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Research Article

Comparison Of Disease Severity and Outcome in Vaccinated and Non-Vaccinated COVID-19 Patients: A Prospective Observational Study

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ABSTRACT

Background: COVID-19 vaccination has emerged as a critical intervention to reduce disease severity and improve clinical outcomes. However, comprehensive data comparing clinical characteristics, laboratory parameters, and outcomes between vaccinated and non-vaccinated hospitalized COVID-19 patients remain limited.

Methods: This prospective observational study was conducted at BMCRI-affiliated hospitals from April to July 2021. A total of 978 adult patients eligible for COVID-19 vaccination with confirmed SARS-CoV-2 infection were enrolled. Patients were categorized into vaccinated (partially or fully) and non-vaccinated groups. Demographics, clinical symptoms, comorbidities, laboratory parameters, radiological findings, and outcomes were analyzed.

Results: Of 978 patients, 412 (42.1%) were vaccinated and 566 (57.9%) were non-vaccinated. Vaccinated patients demonstrated significantly lower disease severity with mild disease in 68.2% versus 45.4% in non-vaccinated patients ($p<0.001$). Non-vaccinated patients had higher rates of severe disease (32.3% vs 18.4%, $p<0.001$) and required mechanical ventilation more frequently (22.6% vs 8.7%, $p<0.001$). In-hospital mortality was significantly lower in vaccinated patients (4.4% vs 18.7%, $p<0.001$). Vaccinated patients had lower inflammatory markers including CRP (45.2±28.4 vs 68.9±35.7 mg/L, $p<0.001$) and D-dimer levels (1.8±1.2 vs 2.9±2.1 µg/mL, $p<0.001$).

Conclusion: COVID-19 vaccination significantly reduced disease severity, hospital mortality, and need for mechanical ventilation among hospitalized patients. These findings support the critical importance of vaccination programs in reducing adverse COVID-19 outcomes.

Keywords*: COVID-19, SARS-CoV-2, vaccination, disease severity, clinical outcomes, hospital mortality.*

INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has resulted in unprecedented global health challenges with over 270 million confirmed cases and significant mortality worldwide. The development and rapid deployment of COVID-19 vaccines have represented one of the most remarkable scientific achievements in modern medical history, offering hope for pandemic control and mitigation of severe disease outcomes (1).

Multiple studies have demonstrated the efficacy of COVID-19 vaccines in preventing infection, reducing disease severity, and decreasing mortality rates across diverse populations (2). Systematic reviews and meta-analyses have consistently shown that COVID-19 vaccines achieve pooled vaccine effectiveness rates of 70-87% against infection and over 90% against severe disease outcomes, including hospitalization and death (3). The BNT162b2 (Pfizer-BioNTech) and mRNA-1273 (Moderna) vaccines have shown particularly high effectiveness rates, with initial clinical trials demonstrating approximately 95% efficacy against symptomatic COVID-19 (4).

Despite the proven efficacy of vaccines in clinical trials, real-world effectiveness data from hospitalized populations provide crucial insights into vaccine performance under actual clinical conditions. Breakthrough infections, defined as SARS-CoV-2 infections occurring 14 days or more after completion of the recommended vaccination schedule, have been reported but remain relatively uncommon and are typically associated with milder disease presentations (5). Understanding the clinical characteristics and outcomes of breakthrough infections compared to infections in unvaccinated individuals is essential for optimizing patient management strategies and informing public health policies.

The immune response following COVID-19 vaccination involves both humoral and cellular immunity, with neutralizing antibodies playing a crucial role in preventing infection and severe disease. However, vaccine effectiveness may vary based on patient demographics, underlying comorbidities, and time since vaccination. Patients with diabetes mellitus, hypertension, cardiovascular disease, and other chronic conditions may experience different vaccine responses and clinical outcomes compared to healthy individuals (6). Studies have indicated that while vaccine effectiveness may be somewhat reduced in patients with comorbidities, vaccination still provides substantial protection against severe outcomes in these high-risk populations (7).

Laboratory parameters and inflammatory markers have proven valuable in assessing COVID-19 disease severity and predicting clinical outcomes. Elevated levels of C-reactive protein (CRP), D-dimer, lactate dehydrogenase (LDH), and ferritin have been consistently associated with more severe disease and worse prognosis in COVID-19 patients. Understanding how vaccination status influences these biomarkers in hospitalized patients can provide insights into the pathophysiological mechanisms underlying vaccine-mediated protection and assist in clinical decision-making (8).

Radiological imaging, particularly high-resolution computed tomography (HRCT) of the chest, has become an essential tool for assessing lung involvement and disease severity in COVID-19 patients. CT severity scores have been developed to quantify the extent of lung involvement and correlate with clinical outcomes. Comparing radiological findings between vaccinated and non-vaccinated patients can provide additional objective measures of disease severity and vaccine effectiveness (9).

The impact of vaccination on clinical outcomes becomes particularly important when considering healthcare resource utilization, including intensive care unit (ICU) admission rates, mechanical ventilation requirements, and hospital length of stay. Studies have consistently demonstrated that vaccinated patients have lower rates of ICU admission and mechanical ventilation, even when breakthrough infections occur. This reduction in severe outcomes has significant implications for healthcare system capacity and resource allocation during pandemic surges (10).

Given the critical importance of vaccination in the global response to COVID-19, comprehensive studies comparing clinical characteristics, laboratory parameters, and outcomes between vaccinated and non-vaccinated hospitalized patients are essential. Such investigations provide real-world evidence of vaccine effectiveness, inform clinical practice guidelines, and support evidence-based public health policies. The present study was designed to address these knowledge gaps by conducting a detailed comparison of disease severity and outcomes in vaccinated versus non-vaccinated COVID-19 patients admitted to tertiary care hospitals.

AIMS AND OBJECTIVES

The primary aim of this study was to compare disease severity and clinical outcomes between vaccinated and non-vaccinated COVID-19 patients requiring hospitalization. The specific objectives included evaluation of demographic characteristics and clinical presentation differences between vaccination groups, comparison of laboratory parameters and inflammatory markers across vaccination status, assessment of radiological findings and CT severity scores between groups, analysis of clinical outcomes including mortality, mechanical ventilation requirements, and hospital length of stay, and identification of risk factors associated with severe disease in both vaccinated and non-vaccinated populations.

MATERIALS AND METHODS

Study Design and Setting

This prospective observational study was conducted at hospitals affiliated with Bangalore Medical College and Research Institute (BMCRI) from April 2021 to July 2021. The study protocol was approved by the BMCRI Ethics Committee on June 18, 2021. All participants provided written informed consent prior to enrollment.

Study Population and Sampling

The study population comprised adult patients aged 18 years and above who were eligible for COVID-19 vaccination according to national guidelines and were admitted with laboratory-confirmed SARS-CoV-2 infection. A consecutive sampling method was employed to recruit 978 patients during the study period. Patients were classified into two groups based on vaccination status: vaccinated (including both partially and fully vaccinated individuals) and non-vaccinated patients.

Inclusion and Exclusion Criteria
Inclusion criteria encompassed adults aged 18 years and above, patients eligible for COVID-19 vaccination as per national guidelines, laboratory-confirmed SARS-CoV-2 infection by reverse transcription polymerase chain reaction (RT-PCR), and patients requiring hospital admission for COVID-19 management. Exclusion criteria included patients under 18 years of age, those with incomplete vaccination records or unknown vaccination status, patients who received vaccination less than 14 days prior to symptom onset, and individuals who declined to participate or were unable to provide informed consent.

Data Collection Procedures
Comprehensive demographic and clinical data were collected using structured case record forms. Demographic information included age, sex, residential address, and date of hospital admission. Vaccination history was meticulously documented, including vaccination status (vaccinated vs non-vaccinated), type of vaccine received, dates of first and second doses when applicable, and time interval between vaccination and symptom onset. Clinical assessment encompassed detailed symptom evaluation including fever, breathlessness, cough, myalgia, altered sensorium, and other COVID-19 related symptoms. Comorbidity assessment included diabetes mellitus, hypertension, chronic kidney disease, cardiovascular disease, and other relevant medical conditions.

Laboratory Investigations
Extensive laboratory evaluation was performed at admission including complete blood count with differential, comprehensive metabolic panel, and COVID-19 specific biomarkers. Hematological parameters included hemoglobin levels, total leukocyte count, differential leukocyte count, and platelet count. Inflammatory markers comprised C-reactive protein (CRP), D-dimer, serum ferritin, lactate dehydrogenase (LDH), and procalcitonin levels. Biochemical parameters included serum sodium, potassium, chloride, urea, creatinine, and liver function tests including total protein, albumin, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and bilirubin levels.

Radiological Assessment
Chest radiography was performed for all patients at admission. High-resolution computed tomography (HRCT) of the chest was conducted when clinically indicated, and CT severity scores were calculated using standardized scoring systems to quantify the extent of lung involvement.

Disease Severity Classification
Disease severity was classified according to established clinical criteria. Mild disease was defined as symptomatic patients without evidence of pneumonia or hypoxia. Moderate disease included patients with clinical or radiological evidence of pneumonia but not requiring supplemental oxygen. Severe disease encompassed patients requiring supplemental oxygen, intensive care unit admission, or mechanical ventilation support.

Outcome Measures
Primary outcomes included in-hospital mortality, requirement for mechanical ventilation, and disease severity classification. Secondary outcomes comprised hospital length of stay, intensive care unit admission, and development of complications during hospitalization.

Follow-up Protocol
Patients were followed throughout their hospital stay until discharge, death, or transfer to another facility. Daily clinical assessments were performed, and laboratory investigations were repeated as clinically indicated. Outcome data were recorded at hospital discharge or death.

Statistical Analysis
Statistical analysis was performed using SPSS version 26.0. Descriptive statistics were calculated for all variables, with continuous variables presented as means with standard deviations and categorical variables as frequencies with percentages. Comparative analysis between vaccinated and non-vaccinated groups was conducted using independent t-tests for continuous variables and chi-square tests for categorical variables. Multivariable logistic regression analysis was performed to identify independent predictors of severe disease and mortality. Odds ratios with 95% confidence intervals were calculated for all relevant associations. A p-value of less than 0.05 was considered statistically significant. Missing data were handled using appropriate statistical methods, and sensitivity analyses were conducted to assess the robustness of findings.

RESULTS

Demographic Characteristics
A total of 978 patients with laboratory-confirmed COVID-19 were enrolled in the study, comprising 412 (42.1%) vaccinated and 566 (57.9%) non-vaccinated individuals. The mean age of the study population was 58.7±14.2 years, with vaccinated patients being significantly older than non-vaccinated patients (62.4±13.8 vs 56.1±14.1 years, $p<0.001$). Male predominance was observed in both groups, with 587 (60.0%) males and 391 (40.0%) females. The proportion of males was slightly higher in the vaccinated group compared to non-vaccinated group (63.1% vs 57.8%, $p=0.043$). Urban residence

was more common among vaccinated patients (78.4% vs 65.2%, p<0.001), reflecting differential vaccine access patterns during the study period.

Vaccination Characteristics

Among the 412 vaccinated patients, 298 (72.3%) had received two doses of vaccine (fully vaccinated) while 114 (27.7%) had received only one dose (partially vaccinated). The majority of vaccinated patients received ChAdOx1 nCoV-19 (Covishield) vaccine (334 patients, 81.1%), followed by BBV152 (Covaxin) in 78 patients (18.9%). The median time interval between completion of vaccination and symptom onset was 45 days (interquartile range: 28-67 days) for fully vaccinated patients and 23 days (interquartile range: 15-34 days) for partially vaccinated patients.

Comorbidity Profile

Comorbidities were present in 623 (63.7%) patients overall, with vaccinated patients having a higher prevalence of comorbidities compared to non-vaccinated patients (72.8% vs 57.2%, p<0.001). Diabetes mellitus was the most common comorbidity, affecting 187 (45.4%) vaccinated patients and 198 (35.0%) non-vaccinated patients (p<0.001). Hypertension was present in 165 (40.0%) vaccinated patients compared to 156 (27.6%) non-vaccinated patients (p<0.001). Chronic kidney disease was observed in 43 (10.4%) vaccinated patients versus 31 (5.5%) non-vaccinated patients (p=0.002). Other cardiovascular diseases were documented in 67 (16.3%) vaccinated patients and 45 (8.0%) non-vaccinated patients (p<0.001).

Clinical Presentation and Symptoms

Fever was the most common presenting symptom, reported in 756 (77.3%) patients, with no significant difference between vaccination groups (78.2% vs 76.7%, p=0.542). Breathlessness was significantly more common in non-vaccinated patients (68.4% vs 54.6%, p<0.001), suggesting more severe respiratory involvement. Cough was present in 545 (55.7%) patients overall, with similar frequencies in both groups (56.3% vs 55.3%, p=0.732). Myalgia was reported by 298 (30.5%) patients, with vaccinated patients experiencing this symptom more frequently (35.9% vs 26.7%, p=0.001). Altered sensorium, indicating severe disease, was significantly more prevalent in non-vaccinated patients (15.9% vs 8.5%, p<0.001).

Disease Severity Distribution

Significant differences in disease severity were observed between vaccination groups. Mild disease was documented in 281 (68.2%) vaccinated patients compared to 257 (45.4%) non-vaccinated patients (p<0.001). Moderate disease affected 56 (13.6%) vaccinated patients and 126 (22.3%) non-vaccinated patients (p<0.001). Severe disease was present in 75 (18.2%) vaccinated patients versus 183 (32.3%) non-vaccinated patients (p<0.001). The odds ratio for severe disease in non-vaccinated patients was 2.14 (95% CI: 1.56-2.93, p<0.001) compared to vaccinated patients.

Laboratory Parameters

Significant differences in laboratory parameters were observed between vaccination groups. Hemoglobin levels were similar between groups (11.8±2.1 vs 11.6±2.3 g/dL, p=0.234). Total leukocyte count was significantly higher in non-vaccinated patients (9,847±4,562 vs 8,234±3,891 cells/μL, p<0.001). Lymphocyte count was lower in non-vaccinated patients (1,456±678 vs 1,723±756 cells/μL, p<0.001), indicating more pronounced lymphopenia. Platelet count was significantly reduced in non-vaccinated patients (198,000±89,000 vs 234,000±78,000 cells/μL, p<0.001).

Inflammatory markers demonstrated marked differences between groups. C-reactive protein levels were significantly elevated in non-vaccinated patients (68.9±35.7 vs 45.2±28.4 mg/L, p<0.001). D-dimer concentrations were higher in non-vaccinated patients (2.9±2.1 vs 1.8±1.2 μg/mL, p<0.001). Serum ferritin levels were elevated in non-vaccinated patients (1,245±567 vs 987±445 ng/mL, p<0.001). Lactate dehydrogenase was significantly higher in non-vaccinated patients (456±189 vs 378±156 U/L, p<0.001). Procalcitonin levels were elevated in non-vaccinated patients (2.8±3.4 vs 1.9±2.1 ng/mL, p=0.003).

Biochemical parameters showed several significant differences. Serum sodium levels were lower in non-vaccinated patients (134.2±6.8 vs 136.1±5.9 mEq/L, p<0.001). Urea levels were elevated in non-vaccinated patients (67.8±34.5 vs 56.9±28.7 mg/dL, p<0.001). Serum creatinine was higher in non-vaccinated patients (1.8±1.2 vs 1.5±0.9 mg/dL, p=0.001). Liver function parameters including AST (89.7±67.8 vs 72.4±52.3 U/L, p<0.001) and ALT (76.5±58.9 vs 64.2±45.6 U/L, p=0.004) were significantly elevated in non-vaccinated patients.

Radiological Findings

Chest radiography revealed abnormalities in 712 (72.8%) patients, with bilateral involvement more common in non-vaccinated patients (58.7% vs 45.9%, p<0.001). High-resolution computed tomography was performed in 534 (54.6%) patients when clinically indicated. CT severity scores were significantly higher in non-vaccinated patients (14.8±6.7 vs 11.2±5.9, p<0.001), indicating more extensive lung involvement. Ground glass opacities were the predominant finding, present in 467 (87.5%) of patients who underwent HRCT. Consolidation was more frequent in non-vaccinated patients (42.3% vs 28.7%, p<0.001).

Clinical Outcomes

Hospital mortality was significantly higher in non-vaccinated patients compared to vaccinated patients (106 patients, 18.7% vs 18 patients, 4.4%, p<0.001). The odds ratio for mortality in non-vaccinated patients was 4.98 (95% CI: 2.96-8.37, p<0.001). Mechanical ventilation was required in 128 (22.6%) non-vaccinated patients compared to 36 (8.7%) vaccinated patients (p<0.001). Intensive care unit admission was necessary for 187 (33.0%) non-vaccinated patients versus 89 (21.6%) vaccinated patients (p<0.001).

Hospital length of stay was significantly longer for non-vaccinated patients (12.8±7.4 vs 9.6±5.8 days, p<0.001). Among survivors, the median time to clinical improvement was 8 days (IQR: 5-12) for vaccinated patients compared to 11 days (IQR: 7-16) for non-vaccinated patients (p<0.001). Complications during hospitalization were more frequent in non-vaccinated patients, including acute respiratory distress syndrome (23.1% vs 12.4%, p<0.001), secondary bacterial infections (18.9% vs 9.7%, p<0.001), and acute kidney injury (15.7% vs 8.0%, p<0.001).

Multivariable Analysis

Multivariable logistic regression analysis identified several independent predictors of severe disease. Non-vaccinated status was associated with increased odds of severe disease (adjusted OR: 2.31, 95% CI: 1.64-3.25, p<0.001). Advanced age emerged as a significant predictor (adjusted OR: 1.04 per year, 95% CI: 1.02-1.06, p<0.001). Diabetes mellitus was independently associated with severe disease (adjusted OR: 1.78, 95% CI: 1.28-2.47, p=0.001). Elevated CRP levels (adjusted OR: 1.02 per mg/L, 95% CI: 1.01-1.03, p<0.001) and elevated D-dimer (adjusted OR: 1.35 per μg/mL, 95% CI: 1.18-1.54, p<0.001) were significant predictors of severe outcomes.

For mortality prediction, non-vaccinated status remained a strong independent predictor (adjusted OR: 3.87, 95% CI: 2.15-6.96, p<0.001). Age was the strongest predictor of mortality (adjusted OR: 1.06 per year, 95% CI: 1.04-1.08, p<0.001). Presence of chronic kidney disease (adjusted OR: 2.94, 95% CI: 1.67-5.18, p<0.001) and cardiovascular disease (adjusted OR: 2.15, 95% CI: 1.34-3.45, p=0.002) significantly increased mortality risk. Laboratory predictors of mortality included elevated procalcitonin (adjusted OR: 1.28 per ng/mL, 95% CI: 1.15-1.43, p<0.001) and lymphocyte count below 1000 cells/μL (adjusted OR: 2.67, 95% CI: 1.78-4.01, p<0.001).

Tables

Table 1: Demographic Profile of Study Population

Characteristic	Overall (n=978)	Vaccinated (n=412)	Non-Vaccinated (n=566)	p-value
Age (years)				
Mean ± SD	58.7 ± 14.2	62.4 ± 13.8	56.1 ± 14.1	<0.001
18-39 years	156 (15.9%)	42 (10.2%)	114 (20.1%)	<0.001
40-59 years	398 (40.7%)	154 (37.4%)	244 (43.1%)	
≥60 years	424 (43.4%)	216 (52.4%)	208 (36.7%)	
Gender				
Male	587 (60.0%)	260 (63.1%)	327 (57.8%)	0.043
Female	391 (40.0%)	152 (36.9%)	239 (42.2%)	
Residence				
Urban	691 (70.7%)	323 (78.4%)	368 (65.2%)	<0.001
Rural	287 (29.3%)	89 (21.6%)	198 (35.0%)	
Vaccination Status				
Fully Vaccinated (2 doses)	-	298 (72.3%)	-	-
Partially Vaccinated (1 dose)	-	114 (27.7%)	-	-
Vaccine Type				
ChAdOx1 nCoV-19 (Covishield)	-	334 (81.1%)	-	-
BBV152 (Covaxin)	-	78 (18.9%)	-	-

Table 2: Comorbidities in Study Groups

Comorbidity	Overall (n=978)	Vaccinated (n=412)	Non-Vaccinated (n=566)	p-value
Any Comorbidity	623 (63.7%)	300 (72.8%)	323 (57.2%)	<0.001
Diabetes Mellitus	385 (39.4%)	187 (45.4%)	198 (35.0%)	<0.001
Hypertension	321 (32.8%)	165 (40.0%)	156 (27.6%)	<0.001
Cardiovascular Disease	112 (11.5%)	67 (16.3%)	45 (8.0%)	<0.001

Comorbidity	Overall (n=978)	Vaccinated (n=412)	Non-Vaccinated (n=566)	p-value
Chronic Kidney Disease	74 (7.6%)	43 (10.4%)	31 (5.5%)	0.002
Chronic Respiratory Disease	89 (9.1%)	42 (10.2%)	47 (8.3%)	0.278
Obesity (BMI ≥30)	156 (15.9%)	71 (17.2%)	85 (15.0%)	0.291
Multiple Comorbidities (≥2)	287 (29.3%)	156 (37.9%)	131 (23.1%)	<0.001

Table 3: Vaccination Status vs Disease Severity

Disease Severity	Overall (n=978)	Vaccinated (n=412)	Non-Vaccinated (n=566)	p-value
Mild	538 (55.0%)	281 (68.2%)	257 (45.4%)	<0.001
Moderate	182 (18.6%)	56 (13.6%)	126 (22.3%)	<0.001
Severe	258 (26.4%)	75 (18.2%)	183 (32.3%)	<0.001
Odds Ratio for Severe Disease		Reference	2.14 (1.56-2.93)	<0.001

Table 4: Comparison of Laboratory Parameters by Vaccination Status

Parameter	Vaccinated (n=412)	Non-Vaccinated (n=566)	p-value
Hematological Parameters			
Hemoglobin (g/dL)	11.8 ± 2.1	11.6 ± 2.3	0.234
Total Leukocyte Count (cells/μL)	8,234 ± 3,891	9,847 ± 4,562	<0.001
Lymphocyte Count (cells/μL)	1,723 ± 756	1,456 ± 678	<0.001
Platelet Count (×10³/μL)	234 ± 78	198 ± 89	<0.001
Inflammatory Markers			
CRP (mg/L)	45.2 ± 28.4	68.9 ± 35.7	<0.001
D-dimer (μg/mL)	1.8 ± 1.2	2.9 ± 2.1	<0.001
Serum Ferritin (ng/mL)	987 ± 445	1,245 ± 567	<0.001
LDH (U/L)	378 ± 156	456 ± 189	<0.001
Procalcitonin (ng/mL)	1.9 ± 2.1	2.8 ± 3.4	0.003
Biochemical Parameters			
Serum Sodium (mEq/L)	136.1 ± 5.9	134.2 ± 6.8	<0.001
Urea (mg/dL)	56.9 ± 28.7	67.8 ± 34.5	<0.001
Creatinine (mg/dL)	1.5 ± 0.9	1.8 ± 1.2	0.001
AST (U/L)	72.4 ± 52.3	89.7 ± 67.8	<0.001
ALT (U/L)	64.2 ± 45.6	76.5 ± 58.9	0.004

Table 5: Clinical Outcomes Analysis

Outcome	Vaccinated (n=412)	Non-Vaccinated (n=566)	Odds Ratio (95% CI)	p-value
Primary Outcomes				
Hospital Mortality	18 (4.4%)	106 (18.7%)	4.98 (2.96-8.37)	<0.001
Mechanical Ventilation	36 (8.7%)	128 (22.6%)	3.06 (2.05-4.57)	<0.001
ICU Admission	89 (21.6%)	187 (33.0%)	1.78 (1.34-2.37)	<0.001
Secondary Outcomes				
Hospital Length of Stay (days)	9.6 ± 5.8	12.8 ± 7.4	-	<0.001
Time to Clinical Improvement (days)*	8 (5-12)	11 (7-16)	-	<0.001
Complications				
ARDS	51 (12.4%)	131 (23.1%)	2.13 (1.50-3.04)	<0.001
Secondary Bacterial Infection	40 (9.7%)	107 (18.9%)	2.17 (1.47-3.21)	<0.001
Acute Kidney Injury	33 (8.0%)	89 (15.7%)	2.14 (1.41-3.24)	<0.001

*Median (Interquartile Range) among survivors

Table 6: Multivariable Analysis for Predictors of Severe Disease

Variable	Adjusted OR	95% CI	p-value
Vaccination Status			
Non-vaccinated vs Vaccinated	2.31	1.64-3.25	<0.001
Demographics			
Age (per year)	1.04	1.02-1.06	<0.001
Male vs Female	1.28	0.94-1.75	0.117
Comorbidities			
Diabetes Mellitus	1.78	1.28-2.47	0.001
Hypertension	1.34	0.95-1.89	0.094
Cardiovascular Disease	1.67	1.02-2.73	0.041
Chronic Kidney Disease	2.15	1.21-3.82	0.009
Laboratory Parameters			
CRP (per mg/L)	1.02	1.01-1.03	<0.001
D-dimer (per μg/mL)	1.35	1.18-1.54	<0.001
Lymphocyte count <1000/μL	1.89	1.34-2.67	<0.001

DISCUSSION

This comprehensive prospective observational study of 978 hospitalized COVID-19 patients provides robust real-world evidence demonstrating the significant protective effects of COVID-19 vaccination against severe disease outcomes. The findings consistently show that vaccination, whether partial or complete, substantially reduces disease severity, mortality, and healthcare resource utilization even among patients requiring hospitalization for COVID-19 treatment.

The demographic characteristics of our study population revealed several important patterns consistent with global vaccination rollout strategies. Vaccinated patients were significantly older and had higher rates of comorbidities, reflecting the prioritization of high-risk populations in early vaccination programs (11). Despite this higher baseline risk profile, vaccinated patients demonstrated markedly better clinical outcomes, underscoring the robust protective effects of vaccination even in vulnerable populations. The higher proportion of urban residents among vaccinated patients reflects documented disparities in vaccine access and uptake during the initial phases of vaccination campaigns (12).

The disease severity distribution provides compelling evidence of vaccine effectiveness in reducing severe COVID-19 outcomes. The finding that 68.2% of vaccinated patients had mild disease compared to only 45.4% of non-vaccinated patients aligns with previous studies demonstrating vaccine-mediated attenuation of disease severity (13). The odds ratio of 2.14 for severe disease in non-vaccinated patients represents a clinically significant risk reduction associated with vaccination. These findings are consistent with large-scale observational studies from Europe and North America that have consistently demonstrated reduced disease severity among breakthrough infections (14).

Laboratory parameter differences between vaccination groups provide insights into the pathophysiological mechanisms underlying vaccine-mediated protection. The significantly lower inflammatory marker levels in vaccinated patients, including CRP, D-dimer, ferritin, and LDH, suggest that vaccination modulates the host inflammatory response to SARS-CoV-2 infection. This attenuation of systemic inflammation likely contributes to the observed reduction in severe outcomes and may explain the lower rates of complications such as acute respiratory distress syndrome and multi-organ dysfunction in vaccinated patients (15).

The preservation of lymphocyte counts in vaccinated patients compared to the profound lymphopenia observed in non-vaccinated patients indicates better maintenance of immune homeostasis following vaccination. This finding suggests that vaccination not only provides specific immunity against SARS-CoV-2 but may also help preserve overall immune function during acute infection. The relationship between lymphopenia and COVID-19 severity has been well-established, and our findings suggest that vaccination may mitigate this immunosuppressive effect of severe COVID-19 (16).

Clinical outcomes analysis revealed striking differences in mortality rates between vaccination groups, with a nearly five-fold reduction in hospital mortality among vaccinated patients. This magnitude of mortality reduction is consistent with systematic reviews and meta-analyses that have documented vaccine effectiveness against death ranging from 85-95% (17). The 4.4% mortality rate among vaccinated patients, while still substantial, represents a dramatic improvement compared to the 18.7% mortality observed in non-vaccinated patients. When considering that vaccinated patients had higher baseline risk factors, this mortality reduction becomes even more remarkable.

The significant reduction in mechanical ventilation requirements and ICU admissions among vaccinated patients has important implications for healthcare system capacity and resource allocation. During pandemic surges, ICU capacity has frequently been overwhelmed, leading to rationing of critical care resources. Our findings suggest that high vaccination coverage could substantially reduce healthcare system strain by decreasing the proportion of COVID-19 patients requiring intensive care interventions (18).

The shorter hospital length of stay and faster time to clinical improvement among vaccinated patients provide additional evidence of vaccine-mediated disease attenuation. These findings not only reflect better clinical outcomes for individual patients but also have economic implications for healthcare systems and patients. Reduced hospital length of stay translates to lower healthcare costs and improved healthcare system efficiency (19).

Multivariable analysis confirmed vaccination status as an independent predictor of both severe disease and mortality, even after adjusting for age, comorbidities, and laboratory parameters. This finding strengthens the causal inference regarding vaccine effectiveness and suggests that the observed benefits cannot be attributed solely to differences in baseline characteristics between vaccination groups. The persistence of vaccination as a significant protective factor after comprehensive adjustment supports the biological plausibility of vaccine-mediated protection.

The comorbidity analysis revealed that while vaccinated patients had higher rates of diabetes, hypertension, and cardiovascular disease, they still experienced better outcomes than non-vaccinated patients. This finding is particularly important for clinical practice, as it demonstrates that vaccination provides substantial protection even in high-risk populations with multiple comorbidities. Previous studies have suggested that vaccine effectiveness may be reduced in immunocompromised populations, but our findings indicate that significant protection is maintained even among patients with chronic medical conditions (20).

Radiological findings supported the clinical observations, with vaccinated patients demonstrating lower CT severity scores and less extensive lung involvement despite similar rates of radiological abnormalities. This pattern suggests that while breakthrough infections can still cause pneumonia, the extent and severity of lung involvement are reduced in vaccinated patients. These radiological findings correlate with the observed differences in clinical severity and oxygen requirements.

The study findings have several important implications for clinical practice and public health policy. First, they provide strong real-world evidence supporting vaccination recommendations for all eligible individuals, regardless of age or comorbidity status. Second, they suggest that even among hospitalized patients, vaccination status should be considered when assessing prognosis and making treatment decisions. Third, they underscore the importance of achieving high vaccination coverage to reduce healthcare system burden and improve population health outcomes.

Our study has several strengths, including the prospective design, comprehensive data collection, large sample size, and inclusion of diverse clinical and laboratory parameters. The consecutive sampling approach minimizes selection bias, and the detailed characterization of vaccination status, including timing and vaccine type, enhances the validity of our findings. The inclusion of both partially and fully vaccinated patients provides insights into dose-response relationships for vaccine effectiveness.

However, several limitations should be acknowledged. The study was conducted during a specific time period when particular SARS-CoV-2 variants were predominant, and vaccine effectiveness may vary against different variants. The observational design, while providing real-world evidence, cannot completely eliminate confounding factors despite multivariable adjustment. Selection bias may exist if vaccinated and non-vaccinated populations differ in unmeasured characteristics that influence hospitalization decisions. Additionally, the study population was limited to hospitalized patients, which may not reflect vaccine effectiveness in preventing mild infections or asymptomatic disease.

Future research should focus on long-term follow-up of vaccinated patients to assess durability of protection, comparative effectiveness of different vaccine platforms and dosing strategies, and vaccine effectiveness against emerging SARS-CoV-2 variants. Studies examining optimal timing for booster doses and effectiveness of updated vaccine formulations will be crucial for maintaining population protection as the pandemic evolves.

CONCLUSION

This prospective observational study provides robust evidence that COVID-19 vaccination significantly reduces disease severity, mortality, and healthcare resource utilization among hospitalized patients. Despite vaccinated patients having higher baseline risk factors including advanced age and multiple comorbidities, they demonstrated markedly better clinical outcomes with a 78% reduction in mortality risk, 65% reduction in mechanical ventilation requirements, and 35% reduction in ICU admission rates compared to non-vaccinated patients. The substantial attenuation of inflammatory markers and preservation of immune function in vaccinated patients provides mechanistic insights into vaccine-mediated protection. These findings strongly support continued vaccination efforts and reinforce the critical importance of achieving high vaccination coverage to reduce COVID-19 morbidity, mortality, and healthcare system burden. The study results have

immediate implications for clinical practice, healthcare resource planning, and public health policy development in the ongoing pandemic response.

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