Characterization of COVID-19 Hospitalized Adult Patients, Vaccinated vs Non-vaccinated in Duhok Province

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Abstract

Objectives: First, to determine prevalence of vaccinated COVID-19 patients among hospitalized patients; second, to determine the epidemiological, clinical, and laboratory characteristics of vaccinated and unvaccinated COVID-19 patients.

Methods: The study was carried out on 300 adult COVID-19 hospitalized patients at Duhok COVID-19 health facilities. A prospective cross-sectional study was used as the study design. Between October 1, 2021, and March 31, 2022, all patients with PCR-confirmed COVID-19 were enrolled.

Results: The majority of people in this study were unvaccinated. Pfizer was most popular among people who had received vaccination. The majority of hospitalized patients were old ages, the mean age was 60.73 ± 15.83 yr. In our study, the unvaccinated females had higher infection rates while vaccinated males had higher hospital admission rates. In our study, vaccinated patients had shorter hospital duration stays. In both vaccinated and unvaccinated patients, predominated cases were severe cases. D dimer was significantly higher among vaccinated patients. The mortality rate was relatively high among both groups. Patients who had received vaccinations tended to experience vomiting and flu-like symptoms more frequently than those who had not. In terms of comorbidities, smoking and malignancy were significant risk factors for COVID-19 infection in unvaccinated patients.

Conclusion: We looked at 300 COVID-19 hospitalized patients. In this study, the majority of people were unvaccinated. Pfizer, had higher prevalence among vaccinated individuals. Majority were elderly. The unvaccinated cases had a higher rate of female hospital admissions than male. The D.Dimer level was significantly different between the two groups. Vomiting and flu-like illness showed higher prevalence in vaccinated cases with significant difference. Smoking and malignancy were significant risk factors for COVID-19 infection in unvaccinated patients. In the fight against a public health disaster like a COVID-19 pandemic, the availability of a COVID-19 vaccines campaign are crucial.

Keywords: COVID-19, vaccinated, unvaccinated

Introduction

The World Health Organization (WHO) declared the coronavirus disease 2019 (COVID-19) a pandemic on March 11, 2020. (WHO).¹ Globally, severe acute respiratory syndrome coronavirus 2 (SARSCoV2), the causative agent of COVID-19 has infected tens of millions of people with significant mortality. The virus is transmitted mainly through exposure to respiratory excretions carrying SARS-CoV-2.² The clinical manifestation ranges from asymptomatic infection to serious life-threatening condition. Mild cases constitute approximately 81%., while severe and critical cases constitute 14% and 5%, respectively.³ SARS-CoV-2 has a particular tendency to involve the lower respiratory tract, resulting in a hazardous complication causing pneumonia.

It has been shown that coexisting diseases like diabetes mellitus (DM), cardiovascular diseases (CVD), chronic lung diseases, ...etc have negative impacts on COVID-19 prognosis, causing an increased risk of developing severe complications such as acute respiratory distress syndrome (ARDS).⁴

The diagnosis of COVID-19 is established by detecting the virus in the clinical specimen by molecular assays.⁵ However, other laboratory parameters are fundamental in evaluating the disease severity such as complete blood count (CBC), c-reactive protein (CRP), D-dimer, S. ferritin, lactate dehydrogenase (LDH), ...etc.⁶ Current management strategies are not satisfactory enough to prevent the disease complications, particularly among patients with severe illnesses and comorbid diseases. Hence, it is essential to have an alternative measure to control the disease. The introduction of COVID-19 vaccine has revolutionized the disease magnitude. In Iraq, three COVID-19 vaccines were introduced to the community, namely: mRNA vaccine "Pfizer BioNTech", the adenoviral vector vaccines ChAdOx1 nCoV-19 (AstraZeneca-Oxford), and Sinopharm (Beijing).⁷ Globally, Pfizer on December 24, 2020, AstraZeneca on January 28, 2021, and Sinopharm on September 10, 2021 were granted emergency use authorization by Food and Drug Administration (FDA).⁸ The first vaccine administered to the Iraqi population in March 2021 was Sinopharm.⁹

COVID-19 vaccines proved to be effective in preventing hospitalization.¹⁰ Fully vaccinated people might develop COVID-19 infection in an attenuated form. However, severe vaccine breakthrough infection is not uncommon, particularly among people with several months of vaccine administration as their immunity fades over time.¹¹ To the best of our knowledge, there is little information regarding the prevalence and characteristics of hospitalized vaccinated COVID-19 patients in Iraq. Therefore, the objectives of this study were: first, to determine prevalence of vaccinated COVID-19 patients among hospitalized patients; second, to determine the epidemiological, clinical, and laboratory characteristics of vaccinated and unvaccinated COVID-19 patients.

Patients and Methods

Setting

The study was conducted in Duhok COVID-19 health facilities. First, Duhok COVID-19 hospital consisting of 50 ward beds and 20 ICU beds was mainly used for severe and critical cases. Second, a 100-bed hospital, called Lalav, primarily met patients with moderate to severe presentations.

Study Design and Patients

The study design was a prospective cross-sectional study on adult COVID-19 hospitalized patients. All PCR confirmed COVID-19 patients from October 1, 2021 until March 31, 2022 were enrolled. COVID-19 cases diagnosed based on other methods were excluded from the study. Clinico-demographic, including vaccination status and laboratory parameters, was recorded in a standardized questionnaire. The study was approved by the Research Ethics Committee, Duhok Directorate General of Health on October 24, 2021 under reference number: 24102021-10-10.

Diagnosis and Measures

COVID-19 hospitalized patients were classified for disease severity into mild, moderate, severe, and critical according to.¹²

Asymptomatic: Patients who test positive for SARS-CoV-2 via a virologic test (such as an antigen or nucleic acid amplification test [NAAT]), but who do not exhibit symptoms that are typical with COVID-19.

Mild Illness: Patients who exhibits any of the COVID-19's many symptoms (such as a fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, and a loss of taste and smell) but do not exhibit dyspnea, shortness of breath, or abnormal chest imaging.

Moderate Illness: Patients with an oxygen saturation (SpO₂) of less than 94% in ambient air at sea level and who exhibit signs of lower respiratory illness during clinical evaluation or imaging.

Severe Type: Patients with a blood oxygen saturation (SpO_2) of less than 94% on room air at sea level, a PaO₂/FiO₂ ratio less than 300 mm Hg, a respiratory rate greater than 30 breaths per minute, or lung infiltrates greater than 50%.

Critical Type: Patients who develop respiratory failure, shock, and multiple organ dysfunction.

The patients were grouped into the following categories according to **Centers for Disease Control and Prevention** (**CDC**), Morbidity and Mortality Weekly (MMWR) Report¹³ for vaccination status:

- 1. Unvaccinated: Individuals who are not vaccinated with any dose of COVID-19 vaccine or vaccine administration by 14 days or less.
- 2. Partially vaccinated: Individuals who were vaccinated with the first dose for more than 14 days, or individuals who were vaccinated with two doses and have not reached 14 days post second vaccine.
- 3. Fully vaccinated: Individuals who were vaccinated with two doses with the second dose \geq 14 days.

All COVID-19 patients underwent laboratory testing including complete blood count (CBC), C-reactive protein (CRP), Lactate dehydrogenase (LDH), Serum ferritin, and D-dimer.

Statistical Analyses

The general information of the patients was presented in mean and Sta. deviation or number and percentage. The mortality rate and vaccination were determined in number and percentage. Comparisons of general and medical information between vaccinated and unvaccinated individuals were examined in an independent *t*-test and Pearson chi-squared test. Comparisons of biomedical measurements between vaccinated and unvaccinated individuals were examined in an independent *t*-test. Comparisons of outcomes between vaccinated and unvaccinated individuals, Association of vaccination by symptoms among individuals, and symptoms by outcomes were examined in Pearson chi-squared tests. The significant level of difference was determined in a *P*-value of less than 0.05. The statistical calculations were performed in JMP pro 14.3.0.

Results

In total, there were 300 patients with a mean age of 60.73 years. There were 142 (47.33%) males and 158 (52.67%) females. Only 28 (9.33%) patients were vaccinated (Table 1).

Table 2 presents the comparison of demographic, clinical, and laboratory parameters between vaccinated and unvaccinated patients. In the vaccinated group, there were 17 (11.97%)

Table 1. Demographic and clinical characteristics of the hospitalized patients

	Statistics				
Parameter (<i>n</i> = 300)	No (0/)	95% CI			
	NO (%)	Lower CI to Upper CI			
Age (yrs.)	60.73 (15.83)	58.93-62.53			
Sex Male Female	142 (47.33) 158 (52.67)	41.75–52.98 47.02–58.25			
Vaccine status Unvaccinated Vaccinated	272 (90.67) 28 (9.33)	86.84–93.46 6.54–13.16			
Type of vaccine Unvaccinated AstraZeneca Pfizer Sinopharm	272 (90.67) 7 (2.33) 15 (5.00) 6 (2.00)	86.84–93.46 1.13–4.74 3.05–8.08 0.92–4.29			
Partially vaccinated (days) No Yes	295 (98.33) 5 (1.67)	96.16–99.29 0.71–3.84			
Fully vaccinated (days) No Yes	277 (92.33) 23 (7.67)	88.76–94.84 5.16–11.24			
Disease severity Moderate Severe Critical	11 (3.67) 221 (73.67) 68 (22.67)	2.06-6.45 68.41-78.33 18.29-27.73			

The infection after first dose (days) was between 2 and 150 days infection after the second dose (days) was between 2 and 220 days.

	Vaccination st	D value	
General characteristics	Unvaccinated (<i>n</i> = 272) (no/%)	Unvaccinated Vaccinated (n = 272) (no/%) (n = 28) (no/%)	
Infection before vaccination No Yes Do not know		6 (21.43) 5 (17.86) 17 (60.71)	
Sex Male Female	125 (88.03) 147 (93.04)	17 (11.97) 11 (6.96)	0.1364ª
Age (year)	60.40 (16.19)	63.89 (11.55)	0.2676 ^b
Symptoms duration (days) mean (SD)	9.41 (3.09)	9.89 (2.62)	0.4273 ^b
Hospitalization duration (day) mean (SD) Range	11.14 (7.72) 1–77 days	8.17 (3.68) 1–60 days	0.0700 ^b
Hospitalization duration < one week 7–14 days 15–21 days 22–28 days > one month	83 (30.51) 81 (29.78) 46 (16.91) 24 (8.82) 38 (13.97)	9 (32.14) 12 (42.86) 3 (10.71) 1 (3.57) 3 (10.71)	0.5484ª
Disease severity Moderate Severe Critical	10 (3.68) 201 (73.90) 61 (22.43)	1 (3.57) 20 (71.43) 7 (25.00)	0.9532ª
Oxygen requirement No Yes	10 (3.68) 262 (96.32)	1 (3.57) 27 (96.43)	0.9775ª
CPAP requirement No Yes	178 (65.44) 94 (34.56)	21 (75.00) 7 (25.00)	0.3081ª
Invasive ventilation requirement No Yes	270 (99.26) 2 (0.74)	27 (96.43) 1 (3.57)	0.1509ª
Outcome of patients Died Recovered OR (95%): 1.29 (0.58–2.87)	148 (54.41) 124 (45.59)	17 (60.71) 11 (39.29)	0.5233ª
Biomedical measurements ALC LDH CRP D. Dimer	0.89 (0.43) 620 (148.40) 78.59 (57.99) 1305.58 (971.42)	0.98 (0.63) 429.5 (380.10) 68.14 (46.23) 1760.48 (1195.38)	0.3135 ^b 0.2633 ^b 0.4118 ^b 0.0390 ^b

Table 2. Comparisons of general characteristics between vaccinated and unvaccinated patients

^aPearson chi-squared test and ^bAn independent *t*-test. SD, Standard Deviation; OR, Odd Ratio; CPAP, Continuous positive airway pressure; SOB, Shortness of breath; ALC, Absolute Lymphocyte Count; LDH, Lactate Dehydrogenase; CRP, C-reactive protein.

males and 11 (6.96%) females, while the unvaccinated group consisted of 125 (88.03%) males and 147 (93.04%) females. The mean age of unvaccinated patients was 60.4 and of vaccinated patients was 63.89 years. The mean duration of symptoms was 9.41 and 9.89 days of unvaccinated and vaccinated groups, respectively. Detailed information is demonstrated in Table 2. Figure 1 shows the patient outcome according to vaccination status.

The comparison of D-dimer level among vaccinated and unvaccinated patients showed a significant higher level of D-dimer among patients who received Sinopharm vaccine (Table 1, Figure 2). The most frequent sign and symptoms were SOB, fever, and cough as shown in Table 4.

In term of frequency of vomiting and flu like symptoms between vaccinated subgroups and unvaccinated cases. Pfizer vaccine was significantly associated with vomiting (P = 0.0047) while Sinopharm vaccine was associated with flu like illness (P = 0.032). (Table 5).

Regarding the comorbidities, CVD followed by DM were the most common risk factors associated with COVID-19 infection in both groups. Malignancy and smoking were significant risk factors for COVID-19 infection in the unvaccinated group (Table 6).

Discussion

COVID-19 vaccine has proven to be an important tool in controlling SARS-CoV-2 pandemic and in reducing disease severity among hospitalized patients. We investigated 300 hospitalized COVID-19 patients with a variety of demographic, clinical, and laboratory profiles. In the current study, the vaccination coverage was 9.33%, which was low in comparison to studies from Iran,14 Turkey,15 Saudi Arabia,16 and India.17 On the contrary, only few studies reported a lower vaccination coverage for e.g. Peru (4.8%).18 This may be related to the lack of knowledge that COVID-19 vaccines prevent or attenuate diseases severity, concerns about the vaccination's composition, and side effects. Consequently, raising awareness concerning vaccine safety and uptake are highly mandatory. The most common administered vaccine in this study was Pfizer, which is in line to our previous study in evaluating COVID-19 vaccination program in Duhok.¹⁹ In the present study, the



Fig. 1 Comparisons of patient outcomes according to vaccination status in hospitalized patients.



Fig. 2 Comparisons of D-dimer among patients with different types of COVID-19 vaccines.

mean age of the hospitalized patients was 60.73 ± 15.83 yr, which was consistent with other studies.²⁰ Generally, older adults are more prone to infections with a more severe course because of increasing incidences of coexisting comorbid diseases, hence a weakened immune system.²¹

In our study, the unvaccinated females were more infected, while vaccinated males had higher rates of hospital admissions. Ambrosino et al. in a review considered gender difference in COVID-19 patients, documenting a higher rate in males²¹ that was in contrast to our finding, which may be clarified by the study being limited to hospitalized patients and a small sample size. Whereas, the high rate of hospitalized vaccinated male patients could be linked to sex hormones, gender-related behavior, and differences in immunological function linked to the X chromosome.²²

In our study, vaccinated patients had shorter hospital duration stays, which signifies the beneficial effect of COVID-19 vaccines. In agreement, several studies documented this finding, indicating its efficacy in reducing burden on the healthcare system.²³

In the current study, severe cases were predominated in both vaccinated and unvaccinated patients. This is justified according to our local COVID-19 management guidelines, as we admit only severe and critical cases to the hospitals.²⁴ Hence, assessing COVID-19 vaccine effectiveness on the general population was unfit as only hospitalized patients were considered. However, though not statistically significant, the frequency of continuous positive airway pressure (CPAP) requirement was higher among unvaccinated group, which indicates the vaccine's efficiency in reducing disease severity.²⁵

Scanning laboratory variable, D dimer was significantly higher among vaccinated patients (P = 0.0390). Furthermore, comparing D-dimer among vaccine administered patients, Sinopharm was significantly associated with higher level (P = 0.0009). Our finding was in contrast to studies from Thailand²⁶ and Turkey.²⁷ The exact elucidation is dense at the moment; however, the higher D dimer level among Sinopharm patients might be related to patients having had received the vaccine at the beginning of COVID-19 vaccine campaign,^{7,28} having its effectiveness faded due to the long duration since patients acquired the infection.

In this study, the mortality rate was relatively high among both vaccinated (60.71%) and unvaccinated (54.41%) patients. On contrary, other studies reported lower death rates.^{29,30} The high mortality rate in the current study is attributed first, to the admission of severe and critical cases in our hospitals while other studies included mild, moderate, and severe cases; second our study period was coincident majorly with the delta variant, hence worse prognosis of this variant, whereas other studies included other variants.

Interestingly, we found that the incidence of vomiting and flu-like illness were higher among vaccinated than unvaccinated patients. Vomiting and flu-like illness were significantly associated with Pfizer (P = 0.0047) and Sinopharm vaccines (P = 0.0328), respectively. There are reports about

Table 3. D-dimer level among hospitalized patients according to the vaccination status					
	AstraZeneca	Pfizer	Sinopharm	Unvaccinated	P-value
D-Dimer	1631 (1085.58)	1684.42 (1246.27)	3030.17 (2598.60)	1305.58 (971.42)	0.0009

ANOVA one-way tests were performed for statistical analyses.

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Symptoms	Unvaccinated ($n = 272$)		Vaccinated ($n = 28$)		<i>P</i> -value
	Number	Percentage	Number	Percentage	
Fever	205	75.37	19	67.86	0.3843
Chill	59	21.69	5	17.86	0.6372
Rigor	32	11.76	2	7.14	0.4626
SOB	272	100.00	28	100.00	NA
Cough	175	64.34	19	67.86	0.7107
Vomiting	32	11.76	8	28.57	0.0127
Chest pain	70	25.74	4	14.29	0.1808
Chest tightness	34	12.50	3	10.71	0.7844
Sore throat	39	14.34	3	10.71	0.5987
Voice change	27	9.93	2	7.14	0.6351
Loss of appetite	68	25.00	8	28.57	0.6791
Abdominal pain	14	5.15	1	3.57	0.7157
Flu-like illness	27	9.93	8	28.57	0.0034
Epigastric pain	42	15.44	3	10.71	0.5048
Constipation	45	16.54	5	17.86	0.8591
Headache	36	13.24	3	10.71	0.7057
Interscapular pain	28	10.29	1	3.57	0.2517
Nasal obstruction	18	6.62	0	0.00	0.1603
Loin pain	12	4.04	1	3.57	0.8353
General bodyache	55	20.22	5	17.86	0.7659
Fatigue	95	34.93	9	32.14	0.7682
Anosmia	26	9.56	3	10.71	0.4838
Parosmia	26	9.56	3	10.71	0.8438
Burning	10	3.68	1	3.57	0.9775
Ageusia	3	1.10	0	0.00	0.5765
Bitter taste	30	11.03	2	7.14	0.5258
Dry mouth	48	17.65	3	10.71	0.3524
Eye pain	18	6.62	1	3.57	0.5286
Sweating	36	13.24	4	14.29	0.8763
Nausea	20	7.35	4	14.29	0.1979
Backache	22	8.09	3	10.71	0.6321
Joints pain	34	12.50	4	14.29	0.7868
Diarrhea	25	9.19	1	3.57	0.3142

Table 4 Comparisons of symptomatology between vaccinated and unvaccinated natients

Table 5. Prevalence of vomiting and flu like symptoms with types of vaccinations

Cumutous	Type of vaccination no (%)				
Symptoms	AstraZeneca	Pfizer	Sinopharm	Unvaccinated	P-value
Vomiting					
No	7 (100)	9 (60.00)	4 (66.67)	240 (88.24)	0.0047
Yes	0 (0.00)	6 (40.00)	2 (33.33)	32 (11.76)	0.0047
OR (95%CI)	Infinity	0.2 (0.07-0.6)	0.27 (0.05-0.51)	Reference	
Flu-like illness					
No	5 (71.43)	11 (73.33)	4 (66.67)	245 (90.07)	0.0220
Yes	2 (28.57)	4 (26.67)	2 (33.33)	27 (9.93)	0.0328
OR (95%CI)	0.28 (0.05-1.49)	0.3 (0.09-1.02)	0.22 (0.04-1.26)	Reference	

Pearson chi-squared test was performed for statistical analyses. OR, Odd Ratio; CI, Confidence Interval.

	Vaccine status				
Risk factors	Unvaccinated (<i>n</i> = 272)		Vaccinated (<i>n</i> = 28)		P-value
	Number	Percentage	Number	Percentage	(two-sided)
DM	71	89.87	8	10.13	0.7776
CVD	149	90.85	15	9.15	0.9925
Preexisting lung disease	13	92.86	1	7.14	0.7729
Hookah	2	100.00	0	0.00	0.6489
Malignancy	7	70.00	3	30.00	0.0223
Obesity	22	100.00	0	0.00	0.1180
Immunosuppressive	8	100	0	0.0	0.4522
CKD	18	100.00	0	0.00	0.1603
Smoking	7	70.00	3	30.00	0.0223
Pregnancy	2	100.00	0	0.00	0.6489
Alcoholic	1	50	1	50	0.8824
Liver cirrhosis	3	100.00	0	0.00	0.5765

Table 6. Association of comorbidities with vaccination status among hospitalized patients

Pearson chi-squared tests were performed for statistical analsyes. DM, Diabetese Mellitus; CVD, Cardiovascular Disease; CKD, Chronic Kidney Disease.

gastroparesis manifested as nausea and vomiting following Pfizer vaccine administration.³¹ The more frequent flu-like illness among Sinopharm receivers could be attributed to the faded effect of this vaccine among patients as explained earlier. Therefore, they were presented with this illness as a frequent symptom of COVID-19.

In the present study, considering comorbidities, smoking and malignancy were significant risk factors for COVID-19 infection in unvaccinated patients. Smoking increases risk for acute respiratory infection in general, and increases entry of SARS-CoV-2 to host by upregulation of the angiotensin converting enzyme 2 (ACE2) receptor in particular.³² Whereas, malignancy in addition to chemotherapy regimens can weaken immune cells and create immunosuppressive state to patients, hence increase susceptibility to the infection.³³

The study had several limitations, first, the study period was limited to a few months, and accordingly this could be a barrier for evaluating the true prevalence of the circulating strain. Second, the study depended on the outbreak magnitude, so the disease declining incidence often had an impact on sample size.

Conclusion

The SARS-CoV-2 pandemic can be controlled with the use of the COVID-19 vaccine, which has also been shown to lessen the severity of illness in hospitalized patients, we looked at 300 COVID-19 patients who were hospitalized and had different demographic, clinical, and laboratory profiles. In this study the majority of population were unvaccinated. Among those who had received vaccinations, Pfizer was most popular. The majority of cases were old ages. The unvaccinated females were more infected, while vaccinated males had higher rates of hospital admissions. The unvaccinated group had longer duration in hospital stay. About three quarter of study population were severe cases. D dimer was significantly higher among vaccinated patients (P = 0.0390). According to the data, the mortality rate was relatively high among both groups. Regarding the clinical characteristics, vomiting and flu-like illness showed higher prevalence in vaccinated patients with significant difference. In terms of comorbidities, smoking and malignancy were significant risk factors for COVID-19 infection in unvaccinated patients. The presence of a COVID-19 vaccine and the proper implementation of a worldwide vaccination campaign are essential in the fight against a public health emergency like a COVID-19 pandemic.

Abbreviations

WHO: World Health Organization, COVID-19: Coronavirus Disease 2019, SARS CoV 2: severe acute respiratory syndrome coronavirus 2, DM: diabetes mellitus, CVD: cardiovascular diseases, ARDS: acute respiratory distress syndrome, CBC: complete blood count, CRP: c-reactive protein, LDH: lactate dehydrogenase, mRNA: Messenger Ribonucleic acid, FDA: Food and Drug Administration, PCR: Polymerase Chain Reaction, NAAT: nucleic acid amplification test, SpO₂: Saturation of Peripheral Oxygen, PaO,/FiO,: Partial pressure of oxygen in arterial blood /Fraction of Inspired Oxygen, CDC: Centers for Disease Control and Prevention, MMWR: Morbidity and Mortality Weekly, CI: Confidence Interval, SD: Standard Deviation, OR: Odd Ratio, SOB: Shortness of breath, CKD: Chronic kidney disease, US: United States, MoH: Ministry of Health, CPAP: Continuous positive airway pressure, ACE2: angiotensin converting enzyme 2.

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Conflict of Interest

The authors affirm that they do not have any conflict of interests.

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