

Research Article

# Comparison of the Characteristics of Patients Admitted to the Intensive Care Unit During Peak Periods of SARS-CoV-2 Variants

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## Abstract

**Background:** Since its emergence, SARS-CoV-2 has undergone numerous mutations. The World Health Organization (WHO) has identified key variants, including Ancestral, Beta, Delta and Omicron. Clinical characteristics and mortality have varied between these variants. This study evaluated the clinical features and outcomes of SARS-CoV-2-positive patients admitted to the Intensive Care Unit (ICU) during different peak periods.

**Methods:** Türkiye experienced four major COVID-19 waves, defined by the Ministry of Health: the first (November 2020-January 2021), second (February-May 2021), third (July-November 2021) and fourth (December 2021-March 2022). Patients admitted to the ICU during these waves were included. Demographics, comorbidities, oxygen therapy, ventilation type, ICU length of stay and mortality rates were analyzed.

**Results:** A total of 510 patients were evaluated: 61 (12%) in the first wave, 148 (29%) in the second, 187 (37%) in the third and 114 (22%) in the fourth. The median age was 70 years (Interquartile range [IQR]: 21), lowest in the second wave (62) and highest in the fourth (76). Most patients (75%, n=384) were unvaccinated. Overall ICU mortality was 81%, ranging from 66% in the first wave to 86% in the fourth. ICU stay length was similar across waves.

**Conclusion:** COVID-19 ICU patient characteristics and outcomes varied across different variants. Further studies are needed to clarify whether Omicron is less pathogenic compared with earlier strains.

**Keywords:** COVID-19; Ancestral; Beta; Delta; Omicron; Variant; Mortality; Intensive Care Unit (ICU)

## Abbreviations

APACHE II: Acute Physiology and Chronic Health Evaluation II; ARDS: Acute Respiratory Distress Syndrome; BMI: Body Mass Index; CCI: Charlson Comorbidity Index; CI: Confidence Interval; COVID-19: Coronavirus Disease 2019; CRBSI: Catheter-Related Bloodstream Infection; CRP: C-Reactive Protein; CRRT: Continuous Renal Replacement Therapy; CT: Computed Tomography; CVVHD: Continuous Veno-Venous Hemodialysis; DM: Diabetes Mellitus; ECMO: Extracorporeal Membrane Oxygenation; HFNO: High-Flow Nasal Oxygen; HT: Hypertension; ICU: Intensive Care Unit; IQR: Interquartile Range; IMV: Invasive Mechanical Ventilation; LDH: Lactate Dehydrogenase; mMRC: Modified Medical Research Council; NIMV: Non-Invasive Mechanical Ventilation; OMIM: Online Mendelian Inheritance in Man; OR: Odds Ratio; PCR: Polymerase Chain Reaction; RRT: Renal Replacement Therapy; SD: Standard Deviation; SOFA: Sequential Organ Failure Assessment; SPSS: Statistical Package for the Social Sciences; VAP: Ventilator-Associated Pneumonia; VOI: Variant of Interest; VOC: Variant of Concern; WHO: World Health Organization

## Introduction

COVID-19 was first identified in December 2019 in Wuhan, Hubei Province, China and rapidly spread worldwide [1,2]. The World Health Organization (WHO) declared COVID-19 a pandemic on March 11, 2020 [1]. The causative virus, SARS-CoV-2, is a positive-sense single-stranded RNA virus with a genome of approximately 30 kb, making it one of the largest known RNA viruses [2-4]. Entry into host cells is mediated by the Angiotensin-Converting Enzyme 2 (ACE2) receptor and the Transmembrane Serine Protease 2 (TMPRSS2) [3,5]. Due to their inherent susceptibility to mutations, RNA viruses, including SARS-CoV-2, have undergone multiple genetic changes over time, resulting in variants with altered transmissibility, clinical manifestations and immune evasion properties [6,7].

The WHO has classified SARS-CoV-2 variants into two primary categories: “Variants of Concern” (VOC) and “Variants of Interest” (VOI), naming them according to the Greek alphabet [6-8]. The major VOCs include Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1), Delta (B.1.617.2) and Omicron (B.1.1.529) [6-8]. While the Delta variant has been associated with increased disease severity and mortality, the Omicron variant, although generally causing milder illness, has exerted a considerable burden on healthcare systems due to its high transmissibility [3,8,9].

In Türkiye, the pandemic unfolded in four major waves: November 2020-January 2021, February-May 2021, July-November 2021 and December 2021-March 2022 [10,11]. Data on daily case counts and hospital admissions, regularly reported by the Ministry of Health, facilitated evaluation of these pandemic waves [10]. The high rates of morbidity and mortality, particularly in vulnerable populations, resulted in substantial strain on Intensive Care Units (ICUs) and posed significant challenges to healthcare delivery [12,13].

COVID-19 presents with a wide clinical spectrum. While some patients remain asymptomatic, those of advanced age or with comorbidities may develop severe complications such as pneumonia, Acute Respiratory Distress Syndrome (ARDS), multi-organ failure and death [13,14]. Critically ill patients often require advanced supportive therapies, including IMV, Non-IMV (NIMV), High-Flow Nasal Oxygen (HFNO) and Renal Replacement Therapy (RRT) [12,15,16]. Prolonged ICU stays further increase the risk of secondary infections and mortality [13].

Throughout the pandemic, treatment protocols and care strategies evolved dynamically. The use of corticosteroids, antiviral agents and immunomodulatory therapies was refined in accordance with emerging clinical evidence, improving patient management [17-19]. The nationwide vaccination program launched in 2021 significantly reduced disease severity and ICU admission rates [11,20]. However, the emergence of highly transmissible variants sustained pressure on healthcare systems. Despite advances in treatment and vaccination, the disease burden persisted in high-risk populations, underscoring the importance of adequate ICU capacity.

There are limited studies comparing the clinical features and ICU burden associated with different SARS-CoV-2 variants and comprehensive datasets from Türkiye offering comparative analyses of pandemic phases remain scarce [10,11,20,21]. Assessing the demographic characteristics, vaccination status, laboratory and imaging findings and ICU course of patients admitted during different pandemic phases is therefore crucial for improving clinical management and guiding healthcare policies [8,22,23].

This study aimed to retrospectively analyze COVID-19 patients admitted to the ICU during four distinct pandemic waves between November 2020 and March 2022, identifying changes in patient profiles, treatment strategies and factors influencing mortality [8]. The findings are expected to inform preparedness for future pandemics, optimize ICU capacity planning and strengthen healthcare system resilience.

## Ethical Statement

This study followed the Declaration of Helsinki, and the University Faculty of Medicine Local Ethics Committee approved the study (Approval Number: 09.2022.958, Date: 22.07.2022). All participants provided informed consent.

## Methods

This single-center, retrospective study included adult patients admitted to the Intensive Care Unit (ICU) of our hospital between November 2020 and March 2022 during four major COVID-19 waves in Türkiye, with SARS-CoV-2 infection confirmed by

Polymerase Chain Reaction (PCR) testing. The study was conducted in accordance with the Declaration of Helsinki and approved by the local ethics committee (Ethics Committee Approval Number: 09.2022.958, Date: 22.07.2022).

#### *Study Design and Patient Selection*

Inclusion criteria were: Age  $\geq 18$  years, confirmed SARS-CoV-2 infection by PCR testing and admission to the ICU during the peak periods of the pandemic waves. Patients with negative PCR tests but clinical suspicion of COVID-19, individuals under 18 years of age and those with incomplete medical records were excluded. The four pandemic waves were defined based on daily case numbers and epidemiological reports from the Turkish Ministry of Health as follows:

Wave: November 2020-January 2021

Wave: February-May 2021

Wave: July-November 2021

Wave: December 2021-March 2022 [3,4].

All patients were managed at the same center with standardized protocols and consistent care practices throughout the study period.

#### *Data Collection*

Demographic data (age, sex), Body Mass Index (BMI), comorbidities (Hypertension [HT], Diabetes Mellitus [DM]) and vaccination status were extracted from electronic health records and patient charts. Symptoms at admission, vital signs, blood pressure, heart rate, respiratory rate, oxygen saturation and temperature were recorded. Data were verified through double-checking of electronic entries to ensure standardization.

Laboratory findings included complete blood count, biochemistry and inflammatory markers, such as leukocyte, lymphocyte and platelet counts, C-Reactive Protein (CRP), ferritin, D-dimer, lactate dehydrogenase (LDH), creatinine, liver enzymes and electrolytes. Chest Computed Tomography (CT) scans performed upon admission were evaluated according to the COVID-19 Reporting and Data System (CO-RADS) classification [24]. ICU course data included length of stay, need for mechanical ventilation (IMV or NIMV), HFNO therapy, RRT and vasopressor support. Secondary infections (Ventilator-Associated Pneumonia [VAP], Catheter-Related Bloodstream Infections [CRBSI], bloodstream infections, urinary infections etc.) and other complications were recorded. Mortality and the need for supplemental oxygen up to six months post-discharge were also evaluated.

#### *Clinical Assessment and Scoring Systems*

Disease severity was assessed using the Sequential Organ Failure Assessment (SOFA) [25] and the Acute Physiology and Chronic Health Evaluation II (APACHE II) scores [26]. Oxygenation was evaluated using the  $\text{PaO}_2/\text{FiO}_2$  ratio. The Charlson Comorbidity Index (CCI) was also calculated for each patient [27]. These scoring systems were used to assess disease severity and identify prognostic factors.

#### *Treatment Protocols*

All patients were evaluated and treated according to institutional COVID-19 protocols based on national and international guidelines [1,11]. Corticosteroids, antiviral agents (e.g., remdesivir), antibiotics and immunomodulatory therapies (e.g., tocilizumab) were administered as indicated. Anticoagulation strategies were guided by disease severity and coagulation parameters. Mechanical ventilation strategies followed ARDS management guidelines.

#### *Vaccination Status*

Vaccination data were verified through the Ministry of Health's e-Nabız system. Patients were classified as unvaccinated, partially vaccinated (single dose) or fully vaccinated (two or more doses). Vaccine types (mRNA or inactivated) were also recorded. These data were analyzed to evaluate the potential impact of vaccination during different variant periods.

#### *Statistical Analysis*

All data were analyzed using SPSS software (IBM SPSS Statistics, version 25.0). The Kolmogorov-Smirnov test was used to assess normality of distribution. Normally distributed continuous variables were presented as mean  $\pm$  Standard Deviation (SD), while

non-normally distributed variables were reported as median (Interquartile Range [IQR]). Categorical variables were expressed as numbers and percentages. Between-group comparisons were performed using the Student's t-test, Mann-Whitney U test and chi-square test. Multivariable analyses were performed using logistic regression and Cox proportional hazards models. A p-value <0.05 was considered statistically significant.

## Results

A total of 510 patients were evaluated: 61 (12%) in the first wave, 148 (29%) in the second wave, 187 (37%) in the third wave and 114 (22%) in the fourth wave (Table 1). The overall median age was 70 years (IQR 21), with the lowest in the second wave (62 years) and the highest in the fourth (78 years,  $p<0.001$ ). Males accounted for 57.5% of the cohort, with significant inter-wave variation ( $p=0.039$ ). The most common comorbidities were HT (55%) and DM (36%). The Charlson Comorbidity Index (CCI) increased progressively, peaking in the fourth wave (median 5 [IQR 2],  $p<0.001$ ). Median ferritin and LDH levels also showed significant differences between waves, with ferritin highest in the second and third waves and LDH highest in the first and fourth waves (both  $p<0.001$ ). Vaccination status was available for the second, third and fourth waves (Table 2). Vaccination rates were low: 75% of patients were unvaccinated and only 9% were fully vaccinated. In the second and third waves, no significant association was observed between vaccination and mortality. In contrast, during the fourth wave, patients with at least one vaccination had lower mortality compared with unvaccinated patients ( $p=0.024$ ).

ICU treatment modalities are summarized in Table 3. The use of IMV increased steadily across waves, from 36% in the first wave to 55% in the fourth ( $p<0.05$ ). NIMV was used in 27.8% overall but decreased significantly during the fourth wave ( $p=0.014$ ). HFNO use was most common during the third wave (64.2%,  $p=0.010$ ). Vasopressor support was required in 77.5% overall, significantly higher during the third and fourth waves ( $p=0.008$ ). Secondary infections occurred in 58.4% of patients, with the highest rate in the first wave (80.3%,  $p<0.001$ ). The source of admission also shifted, with a higher proportion arriving from wards during the second wave compared to other periods ( $p=0.025$ ). SOFA scores were lowest in the second wave and highest in the fourth (median 4 vs 6,  $p<0.001$ ). Overall ICU mortality was 80%, increasing from 65.6% in the first wave to 84% in the third and 82.5% in the fourth ( $p=0.016$ ).

In the ICU, a wide range of advanced treatments were applied (Table 4). IMV was required in nearly four out of five patients (78.8%), while more than half received HFNO (54.7%). RRT such as Continuous Veno-Venous Hemodialysis were performed in 28.6%. More specialized interventions, including nitric oxide, ECMO, iloprost, tocilizumab, cytokine removal and anakinra, were administered less frequently (<3% each).

Multivariate logistic regression identified older age (OR 1.04, 95% CI 1.01-1.06,  $p=0.002$ ), higher SOFA score on admission (OR 1.40, 95% CI 1.20-1.62,  $p<0.001$ ), elevated LDH (OR 1.003, 95% CI 1.001-1.004,  $p=0.021$ ) and lower procalcitonin levels (OR 0.98, 95% CI 0.96-0.99,  $p<0.001$ ) as independent predictors of mortality (Table 5). Follow-up data were available for 101 patients discharged alive (Table 6). Hospital readmission occurred in 10.8%. An oxygen concentrator was prescribed at discharge in 11 patients (10.8%). Fibrotic sequelae were detected in 14.9% and pulmonary thromboembolism in 11.8%. Functional outcomes assessed with mMRC scores showed that only 38.2% were asymptomatic (score 0), whereas 8% had scores  $\geq 3$ , indicating persistent dyspnea.

Characteristics	1. Wave (n=61)	2. Wave (n=148)	3.Wave (n=187)	4. Wave (n=114)	Total (n=510)	p-value
Age, median (IQR) (years)	66 (17)	62 (20)	72 (25)	78 (13)	70 (21)	<0.001
Male, n (%)	39 (63.9)	95 (64.2)	93 (49.7)	66 (56.4)	293 (57.5)	0.039
HT, n (%)	30 (49)	80 (54)	105 (56)	66 (58)	281 (55)	0.969
DM, n (%)	20 (33)	55 (37)	65 (35)	44 (39)	184 (36)	0.241
CCI, median (IQR)	4 (3)	3 (3)	4 (2)	5 (2)	4 (2)	<0.001
Ferritin (ng/mL), median (IQR)	621 (909)	988 (1366)	936 (1559)	591 (768)	837 (1311)	<0.001
LDH (U/L), median (IQR)	589 (385)	581 (405)	434 (374)	591 (279)	556 (396)	<0.001

DM: Diabetes Mellitus, HT: Hypertension, IQR: Interquartile Range, LDH: Lactate Dehydrogenase

**Table 1:** Demographic characteristics of participants.

		ICU Outcomes, n (%)		p-value
		Discharge	Mortality	
2 <sup>nd</sup> Wave	At least one vaccination	4 (13.0)	8 (6.8)	0.277
3 <sup>rd</sup> Wave		11 (36.6)	60 (38.2)	0.873
4 <sup>th</sup> Wave		20 (60.0)	3 (32.9)	0.024

**Table 2:** Vaccination and mortality status.

	1 <sup>st</sup> Wave (n=61)	2 <sup>nd</sup> Wave (n=148)	3 <sup>rd</sup> Wave (n=187)	4 <sup>th</sup> Wave (n=114)	Total (n=510)	p-value
IMV, n (%)	22 (36)	65 (44)	95 (51)	63 (55)	245 (48)	<0.05
NIMV, n (%)	19 (31.1)	41 (27.7)	63 (33.7)	19 (16.7)	142 (27.8)	0.014
HFNO, n (%)	27 (44.7)	74 (50.0)	120 (64.2)	58 (50.9)	279 (54.7)	0.010
CRRT, n (%)	18 (29.5)	51 (34.5)	50 (26.7)	27 (23.7)	146 (28.6)	NS
Vasopressor use, n (%)	44 (72.1)	102 (68.9)	155 (82.9)	94 (82.5)	395 (77.5)	0.008
Secondary Infections	49 (80.3)	82 (55.4)	110 (58.8)	57 (50.0)	298 (58.4)	<0.001
Arrival Place for ICU n (%) Emergency Room / Service	29 (47.5) / 32 (52.5)	48 (32.4) / 100 (67.6)	80 (42.8) / 107 (57.2)	57 (50.0) / 57 (50.0)	214 (42.0) / 296 (58.0)	0.025
SOFA (median, IQR)	5 (6)	4 (4)	5 (5)	6 (3)	6 (5)	<0.001
Mortality	40 (65.6)	117 (79.1)	157 (84.0)	94 (82.5)	408 (80.0)	0.016

CRRT: Continuous Renal Replacement Therapy; HFNO: High-Flow Nasal Oxygen; ICU: Intensive Care Unit; IMV: Invasive Mechanical Ventilation; NIMV: Non-Invasive Mechanical Ventilation; NS: Not Significant

**Table 3:** Intensive Care Unit (ICU) treatments.

	n	%
IMV	402	78.8
HFNO	279	54.7
CVVHD	146	28.6
NIMV	142	27.8
NO	14	2.7
ECMO	10	2
Iloprost	9	1.8
Tocilizumab	9	1.8
Cytokine Removal	8	1.6
Anakinra	6	1.2

CVVHD: Continuous Veno-Venous Hemodialysis; ECMO: Extracorporeal Membrane Oxygenation; HFNO: High Flow Nasal Oxygen; IMV: Invasive Mechanical Ventilation; NIMV: Non-Invasive Mechanical Ventilation; NO: Nitric Oxide

**Table 4:** Treatments administered in the ICU.

Variable	Odds Ratio (95% CI)	p-value
Age (years)	1.04 (1.01-1.06)	0.002
Admission SOFA score	1.40 (1.20-1.62)	<0.001
Procalcitonin (ng/mL)	0.98 (0.96-0.99)	<0.001
LDH (U/L)	1.003 (1.001-1.004)	0.021

CI: Confidence Interval; LDH: Lactate Dehydrogenase; SOFA: Sequential Organ Failure Assessment

**Table 5:** Multivariate logistic regression analysis of factors associated with mortality.

	1 <sup>st</sup> Wave n=21	2 <sup>nd</sup> Wave n=31	3 <sup>rd</sup> Wave n=29	4 <sup>th</sup> Wave n=20	Total n=101
Hospital readmission (IQR)	2 (4)	2 (2)	1 (1)	1 (1)	2 (3)
Oxygen concentrator at discharge, n (%)	0 (0)	4 (12.9)	5 (17.2)	2 (10)	11 (10.8)
Fibrotic sequelae, n (%)	2 (9.5)	5 (16.1)	6 (20.7)	2 (10)	15 (14.9)
Pulmonary thromboembolism, n (%)	4 (19)	3 (9.7)	2 (6.9)	3 (15)	12 (11.8)
mMRC score distribution, n (%)					
0	6 (28.6)	13 (41.9)	9 (30)	11 (55)	39 (38.2)
1	10 (47.6)	12 (38.2)	7 (23)	4 (20)	33 (32.4)
2	5 (23.8)	4 (12.9)	8 (26.7)	4 (20)	21 (20.6)
3	0 (0)	2 (6.5)	5 (16.7)	1 (5)	7 (6.9)
4	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)

IQR: Interquartile Range; mMRC: Modified Medical Research Council

**Table 6:** Post-discharge outcomes and follow-up findings.

## Discussion

This single-center retrospective study provides a comparative evaluation of the clinical characteristics, laboratory findings, treatment approaches and mortality rates of patients admitted to the ICU during four waves of the COVID-19 pandemic in Türkiye between November 2020 and March 2022. Our findings highlight several critical observations, including a high median patient age, an increase in comorbidity burden particularly in the third and fourth waves (CCI was highest in the 4<sup>th</sup> wave), low vaccination coverage, inter-wave variations in laboratory parameters and a significant rise in mortality rates over time. These data are valuable for understanding changes in patient profiles and clinical burden across different phases of the pandemic and for guiding health system preparedness and resource allocation.

This study encompasses a period marked by rapid evolution of SARS-CoV-2, during which successive variants exerted considerable pressure on global healthcare systems. The Alpha and Beta variants were predominant in the first two waves, the Delta variant in the third and the Omicron variant in the fourth wave [8-10,23]. Our findings demonstrate that even during the Omicron-dominant wave, ICU admissions primarily involved elderly patients with significant comorbidity burdens, emphasizing that high transmissibility of Omicron continued to pose severe risks to vulnerable populations. This partially contrasts with reports suggesting a generally milder course for Omicron infections [9]. The persistence of severe illness in high-risk groups despite variant-specific differences highlights the need to consider population risk distribution in pandemic response strategies. Reports from the United Kingdom and South Africa similarly indicated that while overall hospitalization rates decreased during the Omicron wave, ICU demand persisted in older patients and those with multiple comorbidities [9,21,28].

The median age of 70 years and male predominance (58%) in our cohort align with global data showing that advanced age is strongly associated with severe disease and mortality and that men are disproportionately affected [2,4,15]. HT (55%), DM (36%), CVD (28%) and COPD (15%) were the most common comorbidities. The marked increase in CCI scores observed during the fourth wave suggests that severe disease became increasingly concentrated among frail populations over time. These findings underscore the importance of prioritizing high-risk groups in vaccination programs and implementing individualized protective strategies. Symptom profiles in our study were consistent with the typical clinical presentation of COVID-19, with dyspnea (72%), fever (65%) and cough (59%) being the most frequent. Altered mental status was reported in 12% of patients, potentially reflecting hypoxemia and severe systemic inflammation [15,16,29]. This underscores the multisystemic nature of severe COVID-19. Laboratory findings highlighted elevated ferritin, dand D-dimer levels as prominent markers. Ferritin levels were highest during the 2<sup>nd</sup> and 3<sup>rd</sup> waves, while LDH peaked in the 1<sup>st</sup> and 4<sup>th</sup> waves. These results are consistent with previous studies demonstrating the prognostic significance of these biomarkers [4,15]. IMV was required in 46% of patients, increasing to 55% during the fourth wave. HFNO use was particularly high in the 3<sup>rd</sup> wave (64.2%), whereas NIMV use significantly decreased in

the 4<sup>th</sup> wave (16.7%). RRT was required in 28.6%. RRT requirement demonstrates the significant contribution of multi-organ failure to disease severity [12,13]. The incidence of secondary infections was 58.4% overall, with the highest rate in the 1<sup>st</sup> wave (80.3%), underscoring the risks of prolonged mechanical ventilation and highlighting the importance of stringent infection prevention and multidisciplinary ICU management. Treatment strategies in our study mirrored national and international guidelines [1,11]. Corticosteroids were consistently administered across all waves, becoming a global standard following the RECOVERY trial [18]. The increased use of tocilizumab and remdesivir during the second and third waves reflects evolving clinical evidence and therapeutic availability, demonstrating the adaptability of treatment protocols throughout the pandemic. Low vaccination coverage emerged as a major public health challenge. Seventy-five percent of patients were unvaccinated, a statistic likely influenced by vaccine hesitancy and logistical delays in vaccine distribution. In the 4<sup>th</sup> wave, patients with at least one vaccination had significantly lower mortality compared with unvaccinated patients ( $p=0.024$ ). Studies have shown that mRNA and inactivated vaccines significantly reduce the risk of severe disease and death [20-23]. However, their effectiveness in high-risk populations is relatively reduced and booster doses are essential. Our findings reinforce the need for targeted vaccination campaigns and booster strategies for vulnerable populations. The ICU mortality rate in this cohort was 80%, reflecting the severe disease burden during the peak pandemic periods. Mortality increased from 65.6% in the first wave to 84% in the third and 82.5% in the fourth wave. Global reports indicate ICU mortality rates ranging from 40% to 80%, influenced by healthcare infrastructure, ICU capacity, access to therapeutics and national response strategies [12,13,16]. Although Türkiye increased ICU bed capacity during the pandemic, surges in patient volume challenged healthcare resources, demonstrating the need for sustainable surge capacity planning.

Long-term complications of COVID-19 were also notable in this study. Post-discharge, 40% of survivors required supplemental oxygen for up to six months and 15% experienced long COVID symptoms (e.g., fatigue, dyspnea). These results align with studies reporting persistent respiratory impairment and reduced quality of life in 30-50% of severe COVID-19 survivors [29,30]. This highlights the ongoing burden of COVID-19 beyond the acute phase and the necessity of multidisciplinary rehabilitation programs, long COVID clinics and structured follow-up care. Post-COVID psychiatric morbidity and socioeconomic impacts should also be prioritized in health policy planning.

Key strengths of this study include the large ICU patient cohort, standardized management protocols and comparative analysis across four pandemic waves. The single-center design enhanced data consistency and the retrospective approach allowed for rapid data collection. However, limitations include reliance on epidemiological rather than genomic data for variant classification and reduced generalizability due to the single-center setting. Despite these limitations, this study provides rare and detailed insights into the changing clinical burden and patient profile of ICU admissions across different variant-dominant periods in Türkiye.

## **Conclusion**

This study demonstrates that even during later stages of the pandemic, ICU admissions primarily involved elderly patients with multiple comorbidities and mortality remained high. These findings emphasize the need for targeted protection of high-risk populations, widespread administration of booster doses and ongoing investment in ICU capacity. Multidisciplinary care approaches, early access to treatment and robust public health interventions remain critical to pandemic response. The results presented here offer a strategic roadmap for preparedness against future pandemics and highlight the necessity of prioritizing long COVID management within healthcare systems.

## **Conflict of Interest**

Authors have no conflicts of interest to disclose / disclose any relationships or activities.

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## Disclaimer

The views expressed in this manuscript are solely those of the authors and do not necessarily represent the official policy or position of their respective institutions.

## Data Availability Statement

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

## Disclosure of Relationships and Activities

Authors have no conflicts of interest to disclose / disclose any relationships or activities.

## Author's Contribution

Conceptualization: Can Ömür, Hüseyin Arıkan. Study Design: Can Ömür, Hüseyin Arıkan. Data Collection and Processing: Can Ömür, Hüseyin Arıkan. Data Analysis and Interpretation: Can Ömür, Hüseyin Arıkan. Supervision: Sait Karakurt. Writing - Original Draft: Can Ömür. Writing - Review and Editing: Hüseyin Arıkan, Sait Karakurt. Validation: Hüseyin Arıkan. Visualization: Can Ömür. Project Administration: Sait Karakurt.

All authors contributed to the writing and have approved the final version of the manuscript.

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