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# Critical care trends across five waves of COVID-19 in Pakistan: A multi-center observational study from the Pakistan Registry of Intensive CarE (PRICE)

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## Abstract

**Background** COVID-19 emerged as a global health crisis with multiple waves of infection ranging from asymptomatic to critical cases requiring intensive care. In Pakistan, dearth of ICU data limit understanding of critical care admissions and outcomes, making it difficult to understand critical care admissions and outcomes. This study aims to describe demographics, clinical characteristics, and outcomes of patients with SARS-CoV-2 infection admitted to 69 intensive care units (ICUs) during five waves of pandemic in Pakistan.

**Methods** This study analyzed prospectively collected data of adult COVID-19 patients admitted to Pakistan Registry of Intensive Care (PRICE) ICUs from April 2020 to March 2022.

**Results** 9,102 ICU admissions were reported during the study period, with highest in Wave 1 ( $n=2,704$ ) and Wave 2 ( $n=2,563$ ). Most admissions were male, and predominant age group was 60–79 years. Patients aged > 80 years increased from 8.9% in Wave 4 to 18.6% in Wave 5. Common presenting symptoms were shortness of breath, fever, and cough with no sputum. Highest mortality was recorded during Waves 3 and 4 (41%). Among patients requiring organ support, mortality increased from 50% in Wave 1 to 65% in Wave 4. Cox regression showed younger age, low oxygen saturation, and cardiovascular disease were associated with higher risk of invasive mechanical ventilation (IMV).

**Conclusion** Mortality was highest during Waves 3 and 4, particularly among patients requiring organ support. Younger patients, those with low oxygen saturation, and individuals with cardiovascular diseases were at increased risk for IMV.

**Clinical trial number** Not applicable.

**Keywords** Critical care registry, Informatics, COVID-19, Severe acute respiratory infection, Pandemic surveillance, Pandemic preparedness

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## Introduction

SARS-CoV-2, first identified in Wuhan, China, in late 2019, has remained a major global health challenge [1]. Recognizing its widespread impact, the World Health Organization (WHO) declared COVID-19 a Public Health Emergency of International Concern on January 30, 2020 [2]. By the end of the pandemic in 2023, over 765 million confirmed cases and 6.92 million deaths had been recorded worldwide [3].

The pandemic evolved in distinct waves, each characterized by a rise, plateau, and trough and declining cases, influenced by changes in viral transmissibility, vaccination coverage, public health interventions, and population immunity [4, 5]. In Pakistan, 1.53 million COVID-19 cases were reported from May 2020 to March 2022, with 30,656 fatalities in five distinct waves [6]. To coordinate the national response, the National Command and Operations Centre (NCOC) was established in April 2020 to provide daily updates on new cases, recoveries, deaths, critically ill patients, and vaccination coverage. These data supported timely policy decisions, including targeted “smart lockdowns.” Pakistan was later recognized among the top three countries for effectively managing the pandemic [7].

The rapid increase in severe cases strained healthcare systems globally, including shortages of hospital beds, ventilators, personal protective equipment (PPE), and trained staff [5, 8]. The surge in patients requiring respiratory support exposed major gaps in critical care capacity. Accurate disease characterization is therefore essential to identify risk factors, predict organ support needs, and guide resource allocation [9]. While national surveillance tracked overall cases, it lacked detailed patient-level data on ICU admissions. The Pakistan Registry of Intensive Care (PRICE), established in 2018, helped fill this gap by providing near real-time data on ICU admissions, clinical characteristics, and outcomes during the pandemic [10].

In this study, we present the demographics, clinical characteristics, and outcomes of COVID-19 patients admitted to sixty-nine intensive care units (ICUs) during five waves of the pandemic in Pakistan. The outcomes analyzed were length of stay, need for invasive mechanical ventilation, and mortality.

## Methodology

### Study design and setting

This multicenter observational cohort study included prospectively collected data from all COVID-19 patients admitted to ICUs who participated in the Pakistan Registry of Intensive Care (PRICE) from April 2020 to March 2022. The timeline defined by the NCOC [7] for the pandemic waves is shown in Table 1.

PRICE prospectively collects clinical and demographic data on consecutive adult ICU admissions to provide information on case mix (including presentation, diagnosis, and comorbidities), severity of illness, organ support days, risk-adjusted ICU mortality, and care processes [11]. Operational in 69 units, it covers critical care services in five of the country’s seven administrative regions. Demographic, diagnostic, comorbid, and severity of illness data are captured on admission to the ICU; treatment characteristics in the first 24 h, highest ventilation support, and outcomes at ICU discharge. Outcomes (censored at 60 days) are recorded as death in ICU, step down to ward, discharge home, discharge for end-of-life care, and transfer to a specialist unit.

At the time of the WHO declaration of a global pandemic, the International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC) WHO Clinical Characterization Protocol (CCP) was embedded in the PRICE platform. The additional dataset included SARI symptoms at presentation, respiratory symptoms, travel history, and laboratory confirmation of infection. Using the PRICE core and the SARI CCP dataset, clinical characteristics and outcomes of patients admitted to ICU for COVID-19 were described. Patient outcomes were stratified based on the requirement for organ support which included invasive mechanical ventilation, cardiovascular support, and renal replacement therapy. Independent risk factors associated with mortality were identified.

The ISARIC WHO CCP is a sleeper protocol that can be rapidly deployed to provide globally relevant observational data that can inform future clinical and epidemiological research and trials designed to identify strategies to optimize clinical outcomes [12]. The open-access protocols use standardized and refined case report forms, information, and consent documents and offer a tiered (0–3) biological sampling schedule. The WHO Ethics Review Committee approved a global master protocol for the ISARIC CCP and endorsed its use in outbreaks

**Table 1** Timeline for the COVID-19 pandemic in Pakistan

Wave number	Wave 1	Wave 2	Wave 3	Wave 4	Wave 5
Dates	April - September 2020	October 2020 - February 2021	March 2021 - June 2021	July - November 2021	December 2021 - March 2022

of public health interest [13]. The CCP was aligned with the existing PRICE core dataset. Variables were added via a standardized nomenclature (CT SNOMED) already operationalized in the platform [14], enhancing interoperability at the organizational level and facilitating sharing with ISARIC while complying with the FAIR principles for healthcare data collaboration [15].

Leveraging the existing PRICE data collection methods, training was provided to existing data collectors and clinical leads in the additional dataset and in dashboard navigation [11]. Training and implementation were supported by the Wellcome-funded CRIT Care Asia registry development and implementation team based in Sri Lanka [16]. Data quality for surveillance and subsequent research is outlined by the recently published DAQCord guidance for observational research [17].

### Participants and data collection

Patients aged 18 years or older who were admitted to one of the 69 PRICE ICUs during the study period and who met the ISARIC CCP v.10.2 definition for severe acute respiratory infection (SARI), defined as fever ( $\geq 38.0$  °C), cough, or dyspnoea/tachypnoea, admitted to the ICU with confirmed COVID-19 by reverse transcriptase polymerase chain reaction (PCR) [18]. Patients admitted to the ICU on suspicion of COVID-19 who subsequently tested positive for COVID-19 during their ICU admission and at discharge were also included. Patients aged < 18 years were excluded from this study.

### Statistical analysis

We conducted a descriptive analysis of registry-embedded COVID-19 data to understand and assess demographic trends, clinical characteristics, and outcomes of patients with SARS-CoV-2. The patient-level variables analyzed included age group, gender, and organ support, categorized by the presence of ventilatory, cardiovascular, or renal support. Ventilatory support was further

classified into invasive mechanical ventilation (comprising an endotracheal tube (ETT) or tracheostomy) and noninvasive ventilatory support. Reported comorbidities such as diabetes, cardiovascular diseases, hypertension, and mortality outcomes were also included. The main outcomes were ICU admissions, organ support (on admission and during ICU stay), and ICU mortality. All patients were divided into groups based on their period of admission, corresponding to the five pandemic waves. The method of data collection (via PRICE) was identical across all waves.

Descriptive analyses were performed to summarise patient demographics, comorbidities, and clinical characteristics across pandemic waves. Categorical variables were presented as frequencies and percentages, while continuous variables were summarised using medians and interquartile ranges (Q1–Q3). These univariate summaries are presented in Tables 2 and 3. Unadjusted time-to-event analyses included cumulative incidence functions for ICU length of stay and discharge outcomes (death or survival), stratified by organ support status and pandemic wave (Fig. 5). Median time from hospital admission to ICU transfer and to initiation of invasive mechanical ventilation was also reported for survivors and non-survivors (Table 3).

Multivariable time-to-event analyses were conducted using Cox proportional hazards regression to evaluate the association between patient-level factors and two outcomes: initiation of invasive mechanical ventilation (Model 1) and ICU mortality among ventilated patients (Model 2). Pandemic wave was modeled as a categorical fixed effect, and both models were adjusted for age, sex, admission oxygen saturation, hypertension, diabetes, cardiovascular disease, and vaccination status. These variables were selected based on prior evidence of their association with COVID-19 outcomes in critically ill patients [19, 20]. Age and admission oxygen saturation were modeled using orthogonal polynomials of degree 3

**Table 2** Progression from hospital admission to the ICU. Values are shown as median (Q1–Q3) for continuous variables and number (percentage) for categorical variables

	Wave 1 April 2020 to September 2020	Wave 2 October 2020 to February 2021	Wave 3 March 2021 to June 2021	Wave 4 July 2021 to November 2021	Wave 5 December 2021 to March 2022
Total Number of Admissions	2704	2563	1393	1664	788
<b>Progression from Hospital Admission to ICU</b>					
Hospital to ICU admission days	2(1–3)	1(1–4)	1(1–3)	2(1–5)	1(1–3)
ICU admission within 24 h of hospitalization	1602(59.2%)	1513(59.1%)	796 (57.1%)	987 (59.3%)	502 (64.5%)
Mortality n (%)	9359(34.5%)	1009(39.3%)	573(41.1%)	695(41.7%)	161(20.4%)
Length of stay Survivors	3(2–7)	3(1–6)	3(1–6)	3(1–5)	2(1–4)
Length of stay Non-survivors	3(1–7)	5(2–8)	4(2–8)	3(1–7)	4(1–7)

**Table 3** Respiratory Support. Values are shown as median (Q1–Q3) for continuous variables and number (percentage) for categorical variables

	Wave 1 April 2020 to September 2020	Wave 2 October 2020 to February 2021	Wave 3 March 2021 to June 2021	Wave 4 July 2021 to November 2021	Wave 5 December 2021 to March 2022
<b>Invasive Mechanical Ventilation (IMV)</b>					
Number of patients on IMV at the time of ICU Admission	516(19.1%)	615(24.1%)	339(24.3%)	374(22.4%)	117(15%)
Number of patients on IMV at any time during ICU stay	939(34.7%)	1001(39%)	548(39.3%)	751(45.1%)	272(34.5%)
Hospital Admission to IMV days	2 (1–6)	3(1–7)	4 (2–7)	4(2–8)	3(2–6)
Survivors: Hospital admission to IMV days	1(1–3)	1(1–2)	1(1–2)	2(1–5)	2 (1–4)
Non survivors Hospital admission to IMV days	2 (1–4)	2 (1–4)	2 (1–5)	2 (1–5)	2 (1–3)
ICU Admission to IMV -	2 (1–4)	2 (1–5)	3 (1–5)	2 (1–5)	2 (1–4)
<b>High Flow Nasal Cannula (HFNC)</b>					
At the time of Admission	1026 (37.9%)	598(23.3%)	663(47.5%)	512(30.7%)	141(18.1%)
<b>Non-Invasive Ventilation (NIV)</b>					
Median Days for NIV	1(1–3)	2(1–4)	3(1–5)	2.5(1–5)	2(1–4)
Anytime during ICU admission	601 (22.2%)	658 (25.6%)	333 (23.9%)	522 (32.3%)	236(30.1%)

to capture potential nonlinear relationships with the outcome, while maintaining numerical stability and reducing multicollinearity between polynomial terms.

Cox models were selected to accommodate time-to-event outcomes in the presence of competing risks, which are common in ICU settings. For Model 1, the competing events were death or discharge without invasive mechanical ventilation; for Model 2, discharge alive was treated as a competing event.

Missing data were observed only for the oxygen saturation variable, recorded at admission, affecting approximately 4% of observations. Initial multiple imputation attempts using clinically relevant predictors (wave number, age, gender, hypertension, diabetes, cardiovascular support, ventilatory support, and survival status) failed to converge reliably. To improve model stability, we applied the Least Absolute Shrinkage and Selection Operator (LASSO) regression to identify a suitable predictor set; however, several LASSO-selected variables introduced singularity into the imputation design matrix and were subsequently dropped by the Multiple Imputation by Chained Equations (MICE) algorithm, likely due to collinearity, sparse distributions, or deterministic relationships. These exclusions compromised the integrity of the imputation model and introduced instability across imputations. We therefore proceeded with single imputation ( $m=1$ ) using the initially selected predictors. To evaluate the robustness of this approach, we conducted a sensitivity analysis comparing single imputation ( $m=1$ ), multiple imputation ( $m=5$ ), complete-case analysis, and mean imputation. All approaches yielded consistent estimates, with no meaningful differences in effect size or directionality.

Both regression analyses accounted for competing risks: death in the hospital and discharge alive without invasive mechanical ventilation for Model 1, and

discharge dead for Model 2. In both models, patient outcomes were assessed for up to 28 days, and results are presented as hazard ratios (HRs) with 95% confidence intervals (95% CIs). Proportional hazards assumptions were evaluated using scaled Schoenfeld residuals. Full results of the proportional hazards diagnostics are provided in the Supplementary Appendix. All analyses were performed in RStudio version 2023.12.1 using R version 4.3.2.

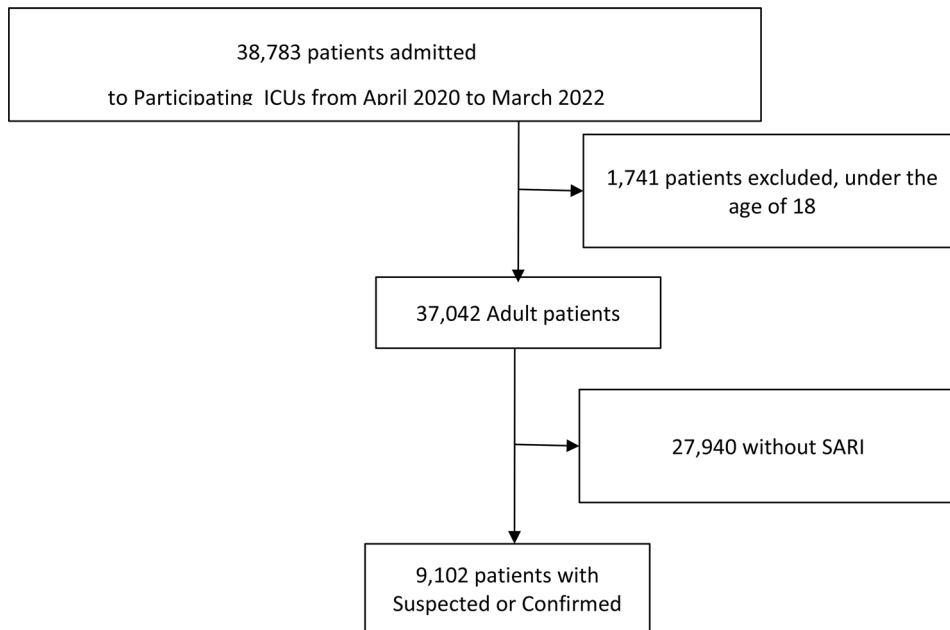
## Results

During the study period, 38,783 patients were admitted to 69 PRICE collaborating ICUs, with 9,102 meeting the eligibility criteria (Fig. 1).

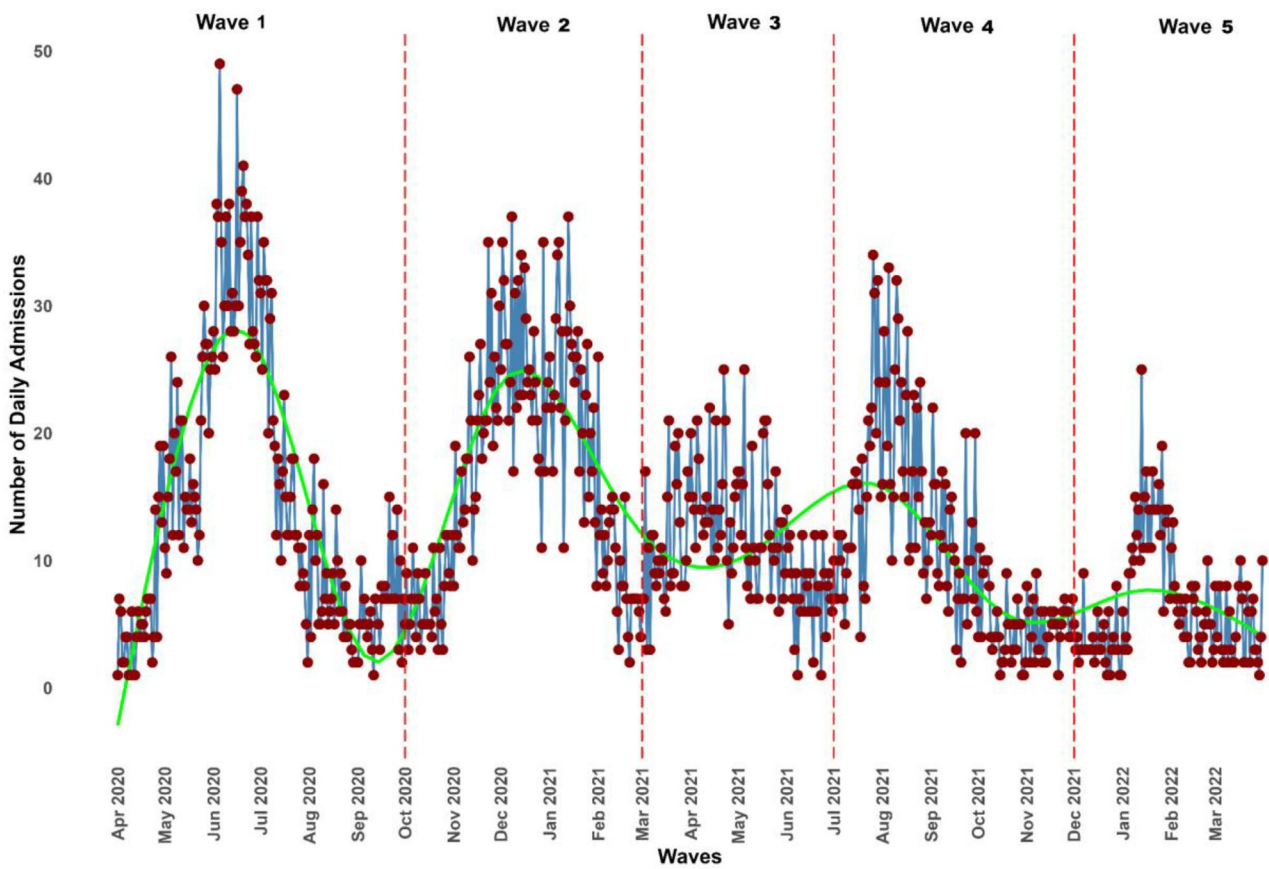
Across all five pandemic waves combined, the median age was 60 years (50–70 years) and 61% were male. Hypertension (47.6%) was the most common comorbidity, followed by type 2 diabetes (15.2%) and cardiovascular diseases (8.6%). The most prevalent symptoms identified were shortness of breath (77.3%), fever (72.4%), and cough (26.9%). The proportion of patients requiring organ support on admission was 41.5%. The overall mortality rate was 37% and the median length of ICU stay was 3 days. At the time of ICU admission, 16.9% of patients received invasive mechanical ventilation (IMV) while 21.5% required IMV at any time during ICU stay.

### Number of admissions

The duration of pandemic waves ranged from four months (Wave 3: 121 days) to six months (Wave 1: 182 days), with ICU admission days varying within each wave (Fig. 2). The highest number of ICU admissions occurred during the first ( $n=2,704$ ) and second ( $n=2,563$ ) waves. The single-day peak was recorded on June 5, 2020, with 49 ICU admissions.



**Fig. 1** Study flowchart for patient inclusion. SARI stands for severe acute respiratory infection



**Fig. 2** COVID-19 admissions to the ICU across the COVID-19 waves

**Demographics**

The majority of ICU admissions were male across the first four waves (Fig. 3). Within each pandemic wave, 60–79 years was the most common age bracket for both males and females. The proportion of patients over 80 years of age increased from 8.9% in the 4th wave to 18.6% in the 5th wave.

**Clinical presentation**

The most prevalent symptoms among both sexes in all waves were shortness of breath, fever, and cough with no sputum (Fig. 4). Fever ( $n = 1,342$ ; 80.6%) was marginally more common than shortness of breath ( $n = 1,192$ ; 71.6%) during the fourth wave.

**Hospital admissions to ICU**

In the first and fourth waves, the median time from hospital to ICU admission was 1 day; during the remaining waves, it was 2 days. The majority of patients were admitted to ICU within 24 h of hospital admission. The highest mortality was observed in waves 3 and 4 (41%) (Table 2).

**Respiratory support**

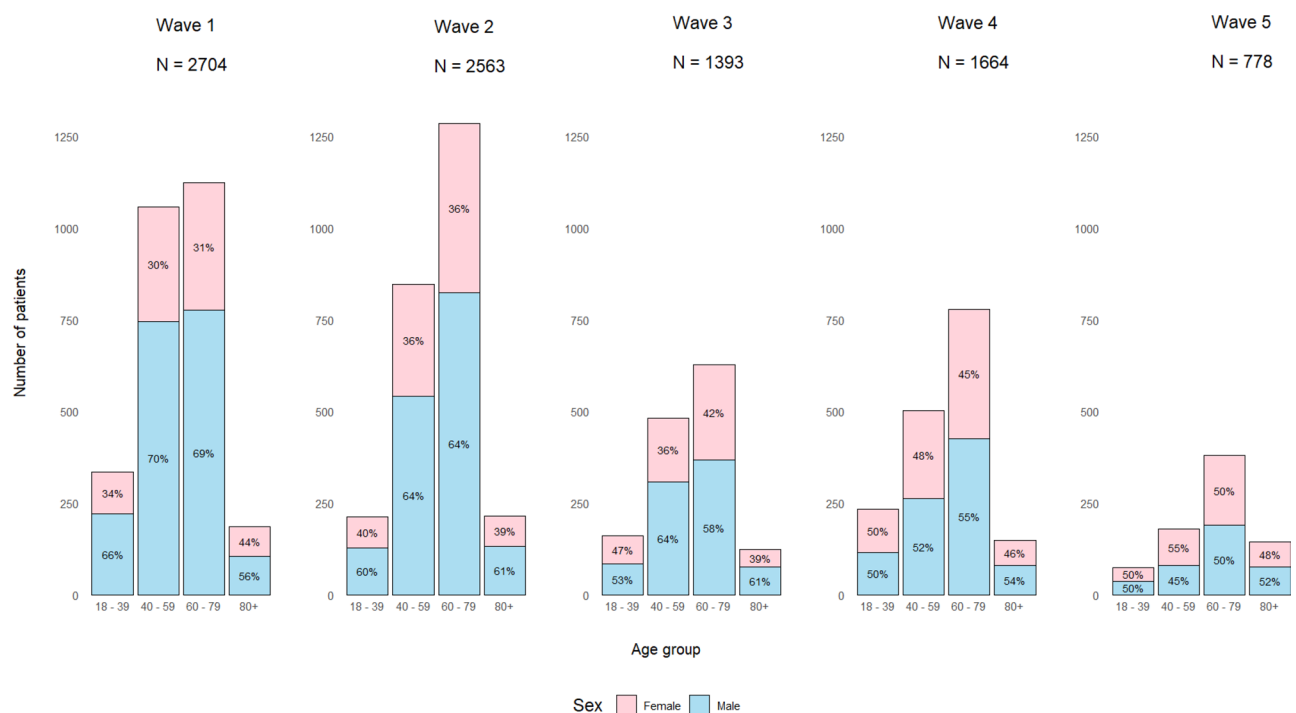
The median time from hospital admission to IMV was 2–3 days throughout the waves with survivors requiring mechanical ventilation sooner. The use of high-flow nasal cannulas (HFNCs) increased to 47.5% in wave 3 (Table 3).

**Mortality and length of stay**

Patient outcomes across all five waves highlighted strong differences between patients with and without organ support during ICU admission (Figure 5). Across all five waves, approximately 80% of patients who did require organ support were discharged within 28 days of ICU admission. The cumulative incidence functions for this patient group indicated that most discharges occurred within the first 10 days of ICU admission. In contrast, mortality incidence among patients who required organ support steadily increased across the first four waves, from 50% in Wave 1 to 65% in Wave 4.

**Multivariate analysis: Invasive mechanical ventilation and mortality**

Cox regression results for the initiation of invasive mechanical ventilation (Model 1) are summarized in Fig. 6. The results revealed that younger patients and individuals with low oxygen saturation at admission had a greater risk of requiring invasive mechanical ventilation. The risk of requiring mechanical ventilation was highest: the hazard ratio (HR) (95% CI) in the 4th wave was 1.21(1.091.34) and that in the 5th wave was 1.28 (1.101.50) relative to that at the start of the COVID-19 pandemic. Additionally, the presence of cardiovascular disease significantly increased the risk of patients being placed on invasive mechanical ventilators (HR:1.16; 95% CI: 1.04–1.31).



**Fig. 3** Sex distribution of admissions by age during the COVID-19 waves

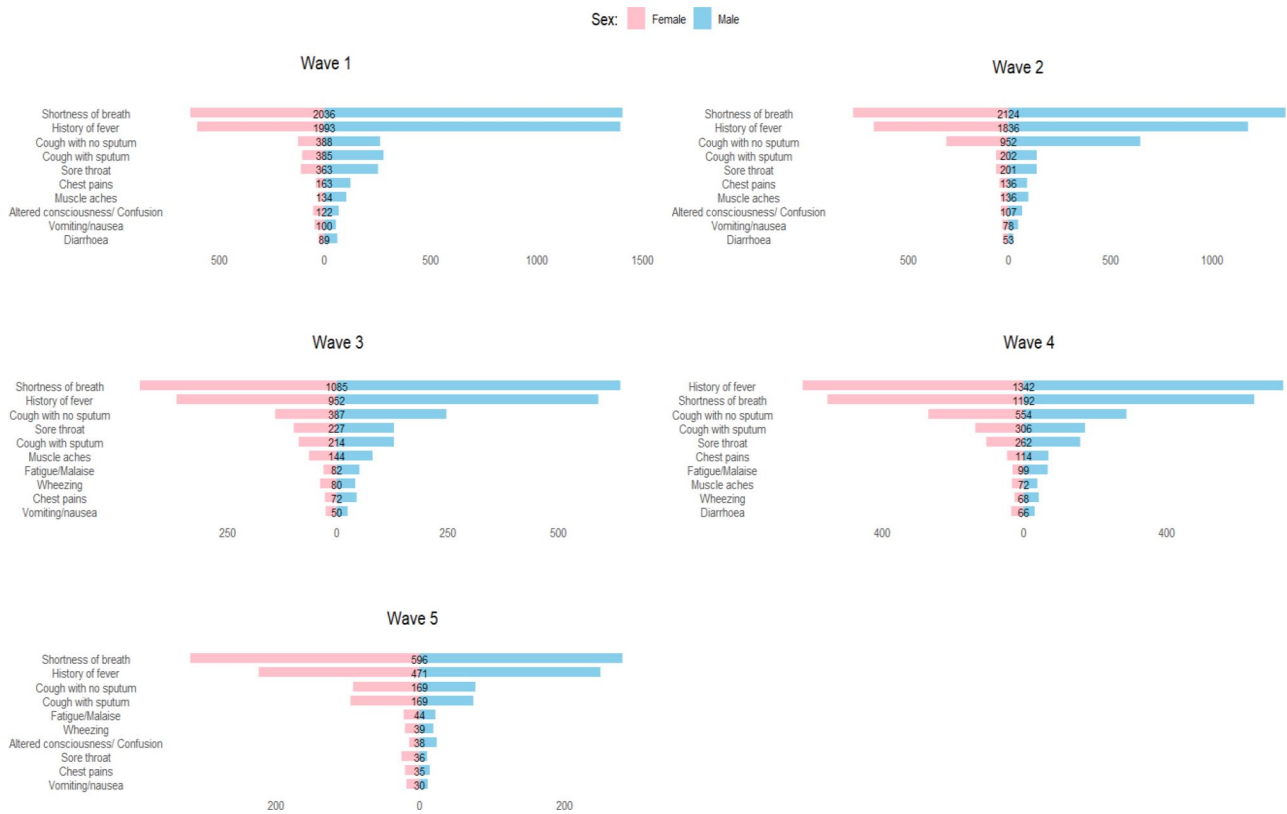


Fig. 4 Gender-specific symptoms across the waves

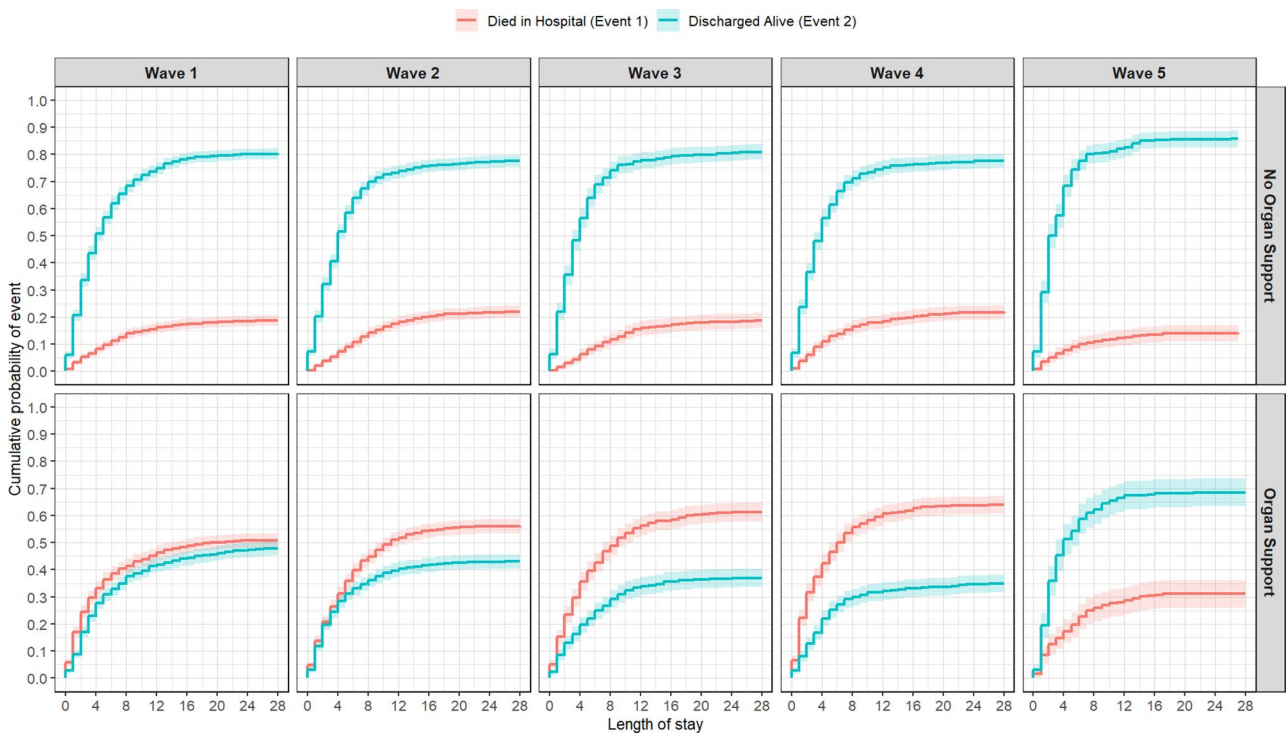
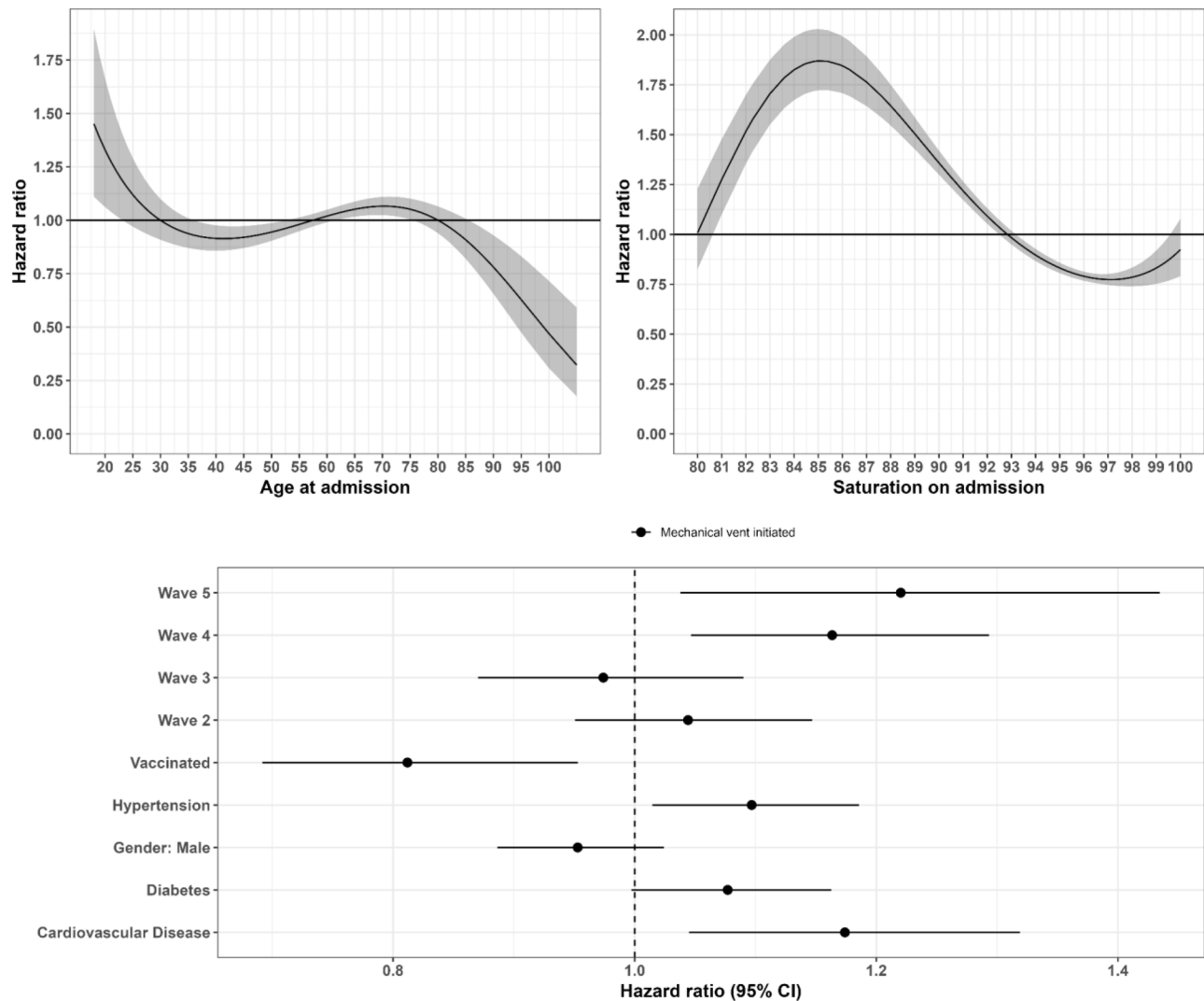


Fig. 5 Cumulative probability of mortality and survival, comparing those requiring organ support vs. no organ support across different waves



**Fig. 6** Hazard ratios for the initiation of invasive mechanical ventilation

Figure 7 summarizes Cox regression results for 28-day in-hospital mortality following the commencement of invasive mechanical ventilation (Model 2). The results indicated age-related associations with mortality risk; higher oxygen saturation on admission was associated with a greater risk of mortality. In addition, the periods of the 4th and 5th waves posed the highest risk for mechanically ventilated patients compared with the first pandemic wave: HR (95% CI); 2nd wave 1.02(0.93 to 1.12); 3rd wave 1.01(0.90 to 1.12) and 4th wave 1.21(1.09 to 1.34).

**Discussion**

**Summary of key findings**

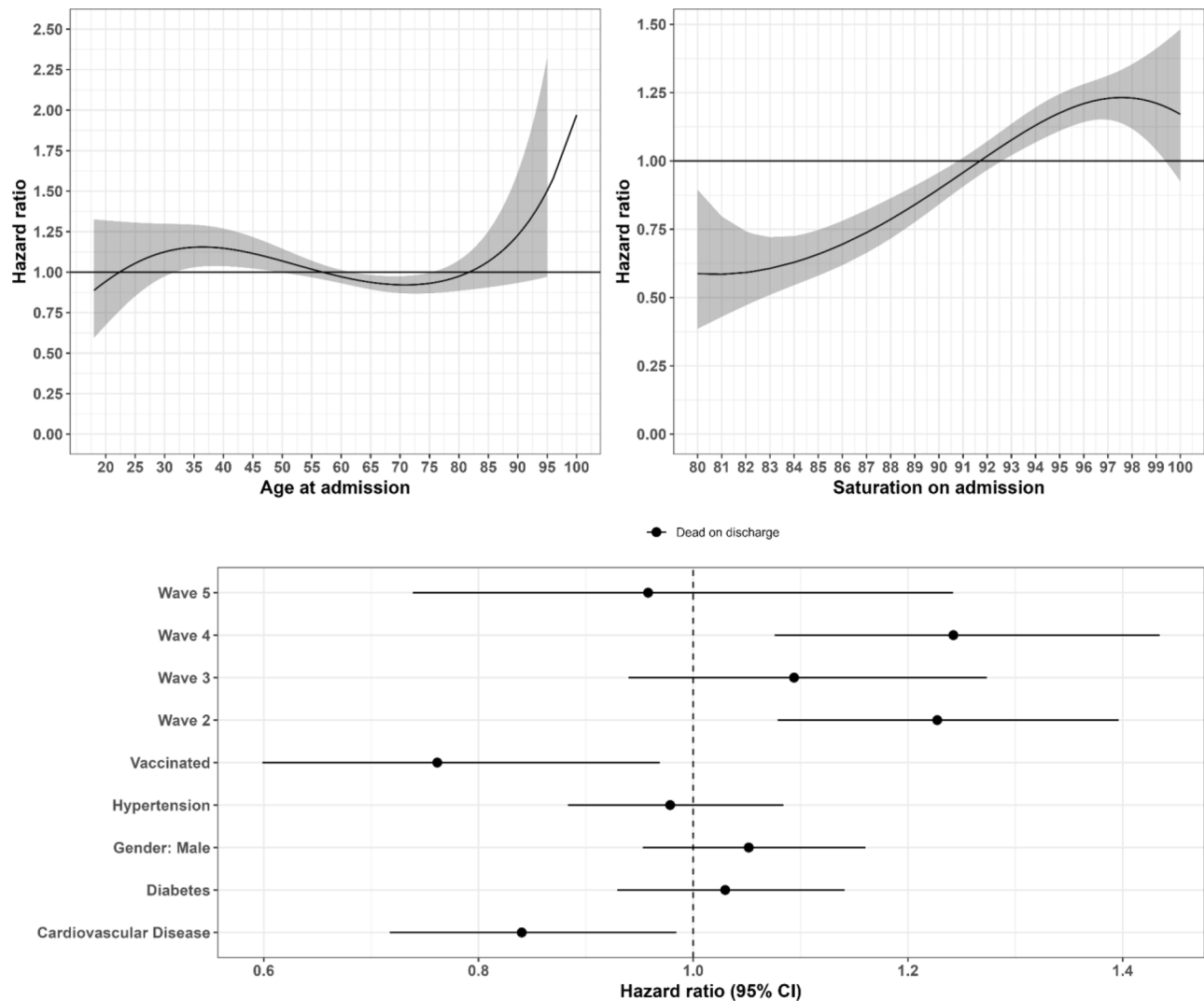
In this multicenter study of 9,102 ICU patients with COVID-19 across five waves in Pakistan, most admissions were male. The majority of patients across all waves were in the 60–79 year age group. Shortness of breath,

fever, and cough were the most frequent presenting symptoms. Mortality reached 41% during Waves 3 and 4. The risk of requiring invasive mechanical ventilation was highest in Waves 4 and 5. Younger patients with low oxygen saturation at admission and cardiovascular disease were significant predictors of invasive ventilation.

**COVID-19 waves: challenges and responses**

Between April 2020 and March 2022, Pakistan experienced five distinct waves of COVID-19, each influenced by emerging variants, changing public health measures, and the gradual evolution of the national pandemic response. These contextual factors are critical to understanding variations in ICU admissions and outcomes observed in the PRICE registry.

The first wave (April–September 2020) occurred earlier than in other South Asian countries [21]. The original strain caused a wide range of symptoms, and a



**Fig. 7** Hazard ratios for death in patients on invasive mechanical ventilation

nationwide lockdown was imposed. Thirty-five hospitals with 2,942 beds were designated for treatment [22], and the mortality rate remained relatively low. The second wave (October–December 2020), associated with the Beta variant, led to moderate increases in cases [23]. “Smart” lockdowns were implemented [24], but poor compliance resulted in overwhelmed ICUs and ventilator shortages.

The third wave (March to June 2021) coincided with the emergence of the alpha variant. This variant has mutations that evade the immune response, leading to moderate-to-severe cases, particularly in areas with low vaccine coverage [25]. Although Pakistan initiated its vaccination campaign by early 2021, a large proportion of the population remained unvaccinated, leading to higher mortality rates.

The third wave (March–June 2021) was driven by the Alpha variant, which partially evaded immune responses

[25]. Although vaccination began early in 2021, low coverage and hesitancy led to more severe cases and higher mortality. The fourth wave (July–November 2021), driven by the Delta variant, was the most severe, with higher transmissibility and hospitalizations [26]. ICU capacity and medical supplies were critically strained, and mortality increased among unvaccinated individuals [27]. The fifth wave (December 2021–March 2022), caused by the Omicron variant, was less severe but highly transmissible, increasing hospital admissions [28, 29].

Throughout the pandemic, Pakistan faced recurring challenges such as limited testing, underreporting, and poor adherence to preventive measures [30]. Economic instability and unemployment also contributed to public resistance to the following guidelines, as many prioritized financial survival over safety [31, 32]. Vaccination began during the third wave, but people were reluctant to get

vaccinated due to misinformation and a lack of awareness, contributing to severe cases [33, 34].

To overcome these challenges the National Command and Operation Centre (NCOC) coordinated with provincial governments to distribute resources including ventilators, oxygen supplies, and PPE [7]. Vaccination was prioritized, especially for healthcare workers and the elderly population. Online portals such as the National Immunization Management System (NIMS) were introduced for vaccine registration and tracking [35]. Mobile vaccination units deployed in remote areas to overcome accessibility issues [36]. The NCOC ran campaigns in local languages to dispel myths and misinformation, aiming to increase public participation in the country's response to and efforts towards the pandemic [7]. A centralized monitoring system was also developed to track hospital occupancy and ICU bed availability for the management of hospitals [7]. These steps by the NCOC and the government helped mitigate the overall situation during the five waves of the pandemic.

#### **Cumulative data trends**

Analysis of the PRICE registry showed that patients admitted to ICUs in Pakistan were generally older (median age 60 years) compared with similar cohorts globally, where a meta-analysis of 11 countries reported a median age of 47 years [37]. The higher age profile in Pakistan may reflect the greater vulnerability of older adults with chronic comorbidities. Conditions such as hypertension, diabetes, and cardiovascular disease increase the risk of severe COVID-19 through impaired immunity and chronic inflammation [38, 39]. These comorbidities, combined with lower vaccination coverage among the elderly, likely contributed to higher ICU admissions and mortality in this group.

Males accounted for more than half of ICU admissions, consistent across all waves. This aligns with global evidence showing higher infection rates and mortality among males [40], suggesting a biological or behavioral predisposition that increased disease severity in men.

The comorbidity pattern seen in the PRICE cohort is similar to that reported in ICU populations from other middle-income countries. Hypertension, diabetes, and cardiovascular disease were the most common conditions, reflecting a high burden of cardiometabolic illness among critically ill patients. Comparable findings were reported in a multicenter one-day point prevalence study from Turkey that included 811 ICU patients with COVID-19, where these comorbidities were also highly prevalent [38]. This similarity indicates that the distribution of non-communicable diseases, rather than geographic location alone, largely influences ICU case-mix and disease severity in resource-limited settings. These conditions are associated with an increased risk of severe

disease, hospitalization, and mortality due to impaired immune response and chronic inflammation.

The most common presenting symptoms were shortness of breath, fever, and cough, consistent with international data from the ISARIC database covering more than 60 countries [39]. These findings confirm that local clinical presentations align with global trends, although symptom severity varied with age, comorbidities, and circulating variants.

At ICU admission, over 40% of patients required organ support, highlighting the severity of the disease. The need for support varied by wave, influenced by changing patient profiles, evolving treatment protocols, and variant characteristics. Meta-analyses report higher rates globally, 69% requiring invasive mechanical ventilation and 34% requiring renal replacement therapy [41], while another study found that 67% of critically ill patients required vasopressors [42]. These differences may reflect variations in ICU resources, patient demographics, and admission criteria across regions.

Mortality among ICU patients in the PRICE registry remained high, likely due to the advanced disease stage at admission and limited healthcare capacity. Internationally, ICU mortality ranged from 26% in Europe to 40% in North America, with a pooled global rate of 34% [43]. Differences in treatment strategies, reporting standards, and outbreak timing likely contributed to these disparities.

The median ICU stay was three days, shorter than the global range of 5–19 days [44]. In low- and middle-income countries, shorter stays often result from early mortality, rapid discharge to free ICU beds, or limited access to advanced life-support equipment. In Pakistan, these factors, along with high patient turnover, may explain the shorter length of stay observed in the registry.

#### **Organ support and patient outcomes across the waves**

The need for invasive mechanical ventilation (IMV) was highest during Waves 2, 3, and 4, coinciding with the emergence of more virulent COVID-19 variants that caused severe respiratory failure. These variants, with greater transmissibility and pathogenicity, led to a rise in critically ill patients requiring advanced respiratory support. A systematic review and meta-analysis reported that nearly half (47%) of patients requiring IMV did not survive [45]. Mortality among ventilated patients is likely due to prolonged lung injury, ventilator-associated complications, and the aggressive inflammatory response seen in severe disease.

During the early waves, clinicians frequently opted for early intubation due to limited understanding of disease progression. As evidence evolved, the use of noninvasive ventilation and corticosteroids increased, reducing intubation rates. However, the emergence of the Delta variant

again increased IMV demand due to more severe respiratory failure.

Multivariate analysis showed a significantly higher risk of IMV use during the later stages of the pandemic. A multicenter study across 21 hospital systems similarly found increased mortality among patients on IMV during the Delta wave [46]. Although the Delta variant's severity played a role, waning immunity and uneven vaccine coverage also contributed. Differences in healthcare capacity further influenced outcomes: regions with stronger infrastructure managed severe cases more effectively, while resource-limited areas experienced higher IMV use and mortality due to delayed hospital presentation and limited critical care services.

Our analysis also found that younger patients and those presenting with low oxygen saturation were more likely to require IMV. This contrasts with findings from high-income countries, where older age predicted higher disease severity [47]. Data from the PRoVENT-COVID study showed that age did not affect ventilator management, but older patients experienced more complications and longer ICU stays [48]. In Pakistan's resource-limited context, younger patients were often prioritized for IMV because of higher expected survival, reflecting triage practices during critical surges.

ICU mortality in our cohort reached 41% during Waves 3 and 4, exceeding the global average of 28.3% and the rates reported in Europe (26%) and North America (40%) [49, 50]. Comparable outcomes have been reported from other middle-income settings. A multicenter retrospective study from Turkey involving critically ill pregnant and puerperal women with COVID-19 reported a maternal mortality of 30.3% and a requirement for invasive mechanical ventilation in 46.6% of cases [51]. In contrast, high-income countries generally report lower ICU and IMV mortality, reflecting stronger critical care capacity, whereas low- and middle-income countries (LMICs) consistently experience higher mortality rates [52]. The elevated mortality observed in our cohort likely results from a combination of factors, including the circulation of more virulent variants (Alpha and Delta), delayed hospital presentation, limited ICU capacity, low vaccination coverage, and uneven public health responses.

### Limitations

Our analysis was limited to variables included in the PRICE registry case report form, which was standardized across all contributing study sites. Although we described overall organ support use, the registry did not record when these interventions were initiated during ICU stay. Some treatment variables were captured only as binary responses ("yes" or "no"), limiting assessment of treatment timing in multivariable analyses. Furthermore, Vaccination data were also limited, as the national campaign

began midway through Wave 3, and uptake remained low through Wave 5 due to hesitancy. Consequently, outcomes could not be stratified by vaccination status. Variant classification was based on national and global surveillance rather than patient-level sequencing and may not fully reflect the diversity of circulating strains.

Our research focused on patients admitted to the PRICE collaborating ICUs, so we cannot draw broader conclusions about triage practices or outcomes in general hospital wards throughout the various waves.

### Conclusion

The five waves of COVID-19 in Pakistan, as observed through the PRICE registry, show variations in disease outcomes. Mortality was higher in the third and fourth waves, where the majority of deaths occurred among patients needing intensive organ support. Younger patients, those with severe hypoxia, and individuals with preexisting cardiovascular conditions face elevated risks for invasive ventilation and adverse outcomes.

### Abbreviations

PRICE	Pakistan Registry of Intensive Care
ICU	Intensive Care Unit
IMV	Invasive Mechanical Ventilation
PRoVENT-COVID	Practice of VENTilation in COVID-19 Patients
PHEIC	Public Health Emergency of International Concern
WHO	World Health Organization
HRs	Hazard Ratios
HFNCs	High-Flow Nasal Cannulas
ETT	Endotracheal Tube
ARDS	Acute Respiratory Distress Syndrome
NIMS	National Immunization Management System
ISARIC	International Severe Acute Respiratory and Emerging Infections Consortium
NCOC	National Command and Operations Centre
PPE	Personal Protective Equipment
SARI	Severe Acute Respiratory Infection
PCR	Polymerase Chain Reaction

### Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12879-026-13012-3>.

Supplementary Material 1

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### PRICE Collaborators

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All authors contributed to the writing and review of the manuscript. Each author reviewed the content and approved the final version of the manuscript prior to submission.

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#### Data availability

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

#### Declarations

##### Ethics approval and consent to participate

Ethical review and approval were obtained from the National Bioethics Committee of Pakistan. The study was awarded a waiver of consent by the "Research Ethics Committee" of "National Bioethics Committee" (Ref: No.4-87/NBC-470/COVID01-/20) and there is also international precedence from WHO and ISARIC that this type of observational and evaluative study does not require individual patient consent. This study complies with the principles set out in the Declaration of Helsinki and the Principles of Good Clinical Practice (ICH 1996).

##### Consent for publication

All authors have reviewed and approved the manuscript for publication.

##### Competing interests

The authors declare no competing interests.

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