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**CASE SERIES** **CORONA EXPERIENCE**

# Clinical characteristics and outcomes of vaccinated critical COVID-19 patients: A case series from a low middle-income country

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## Abstract

**Background:** Vaccination plays an important role in the prevention of some infectious diseases but does it change the outcome in critically ill patients is obscure. Though vaccination leads to decreased emergency and hospital admission, still the vaccinated patients with severe diseases requiring intensive care are being reported. This case series reports the outcome of 20 critically ill patients admitted to the COVID Intensive Care Unit (ICU).

**Methodology:** All vaccinated patients admitted to COVID-ICU at the University Hospital between January 2021 and June 2021 were reviewed. The demographics, comorbidities, vaccination status, systemic manifestations, organ support, complications, pharmacological therapy, outcome and length of ICU as well as hospital stay were recorded. To draw a comparison for all the demographics and clinical characteristics of patients, stratification analysis was performed for the outcome variables.

**Results:** A total of 20 patients were included in the study among which only 7 (35%) survived. The mortality rate for patients over 60 was 84.6 %. Four of the patients had no comorbidities and all of them survived. Among the complications, acute kidney injury was the most common (70%). The median (IQR) ICU stay was 10 (7) days and hospital stay was 13.5 (11) days.

**Conclusions:** The vaccinated patients admitted with COVID-19 ICU had a poor outcome and irrespective of the type of vaccine. The factors leading to increased mortality in this group of patients were male gender, age ≥ 60 years, and associated chronic medical illness.

**Key words:** COVID-19, COVID-19 Vaccines; Critical Care Outcomes; Hospital-Associated Pneumonia; Respiratory Insufficiency

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**Table 1A: Demographics of patients**

| Variable | | Outcome | |
|---|---|---|---|
| | | Death = 13 (65) | Survived = 7 (35) |
| Gender | Male | 12 (70.6) | 5 (29.4) |
| | Female | 1 (33.3) | 2 (66.7) |
| Age (y) | < 60 | 2 (28.6) | 5 (71.4) |
| | ≥ 60 | 11 (84.6) | 2 (15.4) |
| BMI (kg/m$^2$) | < 25 | 2 (40) | 3 (60) |
| | ≥ 25 | 11 (73.3) | 4 (26.7) |
| Comorbidities | | 13 (76.47) | 4 (23.53) |

*Frequency (%) is presented for qualitative variable*

# 1. Introduction

Coronavirus disease 2019 (COVID-19) emerged as a pandemic in the year 2020. The clinical spectrum ranges from asymptomatic to septic shock, and multi-organ dysfunction.[1] The rate of COVID-19 patients for ICU admission goes as high as 32%.[2] The bulk of the data is available from the developed countries. There is a paucity of COVID-19 relevant research published from the low-middle income countries. In Pakistan emergency approval was given to Sinopharm Covilo, Sinovac CoronaVac, CanSino Convidecia (all of Chinese origin) and Gameleya Sputnik V (Russian origin). Currently, there is no data available regarding the outcome of vaccinated critically ill patients with COVID-19. This case series examines the characteristics and outcomes of critically ill patients who were vaccinated and admitted to intensive care after exhibiting severe organ dysfunction.

# 2. Methodology

In this study, the hospital record of patients admitted to COVID-ICU of a University Hospital between 1st January 2021 to 30 June 2021, were reviewed. Data was collected after approval from the departmental research committee and exemption from the ethical review committee of the hospital (ERC number 2021-6791-19399). The number of vaccinated patients in this period was 20 out of 130 admissions. The primary objective was to determine the impact of the COVID-19 vaccine and the patient outcomes admitted to ICU. The secondary objective was to ascertain the effect of the COVID-19 vaccine on the length of hospital and ICU stay of these patients. We included all partially or fully vaccinated patients admitted during the study period. COVID-19 was confirmed in all 20 patients using the polymerase chain reaction (PCR) with either a nasal swab for non-intubated patients or a mini-bronchoalveolar lavage for intubated patients.

The demographics, comorbidities, vaccination status, type of vaccine, the severity of the disease, and need for respiratory support before ICU admission were noted. Upon admission to the intensive care unit, acute respiratory distress syndrome, respiratory support (mechanical ventilation), need for prone position, cardiovascular support (inotropes and vasopressors), renal replacement therapy, as well as pharmacological therapy (e.g., antibiotics, antifungals, steroids, antivirals, immunosuppressant) was noticed. In addition, systemic infections and complications during the hospital stay, duration of ICU and hospital stay, and the outcomes were determined. For assessing the severity of illness, Acute Physiology Assessment and Chronic Health Evaluation II (APACHE II) was used.

**Statistical analysis:** RStudio 4.1.2 (R Foundation for Statistical Computing) was used for statistical analysis. For the laboratory parameters, median interquartile range (IQR) estimates are reported. For the qualitative characteristics of the patients, the frequencies and percentages are computed. To draw a comparison for all the demographics and clinical characteristics of the patients, stratification analysis is performed for the outcome (death/alive discharge) variable.

# 3. Results

## Patient characteristics

The demographics and clinical features are shown in (Table 1A and 1B).

The majority were male 17 (85%). There were only four patients without comorbidities, and all of them survived. In the ones with comorbidities, hypertension (41.66%) was most common followed by diabetes mellitus (36.1%). All patients with chronic kidney disease (15%) died. The

mortality rate for ≥ 60 years was 84.6%. About 80% had critical COVID-19 (CC-19) infection. Ninety percent were fully vaccinated and their vaccination histories are shown in (Table 1B). Sinopharm Covilo (75%) was the most common vaccine. The median (IQR) $PaO_2/FiO_2$ ratio on ICU admission was 110 (33.4). The rest of the laboratory variables can be seen in (Table 2)

## Respiratory failure

The most common hospital admission diagnosis was respiratory failure (95%). On admission to the ICU, 80% of patients with respiratory failure had severe acute respiratory distress syndrome. The patients were initially managed with respiratory support such as non-rebreathing masks, and noninvasive ventilation in the

 

**Table 1B: Clinical Characteristics of Patients**

| Variable | | Death = 13 (65%) | Survived = 7 (35%) |
|---|---|---|---|
| APACHE II score on admission | Median (IQR) | 20 (15) | 18 (7) |
| On ICU admission COVID classification | Critical | 11 (68.8%) | 5 (31.2%) |
| | Severe | 2 (50.0%) | 2 (50.0%) |
| Vaccination status | Partial vaccination | 0 (0%) | 2 (100%) |
| | Complete vaccination | 13 (72.2%) | 5 (27.8%) |
| Type of vaccine | CanSino Convidecia | 2 (100%) | 0(0%) |
| | Janssen (Johnson & Johnson): Ad26.CoV2.S | 0 (0%) | 1 (100%) |
| | Sinopharm Covilo | 9 (60%) | 6 (40%) |
| | Sinovac CoronaVac | 2 (100%) | 0 (0%) |
| Respiratory support | Non-invasive ventilation | 13 (72.2%) | 5 (27.7%) |
| | ARDS on ICU admission | 12 (75%) | 4 (25%) |
| | ICU invasive ventilation | 13 (68.4%) | 6 (31.6%) |
| | ICU prone position | 10 (62.5%) | 6 (37.5%) |
| Cardiovascular support | Epinephrine | 3 (75%) | 1 (25%) |
| | Norepinephrine | 2 (40%) | 3 (60%) |
| | Norepinephrine + Vasopressin | 11 (100%) | 0 (0%) |
| Pharmacological therapy | Remdesivir | 11 (68.8%) | 5 (31.2%) |
| | Tocilizumab | 9 (81.8%) | 2 (18.2%) |
| Complications during ICU stay | Acute Kidney Injury | 10 (71.4%) | 4 (28.6%) |
| | Seizure | 2 (66.7%) | 1 (33.3%) |
| | Pneumothorax + Pneumomediastinum | 5 (100%) | 0 (0%) |
| | Cardiac arrhythmia requiring therapy | 4 (66.7%) | 2 (33.3%) |
| | Myocarditis | 0 (0%) | 2 (100%) |
| | Gastrointestinal bleeding | 4 (100%) | 0 (0%) |
| Total ICU duration (days) | Median (IQR) | 11 (7) | 8 (5) |
| Total hospital duration (days) | Median (IQR) | 13 (13) | 14 (8) |

*Frequency (%) is presented for qualitative variable. Median (IQR) is presented for quantitative variable. ARDS, Acute Respiratory Distress Syndrome; BMI, Body Mass Index; IQR, interquartile range*

COVID-19 high dependency unit. Later, 19 patients required invasive ventilation. The median (IQR) length of invasive mechanical ventilation was 8.5 days (8). Patients were placed prone either the same day or the second day after admission to the ICU. Around 16 (80%) patients were positioned prone, however, only 6 (37.5%) survived. Nine patients were extubated during their stay in the ICU. Two of these patients later died after being reintubated.

## Shock

Sixteen patients required vasopressor infusions due to sustained hypotension in COVID ICU. All 4 patients in which vasopressors were not needed had 100% survival. All patients with the need for double vasopressors (norepinephrine + vasopressin) died.

## Infections

As per hospital guidelines on admission, a complete set of blood chemistry and infectious markers were sent. Nine patients (45%) had bacterial co-infection on ICU admission. The distribution of infections can be seen in Figure 1.

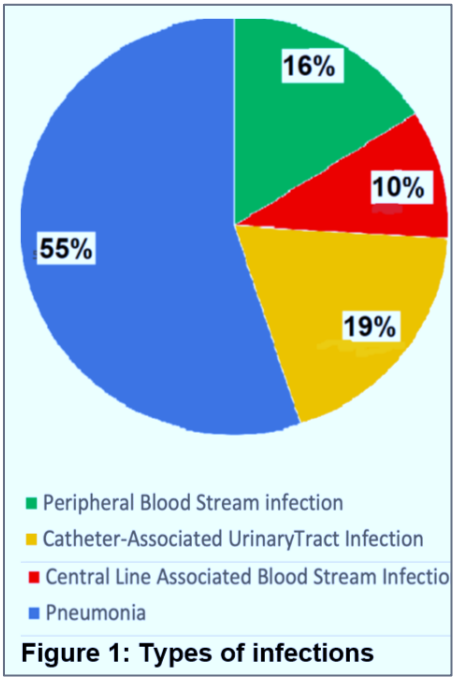


**Figure 1: Types of infections**

## Complications

Among the complications, acute kidney injury was the most common (70%). Renal replacement therapy was used in 5 (25%) patients. Prophylactic (30%) and

 

therapeutic anticoagulants (70%) in the form of unfractionated heparin and low molecular weight heparin were used. Hemorrhagic complications were most prevalent in patients with therapeutic anticoagulation (80%). Atrial fibrillation was the most common cardiac arrhythmia for which therapy (pharmacological or cardioversion) was required. The rest of the complications can be seen in (Table 1B). All those who developed pneumothorax & pneumomediastinum did not survive.

### Outcomes

Steroids were used in all patients. Remdesivir was given to 16 patients out of which only 5 survived. Tocilizumab was also given to 11 patients and 2 survived. The median (IQR) APACHE of 20 (15) was associated with mortality. The median (IQR) ICU stay was 10 days (7) and hospital stay was 13.5 days (11). Out of a total of 20 vaccinated patients, only 7 (35 %) patients survived.

**Table 2: Laboratory Parameters on Hospital Admission**

| Laboratory parameters | Median (IQR, Q1 – Q3) |
|---|---|
| White blood cell count | 13.7 × $10^9$/L (6.7, 11.07–17.77) |
| C-Reactive Protein | 58.65 mg/L (106.69, 19.48 – 126.17) |
| Procalcitonin | 0.29 ng/ml (0.80, 0.14, 0.94) |
| Ferritin | 1177 ng/ml (1371, 718−2089) |
| Interleukin-6 | 75.83 pg/ml (148.32, 25.08−173.40) |
| D- Dimer | 2.3 mg/ml FEU (2.90, 1.80−4.70) |
| $PaO_2/FiO_2$ ratio | 110 (30.80, 94.7−125.5) |

*Median (IQR, Q1 (first quartile) and Q3 (third quartile) reported in table.*

## 4. Discussion

The vaccination data from low-middle income countries like Pakistan is evolving. The approved vaccines are inactivated (Sinovac CoronaVac, Sinopharm Covilo), non-replicating viral vector (oxford/ AstraZeneca vaxzevria, Gamaleya Sputnik V, CanSino Convidecia), and mRNA (Moderna Spikevax, Pfizer/ BioNTech Comirnaty). The inactivated vaccine was one of the first vaccines used in Pakistan. Therefore, most of our population was vaccinated with these vaccines.

The outcome of patients with COVID-19 depends on multiple factors which include demographic variables and comorbidities. In one of the systematic reviews, advanced age and male gender were significantly associated with mortality in patients with COVID-19.[3] In our study too, hospital mortality was more in the male population (70.6%) and patients aged ≥ 60 years (84%). We observed that medical comorbidities increase the risk of mortality even in vaccinated patients with CC-19.

COVID-19 is associated with increased maternal morbidity, mortality, and neonatal complications in pregnant patients.[4] The pregnant vaccinated patient in our series was admitted and mechanically ventilated. Despite gestation age of 32 weeks being one major obstacle, 3 prone sessions were applied. Later, she was discharged after 10 days with a viable fetus.

Our hospital is a tertiary care referral center, thus some of the patients were shifted from other hospitals and presented late. Along with COVID-19, 45% of the patients had a bacterial infection at the time of admission. Cardiovascular support was required in these patients because of septic shock, and only one of them survived. Nosocomial infection in patients with COVID-19 leads to increased length of ICU stay and mortality.[5] The use of immunomodulatory agents and high-dose steroids also predisposes to infection. All of the patients in our series received high-dose steroids and 11 patients received tocilizumab. Thus, 90% of our patients developed a nosocomial infection. The infections included pulmonary, central line-associated bloodstream, peripheral bloodstream, and catheter-associated urinary tract infections.

In this population, bacterial infections are sustained by Gram-negative bacteria like *Enterobacterales, Acinetobacter baumannii, Pseudomonas aeruginosa*, and *Mycoplasma pneumonia* as the most common pathogens.[5] In our patients, the most common isolated bacterial pulmonary pathogen included *Acinetobacter baumannii*. Aspergillus was the most prevalent fungal pulmonary infection.

In contrast to the United States of America and Europe where mRNA and non-replicating viral vector vaccines were mainstream, in Southern Asia, it was the inactivated vaccine. Due to a similar rate of hospital and critical care admission in comparison to mRNA and viral vectored vaccine, M Manoj et al. concluded that the Sinopharm Covilo vaccine was highly valuable especially in underdeveloped and low-middle-income countries.[6] Moreover, unlike the mRNA vaccine, the storage and shipment requirements are not rigorous for

 

inactivated vaccines. The efficacy of Sinopharm Covilo was reported at 78%−79% (in Brazil and China).[7]

There is scarce data from the South Asian countries. Regarding the severity of symptoms in our population, one prospective study showed that mechanical ventilation was needed for 38.8% of patients in one hospital.[8] J Khan et al. compared the outcome of vaccinated and non-vaccinated patients during the delta wave. The vaccinated patients had better outcomes ($P < 0.05$). Out of 884 patients, 504 were vaccinated, though 4.37% developed CC-19. We could not find literature regarding the outcome of vaccinated patients with CC-19.[9] In this case series, we have assessed particularly this population. This makes this case series distinctive in regards to patient selection.

The existing data, especially on vaccinated critical patients with COVID-19, is limited. For now, the use of steroids, lung-protective ventilation, prone position, organ support, and reinforcement on infection prevention in the ICU remain the methods to improve outcomes in these patients.[10]

From 2020 till this day, we have emerged from pneumonia with an unrecognized pathogen to the development of targeted antiviral therapy and vaccine. Still, the outcome of patients with the greatest severity of illness (the ICU population) remains poor even in the vaccinated patients.

# 5. Conclusions

The outcome of vaccinated patients admitted with critical COVID-19 was poor and irrespective of the type of vaccine. The demographic factors leading to increased mortality in this group of patients were male gender, age ≥ 60 years, and chronic medical illness. It would be useful to see a larger cohort of COVID-19 vaccinated patients to identify risk factors that affect outcomes for these patients.

## 6. Key Messages

1. In moderate to severe COVID, the vaccine could help; however, for a critical infection, more research is needed.
2. The outcome of critical COVID-19 (CC-19) patients remains poor irrespective of the type of vaccine.

## 7. Availability of data

The numerical data generated in this study are available with the authors.

## 8. Funding

None declared by the authors.

## 9. Conflict of interests

None of the authors had any conflict of interests.

## 10. Authors' contribution

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