çocuk dahil edilmiştir. Triaj sırasında değerlendirilen yaşamsal bulgular incelendiğinde, influenza grubundaki hastalarda anlamlı derecede daha yüksek ateş, taşipne ve taşikardi saptanmıştır (p=0,001). Akciğer grafisi bulguları açısından COVID-19 grubundaki çocukların %82,2'sinde normal akciğer grafisi izlenirken (p=0,001), influenza grubundaki çocuklarda daha fazla yama tarzı tutulum (p=0,003) ve konsolidasyon (p=0,001) tespit edilmiştir. COVID-19 grubunda trombosit seviyeleri, influenza grubuna kıyasla anlamlı derecede daha yüksek bulunmuştur (p=0,001). Enfeksiyonla ilişkili

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Abstract

Conclusion: Our study objectively compares the severity of COVID-19 in children with influenza, a related serious respiratory illness with regular seasonal or pandemic outbreaks, and with a high patient count in both groups. Our study confirmed that influenza and COVID-19 cohorts are compared. Influenza is more symptomatic, associated with higher fever levels, more viral coinfection, longer and higher rates of hospitalization, greater need for respiratory support, and death.

Keywords: Children, influenza, COVID-19, pandemic

Öz

biyobelirteçler değerlendirildiğinde, influenza grubundaki C-reaktif protein seviyesi, COVID-19 grubuna kıyasla anlamlı derecede daha yüksek saptanmıştır (4,92 mg/L vs. 0,94 mg/L, p=0,001).

Sonuç: Çalışmamız, çocuk hastalarda COVID-19'un, düzenli mevsimsel veya pandemik salgınlarla ortaya çıkan ciddi bir solunum yolu hastalığı olan influenza ile objektif olarak karşılaştırmasını yapmaktadır. Bulgularımız, influenza grubunun COVID-19 grubuna kıyasla daha semptomatik olduğunu, daha yüksek ateş seviyeleri, daha fazla viral koinfeksiyon, daha uzun ve yüksek oranda hastane yatışı, daha fazla solunum desteği ihtiyacı ve daha yüksek mortalite ile ilişkili olduğunu doğrulamaktadır.

Anahtar Kelimeler: Çocuklar, influenza, COVID-19, pandemi

Introduction

The coronavirus disease-2019 (COVID-19) emerged as a global health crisis, marked by uncertainty and widespread transmission. While the World Health Organization has declared that COVID-19 is no longer a "global health emergency," the virus remains a public health concern due to its continued transmissibility.[1] As the pandemic declines, other respiratory viral infections are becoming increasingly prevalent, similar to past winter seasons. Early in the pandemic, it was noted that children were less affected by severe COVID-19 than adults.[2,3] However, their role in transmission remains unclear. Several studies have compared presentations of COVID-19 and influenza in adults.[4] Identifying clinical and laboratory features that allow healthcare professionals to distinguish COVID-19 from seasonal influenza is critical to effective containment, given the significant health, social and economic impact of COVID-19 worldwide. This distinction is particularly important in the pediatric population, as children are more susceptible to influenza due to behavioral factors, such as poor hygiene compliance and immature immune system responses. We conducted this study at our pediatric emergency outpatient clinic, which annually serves an average of 90.000 patients, in Ankara, Türkiye's capital, at its most comprehensive tertiary academic and university hospital. The objective of this study was to determine the differences between COVID-19 and influenza, particularly in pediatric patients. As the COVID-19 pandemic continues, it is critical for pediatricians to compare the demographic and clinical characteristics of the disease in children with influenza infections. COVID-19 can present with a wide clinical spectrum from asymptomatic to respiratory failure. The influenza viruses commonly encountered in children can present with similar symptoms. In this study, we focused on identifying clinical and laboratory characteristics that enable healthcare workers to differentiate COVID-19 from influenza.

Materials and Methods

This retrospective cohort study includes children admitted to the pediatric emergency department (PED) between January 1, 2019, and December 31, 2021, with COVID-19 or influenza confirmed by real-time polymerase chain reaction (RT-PCR) testing. Hacettepe University PED is in Ankara, the capital of Türkiye. Our PED is a referral tertiary academic hospital, serving approximately 90.000 patients annually. Data on patients' presenting complaints, physical examination findings, laboratory and radiological results, treatments and interventions, pediatric intensive care unit (PICU) admission, length of hospital stay, mortality, and clinical outcomes were extracted from medical records. Additionally, the results of COVID-19 RT-PCR and multiplex viral PCR panels for respiratory tract pathogens from nasopharyngeal swab samples, as well as complete blood count, C-reactive protein (CRP), and chest radiography findings, were recorded.

Viral tests were performed on all asymptomatic children with a history of COVID-19 or influenza exposure, as well as on patients who were admitted to the PED, general pediatric ward, or PICU, with a diagnosis of lower respiratory tract infection. Only patients with a positive viral respiratory panel were included in our study. Patients with missing or unavailable laboratory test results were excluded from the study. Respiratory specimens from each child were collected by qualified medical personnel within 24 hours of hospital admission. The extraction and detection of COVID-19 ribonucleic acid in nasopharyngeal swabs were performed according to the manufacturer's instructions using a commercial viral nucleic acid transport buffer and tubes (vNAT, Bioeksen, Türkiye), and an RT-PCR kit (Bio-Speedy severe acute respiratory syndrome-coronavirus-2 N RT-qPCR kit, Bioeksen, Türkiye). Patients with positive RT-PCR results for COVID-19 were classified as the COVID-19 PCR-positive group.

The study was approved by the Ethics Committee of Hacettepe University under registration code GO22/1242, date: 13.12.2022. The ethics committee reviewed our study and waived the need for informed consent, as all data and samples were analyzed retrospectively and collected as part of routine clinical practice in accordance with current guidelines.

To identify other viral respiratory pathogens, multiplex real-time PCR (Bosphore Respiratory Pathogens Panel kit v4, Anatolia Gene Works, Türkiye) was conducted on nasopharyngeal swabs following the manufacturer's protocol. The viral panel tested for adenovirus, respiratory syncytial virus (RSV) types A and B, influenza virus, parainfluenza virus types 1-3, human metapneumovirus, rhinoviruses, human coronaviruses (OC43, 229E, NL63), human bocavirus, and human polyomaviruses KI and WU. Patients who did not meet the collective and probable/definite case definitions or had incomplete data were excluded from the study. The severity of COVID-19 and influenza was classified based on clinical presentation, laboratory findings, and radiological imaging as follows:

Classification of Disease Severity[5,6]

Asymptomatic

No clinical symptoms or signs, with normal chest imaging, despite a positive viral PCR test.

In our hospital, COVID-19 tests were conducted on children with respiratory system symptoms or a contact history, to determine epidemiological characteristics. As a result, an asymptomatic patient group emerged.

Mild

Symptoms of an acute upper respiratory tract infection, including fever, fatigue, myalgia, cough, sore throat, runny nose, and sneezing, or gastrointestinal symptoms, such as nausea, vomiting, abdominal pain, and diarrhea. Physical examination findings may include pharyngeal congestion, but auscultation reveals no abnormalities.

Moderate

Presence of clinical signs of pneumonia, including fever and cough (initially dry, later productive), and possibly wheezing, shortness of breath, or lung crackles. However, there is no significant hypoxemia (pulse oxygen saturation >92%). Some patients may be asymptomatic, but thoracic computed tomography may reveal subclinical lung lesions.

The condition is severe, characterized by disease progression with dyspnea and central cyanosis. Oxygen saturation is less than 92%, accompanied by other manifestations of hypoxia.

Critical

Rapid progression to acute respiratory distress syndrome or respiratory failure. Patients may also develop sepsis, shock, encephalopathy, myocardial injury, or heart failure, coagulation dysfunction, or acute kidney injury. Multiorgan dysfunction can be life-threatening.

Chest radiography findings were categorized as follows: normal, patchy atelectasis and/or hyperinflation and/or bronchial wall thickening, focal consolidation, multifocal consolidation, diffuse alveolar changes.[7]

The vital signs of children were evaluated based on the American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Pediatric Basic and Advanced Life Support, which are also used in our triage system.[8,9]

Statistical Analysis

The demographic information, clinical characteristics, laboratory results, and radiological findings of all patients were analyzed using the IBM SPSS Statistics 23.0 software for Windows. Quantitative data were presented as mean ± standard deviation and median (interquartile range), while qualitative data were expressed as frequencies and percentages. Associations between qualitative variables were assessed using cross-tabulations and the chi-square test. Quantitative variables were compared using the Student's t-test for normally distributed data and the Mann-Whitney U test for non-normally distributed data. A p-value of <0.05 was considered statistically significant.

Results

A total of 661 children diagnosed with COVID-19 and 499 children diagnosed with influenza were included in the study. Baseline clinical characteristics are presented in Table 1. The mean age of patients with COVID-19 was 117.8 months, which was significantly higher than that of patients with influenza, with a median of 51.8 months (p=0.001). There was no significant difference between the two cohorts in terms of gender distribution or the presence of underlying chronic diseases, including chronic respiratory diseases, neuromuscular disorders, epilepsy, obesity, asthma, type 1 diabetes mellitus, and pediatric hemato-oncological malignancies.

The body temperature of patients with influenza was significantly higher than that of patients with COVID-19 (≥38.1 °C, p=0.001). Compared to those with COVID-19, patients with influenza exhibited significantly higher prevalence of cough (p=0.001), respiratory distress (p=0.001), runny nose (p=0.001), abdominal pain, and nausea/vomiting (p=0.001), conjunctivitis (p=0.001), and rash (p=0.001). However, the prevalence of headache and loss of taste or smell was significantly higher in the COVID-19 cohort than in the influenza cohort (p=0.001).

Table 1. Comparison of baseline characteristics patients with influenza and COVID-19

	COVID-19 n (%)	Influenza n (%)	p-value
Gender			
Female	335 (50.6)	229 (45.8)	
Male	326 (49.4)	270 (54.2)	
Age (years, mean ± SD)	9.8±5.9	4.3±3.5	0.001
Presence of fever	427 (64.6)	449 (89.9)	0.001
≤37.5 °C	249 (37.6)	76 (15.3)	
37.6-38 °C	144 (21.7)	62 (12.4)	
38.1-39 °C	195 (31.5)	189 (37.8)	
>39 °C	31 (4.6)	171 (34.2)	
Presence of symptoms	603 (91.2)	482 (96.6)	0.001
Presenting symptoms			
Cough	282 (42.6)	352 (70.5)	0.001
Rhinorrhea	80 (12.1)	237 (47.4)	0.001
Nausea-vomiting	52 (7.8)	118 (23.6)	0.001
Fatigue	116 (17.5)	78 (15.6)	0.386
Sore throat	124 (18.7)	75 (15)	0.095
Muscle pain	81 (12.2)	69 (13.8)	0.429
Fast breathing	20 (3)	55 (11)	0.001
Diarrhea	77 (11.6)	53 (10.6)	0.583
Stomachache	28 (4.2)	49 (9.8)	0.001
Conjunctivitis	3 (0.4)	29 (5.8)	0.001
Headache	81 (12.2)	26 (5.2)	0.001
Rashes	5 (0.7)	21 (4.2)	0.001
Chest pain	10 (1.5)	2 (5.2)	0.064
Loss of taste and smell	34 (5.1)	14 (2.8)	0.001
Contact of index patient	380 (57.4)	105 (21)	0.001
Comorbid conditions	99 (14.9)	94 (18.8)	0.08
Cystic fibrosis	33 (4.9)	11 (2.2)	
Asthma	24 (3.6)	7 (1.4)	
Epilepsy	22 (3.3)	32 (6.4)	
Malignancy	9 (1.3)	9 (1.8)	
Genetic syndromes	6 (0.9)	10 (2)	
Diabetes mellitus type 1	3 (0.4)	-	
Obesity	-	2 (0.4)	
Other	1 (0.1)	5 (1)	
Autoimmune and autoinflammatory disease	1 (0.1)	7 (1.4)	
Congenital heart disease	-	8 (1.6)	
Immunodeficiency	-	3 (0.6)	
Vital sign on admission/triage			
Hypoxia	10 (1.5)	39 (7.8)	0.001
Fever	427 (64.6)	449 (89.9)	0.001
Tachypnea	9 (1.4)	27 (5.4)	0.001
Tachycardia	8 (1.2)	44 (8.8)	0.001
Hypotension	1 (0.2)	2 (0.4)	0.407

SD: Standard deviation, COVID-19: Coronavirus disease-2019

In the COVID-19 group, 57.3% of patients and their relatives reported a history of contact with a confirmed case, whereas this rate was 21% in the influenza group. Additionally, positive findings on respiratory system examination were observed in 28.7% of the influenza group compared to only 2.3% of the COVID-19 group (p=0.001). Upon triage and initial examination, patients with influenza exhibited significantly higher rates of fever, tachypnea, and tachycardia compared to those with COVID-19 (p=0.001).

Comparison of Radiologic and Laboratory Findings Between COVID-19 and Influenza

A total of 91.1% of patients in the COVID-19 cohort and 50.5% of those in the influenza cohort underwent chest radiography. Regarding chest X-ray (CXR) findings, 82.2% of children in the COVID-19 group had normal chest radiographs (p=0.001), whereas children in the influenza group exhibited significantly higher rates of patchy lung involvement (p=0.003) and consolidation (p=0.001). Platelet counts were significantly higher in the COVID-19 cohort than in the influenza cohort (p=0.001). Among infection-related biomarkers, CRP levels were significantly elevated in the influenza cohort compared to the COVID-19 cohort (4.92 mg/L vs. 0.94 mg/L, p=0.001). Regarding blood chemistry parameters, albumin and sodium levels were significantly higher in the COVID-19 cohort than in the influenza cohort (4.42 mg/dL vs. 4.02 mg/dL, p=0.01; 137.76 mmol/L vs. 135.92 mmol/L, p=0.011). Levels of aspartate aminotransferase (AST), alkaline phosphatase, serum creatinine, and creatine kinase (CK) were significantly lower in the COVID-19 pneumonia cohort compared to the influenza cohort (p=0.001) (Table 2).

The rate of viral coinfection was significantly higher in the influenza cohort than in the COVID-19 cohort (25.8% vs. 2.5%). The most commonly detected viral pathogens in the influenza cohort were respiratory RSV (20.2%) and rhinovirus (4.6%), (Table 3). Patients in the influenza cohort had more concurrent viral infections than COVID-19 patients. However, all patients with influenza with detected viral co-infections were in the mild disease group. The use of antibiotics and antiviral therapy (oseltamivir) was significantly more frequent among patients in the influenza cohort (p=0.001). Children in the influenza cohort required respiratory support more frequently than those in the COVID-19 cohort (p=0.07) and had a significantly higher need for high-flow nasal cannula therapy (p=0.022). Additionally, the influenza cohort exhibited higher hospitalization rates (p=0.001) and longer hospital stays (p=0.007) compared to the COVID-19 cohort.

Patients in the COVID-19 cohort were less symptomatic in terms of clinical severity, whereas children in the influenza cohort experienced mild, moderate, and severe and critical disease more frequently (p=0.001). Furthermore, the mortality

rate was higher in the influenza cohort (1.2%) than in the COVID-19 cohort (0.2%) (p=0.022) (Table 3).

Discussion

In this pediatric cohort study conducted at a tertiary referral hospital, we identified key factors associated with COVID-19 and influenza PCR-positive patients. Our findings confirm that influenza-infected patients have more severe symptoms, higher fever, higher rates of viral coinfection, longer hospital stays, higher hospitalization rates, greater need for ventilatory support, and significantly higher mortality.

This study provides an objective assessment of the severity of COVID-19 in comparison with influenza a similarly severe respiratory disease known for its seasonal outbreaks and pandemics. Worldwide, respiratory viruses remain a major cause of childhood morbidity and mortality. However, the differences between COVID-19 and other viral infections, particularly in the pediatric population, are not fully understood.[10] Recommendations for COVID-19 in children are derived predominantly from adult data, and without viral studies, it is difficult to differentiate COVID-19 from influenza through clinical findings alone. In meta-analyses and literature, fever and cough are the most common symptoms of COVID-19, and influenza in children. However, high fever, nasal congestion, rhinorrhea, vomiting, and muscle pain are more frequently observed in children with influenza compared to those with COVID-19. In contrast, diarrhea has been reported more commonly in children with COVID-19.[11,12] Notably, loss of smell and taste, which are characteristic symptoms of COVID-19 in adults, has been rarely reported in pediatric cases.[13] In our cohort, patients infected with influenza were significantly more symptomatic, with cough, fever, and rhinorrhea being more common among them. On the contrary, the frequency of nausea-vomiting, stomachache, and conjunctivitis in children with COVID-19 was less common than in patients with influenza. Skin rash was also less frequent in patients with COVID-19. Although erythematous rash or patchy exanthematous red rashes are dermal symptoms of COVID-19, childhood skin rashes are mostly similar to each other and do not contribute much to the differential diagnosis.[14] Although loss of taste and smell are common presenting symptoms in COVID-19 patients, these complaints were found to be less common (5.1%) in children than in adults and more common in patients with influenza.[13,15,16] This situation may be due to the difficulty children have expressing symptoms, such as loss of taste and smell, because infants and children have not fully developed the ability to recognize and express symptoms.

COVID-19 quickly became a pandemic spread quickly and easily among humans through oral and nasal droplets. As infected humans could be isolated due to pandemic measures, contact history was more manageable in the early period.[16] In our cohort, the history of contact for COVID-19 (57.4%) was

Table 2. Comparison of laboratory results in patients with COVID-19 and influenza patients

	Median (min-max)	Median (min-max)	p-value
Hemoglobin (g/dL)	13.4 (7.4-17.9)	12.4 (6.8-17.1)	0.331
Platelet (/mm³)	229000 (3800-570000)	209000 (18000-592000)	0.001
Leukocyte (/mm³)	6000 (400-23500)	6200 (500-25700)	0.485
Lymphocyte (/mm³)	1790 (90-14670)	2000 (100-12680)	0.121
Neutrophil (/mm³)	2965 (20-22000)	2950 (0-19100)	0.317
AST (U/L)	28 (6-526)	48 (16-547)	0.001
ALT (U/L)	17 (6-509)	21 (6-223)	0.06
BUN (mg/dL)	10.1 (2.2-30.1)	9.5 (2.5-46.2)	0.111
Creatinine (mg/dL)	0.5 (0.1-1.2)	0.4 (0.1-1.4)	0.49
Sodium (mg/dL)	138 (129-147)	136 (124-148)	0.011
Creatine kinase (mg/dL)	107 (26-301)	809 (0.3-36445)	0.001
CRP (mg/dL)	0.4 (0-22)	0.7 (0-41.0)	0.001
LDH (U/L)	244 (106-872)	343 (132-1478)	0.001
Total bilirubin (mg/dL)	0.3 (0.1-13.4)	0.3 (0.1-24)	0.173
PT (s)	12.1 (0.3-14.3)	12.5 (0.1-16.3)	0.396
APTT (s)	26.8 (21.6-32)	27.2 (21.6-112.7)	0.576
INR	1.0 (0.9-1.2)	1.1 (0.9-11)	0.019

AST: Aspartate aminotransferase, ALT: Alanin aminotransferaz, BUN: Blood urea nitrogen, CRP: C-reactive protein, LDH: Laktat dehidrogenaz, PT: Prothrombin time, APTT: Activated partial thromboplastin time, INR: International normalized ratio, COVID-19: Coronavirus disease-2019

Table 3. All results of respiratory samples, radiological findings and clinical characteristics in patients with COVID 19 and influenza

	COVID-19 n (%)	Influenza n (%)	p-value
Viral co-infection	17 (2.5)	129 (25.8)	0.001
RSV	1 (0.1)	101 (20.2)	
Human rhinovirus	9 (1.3)	23 (4.6)	
Coronavirus 229E	3 (0.4)	2 (0.4)	
Metapneumovirus	-	3 (0.6)	
Bocavirus	4 (0.6)	-	
Radiologic exam			
CT	25 (3.8)	-	n/a*
Chest X-ray	562 (91.1)	252 (50.5)	0.001
Chest X-ray findings			
Normal	504 (82.2)	42 (76.1)	0.001
Consolidation	13 (2.1)	24 (9.5)	0.001
Bilateral patchy infiltrates	6 (1)	10 (4)	0.003
Peribronchial thickening	44 (7.2)	22 (7.6)	0.435
Lung hyperaeration (bilateral)	-	4 (1.6)	n/a
Respiratory support	9 (1.4)	19 (3.8)	0.007
0_2 (nasal canula/mask)	8 (1.2)	9 (1.8)	0.405
High flow nasal canula	1 (0.2)	6 (1.2)	0.022
Intubation	1 (0.2)	4 (0.8)	0.094
Antibiotics	85 (12.9)	219 (43.8)	0.001
Oseltamivir	4 (0.6)	263 (52.7)	0.001
Disease severity			
Asymptomatic	50 (7.6)	11 (2.2)	0.001
Mild	589 (89.1)	373 (74.7)	0.001
Moderate	19 (2.9)	91 (18.2)	0.001
Serious-critical	3 (0.5)	24 (2.3)	0.001
Exitus	1 (0.2)	6 (1.2)	0.022
Length of stay (day)	2 (1-5)	4 (2-8)	0.007
Hospitalization	93 (14.1)	182 (36.5)	0.001
Transfer to PICU	2 (0.3)	5 (0.6)	0.128

*n/a: Not applicable, RSV: Respiratory syncytial virus, CT: Computed tomography, PICU: Pediatric intensive care unit, COVID-19: Coronavirus disease-2019

significantly higher than for influenza (2.8%), while in the study involving 8886 pediatric patients, this rate was found to be 71.3%.[17] The COVID-19 pandemic has overwhelmed healthcare systems. Therefore, it is important to evaluate patients in triage. There are few studies assessing vital signs in triage. In the triage, 43.1% of COVID-19 positive patients had tachycardia, 30.7% had fever, and 20.4% had hypoxia, which is relatively low in our patient group.[18] Only fever was detected in two-thirds of the COVID-19-positive children, and this rate was 89.9% in influenza-positive children. We also found tachycardia and tachypnea, at a higher rate in triage at admission. CRP levels have been found to be lower in COVID-19 patients compared to those with influenza.[13] While there is no significant difference in total white blood cell count, neutrophil levels have been reported to be lower in COVID-19 cases.[13] Findings from laboratory comparisons vary significantly. Some studies have reported higher levels of CRP, procalcitonin, alanin aminotransferaz, AST, and laktat dehidrogenaz in influenza patients; however, no significant difference in lymphocyte counts has been observed between the two groups.[19,20] We found no difference among patients regarding leukopenia, lymphopenia, and neutropenia. However, elevated CRP was significantly more common in the influenza cohort. There is substantial evidence suggesting that COVID-19 induces a milder inflammatory response in children compared to influenza. Although AST elevation, sodium elevation, and increased creatinine kinase values were more common, in the influenza patient group as biochemistry parameters, neither hemogram nor biochemistry change is indicative of disease differentiation. The underlying pathogenesis of this disorder remains unclear. Influenza is one cause of the benign acute childhood syndrome, so it is not surprising that elevated CK levels are detected in patients with influenza. In COVID-19 patients, coagulation parameters can be helpful in the timely treatment and prognosis, but thromboembolic events are rare in pediatric patients with COVID-19 infection.[21,22]

CXR are an important tool for clinical and epidemiological characteristics. Children are less studied than adults, and rapid diagnosis is challenging due to asymptomatic or mild episodes.[23] Although physicians tend to examine CXR to help diagnose COVID-19 cases of pneumonia, abnormalities in CXR were more often present in the influenza cohort. While 82.2% of the chest radiographs in the COVID-19 cohort were normal, this rate was 76% in the influenza group. Findings are non-specific, therefore, CXR cannot be used to screen for a condition or as a first-line diagnostic test. Therefore, national and international guidelines should be considered when taking CXR in children, and unnecessary radiation should be avoided. Although there are few studies on infections in children, the frequency of coinfection was 4.7% in children at the beginning of the pandemic, while in the systematic review and meta-analysis involving adult patients, 8.9% of the patients had coinfection, and it was 2.5% in our COVID-19 patient group.[24,25] Quick management with oseltamivir reduces the duration of symptoms and the risk of complications (bronchitis, otitis media, and pneumonia), and hospitalization, and decreases mortality among high-risk populations.[26] However, the use of respiratory viral tests remains controversial. Although it is recommended that the patient is immunocompromised, has chronic medical conditions, or is hospitalized, additional care should be considered. It can also be taken more frequently than typical

routine practices to determine the prevalence of diseases and to separate patient cohorts, especially in pandemic conditions such as COVID-19.[26,27] Respiratory PCR tests were taken before starting oseltamivir treatment. Despite this, 52.7% of the patients were started on oseltamivir. Therefore, we recommend starting antiviral therapy for non-severe patients with confirmed-influenza at high risk for severe or complicated illness. In the COVID-19 pandemic, there has been a dramatic shift in the patterns of traditionally seasonal respiratory viruses, which may be the result of changes in children.[28] In addition, due to restrictions and social isolation, other respiratory viruses, besides COVID-19, have started to be seen at all times of the year and have confused their routine seasonal calendar.[29] Therefore, the scope of our study is significant in evaluating the COVID-19 and influenza cases from the beginning of the COVID-19 pandemic until recently. Does COVID-19 present a milder course in children compared to influenza? The key question remains: which poses a greater risk? In our study, when clinical and treatment needs were compared, influenza was more severe and required extended hospitalization, and children with influenza needed more respiratory support. It is now better known that clinical symptoms of COVID-19 in children tend to be milder,[1,30] as supported by the results of our study. Six patients in the influenza group and one in the COVID-19 group died in our patient cohort. While the child who died in the COVID-19 group had an underlying immune deficiency, the three children in the influenza group were previously healthy with no known disease. The results of our study revealed that COVID-19 is commonly a mild disease in children, and a small proportion of children (3.4%) have a moderate to severe course, requiring intensive care support and long-term mechanical ventilation. Furthermore, we confirmed that fatal outcomes with COVID-19 in children are rare. As seen in our study, influenza continues to be a significant cause of mortality and morbidity in children; however, there was low circulation of influenza during the beginning of the COVID-19 pandemic.[30,31] 2023-2024 season in the US. In outpatient settings, children tested for influenza were more likely to have positive results compared to adults.[32] During the 2023-2024 influenza season, the mortality rate of children hospitalized with an influenza diagnosis was found to be 2.2%.[32] This unpredictable situation may be a reminder that influenza will be more challenging for children in the coming months. In all this chaos, children require more protection during the pandemic. Our findings emphasize the importance of vaccination programs for both influenza and COVID-19 to reduce disease burden in children.

Study Limitations

There are some limitations to our study. It is a single-center study. CXR were especially frequently taken at the beginning of the pandemic. We could not include point-of-care ultrasound examinations in our study due to the lack of standardization of lung ultrasound in COVID-19. Also, all children in both cohort groups were unvaccinated. In our study, we only used a viral respiratory tract panel, but not a bacterial panel because, given the volume of patients and the current standard of care, using bacterial panels is not particularly feasible in the emergency department (ED), where they are often not available to guide diagnosis and treatment. Given the presence of different COVID-19 variants during and after the pandemic, this factor could not be evaluated in the analysis. This limitation exists because variant identification was performed by the central government laboratory for epidemiologic surveillance through random sampling. The differentiation between bacterial and viral upper respiratory tract infections represents a significant challenge in clinical practice. To reduce the empiric use of antibiotics and improve outcomes, there is a need for improved diagnostics that can provide practitioners with rapid information regarding the underlying etiology, thereby enabling them to make more informed decisions. To have a global impact, including in low-income settings, such diagnostics should consider the recently defined target infections, as proposed by experts from academic centers and multicenter studies.[33]

Conclusion

In our pediatric cohort, influenza imposed a significantly greater clinical burden than COVID-19, presenting with higher peak fevers, more severe clinical presentation, increased rates of viral coinfections, prolonged hospital stays, greater need for ventilatory support, and notably higher mortality. These findings reaffirm that, while COVID-19 in children is generally mild and self-limiting, influenza continues to be a major driver of severe respiratory morbidity and mortality. Based on these results, several priorities emerge for pediatric emergency care: implementation of rapid, PCR-based viral diagnostics to guide isolation protocols and therapeutic interventions; reinforcement of seasonal vaccination strategies for both influenza and COVID-19 to mitigate preventable illness; and strengthening of multicenter research networks-particularly in vaccinated pediatric populations and utilizing standardized point-of-care tools-to better characterize emerging variants, guide targeted antiviral therapy, and refine triage algorithms. Strengthening these approaches has the potential to reduce unnecessary antibiotic use and alleviate resource burdens in overcrowded ED.

Ethics

Ethics Committee Approval: The study was approved by the Ethics Committee of Hacettepe University under registration

code GO22/1242, date: 13.12.2022. The ethics committee reviewed our study and waived the need for informed consent, as all data and samples were analyzed retrospectively and collected as part of routine clinical practice in accordance with current guidelines.

Informed Consent: Informed consent was not required and therefore not obtained, as the study was conducted retrospectively and involved no direct patient intervention.

Footnotes

Author Contributions

Surgical and Medical Practises: E.G., Ö.T., Concept: E.G., A.Z.B., Ö.T., Design: E.G., H.Y., A.Z.B., Ö.T., Data Collection or Processing: E.G., H.Y., B.A., A.Z.B., A.A., Ö.T., Analysis or Interpretation: E.G., H.Y., B.A., A.Z.B., A.A., Ö.T., Literature Search: E.G., H.Y., B.A., A.Z.B., Ö.T., Writing: E.G., Ö.T.

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