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THE CLINICAL CHARACTERISTICS OF INFLUENZA AND OTHER VIRAL RESPIRATORY INFECTIONS IN THE INTENSIVE CARE UNIT: A ONE-YEAR SINGLE-CENTER RETROSPECTIVE STUDY

YOĞUN BAKIM ÜNİTESİNDE İNFLUENZA VE DİĞER SOLUNUM YOLU VİRAL ENFEKSİYONLARININ KLİNİK ÖZELLİKLERİ: BİR YILLIK TEK MERKEZLİ RETROSPEKTİF ÇALIŞMA

Volkan Alparslan[1*], Özlem Güler[2], Samet Kutlu[1], İpek İzgin Avcı[1], Aynur Karadenizli[3], Nur Baykara[1], Alparslan Kuş[1]

[1]Kocaeli University, Faculty of Medicine, Department of Anesthesiology and Reanimation, Kocaeli, Türkiye. [2]Kocaeli University, Faculty of Medicine, Department of Infectious Diseases and Clinical Microbiology, Kocaeli, Türkiye. [3]Kocaeli University, Faculty of Medicine, Department of Medical Microbiology, Kocaeli, Türkiye.

ABSTRACT

Objective: The aim of this study was to evaluate the clinical features and prognostic factors associated with mortality in respiratory viral infections in intensive care unit patients.

Methods: This retrospective, single-centre study included adult patients aged ≥18 years who were admitted to the intensive care unit of Kocaeli University Faculty of Medicine between March 2024 and March 2025 and whose respiratory viral agent was detected by BioFire® Respiratory 2.1 Plus Panel test. Demographic data, clinical and pneumonia scoring systems (APACHE II, SOFA, PSI, CURB-65), laboratory parameters and patient prognosis (survived/non survived) were analysed.

Results: A total of 547 out of 2719 intensive care unit patients underwent respiratory panel, and at least one viral agent was detected in 95 (17.4%) of them. The most frequently detected viruses were rhinovirus/enterovirus (n=22), SARS-CoV-2 (n=15) and influenza A-H3 (n=23). The intensive care unit mortality rate was 54.3% in viral positive patients. APACHE II, SOFA, PSI and CURB-65 scores as well as urea and procalcitonin levels were found to be significantly higher in patients with non-survived ($p<0.05$). Although mortality rates due to viral agents differed according to subgroups, this difference was not statistically significant ($p=0.215$).

Conclusion: Respiratory viral infections in intensive care unit patients are associated with mortality, especially in individuals with high clinical severity scores and some laboratory parameters. These findings need to be confirmed with larger sample, multicentre, prospective studies.

Keywords: Respiratory viruses, intensive care unit, influenza, COVID-19, APACHE II, SOFA

ÖZ

Amaç: Bu çalışmanın amacı, yoğun bakım hastalarında saptanan solunum yolu viral enfeksiyonlarının klinik özelliklerini ve mortalite ile ilişkili prognostik faktörleri değerlendirmektir.

Yöntem: Bu retrospektif, tek merkezli çalışmaya, Mart 2024 – Mart 2025 tarihleri arasında Kocaeli Üniversitesi Tıp Fakültesi yoğun bakım ünitesine kabul edilen ve BioFire® Respiratory 2.1 Plus Panel testi ile solunum yolu viral etkeni saptanan ≥18 yaş erişkin hastalar dahil edildi. Demografik veriler, klinik ve pnömoni skorlama sistemleri (APACHE II, SOFA, PSI, CURB-65), laboratuvar parametreleri ve hasta prognozu (yaşam/exitus) analiz edildi.

Bulgular: Toplam 2719 yoğun bakım hastasından 547'sine solunum paneli uygulanmış, bunların 95'inde (%17,4) en az bir viral etken saptanmıştır. En sık tespit edilen virüsler rhinovirüs/enterovirüs (n=22), SARS-CoV-2 (n=15) ve influenza A-H3 (n=23) olmuştur. Viral pozitif hastalarda yoğun bakım mortalite oranı %54,3 bulunmuştur. Ölen hastalarda APACHE II, SOFA, PSI ve CURB-65 skorlarının yanı sıra üre ve prokalsitonin düzeylerinin anlamlı derecede yüksek olduğu görülmüştür ($p<0,05$). Alt gruplara göre viral etkenlere bağlı mortalite oranları farklılık gösterse de bu fark istatistiksel olarak anlamlı bulunmamıştır ($p=0,215$).

Sonuç: Yoğun bakım hastalarında görülen solunum yolu viral enfeksiyonları, özellikle klinik şiddet skorları ve bazı laboratuvar parametreleri yüksek olan bireylerde mortalite ile ilişkilidir. Daha geniş örneklemli, çok merkezli, prospektif çalışmalar ile bu bulguların doğrulanması gerekmektedir.

Anahtar Kelimeler: Solunum yolu virüsleri, yoğun bakım, influenza, COVID-19, APACHE II, SOFA

***Corresponding author/İletişim kurulacak yazar:** Volkan Alparslan; Kocaeli University, Faculty of Medicine, Department of Anesthesiology and Reanimation, Kocaeli, Türkiye.
Phone/Telefon: +90 (262) 303 75 75, **e-mail/e-posta:** volkan.alparslan@kocaeli.edu.tr
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Introduction

Bacterial pathogens occur frequently in intensive care, and the diagnosis of viral infections has increased with advances in molecular tests.[1] However, viral infections have threatened global health, as seen with the 2009 H1N1 pandemic and most recently, the 2019 COVID-19 pandemic.[2] Despite advances in the diagnosis of viral infections, antiviral agents used in their treatment are limited compared to antibiotics.[3] The principal defence mechanism against viral infection is vaccination. Viral pathogens can cause life-threatening sepsis, acute respiratory distress syndrome (ARDS), and organ failures.[4] According to studies conducted prior to the COVID-19 pandemic, the incidence of viral respiratory infections can range between 20% and 50%.[5,6] Although the incidence of respiratory viruses has decreased with the use of methods such as masks and disinfection during the COVID-19 pandemic, it has recently begun to rise again as these measures have been lifted.[7] The principal viral respiratory agents most commonly seen in intensive care are influenza, parainfluenza, respiratory syncytial virus, metapneumovirus, coronavirus, adenovirus and rhinovirus.[1]

There is a strong likelihood of a life-threatening pandemic following COVID-19.[8] Therefore, evaluating the clinical effects of viral respiratory infections in intensive care patients is of particular importance. This study aimed to identify the clinical and epidemiological characteristics of patients with viral respiratory infections in the intensive care unit (ICU) of a tertiary hospital between 2024-2025, to determine factors associated with mortality, and to compare these with the current literature. The study hypothesis was that mortality in patients diagnosed with viral respiratory infections would be associated with the causative pathogen, age, comorbidities, severity of infection (Acute Physiology and Chronic Health Evaluation (APACHE) II, Sequential Organ Failure Assessment (SOFA), Pneumonia Severity Index (PSI), Confusion, Blood Urea Nitrogen (BUN, optional), respiratory rate, blood pressure (CURB-65)), and various laboratory parameters.

Methods

This retrospective, single-center study included patients who were followed up at the Kocaeli University Faculty of Medicine General and Postoperative Intensive Care Unit, Turkey, between March 2024 and March 2025. Patients aged 18 years or older and with positive BioFire® Respiratory 2.1 Plus Panel (BioFire Diagnostics, Salt Lake City, UT, USA) tests during admission to the ICU or during their ICU stay were included. Approval for the study was granted by the Kocaeli University Non-Interventional Clinical Research Ethics Committee (Approval number: GOKAEK-2025/05/33). All patient data were anonymized. The study data were retrieved through a hospital information management system and retrospective examination of patient files. Data recorded during routine clinical procedures were used.

The variables investigated included demographic data (age, sex, underlying chronic diseases, the presence of immunosuppression, and malignancy), clinical scores (APACHE II and SOFA), type of respiratory viral pathogen, pneumonia scores (PSI and CURB-65), prognosis (survivors or non-survivors), laboratory findings (leukocyte, neutrophil, lymphocyte, hematocrit, C-reactive protein (CRP), procalcitonin(Pct), aspartate transferase (AST), alanine transaminase (ALT), urea, creatinine, pH, pO_2, lactate, international normalized ratio (INR), and activated partial thromboplastin time values (aPTT), and radiological involvement (single lobe, multilobular bilateral infiltration, and pleural effusion).

Inclusion Criteria

1. Age 18 or over
2. Admission to the Kocaeli University Faculty of Medicine Hospital ICU
3. Being followed up between 31 March, 2024, and 31 March, 2025, and
4. Identification of respiratory infection based on pathogen-specific PCR testing and laboratory confirmation

Statistical Analysis

All statistical analyses were performed using IBM SPSS for Windows version 29.0 (IBM Corp., Armonk, NY, USA). The Kolmogorov-Smirnov and Shapiro-Wilk tests were used to assess the normality assumption. Continuous variables were presented with median and interquartile range (IQR) values since the normality assumption did not hold. Categorical variables were presented as the number of observations and percentages. Comparisons between groups were performed using the Mann-Whitney U test. Associations between categorical variables were examined with the Chi-square test. A p-value <0.05 was considered statistically significant.

Results

BioFire® Respiratory 2.1 Plus Panel (BioFire Diagnostics, Salt Lake City, UT, USA) were applied to 547 of the 2,719 patients admitted to our ICU throughout the study period. At least one respiratory tract virus was detected in 95 patients (17.4%).

The distribution of viral agents detected in the positive cases was as follows:

- Rhinovirus/enterovirus: 22 (23.1%)
- SARS-CoV-2: 15 (15.7%)
- Coronavirus OC 43:2 (2.1%)
- Parainfluenza virus-3: 11 (11.5%)
- Parainfluenza virus-4: 6 (6.3%)
- Parainfluenza virus-1: 2 (2.15)
- Influenza A-H3 + Influenza A: 23 (24.2%)
- Influenza A (H1N1) 2009 + Influenza A: 2 (2.1%)
- Influenza A (only positive): 4 (4.2%)
- Influenza B: 1 (1.0%)

- RSV A/B: 2 (2.1%)
- Human bocavirus: 1 (1.0%)
- Metapneumovirus A/B: 1 (1.0%)
- Adenovirus: 1 (1.0%)
- Coronavirus 229E: 1 (1.05)
- Rhinovirus/enterovirus + Coronavirus OC43 coinfection: 1 (1.0%)

Of the 95 virus-positive patients, 53 (55.8%) were women and 42 (44.2%) were men. As one of these patients was transferred to an external center, the individual was excluded from the analysis. Analysis was performed on the remaining 94 patients. Forty-three (45.7%) of these 94 patients were discharged, and 51 (54.3%) died in intensive care.

A comparison of the survivors and non-survivors revealed significantly higher SOFA, APACHE II, PSI, and CURB-65 scores in non-survivor patients (p=0.006, p=0.014, p<0.001, and p<0.001, respectively). These scores, associated with mortality, have emerged as powerful indicators of clinical severity and prognosis in patients with viral infections.

In terms of laboratory parameters, the non-survivor patients exhibited significantly higher urea levels (62.8 mg/dL (39.1-154.4) vs 35.5mg/dL (19.2-59.1); p<0.001), and procalcitonin levels (0.13 ng/mL (0.09-0.93) vs. 0.775 ng/mL (0.23-2.54); p=0.002). No significant differences were observed between the CRP, white blood cell, lymphocyte, or hematocrit levels of the groups (p>0.05).

In terms of comorbid diseases, the mortality rate was significantly higher in the patients with chronic obstructive pulmonary disease (COPD) (78.9% vs 48.0%; p=0.016). However, no significant association was found between mortality and the presence of hypertension (p=0.309), diabetes mellitus (p=0.649), or chronic heart failure (p=0.761). A comparison of clinical and laboratory parameters between survivors and non-survivors is presented in Table 1.

Table 1. Comparison of clinical and laboratory findings between survivors and non-survivors

	Survivors (n=43)	Non-survivors (n=51)	p
Age	67 (47-76)	71 (58-77)	0.290
PSI	125 (0-140)	155 (127-196)	**<0.001**
CURB-65	1 (0-3)	2 (2-4)	**<0.001**
CRP	100.4 (31.03-153.2)	91.9 (39.2-184.7)	0.306
Procalsitonin	0.13 (0.09-0.93)	0.77 (0.23-2.54)	**0.002**
Urea	35.5 (19.2-59.1)	62.8 (39.1-154.4)	**<0.001**
SOFA	6 (4-7)	8 (5-10)	**0.006**
APACHE II	19 (16-22)	24.5 (18.75-28.25)	**0.014**
WBC	8.26 (6.92-15.9)	11.9 (7.92-18.6)	0.084
Lymphocyte	1.03 (0.69-1.78)	0.76 (0.4-1.64)	0.174
Haematocrit	32.7 (28.1-36.7)	31.6 (26.1-35.2)	0.216

Values are presented as median (IQR). Comparisons between survivors and non-survivors were performed using the Mann–Whitney U test. A p-value <0.05 was considered statistically significant.

IQR: Interquartile range, PSI: Pneumonia severity index, CRP: C-reactive protein, SOFA: Sequential Organ Failure Assessment, APACHE II: Acute Physiology and Chronic Health Evaluation II, WBC: White blood cell

From the perspective of clinical scoring systems, PSI, CURB-65, SOFA, and APACHE II scores were significantly higher in non-survivors than in survivors (p<0.001, p<0.001, p=0.006, and p=0.014, respectively). These differences are shown in boxplots in Figure 1 and Figure 2.

Examination of laboratory parameters associated with mortality in this study revealed significantly higher urea and procalcitonin levels in non-survivors than in survivors (p<0.001 and p=0.002, respectively). These differences are shown in boxplots in Figure 3.

When mortality rates were analyzed according to the most frequently detected viral subtypes, 36.4% of the patients who tested positive for rhinovirus/enterovirus, 66.7% of those positive for SARS-CoV-2, and 50% of those positive for influenza A-H3 were non-survivors. However, these differences were not statistically significant (p = 0.215).

Discussion

Viral respiratory infections were detected in 95 of the 547 patients whose respiratory panels were investigated in the ICU of a tertiary university hospital in this study. This figure (17.4%) is consistent with previously reported rates and is similar to the 22.4% reported by Al-Dorzi et al.[9] in their Saudi Arabia-based study. The mortality rate in viral-positive patients was 54%.

Scores such as APACHE II, SOFA, PSI, and CURB-65, which were significantly associated with mortality in this study, were of prognostic value in this patient group. Similarly, Al-Dorzi et al. identified PSI scores as independent predictors of admission to intensive care and in-hospital mortality.

Despite the prevalence of comorbidities such as hypertension, heart failure, and malignancy in this study, the variables most closely linked to mortality were the PSI and SOFA scores. Immunosuppression and bacterial superinfections increase mortality, particularly in cases of sepsis associated with viral infections.[10]

Viral infections began to increase again with the lifting of protective measures, such as masks and isolation, in the wake of the COVID-19 pandemic. According to the Centers for Disease Control and Prevention data[11], influenza alone produces between 9 and 41 million cases and causes 4,900-51,000 deaths annually.

Another important finding of the present study is that mortality occurred in approximately half of the patients with viral infections. This may be attributed to the limited early diagnosis and effective treatment of viral infections. The limited number of antiviral agents and the fact that priority is usually attached to support therapy is one of the factors contributing to the high mortality in viral infections.

In this study, high mortality rates due to viral respiratory infections were observed in patients under follow-up in the intensive care unit. Similarly, in their extensive 10-year analysis, O'Halloran et al.[12] reported significantly higher influenza-associated hospital admission, intensive care requirement, and in-hospital mortality rates and

noted that these outcomes were more common among socially disadvantaged groups in particular. This shows that epidemiological risk factors should be considered in addition to clinical factors in the management of viral infections.

In our study, when laboratory parameters associated with mortality were evaluated, procalcitonin and urea levels were significantly higher in patients who died. This finding is important in terms of demonstrating the effects of systemic inflammation and organ dysfunction on mortality. Previous studies have shown that procalcitonin levels are associated not only with bacterial superinfection but also with severe inflammatory responses, such as cytokine storms, and are a valuable biomarker for predicting prognosis. The COVIDeF cohort study by Cancella de Abreu et al.[13] also found that elevated procalcitonin levels were independently associated with in-hospital deterioration (ICU admission, mechanical ventilation, ARDS development, or death). In the same study, urea levels were also shown to be significantly associated with poor clinical outcomes, because elevated urea levels may be associated with a severe course of the disease and fatal outcomes, especially through renal dysfunction and tissue perfusion insufficiency. In this context, procalcitonin and urea levels should be considered for early risk stratification and prognosis determination in intensive care unit patients with viral respiratory tract infections.

In subgroup analyses, numerical differences were observed between mortality rates according to viral agents; however, these differences were not statistically significant. This is probably due to the relatively low number of patients infected with each viral agent. Similarly, it has been reported that larger samples are needed to evaluate the effect of viral subtypes on mortality.[14,15]

This study had several limitations. In particular, owing to its single-center and retrospective design, the generalizability of the results may be limited. In addition, the relatively small number of patients may have reduced the statistical power of the comparisons between subgroups. Due to missing laboratory and clinical data in some patients, we were unable to obtain a complete dataset for all variables. Additionally, because the vaccination status of the patients was not known, we were unable to assess the potential effect of vaccination on disease severity or outcomes. In light of these limitations, the study's findings should be interpreted with care. Future multicenter prospective studies with larger samples will yield stronger evidence on this subject.

In conclusion, this study revealed that mortality rates are high in cases of viral respiratory infection followed up in the ICU and that the presence of COPD and clinical scores such as APACHE II, SOFA, PSI, and CURB-65 are significantly associated with mortality. Careful evaluation of clinical scoring systems and early laboratory markers is of critical importance for the early identification of high-risk patients and optimization of intensive care management. Our findings support the importance of risk classification in the management of viral pneumonia, and further prospective studies with larger sample sizes are needed.

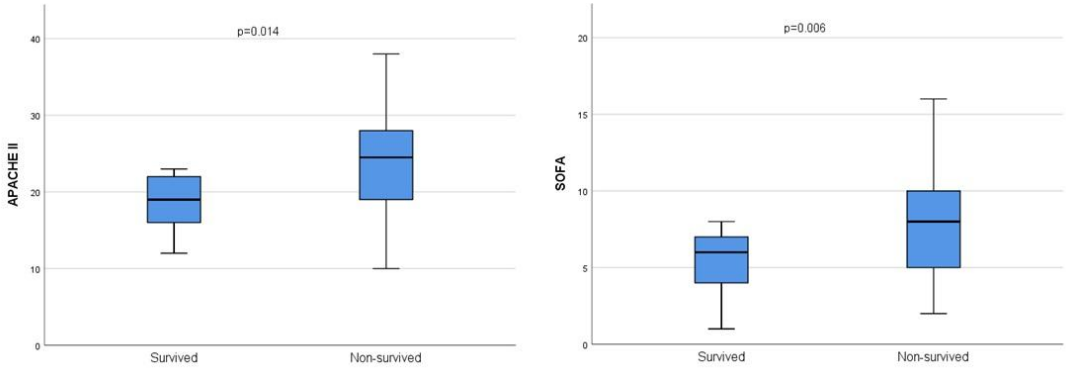

Figure 1. A comparison of APACHE II and SOFA scores in survivors and non-survivors

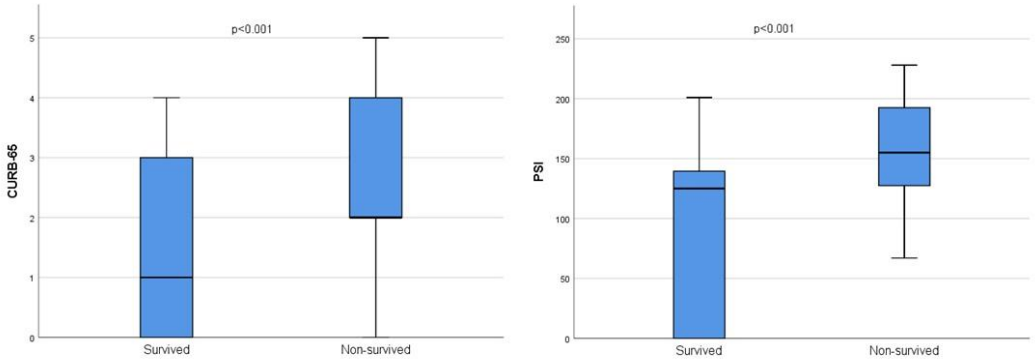

Figure 2. A comparison of CURB-65 and PSI scores in survivors and non-survivors

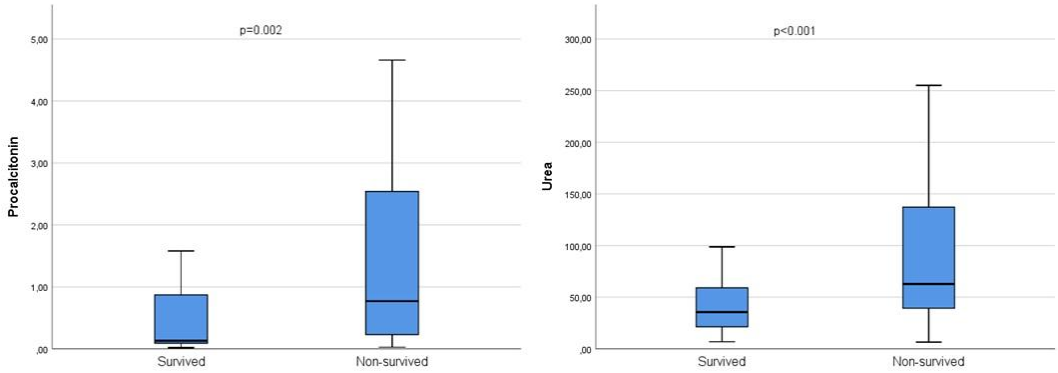

Figure 3. A comparison of procalcitonin and urea levels in survivors and non-survivors

Ethical Approval

Approval for the study was granted by the Kocaeli University Non-Interventional Clinical Research Ethics Committee (Approval number: GOKAEK-2025/05/33).

Conflict of Interest

There is no conflict of interest to declare.

Author Contributions

VA, ÖG: Conceptualization, methodology, formal analysis and investigation, writing-original draft preparation; SK, İİA: Data curation; VA, AK, NB, AK: Writing-review and editing; AK, NB, AK: Supervision

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