Impact of vaccination on morbidity and mortality in adults hospitalized with COVID-19 during the omicron wave in the Jazan Region, Saudi Arabia

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ABSTRACT

الأهداف: تقييم تأثير التطعيم ضد فيروس كورونا المستجد على معدلات الاعتلال والوفيات لدى البالغين الذين يدخلون المستشفى وهم مصابون بفيروس كورونا المستجد خلال موجة أوميكرون في منطقة جازان.

المنهجية: هذه الدراسة كانت دراسة قائمة على الملاحظة مدتها 6 أشهر سجلت مرضى فيروس كورونا المستجد البالغين الذين تم تنويمهم بين يناير ويونيو 2022. تم تصنيف الأفراد إلى 3 مجموعات وفقًا لحالة المناعة لديهم (محصنين و محصنين جزئياً، وغير محصنين). تم تحديد الوفاة والتنويم في وحدة العناية المركزة والتهوية الميكانيكية على أنها نتائج أولية وطول مدة الإقامة في المستشفى لأكثر من أسبوع كنتيجة ثانوية. تم استخدام تحليل الانحدار اللوجستي المتعدد لتقييم العوامل المستقلة والعلاقة بين النتائج وحالة التطعيم.

النتائج: من بين 634 مريضاً مصاباً بفيروس كورونا المستجد والذين تم تنويمهم بمستشفيات منطقة جازان، 46.4% تم تحصينهم بالكامل و19.7% تحصينهم جزئياً و 33.9% لم يتم تحصينهم. كان عدم التحصين مرتبطًا بشكل كبير بدخول وحدة العناية المركزة (نسبة الأرجحية=1.91، فترة الثقة 95%: 1.17-3.11؛ p=0.009) التهوية الميكانيكية (نسبة الأرجحية=2.11، فترة الثقة 95%: 1.25-3.56؛ p=0.005) زيادة مدة الإقامة في المستشفى (نسبة الأرجحية=1.79، فترة الثقة 95%: 1.24-2.59؛ p=0.002) والموت (نسبة الأرجحية=3.03، فترة الثقة 95%: 1.85-4.98؛ p<0.001).

الخلاصة: تؤكد دراستنا على أهمية اتباع نهج شامل لعلاج مرضى فيروس كورونا المستجد يتضمن التطعيم، وإدارة الأمراض المزمنة، واعتبار العمر عامل خطر للنتائج الوخيمة.

Objectives: To evaluate the impact of coronavirus disease-19 (COVID-19) vaccination on morbidity and mortality in adults hospitalized with COVID-19 during the omicron wave in the Jazan Region, Saudi Arabia.

Methods: A 6-month record-based historical prospective study enrolled COVID-19 adult patients admitted between January and June 2022. Individuals were classified into 3 groups according to their immunity status (immunized, partially immunized, and not immunized). Death, intensive care unit (ICU) admission, and mechanical ventilation were identified as the primary outcomes, collectively referred to as "serious outcomes". On the other hand, the length of hospital stays longer than 5 days was categorized as a secondary outcome. Multiple logistic regression analysis was used to evaluate independent factors and the relationship between the outcomes and vaccination status.

Results: Among the 634 COVID-19 patients admitted to Jazan hospitals, 46.4% were fully immunized, 19.7% were partially immunized, and 33.9% were not immunized. Not being immunized was significantly associated with ICU admission (odds ratio [OR]=1.91, 95% confidence interval [CI]: [1.17-3.11]; p=0.009), mechanical ventilation (OR=2.11, 95% CI: [1.25-3.56]; p=0.005), increased length of hospital stays (OR=1.79, 95% CI: [1.24-2.59]; p=0.002), and death (OR=3.03, 95% CI: [1.85-4.98]; p<0.001).

Conclusion: Our study underscores the importance of a comprehensive approach for managing COVID-19 patients that includes vaccination against the disease.

Keywords: COVID-19, morbidity, mortality, vaccination, Saudi Arabia

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In December 2019, an outbreak of pneumonia linked to a fish market was reported in Wuhan, China. The new coronavirus was identified on January 7, 2020.[1] The highly transmissible virus has led to a global health crisis, considered the most significant challenge since World War II.[2] On February 11, 2020, the World Health Organization (WHO) named coronavirus disease 2019 (COVID-19). It is defined as a respiratory infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which belongs to the beta-coronaviruses subfamily.[3] By November 2020, the WHO had reported nearly 259 million COVID-19 cases and 5 million deaths worldwide.[4]

Although the majority of COVID-19 cases are asymptomatic, the clinical picture of SARS-CoV-2 virus infection ranges from mild to severe pneumonia in 15-20% of patients, and approximately 10% of patients require intensive care unit (ICU) admission, mechanical ventilation, and proper management.[5] Coronavirus disease-19 patients usually present with fever, cough, shortness of breath, headache, muscle and bone aches, and malaise. Less common symptoms include nausea, diarrhea, sore throat, productive cough, chest pain, hemoptysis, and confusion.[6] Radiological findings document the progression to pneumonia 1-2 weeks after the beginning of symptoms, with signs including decreased oxygen saturation, patchy/segmental consolidation or multifocal glass ground opacities in chest X-ray or computed tomography, and deterioration of blood gases. Some patients deteriorate to acute respiratory distress syndrome (ARDS), acute renal injury, acute respiratory failure, and multi-organ failure.[6-8]

The COVID-19 pandemic has significantly strained health and economic systems, with increasing demand for inpatient facilities due to the high number of infected cases.[9] By the end of 2021, the omicron variant of the SARS-CoV-2 virus was first identified in South Africa and detected in many other countries worldwide. The variant has rapidly become the dominant strain in many countries, including Saudi Arabia, where it has caused a surge in cases. Several reports suggest that the new variant differs from the delta variant in terms of its transmission rate, infectiousness, severity of illness, and response to preventive and curative measures.[10]

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Vaccination has a cornerstone role in mitigating the pandemic's effects. The COVID-19 vaccines have undergone extensive clinical trials and are authorized by regulatory agencies worldwide for emergency use. The vaccines effectively prevent severe illness, hospitalization, and death from COVID-19. Additionally, vaccination has been demonstrated to reduce viral transmission rates, thereby slowing the spread of the virus and decreasing the likelihood of new variants emerging.[11] However, due to the mutations in its spike protein, several studies suggest that the omicron variant can partially escape the immune response generated by previous infections or vaccination.[12-16]

Predicting factors associated with the need for hospitalization can help prioritize patients, decision-making, and contingency planning.[17] Accordingly, this study aims to evaluate the impact of COVID-19 vaccination on morbidity and mortality during the omicron wave in the Jazan Region of Saudi Arabia.

Methods. A record-based historical prospective study was carried out enrolling all adults (≥18 years old) who were hospitalized in Jazan Region hospitals between January and June 2022, who had confirmed cases of COVID-19 infection, as well as known vaccination statuses and outcomes. Both male and female patients of all ethnic groups were included in the study. Individuals with unknown vaccination statuses or unknown outcomes were excluded.

The Jazan Region is located in southwestern Saudi Arabia and has a relatively homogenous population with similar ethnic and socioeconomic characteristics. More than 20 public and private secondary care hospitals in the region receive thousands of emergency department (ED) visits per year.

Data, including demographics, medical history, and clinical outcomes of admitted COVID-19 patients, were abstracted using electronic medical records from 22 government and private hospitals.

The Ministry of Health Ethics Committee approved the study in the Jazan Region, Saudi Arabia (ethical approval no.: 2192). The data captured will be stored on a secure and confidential computer. The study was carried out in accordance with the principles of Helsinki Declaration.

Immunization status was identified following the Saudi Public Health Authority's definition and the TAWAKALNA application status for COVID-19 tracing at the time of infection; those who got nothing, received only the first dose, or received the second dose more than 8 months after COVID-19 infection were classified as "nonimmunized," whereas those who

received the booster dose of the vaccine or those who received the second dose fewer than 8 months before COVID-19 infection were classified as "immunized".[18] However, our study groups were subdivided to "fully immunized" (including those received booster dose or received the second dose less than 8 months before COVID-19 infection), "partially immunized" (including those received only the first dose or received the second dose more than 8 months before COVID-19 infection), and "not immunized" (including only those patients who got nothing).

Death during hospitalization or within one month after leaving the hospital, the need for ICU admission, and the need for mechanical ventilation were identified as the primary outcomes, collectively referred to as "serious outcomes". On the other hand, the length of hospital stays longer than 5 days was categorized as a secondary outcome. Based on available clinical records, patients were classified according to their final severity of disease following the WHO's categories; those who did not receive oxygen were classified as "mild/moderate," those who received oxygen (or reported needing it) were classified as "severe," and those who received invasive ventilation (or the maximum available respiratory support) were classified as "critically" ill.

The sample size estimation revealed the need to recruit 518 subjects in our study. The sample size was calculated using Epi Info with a confidence level of 95%, a study power of 80%, an unexposed/exposed case-control ratio of 1:2, an odds ratio (OR) of 2.0, and an 11.8% risk of COVID-19 admission based on a study by Alwafi et al.[19]

Statistical analysis. The Statistical Package for the Social Sciences, version 25 (IBM Corp., Armonk, NY, USA) was used. A 2-sided χ^2 test was used to compare sociodemographic characteristics and clinical features. Continuous data were tested for normal distribution, and either a mean (±SD) or median (IQR), a student t-test, or a Mann-Whitney-U test was used for comparison. Multivariate logistic regression analysis was used to evaluate independent factors and the relationship between outcome and vaccination status. Several variables, including age, gender, past medical history, and the presence of comorbidities such as hypertension, diabetes mellitus, heart diseases, chronic renal diseases, and asthma, were included in the logistic regression model. A *p*-value of <0.05 was considered significant for all comparisons, and the results were expressed as OR and 95% confidence intervals (CI) for risk factors and as percentages for immunization status and outcomes.

Results. From January to June 2022, 928 patients were hospitalized with confirmed cases of COVID-19. Of these, 634 were adults who were enrolled in our study, while the rest were excluded because they were either under 18 years of age (252 people) or had an unknown vaccination status (42 people). The mean age of the subjects was 62.4±22.8 years old, and the male-to-female ratio was 1:1. Among the 634 enrolled subjects, 215 (33.9%) were unvaccinated, 78 (13.7%) received only one dose of the COVID-19 vaccine, 244 (38.5%) received 2 doses (206 had not gone 8 months before getting infected, and 47 had gone more than 8 months), and 88 (13.9%) received a booster dose (**Figure 1**). The overall cure rate for the admitted subjects was 79.8%, and the death rate was 20.2% (**Table 1**).

Among the 634 subjects, those who were not immunized had a significantly higher ICU admission rate of 27.4% compared to 16.5% for partially Immunized and 17.4% for those who were fully immunized (p=0.010). Additionally, the median length of hospital stay was higher for nonimmunized subjects at 6.0 days compared to 5.0 days for partially and fully immunized subjects (p=0.001). Furthermore, not immunized subjects had significantly higher rates of critical disease and required mechanical ventilation at 22.3% compared to 10.4% for partially immunized and 11.9% for the fully immunized group (p=0.002). The death rate was also higher for the nonimmunized subjects at 31.6% compared to 18.4% for partially immunized and 12.6% for the fully immunized subjects (p<0.001, **Table 1**).

Regarding outcomes, the mean age of deceased individuals was significantly higher than those who were cured (73.4 vs. 59.6 years; p<0.004), especially among individuals aged 60 years and above. Moreover, when comparing the deceased group with those who were cured, the deceased group was significantly more likely to be diabetic (p<0.001), hypertensive (p<0.001), or have chronic kidney disease (p=0.001, **Table 2**).

The death rate was significantly associated with being unvaccinated (53.1% vs. 29.1%, p<0.001), being a referred case (25.8% vs. 3.2%, p<0.001), and being admitted to the ICU (78.1% vs. 6.1%, p<0.001) compared to the cured group. This noticeably increased the median length of hospital stay (7 vs. 5 days, p<0.001). Moreover, deceased subjects had significantly higher rates of critical disease and need for mechanical ventilation compared to the cured group (53.1% vs. 29.1%; p<0.001, **Table 2**).

A multivariate logistic regression analysis model was used to further analyze the significant factors for mortality and morbidity. The analysis showed that not

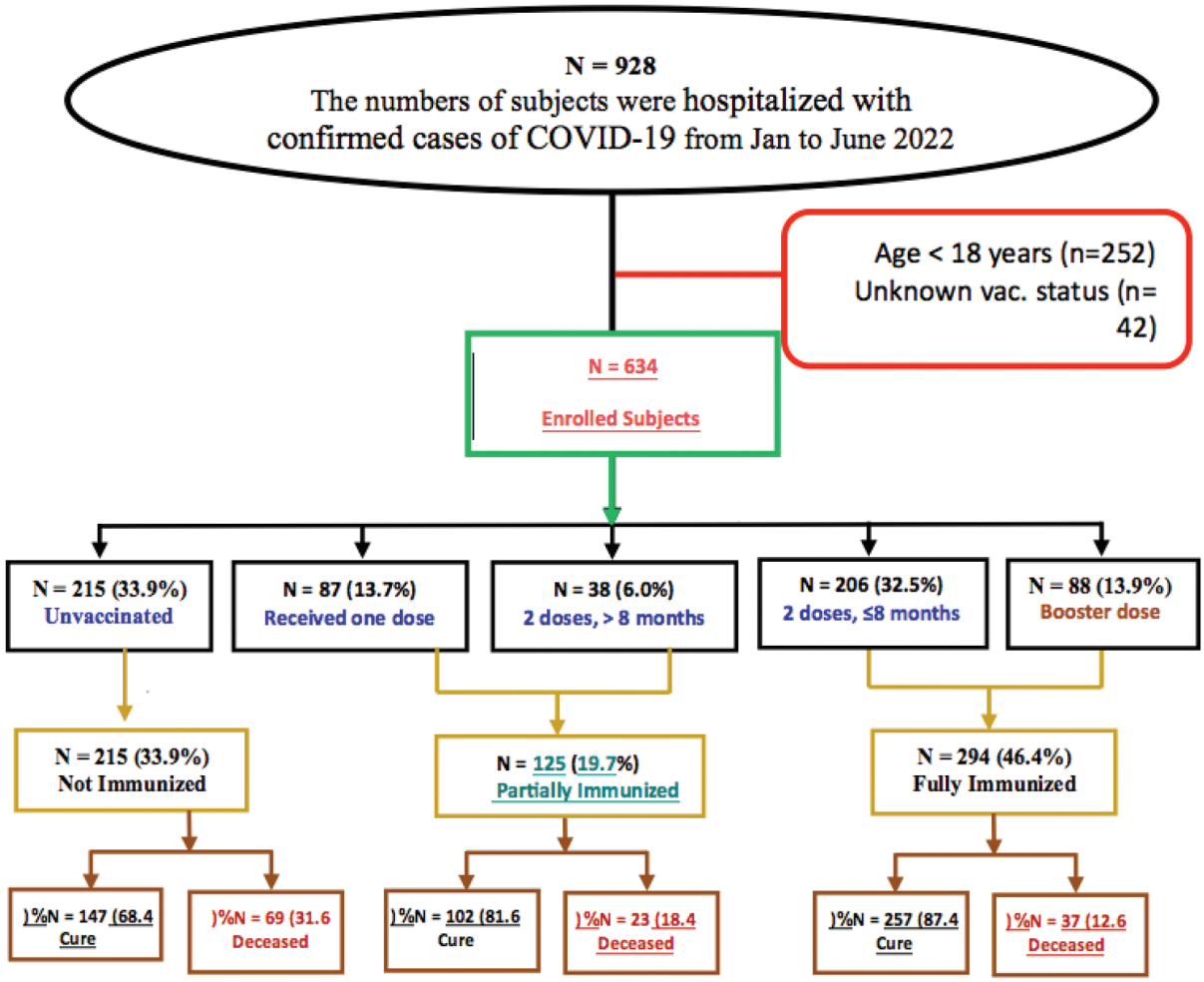

Figure 1 - Flow diagram of the study subjects.

being immunized (OR=3.03, 95% CI: [1.85-4.98]; p<0.001), being aged 60 years or older (OR=2.20, 95% CI: [1.25-3.86]; p=0.006), and having chronic diseases (OR=3.35, 95% CI: [1.55-7.20]; p=0.002) were independent risk factors for death. In contrast, having a history of COVID-19 infection (OR=0.11, 95% CI: [0.01-0.86]; p=0.036) was negatively associated with death (Table 3).

Regarding rates of ICU admission, our study showed that not being immunized (OR=1.91, 95% CI: [1.17-3.11]; p=0.009), being male (OR=1.77, 95% CI: [1.13-2.76]; p=0.012), and having chronic diseases (OR=5.07, 95% CI: [2.40-10.67]; p<0.001), particularly chronic kidney disease (OR=3.98, 95% CI: [1.17-13.47]; p=0.027), were independent risk factors for ICU admission (Table 3).

Regarding the need for mechanical ventilation, our study showed that not being immunized (OR=2.11, 95% CI: [1.25-3.56]; p=0.005), being partially immunized (OR=2.33, 95% CI: [1.15-4.72]; p=0.019) and having chronic diseases (OR=4.76, 95% CI: [2.11-10.77]; p<0.001) were independent risk factors for needing mechanical ventilation (Table 3).

Regarding the length of hospital stay, our study showed that not being immunized (OR=1.79, 95% CI: [1.24-2.59]; p=0.002), being partially immunized (OR=1.80, 95% CI: [1.14-2.84]; p=0.011) and having chronic diseases (OR=3.58, 95% CI: [1.05-12.18]; p=0.041) were independent risk factors for a long hospital stay (Table 3).

Discussion. Based on the multivariate logistic regression analysis, our study identified several independent risk factors affecting the mortality, ICU admission, the need for mechanical ventilation, and the length of hospital stay in COVID-19 patients.

Table 1 - The outcomes characteristics of adult patients hospitalized with coronavirus disease-19 from January to June 2022 according to their immunity (n=634).

Characteristics	All (n=634)	Not immunized (n=215)	Partially immunized (n=125)	Fully immunized (n=294)	*P*-values
Entry to hospital					
Emergency room	486 (76.7)	153 (71.1)	106 (84.8)	227 (77.2)	0.078
In patients	99 (15.6)	42 (19.5)	12 (9.6)	45 (15.3)	
Referral	49 (7.7)	20 (9.3)	7 (5.6)	22 (7.5)	
Admission department					
Ward	490 (77.8)	151 (70.2)	99 (79.2)	240 (81.6)	0.010
Emergency room	13 (2.1)	5 (2.3)	5 (4.0)	3 (1.0)	
ICU	131 (20.7)	59 (27.4)	21 (16.5)	51 (17.3)	
Length of hospital stay in days, median (IQR)	5.0 (3.0-8.0)	6.0 (4.0-10.0)	5.0 (3.0-6.0)	5.0 (3.0-7.0)	0.001
Oxygen therapy and ventilation					
No oxygen	292 (46.1)	81 (37.7)	60 (48.0)	151 (51.4)	0.006
Mask/cannula	180 (28.4)	66 (30.4)	38 (30.4)	76 (25.9)	
Non-invasive	66 (10.4)	20 (9.3)	14 (11.2)	32 (10.9)	
Mechanical	96 (15.1)	48 (22.3)	13 (10.4)	35 (11.9)	
World Health Organization classification for covid-19 severity					
Mild/moderate	292 (46.1)	81 (37.7)	60 (48.0)	151 (51.4)	0.002
Severe	246 (38.8)	86 (40.0)	52 (41.6)	108 (36.7)	
Critical	96 (15.1)	48 (22.3)	13 (10.4)	35 (11.9)	
Clinical outcomes					
Cure	506 (79.8)	147 (68.4)	102 (81.6)	257 (87.4)	<0.001
Death	128 (20.2)	69 (31.6)	23 (18.4)	37 (12.6)	

Values are presented as numbers and precentages (%) or median and interquartile range (IQR). ICU: intensive care unit

In terms of mortality, the study found that being not immunized, being aged 60 years or older, and having chronic diseases were significant independent risk factors, which comes as no surprise, given that the deceased subjects were more likely to suffer from multiple comorbidities.[20,21] In Indonesia, Karyono et al[22] showed that mortality rates were higher among elderly patients with COVID-19 and COVID-19 patients with hypertension, diabetes, and other cardiovascular diseases. Moreover, Djaharuddin et al[23] reported that hypertension, cardiovascular disease, and diabetes were the most common comorbidities in patient death due to COVID-19. The findings highlight the need for targeted care for vulnerable populations, particularly for elderly patients with comorbidities, to reduce their risk of severe outcomes and mortality.

Regarding ICU admission, the study found that being not immunized, being male, and having chronic diseases, particularly chronic kidney disease, were independent risk factors. This was consistent with a recent study by Grasselli et al.[24] On the other hand, not immunized patients were more likely to be admitted to the ICU, in line with previous findings.[25] Another study found that the vaccine effectively prevented severe COVID-19 outcomes, including ICU admission.[26] Specifically, among immunized individuals, the vaccine was 96% effective in preventing ICU admission due to COVID-19 compared to those who were not immunized. The vaccine was also 92% effective in preventing severe COVID-19 outcomes overall, including hospitalization and death.[26] Yet, another study found that the vaccine effectively prevented severe COVID-19 outcomes, including ICU admission.[27] Specifically, among those aged 16 years and older, the vaccine was 87% effective in preventing ICU admission due to COVID-19 compared to those who were unvaccinated. The vaccine was also 89% effective in preventing hospitalization and 91% effective in preventing severe COVID-19 outcomes overall.[27]

Tenforde et al[28] found out that unvaccinated patients hospitalized with COVID-19 were more likely to develop critical conditions such as ARDS, thereby requiring invasive mechanical ventilation. Among patients hospitalized with COVID-19 in our study, the number of patients who required invasive mechanical ventilation and who were in critical condition was significantly higher among the partially immunized, not immunized groups and among the chronic disease group, which further supports the findings of previous research. Even among patients who were intubated due to COVID-19-related ARDS, being immunized has been associated with lower mortality.[29]

Table 2 - Demographic and clinical characteristics of adult patients hospitalized with coronavirus disease-19 from January to June 2022 according to their outcomes (n=634).

Characteristics	All (n=634)	Cure (n=506)	Deceased (n=128)	*P*-values
Age (years), mean±SD	62.4±22.8	59.6±23.5	73.4±16.2	<0.001
<60	246 (38.8)	224 (44.3)	22 (17.2)	<0.001
≥60	388 (61.2)	282 (55.7)	106 (82.8)	
Gender				
Female	317 (50.0)	262 (51.38)	55 (43.0)	0.075
Male	317 (50.0)	244 (48.2)	73 (57.0)	
Nationality				
Saudi	560 (88.3)	447 (88.3)	113 (88.3)	0.985
Non-Saudi	74 (11.7)	59 (11.7)	15 (11.7)	
Past history of COVID-19				
No	594 (93.7)	467 (92.3)	127 (99.2)	0.004
Yes	40 (6.3)	39 (7.7)	1 (0.8)	
Comorbidities (underline chronic diseases)				
No	360 (56.8)	328 (64.8)	32 (25.0)	<0.001
Yes	274 (43.2)	178 (35.2)	96 (75.0)	
Diabetes mellitus				
No	458 (72.2)	398 (78.7)	60 (46.9)	<0.001
Yes	176 (27.8)	108 (21.3)	68 (53.1)	
Hypertension				
No	445 (70.2)	387 (76.5)	58 (45.3)	<0.001
Yes	189 (29.8)	119 (23.5)	70 (54.7)	
Chronic heart disease				
No	610 (96.2)	490 (96.8)	120 (93.7)	0.089
Yes	24 (3.8)	16 (3.2)	8 (6.3)	
Asthma				
No	617 (97.3)	496 (98.0)	121 (94.5)	0.075
Yes	17 (2.7)	10 (2.0)	7 (5.5)	
Chronic kidney disease				
No	619 (97.6)	500 (98.8)	119 (93.0)	0.001
Yes	15 (2.4)	6 (1.2)	9 (7.0)	
Other comorbidities (SCA, obesity, immunosuppression, malignancies, and others)				
No	612 (96.1)	487 (96.0)	125 (96.1)	0.608
Yes	25 (3.9)	20 (4.0)	5 (3.9)	
Vaccination status				
1 dose	87 (13.7)	69 (13.6)	18 (14.1)	<0.001
2 doses	244 (38.5)	210 (41.5)	34 (26.6)	
3 doses	88 (13.9)	80 (15.8)	8 (6.3)	
Not vaccinated	215 (33.9)	147 (29.1)	68 (53.1)	
Entry to hospital				
ER	486 (76.7)	421 (83.2)	65 (50.8)	<0.001
In patients	99 (15.6)	69 (13.6)	30 (23.4)	
Referral	49 (7.7)	16 (3.2)	33 (25.8)	
Admission department				
Word	493 (77.8)	464 (91.7)	26 (20.3)	<0.001
ER	13 (2.1)	11 (2.2)	2 (1.6)	
ICU	128 (20.2)	31 (6.1)	100 (78.1)	
Admission after infection with COVID-19 in days, median (IQR)	0.0 (0.0-2.0)	0.0 (0.0-2.0)	0.5 (0.0-2.5)	0.221
Length of hospital stay in days, median (IQR)	5.0 (3.0-8.0)	5.0 (3.0-7.0)	7.0 (4.0-13.5)	<0.001
Oxygen therapy and ventilation				
No oxygen	292 (46.1)	286 (56.5)	6 (4.7)	<0.001
Mask/cannula	180 (28.4)	158 (31.2)	22 (17.2)	
Non-invasive	66 (10.4)	55 (10.9)	11 (8.6)	
Mechanical	96 (15.1)	7 (1.4)	89 (69.5)	
World Health Organization classification for COVID-19 severity				
Mild/moderate	292 (46.1)	286 (56.5)	6 (4.7)	<0.001
Severe	246 (38.8)	213 (42.1)	33 (25.8)	
Critical	96 (15.1)	7 (1.4)	89 (69.5)	

Values are presented as numbers and precentages (%), mean ± standard deviation (SD), or median and interquartile range (IQR).
SCA: sickle cell anemia, ER: emergency room, ICU: intensive care unit, COVID-19: coronavirus disease-19

Table 3 - Multivariate analysis of the variables predicting morbidity and mortality in adult patients hospitalized with coronavirus disease-19 from January to June 2022 (n=634).

Characteristics	Death		ICU Admission		Mechanical ventilation		Length of hospital stay exceeding 5 days	
	OR (95% CI)	*P*-values	OR (95% CI)	*P*-values	OR (95% CI)	*P*-values	OR (95% CI)	*P*-values
Not immunized	3.03 (1.85-4.98)	<0.001	1.91 (1.17-3.11)	0.009	2.11 (1.25-3.56)	0.005	1.79 (1.24-2.59)	0.002
Partially immunized	1.75 (0.98-3.15)	0.059	1.69 (0.91-3.15)	0.099	2.33 (1.15-4.72)	0.019	1.80 (1.14-2.84)	0.011
Age (≥60 years)	2.20 (1.25-3.86)	0.006	0.78 (0.46-1.32)	0.361	1.20 (0.67-2.16)	0.538	1.20 (0.84-1.74)	0.309
Gender (male)	1.29 (0.83-2.00)	0.263	1.77 (1.13-2.76)	0.012	1.58 (0.97-2.58)	0.066	0.83 (0.60-1.15)	0.268
Past history of COVID-19 (yes)	0.11 (0.01-0.86)	0.036	0.00 (0.00-0.00)	0.997	0.00 (0.00-0.00)	0.997	1.22 (0.63-2.37)	0.543
Comorbidities (yes)	3.35 (1.55-7.20)	0.002	5.07 (2.40-10.67)	<0.001	4.76 (2.11-10.77)	<0.001	1.17 (0.63-2.15)	0.611
Diabetes mellitus (yes)	1.46 (0.80-2.65)	0.221	1.12 (0.63-1.96)	0.707	1.29 (0.69-2.41)	0.421	0.85 (0.55-1.45)	0.551
hypertension (yes)	1.04 (0.55-1.98)	0.899	1.62 (0.88-2.99)	0.124	1.02 (0.53-1.96)	0.962	0.35 (0.77-2.36)	0.293
Asthma (yes)	1.85 (0.57-5.99)	0.304	0.87 (0.26-2.90)	0.823	0.00 (0.00-0.00)	0.998	1.04 (0.36-3.02)	0.947
Chronic heart disease (yes)	0.76 (0.28-1.98)	0.569	0.68 (0.27-1.74)	0.419	1.07 (0.41-2.74)	0.895	0.50 (0.20-1.26)	0.142
Chronic kidney disease (yes)	3.06 (0.99-9.49)	0.053	3.98 (1.17-13.47)	0.027	2.12 (0.68-6.61)	0.196	3.58 (1.05-12.18)	0.041

Values are presented as odds ratio (OR) and 95% confidence interval (CI). References: fully vaccinated, age <60 years, gender (female), past history of COVID (no), comorbidities (no), diabetes mellitus (no), hypertension (no), asthma (no), chronic heart disease (no), and chronic kidney disease (no). COVID-19: coronavirus disease-19, ICU: intensive care unit

Being not immunized, and having chronic diseases as significant risk factors for prolonged hospital stay in COVID-19 patients had been identified by several studies. These studies highlight the importance of early identification and management of these risk factors, including vaccination, management of chronic diseases, and early intervention, to reduce the duration of hospitalization and improve outcomes.[30-32]

Following our multivariate analysis of the factors associated with mortality and morbidity, the study's findings highlight the importance of prior infection of COVID-19 in reducing the risk of severe outcomes and mortality among patients with COVID-19. The findings suggest that patients who have already been infected with COVID-19 are less likely to experience severe outcomes and mortality and therefore enjoy higher chances of recovery. This contradicts the findings reported by Bowe et al,[33] but supports those of others.[34]

These findings highlight the importance of vaccination and the management of chronic diseases in reducing the risk of severe outcomes in COVID-19 patients. The study's results may have important implications for public health interventions aimed at the management of COVID-19 patients, reducing the burden of COVID-19 on healthcare systems, and improving patient outcomes. First, the study highlights the importance of COVID-19 vaccination in reducing the risk of severe outcomes, including mortality, ICU admission, mechanical ventilation, and prolonged hospital stay. This underscores the need for public health interventions aimed at promoting COVID-19 vaccination among eligible populations.

Second, the study identifies chronic disease as a significant risk factor for severe outcomes in COVID-19 patients. This emphasizes the importance of managing chronic diseases, such as hypertension, diabetes, and chronic kidney disease, in COVID-19 patients to reduce the risk of severe outcomes. Healthcare providers should be vigilant in monitoring and managing chronic diseases in COVID-19 patients, particularly those who are not vaccinated. Third, the study highlights the importance of age and gender as risk factors for severe outcomes in COVID-19 patients. Old age has been consistently identified as a risk factor for severe COVID-19 outcomes in previous studies, and this study supports these findings. Healthcare providers should be aware of these risk factors when managing COVID-19 patients and consider them when making treatment decisions.

Based on the findings of this study, here are some recommendations that could be applied to improve the management of COVID-19 patients. The study found that not being immunized was a significant risk factor for severe outcomes in COVID-19 patients, accordingly; public health authorities should prioritize efforts to promote COVID-19 vaccination and improve vaccine uptake among eligible populations. To reduce the risk of severe outcomes resulted from chronic diseases, such as hypertension, diabetes, and chronic kidney disease, whereas they were identified as significant risk factors

for severe outcomes in COVID-19 patients, healthcare providers should monitor and manage these conditions in COVID-19 patients carefully.

Healthcare providers should pay attention when managing old-aged COVID-19 patients. Getting older is a risk factor for severe outcomes in such patients.

Public health messaging should emphasize the importance of vaccination and managing chronic diseases in reducing the risk of severe outcomes in COVID-19 patients. Messaging should also be targeted to specific populations, such as older adults, who may be at higher risk for severe outcomes. To effectively manage COVID-19 patients, it is important to ensure access to healthcare services, including vaccination, testing, and treatment. Public health authorities should work to ensure that healthcare services are accessible to all, including those in underserved communities. By implementing these recommendations, healthcare providers and public health authorities can improve the management of COVID-19 patients and reduce the burden of the virus on healthcare systems.

Study limitations. Due to long, complex procedures at the national level, this study was limited in its ability to carry out genomic sequencing to determine which variants caused which infections. Similarity of symptoms of all COVID-19 variants was another challenge when distinguishing omicron from the other variants. However, our study covered most hospitalized cases of COVID-19 in the period between January and June 2022. This period represents the peak period for the omicron wave in the Jazan Region.

It is important to acknowledge that excluding individuals with missing vaccination status or unknown outcomes may introduce some selection bias in our study. However, we took rigorous measures to mitigate this bias. These measures included carefully addressing missing data to prevent its introduction of bias, enrolling all admitted patients in our study, and strictly adhering to inclusion criteria. These steps were crucial in minimizing bias and enhancing the validity and reliability of our study results.

In conclusion, our study underscores the importance of a comprehensive approach for managing COVID-19 patients that includes vaccination against the disease. By implementing such an approach, healthcare providers can improve patient outcomes and reduce the burden of COVID-19 on healthcare systems.

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