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Original article

COVID-19 vaccine had a significant positive impact on patients with SARS-CoV-2 during the third (Omicron) wave in Saudi Arabia



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ARTICLE INFO

Article history:

Received 22 June 2022

Received in revised form 31 August 2022

Accepted 18 September 2022

Keywords:

COVID-19

SARS-CoV-2

Vaccine

Third wave

Saudi Arabia

Omicron

ABSTRACT

Introduction: The third (Omicron) wave had caused significant increase in the number of COVID-19 cases around the globe. The severity of the disease depended on the extent of the vaccination status.

Methods: This is a retrospective study of infected COVID-19 patients during the third (Omicron) wave in a hospital in Saudi Arabia.

Results: A total of 400 patients were included with 220 (55 %) males and 180 (45 %) females, and a mean age (+/- SD) of 36.34 + 16.47 years. The most common presenting symptoms were: sore throat 159 (39.8 %), cough 158 (39.5 %), fever 132 (33 %), headache 122 (30.5 %), and muscle ache 124 (31%). There was no difference in underlying conditions, signs and symptoms between males and females apart from the occurrence of sore throat with an OR of 2.014 (95 % CI: 1.103–3.677, P = 0.023) and need of hospitalization OR 2.457 (95 % CI: 1.168–5.167, P value = 0.018) in a binary logistic regression comparison. The need for hospitalization was inversely related to the number of COVID-19 vaccination doses. The rate of admission was 8 (72.7 %), 34 (12 %), 4 (5.4 %) for one, two, and three doses of COVID-19 vaccine, respectively (P < 0.0001). Of all the patients, 14 (3.5 %) and 8 (2 %) required intensive care (ICU) admission and mechanical ventilation, respectively. The median Ct-value of SARS-CoV-2 was higher in those who had 2 or 3 doses compared to those who had one dose of the COVID-19 vaccine, but the difference did not reach statistical significance. None of the included patients died during the study period.

Conclusion: Omicron variant symptoms among infected patients are generally milder compared to other variants. Prior COVID-19 vaccination may limit disease severity and need for hospitalization.

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1. Introduction

Coronavirus disease-19 (COVID-19), is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and had resulted in a global pandemic with different variants causing multiple waves [1]. In the Kingdom of Saudi Arabia (KSA), the first case of COVID-19 was reported in March 2020 [2]. The first wave in the country began in early March 2020 till the end of December and the second wave

Abbreviations: COVID-19, Coronavirus Disease 2019; SARS-CoV-2, Severe Acute Respiratory Syndrome Coronavirus 2; KSA, Kingdom of Saudi Arabia; ICU, Intensive Care Unit; RT-PCR, Reverse Transcriptase Polymerase Chain Reaction; SOB, Shortness of breath

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<https://doi.org/10.1016/j.jiph.2022.09.005>

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Table 1
Demographic Data and Underlying Comorbidities of the included patients with a comparison between males to females. The Odds Ratio (OR) was done using a binary regression analysis.

	All	Male	Female	Odds ratio (Male to Female)	95% C.I. for Odds Ratio		P-value
					Lower	Upper	
Number	400	182	218	—	—	—	—
Mean age (SD)	36.34 (16.47)	36.8 (17.2)	35.9 (15.8)	—	—	—	—
Obesity	4 (1)	1 (0.5)	3 (1.4)	2.864	0.269	30.516	0.383
Diabetes Mellitus	42 (10.5)	16 (8.8)	26 (11.9)	0.612	0.249	1.506	0.285
Hypertension	30 (7.5)	14 (7.7)	16 (7.3)	1.308	0.448	3.821	0.624
Cardiovascular disease	7 (1.8)	4 (2.2)	3 (1.4)	3.392	0.523	22.014	0.200
Lung Disease	5 (1.3)	3 (1.6)	2 (0.9)	1.800	0.237	13.671	0.570
Immunosuppressant drug Use	4 (1)	0	4 (1.8)	—	—	—	—
Contact with a positive case	43 (10.8)	21 (11.5)	22 (10.1)	0.910	0.415	1.996	0.814
Fever	132 (33)	58 (31.9)	74 (33.9)	1.233	0.681	2.231	0.489
Sore throat	159 (39.8)	62 (34.1)	97 (44.5)	0.453	0.245	0.837	0.011*
Cough	158 (39.5)	65 (35.7)	93 (42.7)	0.813	0.462	1.430	0.473
Shortness of breath (SOB)	23 (5.8)	8 (4.4)	15 (6.9)	0.560	0.181	1.728	0.313
Runny nose	75 (18.8)	31 (17)	44 (20.2)	0.982	0.547	1.761	0.950
Chest pain	10 (2.5)	4 (2.2)	6 (2.8)	1.523	0.333	6.977	0.588
Headache	122 (30.5)	52 (28.6)	70 (32.1)	0.820	0.406	1.655	0.580
Muscle ache	124 (31)	55 (30.2)	69 (31.7)	1.626	0.771	3.426	0.201
Diarrhea	7 (1.8)	2 (1.1)	5 (2.3)	0.622	0.112	3.471	0.589
Hospital admission	56 (14)	20 (11)	36 (16.5)	2.457	1.168	5.167	.018*
ICU admission	9 (2.3)	6 (3.3)	3 (1.4)	0.258	0.050	1.337	0.106
Mechanical ventilation	3 (0.8)	1 (0.5)	2 (0.9)	0.570	0.029	11.138	0.711

ICU: intensive care unit; *denotes statistical significance

began in January 2021 [3]. As part of the strategy to limit the pandemic, KSA applied multiple steps including vaccination to decrease the spread of the disease [4]. However, the emergence of the Omicron variant had caused a significant increase in the number of positive cases and by mid-January 2022, the daily reported cases were more than 4000 positive cases per day compared to an average of less than 100 positive cases in the preceding months.

Early reports suggested infection with the Omicron variant was less severe than those caused by other variants [5–7]. Hospital admission rates in South Africa of those infected with the Omicron variant was significantly lower than the rates in previous waves caused by other variants [6–9]. A study of the first 1119 Omicron cases in France reported significantly lower rates of hospitalization, intensive care admission, and mortality compared with 3075 cases due to the delta variant [10].

Previous studies from KSA described the epidemiology, clinical features, intensive care unit (ICU) admission and therapy of COVID-19 patients mainly during the first wave of the pandemic [3,11–14]. However, we are not aware of any previous studies from KSA about the epidemiology and clinical characteristics of COVID-19 during the Omicron wave. In this study, we compare the characteristics of patients, clinical presentation, risk of hospital admission, vaccine impact and outcome during the third wave of the pandemic.

2. Material and methods

We conducted a retrospective study of all cases of COVID-19 from a single medical center in KSA from 25th December 2021 to February 30, 2022. The collected data were the demographics, clinical presentation, underlying comorbidities, vaccination status, number of vaccine doses, the date of the last dose and the date of SARS-CoV-2 infection. Each case was also reviewed in relation to the need of hospital or ICU admission and expressed the proportion of such patients in relation to the number of COVID-19 vaccine doses. In addition, we compared patients who required and did not require hospitalization.

We calculated the time from the last vaccine dose to the following infection in days. SARS-CoV-2 infection was based on a positive SARS-CoV-2 by real-time RT-PCR using swab samples from the upper respiratory tract (nasopharyngeal/ oropharyngeal exudate) or

from the lower respiratory tract (sputum/endotracheal aspirate/ Broncho alveolar lavage/bronchial aspirate), as described previously [15]. The study was approved by the institutional board (IRB) (AFHER-IRB-2022–008).

3. Statistical analysis

We summarized continuous and categorical data as numbers and percentages. Characteristics of patients were compared using descriptive statistics. Categorical data were compared using a chi-square test. We compared admitted and non-admitted as well as males and females in relation to other covariates using Chi-square tests. We utilized a binary logistic regression analysis modeling of multiple covariates in relation to admission status as well as gender. A Boxplot of the Ct-values of SARS-CoV-2 rt-PCR in relation to the number of doses of COVID-19 vaccine was constructed. Kaplan-Meier curve was used to show time-to-events (time from last COVID-19 vaccine to the subsequent occurrence of SARS-CoV-2 infection in days). For Kaplan-Meier curve analysis, male to female comparison was done using log rank test (Matel Cox).

Statistical analysis was performed using the Statistical Package for the Social Sciences Program (SPSS), version 28. All statistical tests were performed with two-sided tests and a P value of ≤ 0.05 denoted statistical significance.

4. Results

During the study period, a total of 400 patients with SARS-CoV-2 infection were confirmed by RT-PCR and were included in the analysis. There were 220 (55%) males and 180 (45%) females. The mean age (+/- SD) was 36.34 + 16.47 years. The most common comorbidities were diabetes mellitus 42 (10.5%) and hypertension 30 (7.5%). The presence of other comorbidities is shown in Table 1. The most common presenting symptoms were: sore throat 159 (39.8%), cough 158 (39.5%), fever 132 (33%), headache 122 (30.5%), and muscle ache 124 (31%) (Table 1). There was no difference in underlying conditions, signs and symptoms between males and females (Table 1) apart from the occurrence of sore throat with an OR of 2.014 (95% CI: 1.103–3.677, P = 0.023) and need of hospitalization OR

Table 2

Percentage of patients requiring hospitalization in relation to the number of COVID-19 doses based on 365 patients with verified vaccination.

Number of vaccines received	Admitted		Total
	Yes	No	
One Dose	8 (72.7)	3 (27.3)	11
Two Doses	34 (12)	247 (88)	281
Three Doses	4 (5.4)	69 (94.5)	73
Total	46	319	365

P < 0.0001

2.457 (95 % CI: 1.168–5.167, P value = .018), in a binary logistic regression comparison.

Of all the patients, 56 (14 %) required hospital admission, and the rate of hospitalization was inversely significantly associated with the number of COVID-19 doses, based on 365 patients with verified vaccination doses (Table 2). The rate of admission was 8 (72.7 %), 34 (12 %), 4 (5.4 %) for one, two, and three doses of COVID-19 vaccine, respectively (P < 0.0001). Of all the patients, 14 (3.5 %) and 8 (2 %) required ICU admission and mechanical ventilation, respectively. The mean duration (+/- SD) of ICU admission and mechanical ventilation was 9.8 (+/- 12.9) and 6.1 (+/- 6) days, respectively.

A binary logistic regression analysis comparing admitted to non-admitted patients is shown in Table 3. The following parameters were significantly associated with admission to the hospital: headache OR 18.06 (95 % CI: 2.211–147.665; P value = 0.007), and sore throat OR 4.643 (95 % CI: 1.282–16.814; P value = 0.019) and the following factors were less associated with admission: fever OR 0.276 (95 % CI: 0.096–.796; P value = 0.017), and diabetes mellitus OR 0.249 (95 % CI: 0.083–0.747; P value = 0.013) (Table 3).

The median viral Ct value was higher in those who had 2 or 3 doses compared to those who had one dose of COVID-19 vaccine (Fig. 1). The median and 95 % CIs were: 8.8 (6.52–15.66), 11.7 (12.7–14.2), 12.5 (12.9–15.5) for one, two, and three doses, respectively. However, this difference did not reach statistical difference (P = 0.37). The mean time to SARS-CoV-2 infection after vaccination was 131.60 (CI: 123.17–140.02) days and it was similar between males (131.3, CI: 119.57–142.99) and females (131.97, CI: 119.83–144.11) (Fig. 2).

5. Discussion

In this study, we evaluated the impact of COVID-19 vaccines on the rate of hospitalization of patients with COVID-19 as well as a

description of the characteristics, presenting symptoms and outcome of patients infected with SARS-CoV-2 during the third (Omicron) wave of the SARS-CoV-2 in Saud Arabia. The most common underlying comorbidities were diabetes mellitus and hypertension. In one study comparing the first and second waves in KSA, the most underlying comorbidities in hospitalized patients were diabetes mellitus, cardiac disease and heart failure [3]. The most important feature of the Omicron wave was the significantly lower hospitalization rate compared to prior waves. The data of hospitalization rate in this study is consistent with other data of patients with Omicron variant infection. Data from South Africa showed that patients with Omicron infection were less likely to require hospitalization compared with the Delta variant and had significantly lower odds of severe disease (62.5 % vs 23.4 %; aOR 0.3, 95 % CI 0.2–0.5), after controlling for other factors [6]. An additional study from South Africa showed that patients presenting with an acute respiratory condition was 31.6 % in the Omicron wave versus a rate of 91.2 % in a previous wave [7]. Data from other countries such as England, and Scotland, showed a reduction in the rate of hospitalizations (15–80 %) in patients who had Omicron compared to the Delta variant [16]. In a binary logistic analysis, the following parameters were significantly associated with admission to the hospital: headache and sore throat. Whereas, fever and diabetes mellitus were inversely associated with hospital admission. A previous study from Saudi Arabia showed that cardiovascular disease and diabetes mellitus were present in the first and second wave and the commonest symptoms were cough, fever and shortness of breath [3]. Differences in these factors likely related to differences in the study population or the interaction between the different factors and the vaccination.

The most common symptoms were sore throat, cough, fever, and headache in this study. Previous studies from KSA revealed similar symptoms during the first and second waves in addition to shortness of breath, which was a frequent complaint at the time of presentation [3]. In another study, sore throat and hoarseness of voice were more consistent symptoms in patients with the Omicron variant than those who had the Delta variant (regardless of the vaccination status) [17]. One study showed that sore throat was seen in 70.5 % of patients with Omicron compared to 60.8% in those who had the delta variant [17]. It was interesting to note a common presentation of odynophagia in cases with Omicron variant as reported in one study [18]. One striking difference was the low occurrence of anosmia among Omicron variant patients, a pathognomonic feature of earlier waves of SARS-CoV-2 infection [19]. This study showed no significant gender variation in comorbidities and symptoms, and no

Table 3

A Comparison between patients who required and did not require hospitalization. The Odd Ratio was done using a binary logistic regression analysis.

	Admitted		Odds Ratio (admitted to non-admitted)	95 % C.I.		P-value
	Yes (Number, %)	No (Number, %)		Lower	Upper	
Obesity	2 (3.6)	2 (0.6)	3.871	0.199	75.263	0.371
Diabetes Mellitus	18 (32.1)	24 (7)	0.249	0.083	0.747	0.013*
Hypertension	11 (19.6)	19 (5.5)	2.406	0.474	12.215	0.289
Cardiovascular disease	7 (12.5)	0	–	–	–	–
Lung Disease	3 (5.4)	2 (0.6)	0.414	0.018	9.750	0.584
Immunosuppressant drug use	1 (1.8)	3 (0.9)	0.782	0.066	9.241	0.846
Contact with positive case	2 (3.6)	41 (11.9)	0.441	0.043	4.539	0.491
Fever	17 (30.4)	115 (33.4)	.276	.096	.796	0.017*
Sore throat	5 (8.9)	154 (44.8)	4.643	1.282	16.814	0.019*
Cough	16 (28.6)	142 (41.3)	.632	.194	2.057	0.446
Shortness of breath	10 (17.9)	13 (3.8)	.329	.080	1.353	0.123
Runny nose	2 (3.6)	73 (21.2)	2.657	.477	14.788	0.264
Chest Pain	4 (7.1)	6 (1.7)	.212	.020	2.206	0.194
Headache	2 (3.6)	120 (34.9)	18.069	2.211	147.665	0.007*
Muscle ache	4 (7.1)	120 (34.9)	1.306	.236	7.221	0.760
Diarrhea	2 (3.6)	5 (1.5)	.226	.014	3.656	0.295
ICU admission	8 (14.3)	1 (0.3)	28.176	2.263	350.809	0.009*

ICU: intensive care unit; *denotes statistical significance

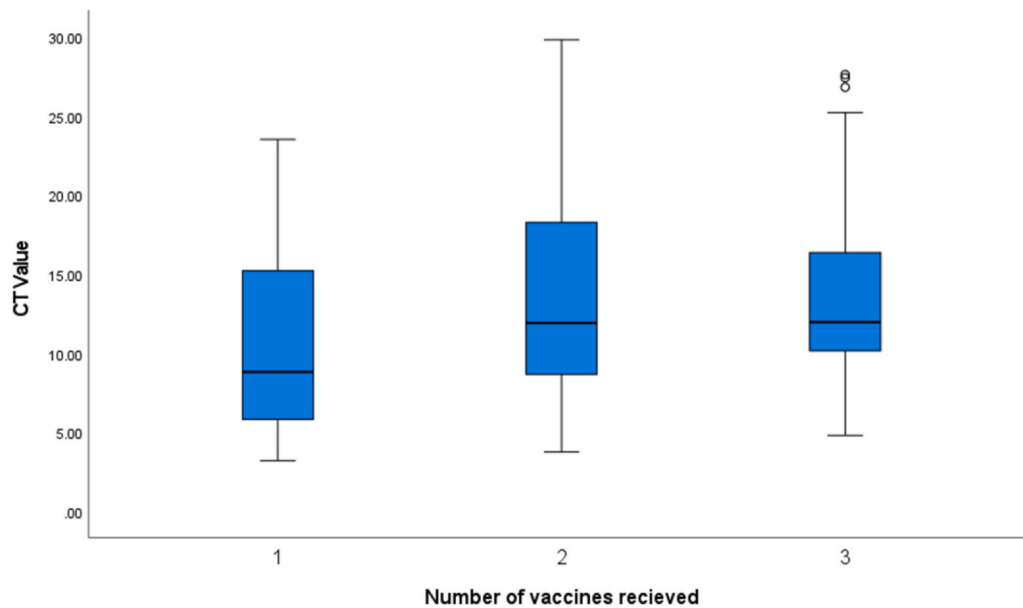


Fig. 1. A Boxplot of the Ct-values of SARS-CoV-2 rt-PCR in relation to the number of doses of COVID-19 vaccine.

other studies had examined gender impact in Omicron wave. However, the occurrence of sore throat in a binary logistic regression showed higher rate among males with an OR of 2.014 (95 % CI:1.103–3.677, $P=0.023$) and a higher need of hospitalization OR 2.457 (95 % CI: 1.168–5.167, P value =.018). The emergence of the COVID-19 had showed a significant racial disparity [20]. In addition, with the Omicron variant there was also significant racial/ethnic and gender disparities in severe clinical outcome [21]. One study showed that females infected with the Omicron variant had fewer hospitalization and ICU admission than male [21].

The median viral Ct value was higher in those who had 2 or 3 doses compared to those who had one dose of the COVID-19 vaccine; however, this difference did not reach statistical difference ($P=0.37$). A previous study comparing the viral Ct value during the first wave showed no change overtime [22]. Studies of Ct values among

patients infected with the Omicron variant showed had higher Ct values in those who had the Omicron variant [23]. One study among healthcare workers showed higher viral Ct values at day 5 of symptoms in those with Omicron than those with the Delta variant [24]. On the other hand, another study showed no difference in the Ct values in relation to variants or vaccine status [25]. However, one study showed higher Ct values in individuals with breakthrough infections [26]. The majority of the patients in the current study were vaccinated and this might had contributed to the increased Ct values. Another explanation is the low sample size in those who had one dose as indicated by the wide 95% confidence interval.

The mean time in days to SARS-CoV-2 infection after vaccination was 131.60 (CI: 123.17–140.02) days and was similar between males and females. It had been shown that the effectiveness of two doses of mRNA COVID-19 vaccine decreased to < 40 % a few months after

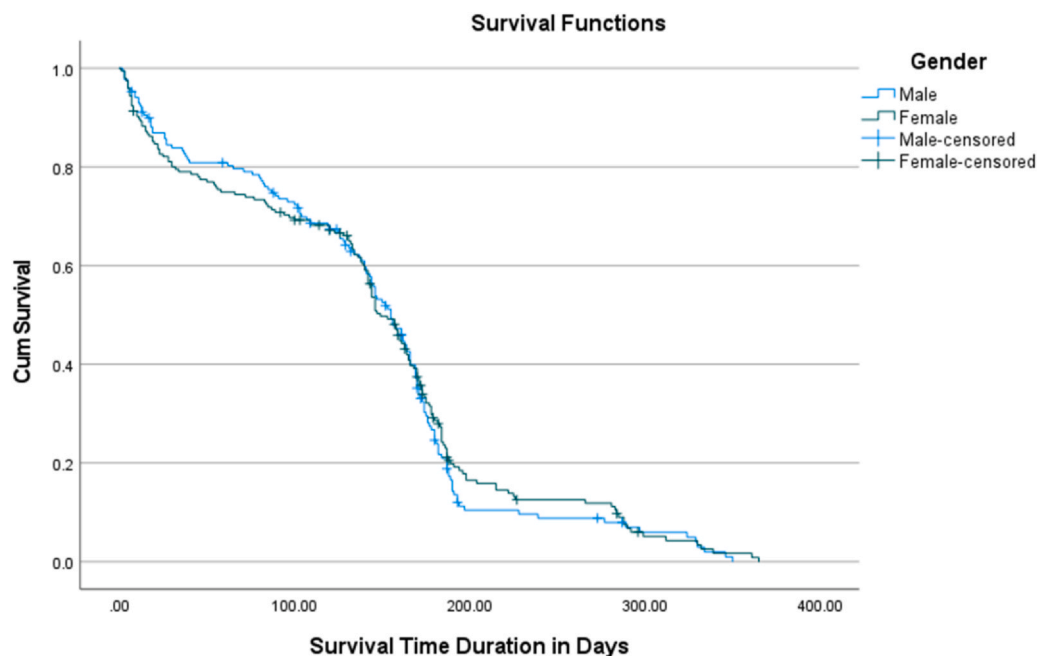


Fig. 2. Kaplan Meier survival curve depicting the time in days from last vaccination dose to the following infection for males and females.

the second dose [27,28]. A third dose of COVID-19 vaccine provides about 70 % protection from infection 2 weeks after the dose [29]. In one study, the effectiveness of mRNA vaccines was about 95 % at 2 months after the first dose and 66.6–80.3 % at 7 months [30]. Waning immunity after vaccination was found in one study to be associated with breakthrough infection but not severe disease [31]. In one study of healthcare workers in South Africa, there was a high rate of breakthrough infection with Omicron variants [32]. The occurrence of breakthrough infections had been associated with reduction in the vaccine efficacy in preventing hospitalization from 91 % after 2 months to 78 % by the fourth month after a third dose [33]. One study showed that COVID-9 vaccination provides different level of protection against SARS-CoV-2 variants with a lower protection for Omicron than Delta variants [34]. Additionally, Omicron variant was shown to escape neutralizing antibodies after two doses of vaccinations due to antigenic shift [35,36].

There are limitations to this study in addition to being observational and retrospective in nature. Also, patients with infections during the third wave were presumed to have Omicron variant, however, there were no genotype studies for confirmation of the specific variants. Lastly, a study conducted retrospectively in one center only may not reflect the entire patients population and thus this may limit the generalizability of the study.

In conclusion, the current study of patients who were diagnosed during the Omicron wave in KSA showed that those patients had milder disease compared to other variants and required less hospitalization and less ICU admission. The fact that most patients had received COVID-19 vaccine shed additional light from real-world data on the importance of COVID-19 vaccination in limiting disease severity and decreasing the need for hospitalization.

Ethical approval

This study was approved by the institutional board (IRB) (AFHER-IRB-2022-008).

Funding

No funding was received for this study.

Author contribution

All authors contributed to the data gathering, analysis, or drafting the first draft. All authors approved the final draft

Data availability

Data available upon reasonable request.

Conflict of interest

All authors have no conflict of interest to declare.

Acknowledgments

N/A.

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