Archives of Anesthesiology and Critical Care (In Press); x(x): xx-xx.

Available online at http://aacc.tums.ac.ir

Research Article

Respiratory Support Patterns, Pneumothorax Incidence, and Factors Associated with Invasive Intubation among Critically Ill COVID-19 Patients Admitted to the ICU

Zahra Rahimi, Behzad Nazemroaya, Zahra Shojaei*

Department of Anesthesiology and Critical Care, School of Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.

ARTICLE INFO

Article history:
Received 23 June 2026
Revised 15 July 2026
Accepted 29 July 2026

Keywords:
COVID-19;
Intensive care unit;
Mechanical ventilation;
Non-invasive ventilation;
Pneumothorax;
Barotrauma;
Mortality

ABSTRACT

Background: Critically ill patients with coronavirus disease 2019 (COVID-19) often require escalation of respiratory support, such as non-invasive ventilation and invasive mechanical ventilation. While invasive ventilation can be lifesaving, it is associated with risks of ventilator-induced lung injury and barotrauma, including pneumothorax. The present study evaluated respiratory support patterns, clinically documented pneumothorax, and factors associated with invasive intubation among critically ill COVID-19 patients admitted to the intensive care unit of Al-Zahra Hospital in Isfahan, Iran.

Methods: This retrospective observational cohort study included 152 adult patients with confirmed COVID-19 admitted to the intensive care unit. Demographic characteristics, recorded hospital stay/duration, early laboratory values, arterial blood gas indices, respiratory support modalities, airway interventions, and clinically documented pneumothorax were extracted from medical records. Patients were compared according to invasive intubation status. Continuous variables were compared using the Mann–Whitney U test, and categorical variables were compared using the chi-square test with continuity correction or Fisher's exact test, as appropriate. Exploratory multivariable logistic regression was performed to identify variables independently associated with invasive intubation.

Results: The mean age was 58.49 ± 13.94 years, and 87 patients (57.2%) were male. Non-invasive ventilation was required in 34 patients (22.4%), while 82 patients (53.9%) underwent endotracheal intubation and invasive mechanical ventilation. Re-intubation occurred in 7 patients (4.6% of the total cohort; 8.5% of intubated patients), and tracheotomy was performed in 6 patients (3.9% of the total cohort; 7.3% of intubated patients). Clinically documented pneumothorax occurred in 2 patients, corresponding to 1.3% of the total cohort and 2.4% of intubated patients. Compared with non-intubated patients, intubated patients were older and had higher blood urea nitrogen, creatinine, $PaCO_2$, activated partial thromboplastin time, D-dimer, C-reactive protein, and ferritin levels, as well as lower hemoglobin concentration, lower platelet count, and lower arterial pH. In exploratory multivariable analysis, higher blood urea nitrogen, lower hemoglobin concentration, lower platelet count, and higher C-reactive protein were independently associated with invasive intubation.

Conclusion: In this single-center cohort of critically ill COVID-19 patients, the requirement for invasive respiratory support was substantial, while clinically documented pneumothorax was infrequent. Patients who required invasive intubation exhibited greater renal, inflammatory, hematologic, coagulation, and acid-base abnormalities compared to non-intubated patients. These findings are hypothesis-generating and non-causal due to the retrospective design, limited ventilatory

The authors declare no conflicts of interest.
*Corresponding author.
E-mail address: behzadnazemroaya797@gmail.com
DOI:

mechanics data, and the small number of pneumothorax events.

Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), rapidly became a major cause of hospitalization and intensive care unit (ICU) utilization worldwide [1].

Although many infected individuals develop mild or moderate disease, a clinically important subgroup progresses to severe viral pneumonia, acute respiratory distress syndrome (ARDS), refractory hypoxemia, and multi-organ dysfunction [2-3]. Among ICU-admitted patients, the need for advanced respiratory support and invasive mechanical ventilation reflects high disease severity and is frequently associated with prolonged hospitalization, complex ICU management, and poor clinical outcomes [2,3,4].

The pulmonary manifestations of severe COVID-19 are driven by direct viral injury, dysregulated host inflammation, endothelial injury, and microvascular thrombosis. SARS-CoV-2 can trigger an exaggerated inflammatory response, with cytokine release and immune-mediated tissue injury contributing to alveolar-capillary damage and systemic complications [5]. In severe disease, these mechanisms may lead to ventilation–perfusion mismatch, impaired gas exchange, altered respiratory mechanics, increased physiological dead space, and severe systemic hypoxemia [6]. As respiratory failure progresses, critically ill patients may require escalation from conventional oxygen therapy to non-invasive respiratory support and, when these measures are insufficient, endotracheal intubation and invasive mechanical ventilation [7].

Although invasive mechanical ventilation can be lifesaving, mechanically ventilated lungs affected by severe inflammation and ARDS are vulnerable to ventilator-induced lung injury and barotrauma. Pneumothorax, pneumomediastinum, and related barotrauma events have been reported in patients with COVID-19, particularly among those receiving invasive mechanical ventilation [8–10].

These complications may worsen oxygenation, complicate ventilator management, increase the need for additional invasive procedures, and further destabilize critically ill patients. Therefore, evaluating pneumothorax incidence in ICU patients with COVID-19 remains clinically relevant, particularly when interpreted alongside respiratory support requirements and airway interventions. Lung-protective ventilation remains a central strategy in the management of ARDS. Low tidal-volume ventilation and limiting plateau pressure reduce ventilator-induced lung injury in acute lung injury and ARDS [11]. Driving pressure has also been identified as an important mechanical variable associated with survival in ARDS [12].

In selected patients with severe ARDS and marked patient–ventilator asynchrony dyssynchrony, neuromuscular blocking agents may improve patient–ventilator synchrony and reduce excessive respiratory effort [13]. However, in many retrospective COVID-19 datasets, detailed ventilatory parameters such as tidal volume, plateau pressure, driving pressure, positive end-expiratory pressure, respiratory-system compliance, prone positioning, recruitment maneuvers, and duration of mechanical ventilation are unavailable. This limits the ability to determine whether observed barotrauma rates are related to ventilation strategy, disease severity, diagnostic intensity, or documentation practices.

The clinical management of critically ill COVID-19 patients also evolved during the pandemic. International guidelines supported structured respiratory support strategies, anticoagulation considerations, infection control measures, and organ-supportive care in critically ill adults with COVID-19 [7].

Corticosteroids became a major component of therapy for hospitalized patients requiring oxygen therapy or mechanical ventilation after evidence demonstrated a survival benefit in this population [14].

Remdesivir was also used in selected hospitalized patients during several phases of the pandemic based on evidence suggesting a shorter time to clinical recovery in some patients [15]. Although pharmacological treatment is not the primary focus of the present analysis, these changes in background care are important when interpreting ICU cohorts treated during the pandemic.

Local ICU data remain clinically useful because thresholds for ICU admission, timing of intubation, access to non-invasive ventilation, resource availability, case mix, and institutional respiratory support practices varied across countries, hospitals, and pandemic waves [4]. Al-Zahra Hospital in Isfahan, Iran, served as a major tertiary referral center during successive COVID-19 surges. Evaluation of patients managed in this setting can help characterize center-specific patterns of respiratory support, clinically documented pneumothorax, airway interventions, and laboratory features associated with invasive intubation. Accordingly, this study aimed to evaluate respiratory support modalities, clinically documented pneumothorax, and factors associated with invasive intubation among critically ill COVID-19 patients admitted to the ICU of Al-Zahra Hospital in Isfahan, Iran.

Methods

Study Design and Setting

This retrospective observational cohort study was conducted at Al-Zahra Hospital, a tertiary university-affiliated referral center in Isfahan, Iran. The study included critically ill adult patients with confirmed COVID-19 who were admitted to the intensive care unit (ICU) during the study period. The study was designed to describe respiratory support patterns, clinically documented pneumothorax, and factors associated with the requirement for endotracheal intubation and invasive mechanical ventilation.

Ethical Considerations

The study protocol was reviewed and approved by the Institutional Review Board and Research Ethics Committee of Isfahan University of Medical Sciences under the ethics code IR.MUI.MED.REC.1402.418. Because of the retrospective design and the use of de-identified medical record data, the ethics committee waived the requirement for individual written informed consent.

All extracted data were anonymized before analysis. Patient confidentiality was maintained throughout data collection, storage, and statistical analysis, in accordance with the principles of the Declaration of Helsinki.

Study Population

The study population consisted of adult patients admitted to the COVID-19 ICU of Al-Zahra Hospital with confirmed COVID-19. Patients were eligible for inclusion if they were 18 years of age or older, had ICU admission because of severe COVID-19-related illness, had a positive SARS-CoV-2 polymerase chain reaction test, and had chest computed tomography findings compatible with COVID-19 pneumonia.

A total of 152 critically ill adult patients fulfilled the eligibility criteria and were included in the final analysis. Patients with unavailable core respiratory support data or insufficient clinical documentation for the main study variables were excluded from analysis.

However, patients were not excluded because of missing values in selected laboratory markers; instead, laboratory variables with missing data were analyzed using available-case analysis.

Data Sources and Data Collection

Data were extracted retrospectively from electronic medical records and available paper-based ICU files using a standardized data collection form. Extracted variables included demographic characteristics, hospital stay duration, early laboratory values, arterial blood gas indices, respiratory support modalities, airway interventions, and clinically documented respiratory complications. The extracted demographic and clinical variables included age, sex, and hospital stay duration. Laboratory and arterial blood gas variables included blood urea nitrogen, serum creatinine, aspartate aminotransferase, alanine aminotransferase, hemoglobin, platelet count, arterial pH, arterial partial pressure of carbon dioxide, arterial partial pressure of oxygen, activated partial thromboplastin time, prothrombin time, D-dimer, C-reactive protein, and ferritin. For variables with missing laboratory values, the number of valid observations was reported separately.

Definitions of Respiratory Support Variables

Respiratory support and airway-related variables included the use of oxygen by cannula or mini-mask, non-invasive ventilation, endotracheal intubation and invasive mechanical ventilation, re-intubation, tracheotomy, and clinically documented pneumothorax.

Non-invasive ventilation was defined as documented use of non-invasive ventilatory support during the clinical course. Invasive intubation was defined as endotracheal intubation followed by invasive mechanical ventilation. Patients recorded as having endotracheal intubation or intubation followed by tracheotomy were classified as invasively intubated for analysis. Re-intubation was defined as documented repeat endotracheal intubation after a previous extubation attempt. Tracheotomy was defined as documented surgical or percutaneous tracheotomy during the ICU or hospital course.

Definition of Pneumothorax

Pneumothorax was defined as a clinically documented diagnosis of pneumothorax in the medical record during the clinical course. The diagnosis was based on documentation by the treating clinical team and available radiological evidence in the medical record.

Because this was a retrospective study, systematic re-evaluation of all chest radiographs or computed tomography scans was not performed. Therefore, small or clinically silent pneumothoraces may not have been captured unless they were explicitly documented in the clinical record.

Outcome Measures

The main descriptive outcomes were the need for non-invasive ventilation, endotracheal intubation, invasive mechanical ventilation, re-intubation, tracheotomy, and a clinically documented pneumothorax. The main comparative outcome was invasive intubation status. Patients were classified as intubated or non-intubated and were compared with respect to demographic, laboratory, arterial blood gas, and clinical variables.

A secondary descriptive comparison was performed according to the need for non-invasive ventilation. Because pneumothorax occurred in only two patients, inferential modeling for it was not performed.

Handling of Missing and Censored Laboratory Data

Laboratory variables were analyzed using available-case analysis. Therefore, the valid sample size was reported for each laboratory variable when missing values were present. Activated partial thromboplastin time, prothrombin time, D-dimer, and ferritin had incomplete data and were reported with their corresponding valid sample sizes.

For laboratory variables with upper-limit or censored values in the clinical record, boundary numeric values were used when necessary for analysis. This approach may underestimate true extreme values and was considered in the interpretation of D-dimer and ferritin results.

Statistical Analysis

Statistical analysis was performed using SPSS software. Continuous variables were summarized using mean ± standard deviation, median and interquartile range, and range, as appropriate. Categorical variables were summarized as frequency and percentage.

Because several continuous variables showed non-normal distributions and clinically relevant skewness, between-group comparisons were performed using the Mann-Whitney U test.

Categorical variables were compared using the chi-square test with continuity correction or Fisher's exact test, as appropriate. Patients were compared according to invasive intubation status. Continuous variables were reported as median and interquartile range in the intubated and non-intubated groups. Categorical variables were reported as frequency and percentage within each group.

A similar exploratory comparison was performed based on the need for non-invasive ventilation. Exploratory multivariable logistic regression was performed to assess variables independently associated with invasive intubation. Variables included in the model were selected based on clinical relevance and significant or near-significant differences in bivariate analyses while avoiding excessive model complexity. To improve interpretability, blood urea nitrogen and C-reactive protein were scaled by 10-unit increases, and platelet count was scaled by 100,000/μL increases. Adjusted odds ratios with 95% confidence intervals were reported. This regression analysis was considered exploratory due to the retrospective design and the absence of a prespecified statistical analysis plan. A two-sided P value of less than 0.05 was considered statistically significant. Given the observational design, all associations were interpreted as non-causal.

Results

Corrected Cohort Characteristics

The corrected dataset included 152 critically ill adult patients with COVID-19 admitted to the ICU. The mean age was 58.49 ± 13.94 years, and the median age was 63.0 years (IQR: 48.0–69.0; range: 27–79). Eighty-seven patients (57.2%) were male, and 65 (42.8%) were female. All patients had chest computed tomography findings compatible with COVID-19 and positive polymerase chain reaction results.

The mean recorded hospital stay/duration was 9.39 ± 8.76 days, with a median of 7.0 days (IQR: 3.0–13.0; range: 1–47).

All patients received oxygen through a cannula or mini-mask during their clinical course. Non-invasive ventilation was required in 34 patients (22.4%). Endotracheal intubation and invasive mechanical ventilation were required in 82 patients (53.9%). Re-intubation occurred in 7 patients, corresponding to 4.6% of the total cohort and 8.5% of intubated patients. Tracheotomy was performed in 6 patients, corresponding to 3.9% of the total cohort and 7.3% of intubated patients. Clinically documented pneumothorax occurred in 2 patients, corresponding to 1.3% of the total cohort and 2.4% of intubated patients. The baseline demographic and clinical characteristics of the cohort are summarized in Table 1.

Table 1- Baseline demographic and clinical characteristics of the corrected cohort

Variable	Mean ± SD or n (%)	Median (IQR)	Range
Age (years)	58.49 ± 13.94	63.0 (48.0–69.0)	27–79
Male (sex)	87 (57.2)	—	—
Female (sex)	65 (42.8)	—	—
Non-invasive ventilation requirement	34 (22.4)	—	—
Invasive intubation	82 (53.9)	—	—
Re-intubation	7 (4.6)	—	—
Tracheotomy	6 (3.9)	—	—
Clinically documented pneumothorax	2 (1.3)	—	—
Oxygen by cannula or mini-mask	152 (100.0)	—	—
Chest CT compatible with COVID-19	152 (100.0)	—	—
PCR positive	152 (100.0)	—	—
Hospital stay/duration, days	9.39 ± 8.76	7.0 (3.0–13.0)	1–47

Values are presented as mean ± standard deviation, median (interquartile range), or number (%), as appropriate. CT: computed tomography; PCR: polymerase chain reaction.

Corrected Laboratory Profile

The corrected laboratory profile demonstrated substantial physiological, hematologic, renal, coagulation, and inflammatory abnormalities.

Median blood urea nitrogen was 23.0 mg/dL (IQR: 16.0–38.5), median serum creatinine was 1.05 mg/dL (IQR: 0.80–1.52), median arterial pH was 7.303 (IQR: 7.221–7.349), median $PaCO_2$ was 51.00 mmHg (IQR: 40.35–60.67), and median PaO_2 was 50.20 mmHg (IQR: 40.20–63.23).

Median C-reactive protein was 85.0, median D-dimer was 1369.0, and median ferritin was 758.0. D-dimer and ferritin had missing values and possible upper-limit/censored values; therefore, these variables should be interpreted cautiously. The corrected laboratory findings are summarized in Table 2.

Comparisons According to Invasive Intubation Status

Patients who underwent endotracheal intubation and invasive mechanical ventilation differed substantially from non-intubated patients. Intubated patients were older than non-intubated patients (median 64.0 vs. 60.0 years; $p = 0.021$).

They also had higher blood urea nitrogen (30.5 vs. 18.0 mg/dL; $p < 0.001$), creatinine (1.45 vs. 0.95 mg/dL; $p < 0.001$), $PaCO_2$ (52.20 vs. 48.20 mmHg; $p = 0.023$), activated partial thromboplastin time (32.00 vs. 30.00 s; $p = 0.034$), D-dimer (1745.5 vs. 903.5; $p = 0.012$), C-reactive protein (116.0 vs. 17.0; $p < 0.001$), and ferritin levels (978.0 vs. 741.0; $p = 0.038$).

In contrast, hemoglobin concentration was significantly lower among intubated patients than among non-intubated patients (10.15 vs. 12.05 g/dL; $p < 0.001$). Platelet count was also lower in the intubated group (129,000 vs. 201,500/μL; $p < 0.001$), and arterial pH was significantly lower among intubated patients (7.248 vs. 7.330; $p < 0.001$).

Hospital stay/duration was longer in intubated patients than in non-intubated patients (10.0 vs. 4.5 days; $p < 0.001$). Aspartate aminotransferase, alanine aminotransferase, PaO_2, and prothrombin time did not differ significantly between groups. Detailed continuous-variable comparisons according to invasive intubation status are presented in Table 3.

Categorical Comparisons According to Invasive Intubation Status

Sex distribution did not differ significantly between intubated and non-intubated patients ($p = 0.852$). The requirement for non-invasive ventilation was also not significantly different between groups ($p = 0.399$). Re-intubation and tracheotomy were observed only among intubated patients, as expected clinically.

Pneumothorax was observed only among intubated patients, occurring in 2 of 82 (2.4%), but the difference between intubated and non-intubated patients was not statistically significant ($p = 0.500$). Categorical comparisons according to invasive intubation status are presented in Table 4.

Comparisons According to Non-Invasive Ventilation Requirement

Most baseline continuous variables did not differ significantly by non-invasive ventilation requirement. However, C-reactive protein was higher among patients requiring non-invasive ventilation than among those not requiring non-invasive ventilation (112.5 vs. 70.5; $p = 0.027$).

Hospital stay/duration was also significantly longer in the non-invasive ventilation group (13.0 vs. 5.0 days; $p < 0.001$). Age, blood urea nitrogen, creatinine, liver enzymes, hemoglobin, platelet count, arterial pH, $PaCO_2$, PaO_2, coagulation parameters, D-dimer, and ferritin did not differ significantly between groups. Continuous-variable comparisons according to the NIV requirement are presented in Table 5.

In exploratory multivariable logistic regression, higher blood urea nitrogen, lower hemoglobin concentration, lower platelet count, and higher C-reactive protein remained independently associated with invasive intubation Table 6.

Table 2- Corrected laboratory findings

Laboratory variable	Valid n	Mean ± SD	Median (IQR)	Range
Blood urea nitrogen (mg/dL)	152	31.99 ± 26.02	23.0 (16.0–38.5)	5–132
Creatinine (mg/dL)	152	1.50 ± 1.23	1.05 (0.80–1.52)	0.50–7.90
Aspartate aminotransferase (U/L)	152	86.09 ± 203.60	58.0 (43.8–87.0)	13–2526
Alanine aminotransferase (U/L)	152	70.11 ± 91.65	51.5 (36.0–72.5)	16–908
Hemoglobin (g/dL)	152	11.16 ± 2.30	11.10 (9.47–13.03)	5.00–17.40
Platelet count (/μL)	152	173,217.11 ± 89,533.37	159,000 (111,000–231,250)	11,000–425,000
Arterial pH	152	7.271 ± 0.135	7.303 (7.221–7.349)	6.504–7.492
$PaCO_2$ (mmHg)	152	53.03 ± 18.83	51.00 (40.35–60.67)	24.40–139.00
PaO_2 (mmHg)	152	54.88 ± 24.76	50.20 (40.20–63.23)	17.60–194.30

Activated partial thromboplastin time (s)	149	35.93 ± 15.16	31.50 (28.00–37.00)	26.00–112.00
Prothrombin time (s)	151	15.50 ± 9.04	13.30 (11.90–16.00)	9.00–105.00
D-dimer	138	3072.67 ± 3381.87	1369.0 (676.25–3949.75)	13.35–10300
C-reactive protein	152	75.89 ± 53.95	85.0 (16.0–125.0)	1–166
Ferritin	129	876.36 ± 568.12	758.0 (406.0–1449.0)	17–1700

Values are presented as mean ± standard deviation, median (interquartile range), and range. Valid n differs for variables with missing data. $PaCO_2$: arterial partial pressure of carbon dioxide; PaO_2: arterial partial pressure of oxygen.

Table 3- Continuous variables according to invasive intubation status

Variable	Not intubated (n = 70), median (IQR)	Intubated (n = 82), median (IQR)	P value
Age (years)	60.0 (41.5–67.0)	64.0 (52.0–71.0)	0.021
Blood urea nitrogen (mg/dL)	18.0 (15.0–23.0)	30.5 (20.0–59.5)	<0.001
Creatinine (mg/dL)	0.95 (0.80–1.10)	1.45 (0.90–2.50)	<0.001
Aspartate aminotransferase (U/L)	54.0 (40.2–82.8)	66.0 (48.5–87.8)	0.087
Alanine aminotransferase (U/L)	55.0 (36.5–87.5)	50.5 (36.0–68.8)	0.207
Hemoglobin (g/dL)	12.05 (10.53–13.45)	10.15 (9.00–11.88)	<0.001
Platelet count (/μL)	201,500 (142,250–274,250)	129,000 (73,500–188,750)	<0.001
Arterial (pH)	7.330 (7.290–7.386)	7.248 (7.170–7.324)	<0.001
$PaCO_2$ (mmHg)	48.20 (39.38–54.67)	52.20 (40.60–68.80)	0.023
PaO_2 (mmHg)	47.05 (37.60–57.67)	51.45 (40.62–68.08)	0.093
Activated partial thromboplastin time (s)	30.00 (28.00–34.00)	32.00 (28.00–38.75)	0.034
Prothrombin time (s)	12.80 (11.83–15.23)	13.50 (12.00–18.00)	0.094
D-dimer	903.5 (564.25–2951.75)	1745.5 (991.5–4459.25)	0.012
C-reactive protein	17.0 (5.25–84.25)	116.0 (71.5–134.0)	<0.001
Ferritin	741.0 (311.0–1083.0)	978.0 (421.0–1650.0)	0.038
Hospital stay/duration (days)	4.5 (2.25–7.0)	10.0 (5.0–15.0)	<0.001

Continuous variables are presented as median (interquartile range). Between-group comparisons were performed using the Mann–Whitney U test. $PaCO_2$: arterial partial pressure of carbon dioxide; PaO_2: arterial partial pressure of oxygen.

Table 4- Categorical variables according to invasive intubation status

Categorical variable	Not intubated (n = 70), n (%)	Intubated (n = 82), n (%)	P value
Female sex	31 (44.3)	34 (41.5)	0.852
Male sex	39 (55.7)	48 (58.5)	—
Non-invasive ventilation: no	57 (81.4)	61 (74.4)	0.399
Non-invasive ventilation: yes	13 (18.6)	21 (25.6)	—
Re-intubation: no	70 (100.0)	75 (91.5)	0.015
Re-intubation: yes	0 (0.0)	7 (8.5)	—
Tracheotomy: no	70 (100.0)	76 (92.7)	0.031
Tracheotomy: yes	0 (0.0)	6 (7.3)	—
Pneumothorax: no	70 (100.0)	80 (97.6)	0.500
Pneumothorax: yes	0 (0.0)	2 (2.4)	—

Categorical variables are presented as a number (%). Between-group comparisons were performed using the chi-square test with continuity correction or Fisher's exact test, as appropriate. Re-intubation and tracheotomy should be interpreted primarily among patients who underwent endotracheal intubation.

Table 5- Continuous variables according to the non-invasive ventilation requirement

Variable	No NIV (n = 118), median (IQR)	NIV required (n = 34), median (IQR)	P value
Age (years)	62.0 (48.0–70.0)	63.0 (51.0–68.0)	0.912
Blood urea nitrogen (mg/dL)	22.0 (15.0–36.75)	25.0 (17.25–42.0)	0.285
Creatinine (mg/dL)	1.10 (0.80–1.58)	1.00 (0.80–1.30)	0.560
Aspartate aminotransferase (U/L)	60.5 (42.0–87.75)	56.0 (50.5–83.75)	0.610
Alanine aminotransferase (U/L)	52.0 (36.25–71.5)	50.5 (35.25–75.0)	0.915
Hemoglobin (g/dL)	11.40 (9.90–13.10)	10.65 (9.03–11.78)	0.180
Platelet count (/μL)	161,000 (121,250–230,250)	153,000 (89,500–225,500)	0.496
Arterial (pH)	7.309 (7.223–7.361)	7.289 (7.223–7.333)	0.378
$PaCO_2$ (mmHg)	50.05 (38.25–60.08)	53.45 (45.00–64.75)	0.086

PaO_2 (mmHg)	50.20 (40.28–65.45)	49.85 (40.43–56.95)	0.436
Activated partial thromboplastin time (s)	31.60 (28.00–37.65)	31.00 (28.00–35.38)	0.995
Prothrombin time (s)	13.50 (12.00–16.30)	12.90 (11.83–14.95)	0.272
D-dimer	1438.5 (684.25–4130.5)	1150.0 (651.5–3151.0)	0.567
C-reactive protein	70.5 (12.25–121.75)	112.5 (28.0–136.5)	0.027
Ferritin	741.0 (346.0–1444.5)	886.0 (592.0–1510.0)	0.284
Hospital stay/duration (days)	5.0 (3.0–10.0)	13.0 (9.0–16.75)	<0.001

Continuous variables are presented as median (interquartile range). Between-group comparisons were performed using the Mann–Whitney U test. NIV: noninvasive ventilation; $PaCO_2$: arterial partial pressure of carbon dioxide; PaO_2: arterial partial pressure of oxygen.

Table 6- Exploratory multivariable logistic regression for invasive intubation

Variable	Adjusted OR	95% CI	P value
Age (per year)	0.98	0.95–1.02	0.359
Blood urea nitrogen (per 10 mg/dL)	1.61	1.11–2.34	0.013
Hemoglobin (per 1 g/dL)	0.69	0.54–0.86	0.001
Platelet count (per 100,000/μL)	0.43	0.23–0.77	0.005
Arterial pH (per 1-unit increase)	0.08	0.00–3.40	0.187
C-reactive protein (per 10-unit increase)	1.21	1.10–1.32	<0.001

OR: odds ratio; CI: confidence interval. The regression analysis was exploratory and should be interpreted as hypothesis-generating due to the retrospective design and the absence of a prespecified statistical analysis plan.

Discussion

This retrospective observational cohort study of 152 critically ill adult patients with COVID-19 admitted to the ICU of Al-Zahra Hospital identified several clinically relevant findings. The requirement for advanced respiratory support was substantial: 22.4% of patients required non-invasive ventilation, and 53.9% underwent endotracheal intubation and invasive mechanical ventilation. Clinically documented pneumothorax was uncommon, occurring in only 1.3% of the total cohort and 2.4% of intubated patients. Patients who required invasive intubation demonstrated greater physiological, renal, inflammatory, hematologic, coagulation, and acid-base abnormalities than non-intubated patients. Specifically, intubated patients had higher blood urea nitrogen, creatinine, $PaCO_2$, activated partial thromboplastin time, D-dimer, C-reactive protein, and ferritin levels, as well as lower hemoglobin concentration, lower platelet count, and lower arterial pH. In exploratory multivariable analysis, higher blood urea nitrogen, lower hemoglobin concentration, lower platelet count, and higher C-reactive protein remained independently associated with invasive intubation. A high proportion of patients requiring invasive mechanical ventilation is clinically plausible because the study population consisted exclusively of critically ill ICU-admitted patients with COVID-19. Severe COVID-19 pneumonia may progress to ARDS, refractory hypoxemia, increased work of breathing, altered respiratory mechanics, impaired gas exchange, and multi-organ dysfunction, all of which may necessitate escalation of respiratory support [1–6]. Large ICU cohorts have consistently shown that mechanically ventilated patients with COVID-19 represent a severely ill subgroup with substantial organ-support requirements and poor outcomes [2-4]. Therefore, the intubation rate observed in the present cohort should be interpreted as a marker of high disease acuity rather than as representative of all hospitalized patients with COVID-19. Patients requiring invasive intubation were older and had more pronounced renal and metabolic abnormalities than non-intubated patients. Higher blood urea nitrogen and creatinine among intubated patients may reflect greater systemic disease severity, renal hypoperfusion, acute kidney injury, pre-existing renal impairment, catabolic stress, or a combination of these factors. Acute kidney injury and renal dysfunction have been reported frequently among hospitalized patients with COVID-19 and are associated with adverse clinical outcomes [16]. In the present analysis, blood urea nitrogen remained independently associated with invasive intubation even after adjustment for selected variables, suggesting that renal or systemic metabolic derangement may help identify patients with more severe critical illness. However, because this was a retrospective observational study, this association must not be interpreted as evidence that elevated blood urea nitrogen directly caused the need for intubation.

The lower hemoglobin concentration observed among intubated patients is also clinically relevant. Anemia may reduce arterial oxygen content and worsen oxygen delivery in patients already experiencing severe hypoxemic respiratory failure. In COVID-19-associated pneumonia or ARDS, reduced oxygen-carrying capacity may aggravate the physiological consequences of impaired gas exchange. In the exploratory regression model, higher hemoglobin concentration was associated with lower odds of invasive intubation. This finding is biologically plausible, but it remains hypothesis-generating. The dataset did not include detailed information regarding chronic anemia, acute bleeding,

transfusion exposure, iron status, inflammatory anemia, or the timing of hemoglobin measurement relative to respiratory deterioration. Therefore, hemoglobin should be interpreted as a marker of severity rather than an independent causal determinant of intubation.

Thrombocytopenia was another important finding. Platelet count was markedly lower among intubated patients and remained independently associated with invasive intubation in the exploratory model. COVID-19 is associated with endothelial injury, inflammatory activation, coagulation abnormalities, and microvascular thrombosis [5-6]. Lower platelet counts may reflect systemic inflammation, platelet consumption, sepsis, bone marrow suppression, drug effects, or disseminated intravascular coagulation-like physiology in severe disease. The association between lower platelet count and invasive intubation in this cohort is consistent with the concept that hematologic and coagulation abnormalities may accompany more severe COVID-19 illness. Nevertheless, the available data do not allow determination of whether thrombocytopenia preceded respiratory deterioration or occurred as part of the same severity trajectory.

Inflammation appeared to be strongly associated with invasive intubation. C-reactive protein was substantially higher in intubated patients than in non-intubated patients and remained independently associated with invasive intubation after adjustment. Severe COVID-19 may involve an exaggerated inflammatory response, cytokine release, endothelial dysfunction, and diffuse pulmonary injury [5]. A higher inflammatory burden may contribute to alveolar-capillary injury, worsening oxygenation, and progression to respiratory failure. However, as with other laboratory markers in this study, the timing of C-reactive protein measurement is central to interpretation. If C-reactive protein was measured after respiratory deterioration or after initiation of invasive ventilation in some patients, reverse causation and severity-related confounding cannot be excluded. The arterial blood gas findings further support the interpretation that intubated patients represented a more severely ill subgroup. Intubated patients had lower arterial pH and higher PaCO2 than non-intubated patients, indicating more severe ventilatory impairment or mixed acid-base disturbance. Hypercapnia and acidemia may occur in advanced respiratory failure, increased physiological dead space, respiratory muscle fatigue, impaired alveolar ventilation, shock, renal dysfunction, or combined metabolic and respiratory derangements. Although arterial pH was significantly lower in bivariate comparisons, it was not independently associated with intubation in the exploratory regression model. The wide confidence interval around the pH estimate indicates statistical instability, most likely because of scaling, limited variability, collinearity with other severity markers, and the retrospective nature of the dataset. Therefore, pH should not be overinterpreted as an independent predictor in this study. The low observed incidence of clinically documented pneumothorax is notable but must be interpreted very cautiously. Pneumothorax occurred in only 2 patients, representing 1.3% of the total cohort and 2.4% of intubated patients. Previous studies have reported barotrauma, pneumothorax, pneumomediastinum, and related complications among patients with COVID-19, particularly those receiving invasive mechanical ventilation [8-10]. The lower rate observed in the present cohort may reflect differences in patient characteristics, disease severity, diagnostic intensity, ventilation practices, duration of invasive ventilation, or documentation patterns. However, because only two pneumothorax events occurred, the estimate is statistically unstable; even a small number of additional missed cases would substantially change the incidence. No causal conclusion can be made regarding the low pneumothorax rate. The dataset did not include key ventilatory variables, such as tidal volume, plateau pressure, peak airway pressure, driving pressure, positive end-expiratory pressure, respiratory system compliance, prone positioning, recruitment maneuvers, or duration of mechanical ventilation. These variables are essential for evaluating the relationship between mechanical ventilation and barotrauma. Lung-protective ventilation with low tidal volumes and limitation of plateau pressure is central to ARDS management [11], and driving pressure has been associated with survival in ARDS [12]. However, because these parameters were not available in the present dataset, the low observed pneumothorax incidence cannot be attributed to lung-protective ventilation, driving pressure limitation, or any specific ventilatory protocol. Under-detection is another plausible explanation for the low pneumothorax rate. In this study, pneumothorax was defined according to clinical documentation in the medical record and available radiological evidence recorded during routine care. Systematic re-evaluation of serial chest radiographs or computed tomography scans was not performed. As a result, small, transient, or clinically silent pneumothoraces may have been missed. Similarly, pneumomediastinum and subcutaneous emphysema were not analyzed as separate barotrauma outcomes. Therefore, the reported incidence should be understood as the incidence of clinically documented pneumothorax, not the true radiological incidence of all barotrauma events.

Re-intubation and tracheotomy were observed only among intubated patients, as expected clinically. Re-intubation occurred in 8.5% of intubated patients, and tracheotomy was performed in 7.3% of intubated patients. These outcomes likely reflect a subgroup with prolonged ventilatory dependence, failed extubation, or complex airway and respiratory management.

Tracheostomy has been used in selected patients with COVID-19 who require prolonged mechanical ventilation, although timing, patient selection, procedural approach, and outcomes vary across centers [17]. In the present study, the absence of data on duration of mechanical ventilation, timing of extubation, cause of extubation failure, timing of tracheotomy, ventilator-free days, decannulation, and post-tracheotomy outcomes limits interpretation. Therefore, reintubation and tracheotomy should be reported descriptively and not overinterpreted as independent prognostic markers.

The comparison of non-invasive ventilation requirements showed that most baseline laboratory and arterial blood gas variables did not differ significantly between patients who did and did not receive non-invasive ventilation. Patients requiring noninvasive ventilation had higher C-reactive protein levels and longer hospital stay/duration. This may indicate a greater inflammatory burden and a more prolonged clinical course in patients managed with non-invasive respiratory support. However, the use of non-invasive ventilation is highly dependent on institutional practice, timing of presentation, oxygenation status, availability of ICU resources, clinician preference, and evolving pandemic protocols. In addition, a longer hospital stay may reflect survival long enough to receive prolonged respiratory support, delayed escalation, or greater illness complexity. Therefore, the NIV-related findings should be considered descriptive rather than causal.

The background management of critically ill COVID-19 patients changed substantially over the pandemic. International recommendations emphasized supportive critical care, appropriate respiratory support, infection control, anticoagulation considerations, and organ support in critically ill adults with COVID-19 [7]. Corticosteroids became standard therapy for many hospitalized patients requiring oxygen or mechanical ventilation after evidence demonstrated benefit in this population [14] , and remdesivir was used in selected hospitalized patients based on evidence suggesting a shorter time to recovery in some settings [15]. These therapeutic developments are important contextual factors when comparing COVID-19 ICU cohorts across pandemic waves. However, the present study was not designed to evaluate treatment efficacy, timing, dose-response relationships, or medication-specific outcomes.

The exploratory regression model provides additional but limited insight. Higher blood urea nitrogen, lower hemoglobin concentration, lower platelet count, and higher C-reactive protein were independently associated with invasive intubation. These variables are clinically plausible markers of severity, reflecting renal or metabolic stress, impaired oxygen-carrying capacity, hematologic and coagulation derangements, and systemic inflammation. Nevertheless, the model was exploratory and was not based on a prespecified statistical analysis plan. Important confounders, including comorbidities, body mass index, baseline functional status, formal ARDS severity category, APACHE II score, SOFA score, oxygenation indices, radiological disease extent, vasopressor use, renal replacement therapy, treatment timing, and ventilatory parameters, were unavailable. For this reason, the model should not be presented as a validated prediction model.

This study has several strengths. It provides center-specific data from a major tertiary referral hospital that managed critically ill patients with COVID-19 during the pandemic. The corrected analysis used a cohort of 152 patients and included respiratory support variables, arterial blood gas indices, routine laboratory markers, and clinically documented pneumothorax. The analysis also avoided unsupported mortality claims and did not attempt statistically unreliable modeling of pneumothorax despite its clinical relevance. This conservative interpretation improves the methodological defensibility of the manuscript.

The study also has important limitations. First, the retrospective single-center design limits causal inference and generalizability. Second, the timing of some laboratory measurements relative to respiratory deterioration and intubation may not have been uniform, which increases the risk of reverse causation and severity-related confounding. Third, detailed ventilatory parameters, including tidal volume, plateau pressure, driving pressure, positive end-expiratory pressure, respiratory-system compliance, prone positioning, recruitment maneuvers, and duration of mechanical ventilation, were unavailable. Therefore, the incidence of pneumothorax cannot be linked to specific ventilatory strategies. Fourth, pneumothorax was identified through clinical documentation rather than systematic radiological review; consequently, clinically silent or undocumented barotrauma may have been missed.

Additional limitations should be acknowledged. D-dimer and ferritin had missing values and possible upper-limit or censored values, which may have affected their descriptive and comparative statistics. Important clinical variables, including comorbidities, body mass index, APACHE II score, SOFA score, ARDS severity category, vasopressor use, renal replacement therapy, treatment timing, and ICU discharge outcome, were not available in the corrected dataset. Mortality was not analyzed because a verified survival/death variable was not available in the analyzable dataset. Finally, because pneumothorax occurred in only two patients, the study was underpowered to identify risk factors for pneumothorax or to compare pneumothorax rates across respiratory support subgroups.

Conclusion

In summary, critically ill COVID-19 patients admitted to the ICU of Al-Zahra Hospital exhibited a high requirement for invasive respiratory support, whereas clinically documented pneumothorax was infrequent. Patients requiring invasive intubation demonstrated greater renal, inflammatory, hematologic, coagulation, and acid-base abnormalities compared to non-intubated patients. Higher blood urea nitrogen, lower hemoglobin concentration, lower platelet count, and higher C-reactive protein were independently associated with invasive intubation in exploratory analysis. These findings are hypothesis-generating and non-causal. Future multicenter studies with standardized laboratory assessment timing, systematic imaging review, comprehensive evaluation of ventilatory mechanics, validated severity scores, and adjusted outcome models are necessary to clarify the determinants of invasive intubation and barotrauma in critically ill COVID-19 patients.

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