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ARAŞTIRMA YAZISI / RESEARCH ARTICLE

SARS-COV-2, İNFLUENZA VE RESPİRATUAR SİNSİTYAL VİRÜS PNÖMONİLERİ NEDENİYLE HASTANEDE YATAN HASTALARIN KLİNİK ÖZELLİKLERİNİN KARŞILAŞTIRILMASI

COMPARISON OF CLINICAL CHARACTERISTICS OF PATIENTS HOSPITALIZED DUE TO SARS-COV-2, INFLUENZA AND RESPIRATORY SYNCYTIAL VIRUS PNEUMONIA

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ÖZET

AMAÇ: İnfluenza, respiratuar sinsityal virüs (RSV) ve şiddetli akut solunum yolu sendromu koronavirüs-2 (SARS-CoV-2) enfeksiyonu damlacıklar yoluyla yayılan, benzer semptom ve radyolojik bulguları olan ve solunum yetmezliğine neden olabilen etkenlerdir. Bu çalışma yeni koronavirüs hastalığı (COVID-19), influenza ve RSV pnömonisi olan hastaların klinik özelliklerini ve mortalite oranlarını karşılaştırmak için yapılmıştır.

GEREÇ VE YÖNTEM: Başkent Üniversitesi Tıp Fakültesi Hastanesi'nde COVID-19, influenza ve RSV pnömonisi nedeniyle yatırılan toplam 182 hasta çalışmaya dahil edildi. Hastalar klinik durumlarına göre gruplandırıldı. Hastaların demografik özellikleri, komorbiditeleri, laboratuvar ve radyolojik bulguları, solunum destek tedavileri ve mortalite oranları kaydedildi ve gruplar arasında karşılaştırıldı.

BULGULAR: Ortalama yaş COVID-19 grubunda (n:115) 69.4±7 yıl, influenza grubunda (n:33) 72,9±17,1 yıl ve RSV grubunda (n:34) 66,5±22,4 yıl idi. Gruplar arasında yaş farkı yoktu (p=0,305). COVID-19 grubunda erkek hastaların hastane yatış oranı daha fazlaydı (p=0,036). Komorbiditeler açısından gruplar arasında fark yoktu (p>0.05). COVID-19, RSV ve influenza hasta grupları arasında mortalite oranları açısından fark yoktu (p=0.260).

SONUÇ: Pulmoner tutulumlu viral enfeksiyonlar kötü klinik seyir gösterebildikleri için özel dikkat gerektirirler. İçinde bulunduğumuz yüzyılda ölümlere neden olan COVID-19 pnömonisinin klinik seyrinin şiddeti, influenza ve RSV gibi viral enfeksiyonların klinik seyrinden farklı değildir.

ANAHTAR KELİMELER: COVID-19, İnfluenza, Pnömoni, Solunum sinsityal virüsü.

ABSTRACT

OBJECTIVE: Influenza, respiratory syncytial virus (RSV), and severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection are agents that spread through droplets, have similar symptoms and radiological findings, and can cause respiratory failure. This study was conducted to compare the clinical features and mortality rates of patients with novel coronavirus disease (COVID-19), influenza, and respiratory syncytial virus pneumonia.

MATERIAL AND METHODS: A total of 182 patients who were hospitalized at Baskent University Medical Faculty Hospital due to COVID-19, influenza, and RSV were included in the study. Patients were grouped according to their clinical status. Demographic characteristics, comorbidities, laboratory and radiological findings, respiratory support treatments and mortality rates of the patients were recorded and compared between the groups.

RESULTS: The mean age was 69.4±7 years in the COVID-19 group (n:115), 72.9±17.1 years in the influenza group (n:33), and 66.5±22.4 years in the RSV group (n:34). There was no difference in age between the groups (p=0.305). The hospitalization rate was higher for male patients in the COVID-19 group (p=0.036). There was no difference between the groups in terms of comorbidities (p>0.05). There was no difference in mortality rates between the COVID-19, RSV, and influenza patient groups (p=0.260).

CONCLUSIONS: Viral infections with pulmonary involvement require special attention because they can have a poor clinical course. The severity of the clinical course of COVID-19 pneumonia, which causes deaths in the current century, is not different from the clinical course of viral infections such as influenza and RSV.

KEYWORDS: COVID-19, Influenza, Pneumonia, Respiratory syncytial virus.

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INTRODUCTION

Community-acquired pneumonia (CAP) is an important cause of mortality and morbidity. Respiratory tract viruses have been identified in approximately 25% of patients with CAP (1). In previous studies, it was reported that Respiratory syncytial virus (RSV) was responsible for 4.1% of hospitalizations due to pneumonia and influenza was responsible for 3.5% (2).

Since the beginning of the novel coronavirus disease (COVID-19) pandemic, the newly identified severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has been compared with other respiratory viruses in daily clinical practice. Due to similar clinical features, it is difficult to diagnose according to symptoms in the early period. Studies have revealed that symptoms such as fever, cough, myalgia, headache, and wheezing are seen in all of these respiratory tract viral infections, however there are differences in symptom frequency (3). This study aimed to compare seasonal influenza RSV infections and with, with the yet unfamiliar SARS-CoV-2 infection in hospitalized patients clinically, laboratory, and radiologically, and to determine their similar and different features.

MATERIALS AND METHODS

Study Population

The study was designed as a retrospective observational study. Patients aged 18 years and older who were hospitalized in Baskent University Medical Faculty Hospital due to influenza and RSV pneumonia (between January 2015-January 2020) and COVID-19 pneumonia (between March 2020-September 2021) were included in the study. The electronic and medical records of the patients were reviewed. Age groups were divided into groups as 20-49, 50-69, 70 and over. The patients' demographic characteristics, comorbidities, vital signs, laboratory and radiological findings, respiratory support treatments, corticosteroid requirements, length of hospital stay, hemodialysis requirements, and mortality rates were recorded. Patients were divided into three groups as influenza patients, RSV patients, and COVID-19 patients. Patients were divided into groups according to their clinical status as mild-moderate pneumonia and severe pneumonia (pneumonia requiring intensive care admission). Grouping was based on national COVID-19 guidelines (4). Radiological evaluations were performed by a double-blind independent radiologist and pulmonologist. Comparisons were made between groups. Comparisons were also made between deceased and living patients.

Virus Identification

RSV Nucleic Acid Detection Kit (Quidel, Sofia RSV FIA, SanDiego, CA92121 USA) and FA/FB Virus Nucleic Acid Detection Kit (Quidel, Sofia Strep A+ FIA, SanDiego, CA92121) were used for the diagnosis of RSV and influenza infection. Nucleic acid kit (Bioeksen, Turkey) was used for polymerase chain reaction (PCR) analysis of nasopharyngeal swab samples for the diagnosis of SARS-CoV-2.

Ethical Committee

This study was approved by Baskent University Medical and Health Sciences Research Board (Project no: KA20/452 date: 15.12.2020) and funded by Baskent University Research Fund.

Statistical Analysis

The suitability of numerical variables to normal distribution was examined with the Kolmogorov-Smirnov test of normality and mean ± standard deviation for normally distributed variables and median (minimum-maximum) values for non-normally distributed variables were given as descriptive statistics. Categorical variables are shown as frequency (n) and percentage (%). Kruskal-Wallis analysis of variance was used to analyze the differences in the measurement variables according to the groups. Post-Hoc Tukey test was performed to define which group or groups are significant from each of them. Chi-square and Fisher Exact Tests were used to test the mortality rates in each group according to the age group and gender and also according to the existence of comorbidities and cancer in each group of patients. In testing the significance of categorical variables between groups, the Pearson Chi-Square test was used in case of assumptions were met and the Fisher Exact Chi-Square test was used if not. Type I error probability was determined as $\alpha=0.05$ in all hypothesis tests and statistical evaluations were made using the SPSS v25.0 software package.

RESULTS

A total of 182 patients were included in the study. The mean age was 69.4±7 years in the COVID-19 group (n:115), 72.9±17.1 years in the influenza group (n:33), and 66.5±22.4 years in the RSV group (n:34). There was no difference in terms of age between the groups (p=0.305). The hospitalization rate was higher for male patients in the COVID-19 group (p=0.036) **(Table 1)**.

Table 1: Demographic characteristics

	COVID-19(n=115)	Influenza(n=33)	RSV(n=34)	p
Age (Mean±sd)	69.4 ±7	72.9±17.1	66.5±22.4	0.305
Female (n,%)	40(34.8)	19(57.6)	17(50.0)	
Male (n,%)	75(65.2)	14(42.4)	17(50.0)	0.036
COPD (n,%)	23(20.0)	8(24.2)	9(26.5)	0.683
Asthma (n,%)	4(3.5)	2(6.1)	3(8.8)	0.385
HT (n,%)	78(67.8)	22(66.7)	23(6.6)	0.992
CAD (n,%)	63(55.8)	13(39.4)	21(6.8)	0.150
Cancer (n,%)	14(12.2)	8(24.2)	2(5.9)	0.083
CRF-CKD (n,%)	27(25.2)	6(18.2)	8(23.5)	0.706
Liver disease (n,%)	8(7.0)	2(6.1)	2(5.9)	0.967
DM (n,%)	39(33.9)	11(33.3)	16(47.1)	0.348

COPD: chronic obstructive pulmonary disease, HT: hypertension, CAD: coronary artery disease, CRF-CKD: chronic kidney disease, chronic kidney failure, DM: diabetes mellitus

p<0.05, significant

The most common comorbidities were a chronic obstructive pulmonary disease, hypertension, coronary artery disease, congestive heart failure, solid organ and hematological malignancies, diabetes mellitus, chronic kidney failure, and chronic liver disease. There was no difference between the groups in terms of comorbidities (p>0.05), (Table 1). Fever was more common in COVID-19; dyspnea was more common in influenza and RSV; cough was more common in COVID-19 and RSV patients (p=0.007, p<0.00, p=0.018, respectively) **(Table 2)**.

Table 2: Distribution of symptoms

	COVID-19 (n=115)	Influenza (n=33)	RSV (n=34)	p
Fever (n,%)	58(50.4)	7(21.2)	12(35.3)	0.007
Cough (n,%)	52(45.6)	6(18.2)	14(41.2)	0.018
Dyspnea (n,%)	56(49.1)	28(84.8)	27(79.4)	0.001
Fatigue (n,%)	58(52.3)	3(60.0)	6(17.6)	0.062
Joint pain (n,%)	18(16.4)	1(3.0)	-	0.171
Nausea (n,%)	5(4.4)	2(66.7)	2(5.8)	0.001
Diarrhea (n,%)	10(8.8)	-	2(66.7)	0.036

*p<0.05, significant

In our study, dyspnea was a notable symptom in patients who died due to COVID-19 infection (p=0.033). Laboratory findings of COVID-19, influenza, and RSV groups are presented in **(Table 3)**. Radiological findings of COVID-19, influenza, and RSV groups are presented in **(Table 4)**.

Table 3: Laboratory findings

	COVID-19 (n=115) Mean±sd	Influenza (n=33) Mean±sd	RSV (n=34) Mean±sd	p
WBC	9.4±5.9	15.6±9	12.2±5.8	0.001
Plt	213.7±91.5	224.4±135.8	213.3±98	0.942
Neutrophil	7.3±5.6	13.4±8.5	10.3±5.6	0.001
N/L	7.9±7.7	20.6±20.2	15±16.2	0.001
Lymphocyte	1.2±0.6	1.3±1.5	1.1±0.9	0.079
AST	28.4±36.1	103.3±377.4	37±73.1	0.447
AST	36.3±39.9	124.2±345	46.2±62.6	0.369
BUN	32.9±23.7	36.9±26.3	33.4±15.4	0.335
Creatine	1.8±1.7	1.6±1.3	1.5±1.2	0.397
Procalcitonin	2.7±9.7	3.8±9.1	5.2±18.6	0.002
CRP	97.3±94.9	120.6±77.4	91.9±75.3	0.094
Ck-MB	2.3±3.3	2.9±2.9	2.9±3.4	0.164
Troponin	230.2±901.9	0.2±0.3	0.5±1.2	0.001
Ferritin	553.7±556.9	175±132.3	578.5±714.9	0.362
D-dimer	3.1±5.4	2.5±1.8	4.0±4.3	0.178

WBC: White blood cell. Plt: Platelet. N/L: Neutrophil/lymphocyte ratio. AST: Aspartate aminotransfer
ALT: Alanine aminotransferase. BUN: Blood urea nitrogen. CRP: C-reactive protein.
Ck-MB: Creatine kinase myocardial band. p<0.05, significant

Table 4: Radiological findings

	COVID-19 (n=115) n (%)	Influenza(n=33) n (%)	RSV(n=34) n (%)	p
Right lung involvement	91 (79.1)	27 (87.1)	22 (66.7)	0.130
Left lung involvement	83 (72.2)	24 (77.4)	20 (60.6)	0.297
Bilateral involvement	77 (67.0)	21 (67.7)	18 (54.5)	0.392
Upper lobe involvement	62 (54.4)	12 (38.7)	8 (25.0)	0.008
Middle lobe involvement	41 (35.7)	10 (32.3)	6 (18.8)	0.193
Lower lobe involvement	79 (69.3)	28 (90.3)	24 (75.0)	0.060
Central involvement	37 (33.9)	-	-	0.129
Peripheral involvement	92 (84.4)	-	-	0.001
Unifocal	20 (17.4)	10 (32.3)	7 (21.9)	0.192
Multifocal	84 (73.0)	18 (58.1)	15 (46.9)	0.014
Ground glass	88 (76.5)	6 (19.4)	9 (28.1)	0.001
Consolidation	38 (33.0)	11 (35.5)	8 (25.0)	0.622
Nodule	17 (14.8)	12 (38.7)	8 (25.0)	0.012
Cavity	4 (3.5)	2 (6.5)	2 (6.3)	0.651
Pleural effusion	37 (32.2)	20 (64.5)	17 (51.5)	0.002

p<0.05, significant

While consolidation including middle lobe involvement and air bronchogram was more common in deceased COVID-19 patients (p=0.028, p=0.037, respectively), no significant radiological finding was observed in deceased influenza and RSV patients. Clinical status and respiratory support treatments of COVID-19, influenza, and RSV groups are presented in **Table 5.**

Table 5: Clinical status and respiratory support treatments

	COVID-19 (n=115)	Influenza (n=33)	RSV (n=34)	p
Clinic status (n,%) mild-moderate	75 (65.2)	9 (27.3)	8 (23.5)	0.001
Clinic status (n,%) severe	40 (34.8)	24 (72.7)	26 (76.5)	
SpO_2 at hospitalization (mean±SD)	90.28±7.5	79.5±7.8	83.2±8.4	0.001
SpO_2 at discharge (mean±SD)	94.4±2.7	91.4±4.2	94.5±3.5	0.001
Length of hospital stay (days) (mean±SD)	7.3±9.4	4.1±4.5	8.1±11.6	0.001
Length of ICU stay (days) (mean±SD)	2.7±4.9	8.2±8.8	9.2±11.5	0.006
Nasal O_2 (n,%)	75 (66.4)	30 (90.9)	30 (88.2)	0.002
HD (n,%)	22 (19.6)	5 (15.2)	9 (26.5)	0.502
HFOT (n,%)	19 (16.8)	12 (36.4)	6 (17.6)	0.045
NIMV (n,%)	9 (8.0)	17 (51.5)	14 (41.2)	0.01
IMV (n,%)	19 (17.0)	15 (45.5)	15 (44.1)	0.01
ECMO (n,%)	1 (0.9)	-	-	0.999
Mortality (n,%)	26 (22.6)	12 (36.4)	10 (29.4)	0.260
Antibiotic use (n,%)	106 (96.4)	32 (97.0)	31 (91.2)	0.520
Steroid (n,%)	66 (58.4)	23 (69.7)	24 (70.6)	0.288
Peripheral or central thrombosis (n,%)	26 (23.9)	5 (15.2)	2(5.9)	0.054

SpO_2: mean oxygen saturation. O_2: oxygen. HD: hemodialysis. HFOT: High flow oxygen therapy. NIMV: Noninvasive mechanical ventilation. IMV: Invasive mechanical ventilation. ECMO: Extracorporeal membrane oxygenation.

p<0.05, significant

There was no difference in mortality rates according to age groups among the COVID-19, influenza, and RSV groups (p=0.051, p=0.255, p=0.263, respectively). There was no difference in mortality rates by gender between the COVID-19, influenza, and RSV groups (p=0.625, p=0.506, p=0.452, respectively). Mortality rates were higher in cancer patients in the influenza group (p=0.009). There was no difference in mortality rates between the groups according to other comorbidities (p>0.05). Corticosteroid (p=0.008), broad-spectrum antibiotic use (p<0.05), and the need for Invasive mechanical ventilation (IMV) were found to be higher in patients in the deceased COVID-19 group (p<0.05). It was observed that the need for IMV was higher in patients who died due to influenza and RSV (p<0.001 and p<0.001). Favipiravir was used in all COVID-19 patients and Oseltamivir was used in all influenza patients. Oseltamivir was used until diagnosis in 38% of RSV patients. No specific antiviral therapy was given for RSV.

In the COVID-19 group, mean neutrophil count (p=0.036), Neutrophil/lymphocyte ratio (N/L) (p=0.040), creatine (p=0.042), D-dimer (p=0.042), lactate dehydrogenase (LDH) (p=0.014), troponin (p=0.004), creatine kinase (Ck-MB) (p=0.046), and blood urea nitrogen (BUN) were elevated in patients who died (p=0.01). Alanine aminotransferase (ALT) (p=0.01), aspartate aminotransferase (AST) (p=0.01), sodium (p=0.007), prothrombin time (PT) (p=0.036) and LDH in patients who died due to influenza infection (p=0.043) values were found to be higher. N/L ratio and D-dimer values were found to be higher in patients who died from RSV infection (p=0.034 and p=0.016, respectively).Peripheral or central thrombosis was significantly more frequent in the COVID-19 group (23.9%) than in influenza (15.2%) and RSV (5.9%) groups (p=0.054) table 5. Of the COVID-19 patients with thrombosis, 43.5% died (p=0.013).

DISCUSSION

In COVID-19, influenza and RSV pneumonia, patients with chronic disease, diabetes, malignancy, obesity, and immunosuppressive diseases, living in nursing homes, and patients over 65 years of age are in the high-risk group for hospitalization and mortality (5 - 13). In our study, in which we compared three viral infection groups with similar clinical courses and lung involvement, no difference was observed in terms of hospitalization rates according to age in all three groups. No difference was found for comorbid diseases. Bradley et al. showed that adults hospitalized for RSV compared to influenza were slightly older and had more comorbidities (14). COVID-19, influenza, and RSV have similar symptoms. Early diagnosis is difficult based on symptoms. However, some symptoms may be more prominent (3). In our study, fever was a more remarkable symptom in patients with COVID-19. Dyspnea was more prominent in influenza and RSV patients. Cough was more common in COVID-19 and RSV patients than in influenza patients.

It has been reported that the most common symptom of influenza in hospitalized patients is cough (96%), followed by fever (64%) (15). Cough, wheezing and shortness of breath are prominent in RSV pneumonia (8). In a study comparing hospitalized patients with a diagnosis of RSV and influenza, it was reported that wheezing was more common in patients with RSV and fever was more com-

mon in patients with influenza (16). It has been reported that the most common symptoms of COVID-19 disease are fever (98.6%), fatigue (69.6%) and dry cough (59.4%) (17).

The high D-dimer, CRP and ferritin values measured during hospitalization in patients with COVID-19, influenza and RSV in our study showed that the changes in these laboratory parameters were not specific to COVID-19. All these findings indicate that laboratory values will not be a distinguishing feature between the three viral infection groups in the initial stage of the disease. In the study of Cobb et al., D-dimer was elevated in both influenza and COVID-19 groups (18). In our study, troponin level was higher in the COVID-19 group. At hospital admission, there was no other early symptomatic laboratory parameter that could be distinguishable for COVID-19, except troponin. In our study, it was observed that the rate of leukocytosis, neutrophilia, and N/L was significantly higher in the RSV and influenza groups than COVID-19 group. Similarly, in the study of Torun et al., leukocyte and neutrophil levels were found to be higher in influenza patients compared to patients with COVID-19 (19). In the study by Cobb et al., consistent with our study, leukocytes were found to be higher in the influenza group than in the COVID-19 group, lymphocyte counts were similar, and D-dimer was higher in both groups (18). Gao et al. reported that lymphopenia is an important laboratory finding in patients hospitalized with the diagnosis of influenza (20). Wang et al also reported that lymphopenia is an important laboratory finding that may also have prognostic potential in COVID-19 (17).

In our study, there was no difference in lymphocyte count between the groups. In our study, high neutrophil, N/L ratio, BUN, creatine, D-dimer, LDH, troponin, Ck-MB values were associated with mortality in COVID-19. In studies, high troponin levels have also been associated with adverse aspects of COVID-19 disease, such as myocardial damage and death (21). High ALT, AST, sodium, PT, LDH values were associated with mortality in influenza. Gao et al also showed in univariate analysis that higher than normal AST level is a risk factor for ARDS in influenza (20). High N/L and D-dimer values were associated with mortality in RSV. Thoracic computed tomography has been a frequently used imaging method in the COVID-19 pandemic in patients presenting with low oxygen saturation and dyspnea symptoms. We observed that there are more and predominantly peripheral and multifocal ground glass infiltrations in COVID-19 compared to influenza and RSV. In the study by Tang et al., ground glass opacities were observed more commonly in COVID-19 patients than in influenza patients (22). Onigbinde et al. analyzed 17 studies on COVID-19 and influenza. They reported that in COVID-19, ground-glass opacities are usually located in the lower lobes and peripherally, whereas in influenza they show a central, peripheral, or random distribution, usually affecting the five lobes (23). Although the radiological findings of most viral pneumonia are similar, the distinguishing radiological findings in COVID-19 were helpful in the diagnosis. As the disease progresses in COVID-19, consolidation becomes the dominant CT finding (24). We observed more frequent consolidations involving air bronchograms in deceased COVID-19 patients.

We found that in our study, hospitalization and discharge oxygen saturations were higher, and nasal oxygen, HFOT, and MV requirements were lower in COVID-19 patients. This situation has been attributed to the fact that patients with a diagnosis of COVID-19 were hospitalized in the early stages, without desaturation, by generalizing the indications for hospitalization. In the study of Cobb et al., the IMV requirement and ARDS rates of influenza and COVID-19 patients were found to be similar. However, they found that critically ill patients with COVID-19 had twice the risk of hospital mortality compared to influenza patients (18). In our study, there was no difference between the COVID-19, influenza, and RSV groups in terms of death rates according to age group and gender. Mortality rates were higher in cancer patients in the influenza group. In the study of Tang et al., the mortality of influenza patients was found to be significantly higher than that of COVID-19 patients (22). The study of Cobb et al. was conducted in the early stages of the pandemic, and corticosteroids, which were shown to improve outcomes in subsequent studies, were not routinely used (18). However, corticosteroid treatment, which was shown to improve outcomes in CO-

VID-19 patients was included in our study and was routinely used in selected cases (25, 26). In our study, the longest intensive care unit (ICU) length of stay was in the RSV group, followed by the influenza group, and the length of ICU stay of COVID-19 patients was considerably shorter than these two groups. These results should not suggest that COVID-19 patients have a shorter need for ICU length of stay and should not create unnecessary optimism, because, in the context of the COVID-19 infection, which caused a pandemic, some severely but stabilized patients were transferred from the ICU to the normal ward to continue their NIMV and HFOT just to quickly make room for new patients in ICU.

Escherichia coli, Staphylococcus aureus, Stenotrophomonas maltophilia, Klebsiella pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii, Aspergillus fumigatus, Candida species were isolated in sputum as coinfection and superinfection, in deep tracheal aspirate and bronchial lavage in all three groups. There was no difference in the distribution of agents. Studies with more participants are needed on this subject. Broad-spectrum antibiotics and antifungal treatments were used in all three groups. Although the clinical process and results are similar, causative isolation should be performed in viral pneumonia, so that viral infections with specific treatment are determined and unnecessary antibiotic treatment is avoided by distinguishing between virus and bacterial infection.

Our study has some limitations. Our data involves hospitalized patients only. Laboratory and radiological findings are values obtained only on the first day of hospitalization and may have changed in the course of the disease. The fact that the number of patients hospitalized due to influenza and RSV pneumonia was insufficient in the data set caused the participant difference. Some of the COVID-19 and influenza patients were not vaccinated. Due to the absence of an FDA-approved vaccine for RSV, an evaluation for vaccination could not be made in our study.

Viral infections with pulmonary involvement require special attention because they can have a poor clinical course. The severity of the clinical course of COVID-19 pneumonia, which causes deaths in the current century, is not different from the clinical course of viral infections such as influenza and RSV.

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