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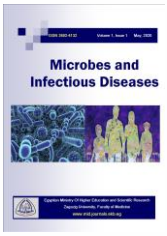

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Original article

Effectiveness of COVID-19 vaccination among patients hospitalized from April 2020 to March 2021: A retrospective cohort study

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ABSTRACT

Background: The COVID-19 pandemic is one of the worst pandemics of recent times. Getting vaccinated against COVID-19 is a preventative strategy that helps in the prevention of the infection and reduces its severity. This study aimed to measure the reinfection and vaccination rates among COVID-19 patients who were admitted to Ain Shams University (ASU) Hospitals during the pre-vaccination era (April 2020–March 2021) and correlate their vaccination status with the incidence and severity of the reinfection. **Methods:** A retrospective cohort study was conducted that includes patients diagnosed with SARS-CoV-2 infection and admitted to ASU Hospitals during the pre-vaccination era. Data about the first COVID-19 infection were extracted from the patient's records and then a random sample of patients was selected and data about vaccination and re-infection rates were collected from them through an interview questionnaire. **Results:** 340 out of the 400 included subjects received COVID-19 vaccination (85%); 4.41% received incomplete doses; 67.06% received full vaccination; and 28.23% received full vaccination with an additional booster dose. 53.61% of booster vaccinations used the same vaccine each time, while 46.39% received different vaccines. Regarding the reinfection rate, it was higher among the unvaccinated group compared to the vaccinated (20% versus 13.82%) but this difference was not statistically significant. Also, the length of stay in hospital during the reinfection was 6 days in both groups. **Conclusion:** Although our results revealed no statistically significant difference between the vaccinated and unvaccinated groups regarding the reinfection rate. But it may show a piece of evidence that COVID-19 vaccination plays an important clinical role in reducing the severity of COVID-19 infection.

Introduction

COVID-19 has caused an unprecedented health crisis since it was initially discovered in Wuhan, with five hundred million documented cases and around 18 million additional fatalities [1,2]. Medical presentations of COVID-19 infection include a wide range of aspects, varying from no symptoms to slight symptoms resembling the flu to pneumonia-like symptoms, acute respiratory failure, and mortality [3]. Respiratory symptoms often have

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a sudden beginning and are associated with systemic consequences, suggesting that COVID-19 stimulates a series of abnormalities in the body's response with an extensive spectrum of immune-inflammatory modifications [4].

Safe and effective COVID-19 vaccines are a powerful tool for ensuring public health and controlling the pandemic [5]. Acquiring vaccination against COVID-19 is a preventative strategy that people can take to decrease the risk and severity of infection. Vaccine breakthrough infection occurs in some vaccinated people, as no vaccine for any disease is 100% effective in preventing infection in every person who receives it [6].

In a study conducted in India to evaluate the effect of vaccination on severity and reinfection rates, results show that only 31.07% experienced COVID-19 infection after receiving the vaccine [7]. Furthermore, in a study carried out in U.S. states, results show that the vaccination diminished the population infection rate by 1.34 percentiles (ranging from 10.10 to 8.76%), hindered nearly 0.12 million admissions to hospitals (ranging from 0.89 to 0.78 million), and diminished the number of new cases by 4.4 million (ranging from 33.0 to 28.6 million) [8].

Also, another study conducted in the U.S. states reveals that the vaccination decreased the total attack rate to 4.6% from 9.0% without the vaccination and markedly decreased adverse effects, with non-intensive care unit (ICU) hospitalizations by 63.5%, ICU hospitalizations by 65.6%, and deaths by 69.3% [9].

Results from a study conducted by **Liu et al.** [10] show that a single dose of the vaccine was 41% efficient at preventing COVID-19 infections, 52% for symptomatic COVID-19, 66% for admission to a hospital, 45% for Intensive Care Unit admissions, and 53% for COVID-19-related mortality. While two doses were 85% efficient at preventing COVID-19 infections, 97% for symptomatic COVID-19, 93% for admission to a hospital, 96% for hospitalizations to the critical care unit, and 95% for fatalities associated to COVID-19, respectively.

Egypt began vaccination against COVID-19 in January 2021. Vaccines such as Moderna, AstraZeneca, Pfizer, Janssen, Sinopharm, and Sinovac were used. More than 108 million doses have been administered in Egypt [11].

To generate more evidence about the role of vaccination in controlling the COVID-19 pandemic, The current study aimed to measure the reinfection and vaccination rates among COVID-19 patients who were admitted to Ain Shams University (ASU) Hospitals during the pre-vaccination era (April 2020–March 2021) and correlate their vaccination status with the incidence and severity of the reinfection.

Methodology

A retrospective cohort study was conducted that includes the patients diagnosed with SARS-CoV-2 infection and admitted to Ain Shams University Hospitals during the pre-vaccination era (April 2020 - March 2021) after exclusion of hospital mortality. The study followed the principles of the Helsinki Declaration and was approved by the Ethical Committee of Ain Shams University (Number:570/2022). Oral informed consent was obtained from all participating patients after an explanation of the study's purpose and procedures. The study was conducted through two phases:

Phase I: Sample selection and data extraction

A study population of total 2578 patients who diagnosed with COVID-19 infection and admitted to Ain Shams University Hospitals was used to obtain a sample size by using Power Analysis and Sample Size Software (PASS 11) (Version 11.0.08) for sample size calculation, setting confidence level at 95% margin of error ±0.05 and after reviewing previous study results [9] which shows that COVID-19 vaccination decreased the total attack rate to 4.6% from 9.0% without the vaccination; based on that, a sample size of at least 400 patients diagnosed with COVID-19 infection and admitted to the hospital in the pre-vaccination period were sufficient to achieve study objective after adjustment of 10% for missing and incomplete data. Patients were selected randomly by using random number generator software. Data extracted from records includes socio-demographic characteristics like (age, gender, education level, area of residence, marital status, and employment status), comorbidities (hypertension, diabetes, chronic lung diseases, heart, liver, and kidney diseases, cancers, etc., and immunosuppressive drugs), tobacco use status (never, former, or current user), and details about the first attack of COVID-19 infection, including assessment for its severity (oxygen saturation, need for ICU admission, and mechanical ventilation), symptoms, and signs (fever

or chills, runny nose, congestion, sore throat, exhaustion, headache, muscle or body aches, nausea, vomiting, diarrhea, and/or shortness of breath).

Phase II: A telephone interview was conducted and a questionnaire was used to collect data about the vaccination history, including the status of vaccination, type of vaccine, number of doses, and date of last dose, reinfection episodes including the number of attacks, time (date) of reinfection concerning vaccination date if the patient was vaccinated (number and severity of post-vaccination attacks), diagnosis of reinfection: based on the patients' reported data regarding the method of diagnosis (whether it was lab-confirmed, clinically assessed, just by symptoms and signs, or the contact with an infected person), assessment for the severity of reinfection for vaccinated patients(the same as the first attack), and assessment of the severity of the post-vaccination attack, symptoms, and signs (fever or chills, runny nose, congestion, sore throat, exhaustion, headache, muscle or body aches, nausea, vomiting, diarrhea, and/or shortness of breath). To improve the validity of the data and standardize the calculated rates the following definitions were used:

1. Severity of COVID-19 infection: Severe COVID-19 infection: Any COVID-19-infected patient who has SpO2 <94%, Shortness of breath, or difficulty breathing requires hospital admission, ICU admission, and mechanical ventilation [6].

2. COVID-19 reinfection: Any COVID-19 infection that occurred after the first attack, diagnosed based on the patients' reported data (whether it was lab-confirmed, clinically assessed, just by symptoms, or contact with an infected person).

Post-vaccination reinfection: should be after 2 weeks from vaccination and within 6 months.

3. Effectiveness of the vaccine will be measured as [5]:

- Comparing the severity of attacks among vaccinated and unvaccinated patients.

- Comparing the severity of attacks between the pre-vaccination period and post-vaccination period in vaccinated patients.

- Attributable risk (Risk for exposed group − Risk for unexposed group divided by Risk for exposed group× 100%).

4. Partially vaccinated: An individual is considered partially vaccinated if the individual has not yet received all the required doses of a Covid-19 vaccine.

5. Fully vaccinated: An individual is defined as fully vaccinated only if they have received the full series of vaccine or a combination of vaccines approved by WHO.

Version 22 of the SPSS statistical software for social science was used for all statistical analyses. Utilizing descriptive statistics to represent the quantitative variables in numerical form (mean, SD, or percentages). When suitable, tabular and diagrammatic representations are utilized to describe the qualitative variables. The significance of the relationships between the variables was evaluated applying the Chi-square test for categorical variables and the Student (t) test for continuous variables with normally distributed data. Chi-square test and Mann-Whitney U test for categorical variables are used to test non-normally distributed data. Findings are considered statistically significant when the p-value is less than 0.05.

Results

As shown in **Table 1**, among the 400 included subjects, 49% were females and 51% were males. Their age ranged between 16-85 years, with a mean value of 52.71 ± 14.13 years. Most of them had severe condition on admission 76.75% and 6.50% were critical. The comorbidity rate was 15.50%, and 4.25% were currently smokers, while 1.75% were ex-smokers. The duration of hospital admission ranged between 1-36 days, with a mean value of 7.49±5.26 days. Out of the 400 included subjects, 29 (7.25%) needed ICU admission. Indication for ICU referral was hypoxia in 26 subjects (6.50%) followed by dyspnea in 2 cases (0.50%) and chest pain in 1 case (0.25%). Only 1 patient need mechanical ventilation (0.25%). All of them survived and discharged from hospital.

As shown in **Table 2**, the vaccination rate among the studied groups was 85% (95% CI 81.22% - 88.23%); among them 4.41% received incomplete doses, 67.06% received full vaccination with 28.23% received full vaccination with additional booster dose. 53.61% of booster vaccinations were by the same vaccine each time while 46.39% received different vaccines.

According to **Figure 1**, the most common types of vaccines used in the vaccinated group were Sinopharm (39.41%) and Astrazeneca (39.41%),

while Johnson and Johnson (7.65%) was the least common.

As shown in **Table 3**, there was no difference between the vaccinated and unvaccinated groups regarding the sociodemographic characteristics. Regarding the reinfection rate, it was higher among the unvaccinated group (20% versus 13.82%) but this difference was not statistically significant (p= 0.214). Also, the length of stay in hospital during the reinfection was the same in both groups.

NB: In 1st infection, others include: insomnia and hypoxia.

NB: In reinfection, others include: loss of smell or taste, runny nose, muscle or body aches, vomiting or nausea.

As shown in **Figure 2**, the most common symptom during the first infection was dyspnea (90%) while during the reinfection was fever (76.27).

As shown in **Table 4**, there is no statistically significant difference between vaccinated re-infected and vaccinated not re-infected subjects as regard age, age group, sex, job and the presence of comorbidities. Reinfection after vaccination was more frequent in working (61.70%) than not working (38.29%) subjects. There is no statistically significant difference between re-infected vaccinated and non-re-infected vaccinated subjects as regard vaccination type and the type of booster doses. There is no statistically significant difference between incomplete, full vaccinated and vaccinated with booster dose subjects as regard reinfection and hospitalization frequency.

Table 1. Socio-demographic and clinical data of the first infection in the studied population (N=400).

	N=400
Age in years	
Mean ±SD	52.71±14.13
Minimum – Maximum	16 – 85
Median (IQR)	55 (42 – 63)
	N (%)
Age groups	
<30	27 (6.75)
30 - < 50	117 (29.25)
50 - < 70	216 (54.0)
≥ 70	40 (10.0)
Sex	
Male	205 (51.25)
Female	195 (48.75)
Job	
Working	219 (54.75)
Not working/retired/housewife	181 (45.25)
Smoking	
None	376 (94.00)
Current	17 (4.25)
Ex-smoker	7 (1.75)
Severity of the condition on admission	
Moderate	67 (16.75)
Severe	307 (76.75)
Critical	26 (6.50)
Source of infection	
Community acquired	393 (98.25)
Contact with patient	7 (1.75)
Presence of comorbidity* (Yes)	62 (15.50)
ICU admission (Yes)	29 (7.25)
Length of stay (Days)	
Mean ±SD	7.49±5.26
Minimum – Maximum	1 – 36
Median (IQR)	6 (4 – 10)
Reinfection after discharge from hospital (Yes)	59 (14.75)

*Comorbidities include hypertension, diabetes, chronic diseases, cancer, immunologic disorders.

Table 2. Frequency and vaccination status of the studied population (N=400).

	N (%)
Vaccination (N=400)	
Vaccinated group	340 (85.0)
Non-vaccinated group	60 (15.0)
Vaccination status (N=340)	
Partially Vaccinate	15 (4.41)
Fully vaccinated	228 (67.06)
Fully vaccinated with booster dose	97 (28.23)
Vaccination type booster dose (N=97)	
Same vaccine	52 (53.61)
Different vaccines	45 (46.39)

Table 3. Comparison between vaccinated and unvaccinated groups (N=400).

	Vaccinated N = 340 (%)	**Unvaccinated N =60 (%)**	**t-test/x^2**	***P*-value**
Age in years (Mean ±SD)	52.85±13.57	51.73±71.10	0.478	0.634
Sex				
Male	178 (52.35)	27 (45.00)	1.104	0.293
Female	162 (47.65)	33 (55.00)		
Job				
Working	161 (47.35)	20 (33.33)	4.046	0.044
Not working	179 (52.65)	40 (66.67)		
Comorbidities				
Yes	52 (15.32)	10 (16.67)	0.073	0.787
No	288 (84.68)	50 (83.33)		
Re-infection				
Yes	47 (13.82)	12 (20.00)	1.547	0.214
No	293 (86.18)	48 (80.00)		
Number of reinfection attacks				
Once	35 (74.46)	8 (66.67)	2.258	0.521
Twice or more	12 (25.54)	4 (33.33)		
Hospital admission				
No	337 (99.12)	59 (98.33)		
Yes	3 (0.88)	1 (1.67)	0.317*	0.573
Length of stay in hospital during the reinfection (days) **(Mean ±SD)**	6 ±1	6	---	----

x^2 = Chi square. * Fisher's exact test.

Table 4. Description of vaccinated group: Comparison between reinfected and not reinfected patients (N = 340)

	Reinfected	**Not reinfected**	**t-test/x^2**	***P*-value**
	n = 47 (%)	**n =293 (%)**		
Age in years (Mean ±SD)	51.15±13.08	53.08±13.64	-0.931	0.355
Age groups				
<30	3 (5.41)	15 (5.13)	0.635	0.888
30 - < 50	13 (27.70)	91 (31.14)		
50 - < 70	28 (59.67)	162 (55.39)		
≥ 70	3 (6.37)	25 (8.54)		
Sex				
Male	23 (48.94)	155 (52.90)	0.255	0.613
Female	24 (51.06)	138 (47.09)		
Job				
Working	29 (61.70)	132 (45.06)	5.712	0.017
Not working	18 (38.29)	161 (54.94)		
Comorbidities				
Yes	9 (19.14)	43 (14.67)	0.626	0.429
No	38 (80.85)	250 (85.32)		
Vaccination completeness				
Partially vaccinated	4 (8.51)	11 (3.75)	0.174	0.677
Fully vaccinated	29 (61.70)	199 (67.91)		
Fully vaccinated with booster dose	14 (29.78)	83 (28.32)		
Type of booster doses	**n-=14**	**n=83**		
Same vaccine	7 (50.0)	45 (54.22)	0.086	0.769
Different vaccine	7 (50.0)	38 (45.78)		

Figure 1. Types of vaccines among vaccinated group (N=340).

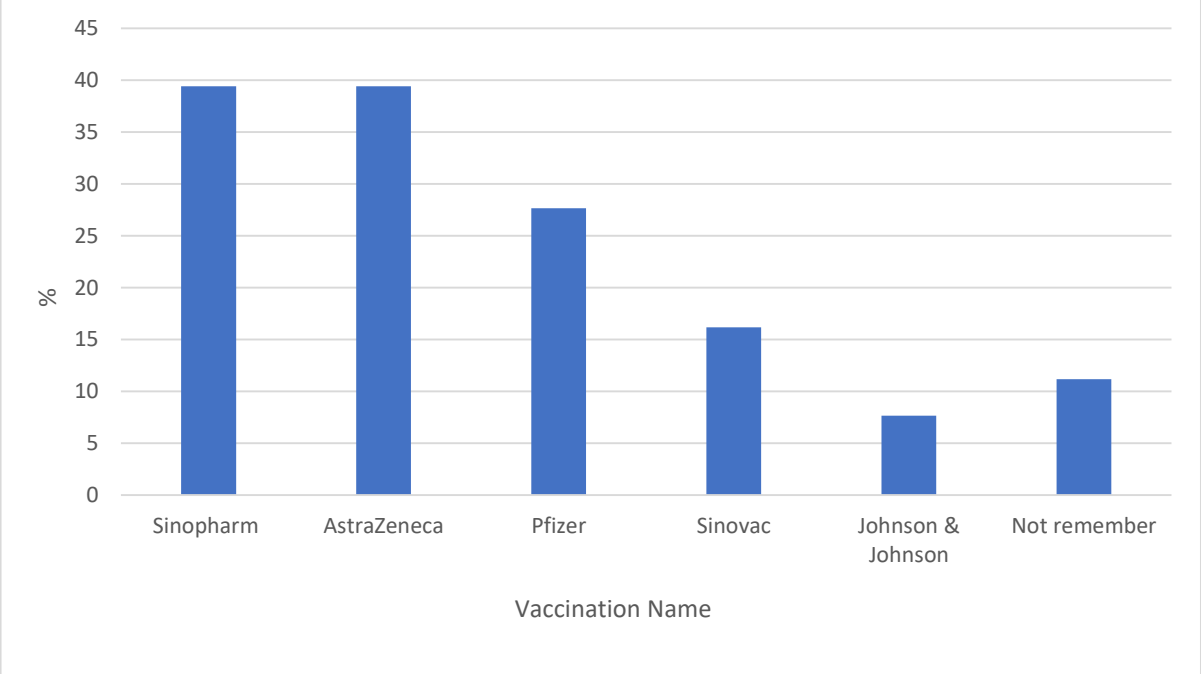
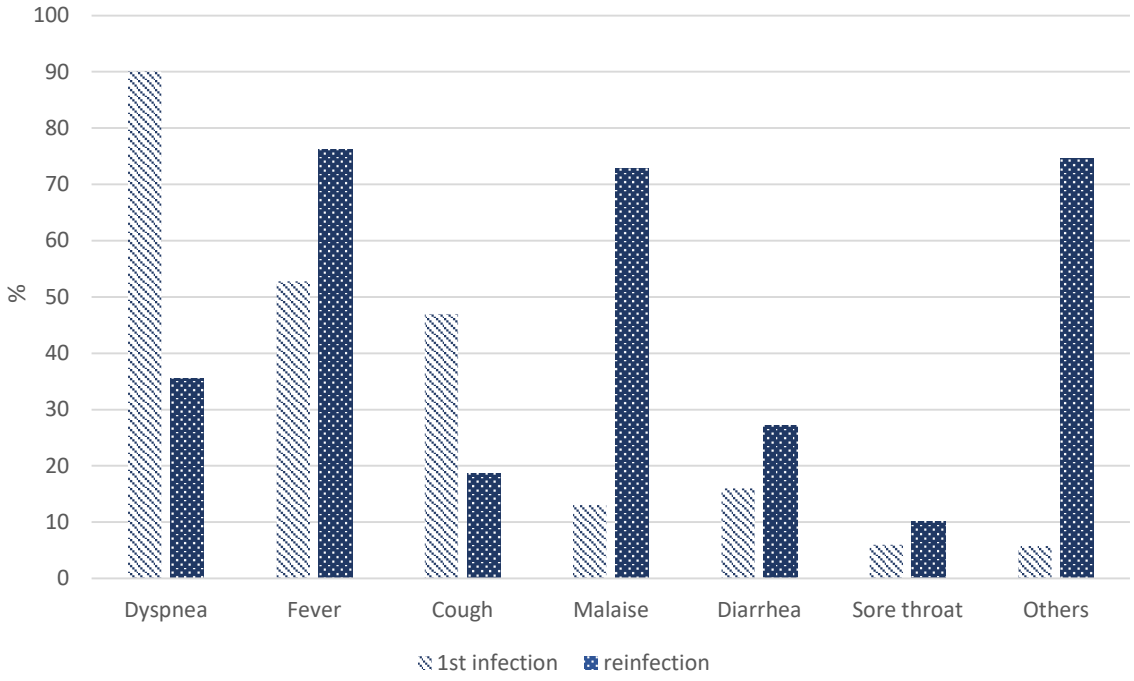


Figure 2. Clinical symptoms of the 1st infection and reinfection in the studied population.



Discussion

This retrospective cohort study was conducted on 400 patients with confirmed COVID-19 infection and admitted to Ain Shams University Hospitals to assess the COVID-19 vaccine effectiveness on reinfection and severity.

Regarding socio-demographics, among the 400 included subjects, 49.00% were females and 51.00% were males. Their age ranged between 16-85 years, with a mean value of 52.71 ± 14.13 years. Most of them had severe conditions on admission; 76.75% and 6.50% were critical. The comorbidity rate was 15.50% and 4.25% were currently smokers, while 1.75% were ex-smokers. The duration of hospital admission ranged between 1-36 days, with a mean value of 7.49±5.26 days.

According to vaccination status, the current study detected that 340 out of the 400 included subjects received COVID vaccination (85%); 4.41% received incomplete doses; 67.06% received full vaccination; and 28.23% received full vaccination with an additional booster dose. 53.61% of booster vaccinations used the same vaccine each time, while 46.39% received different vaccines.

However, **Sayeed et al.**[12] carried out a cohort study within the Sindh Infectious Diseases Hospital and Research Institute, Pakistan, and found that, according to the status of COVID-19 vaccination, the majority of cases 73.13% were not vaccinated, while 26.87% were. Of those who were vaccinated, 42.3% were partially vaccinated, and 57.7% were fully vaccinated. Additionally, **Moline et al.** [13] found that out of 7,280 eligible COVID-NET patients, 5,451 (75%) were not vaccinated, 867 (12%) were partially vaccinated, and 394 (5%) were completely vaccinated.

In a study conducted From 13 September 2021 to 5 December 2021, 278,096 (31.1%) were unvaccinated, 223,198 received ChAdOx1-S 175 days after a second dose and 171,079 received BNT162b2 175 days after a second dose. Of those who had received a booster dose, 89,019 received a ChAdOx1-S primary course and 132,453 received a BNT162b2 primary course [14].

Alnemari et al. [15] revealed that only 265 (25%) patients received one dose of mRNA Pfizer-BioNtech (BNT162b2) or AstraZeneca-Oxford (AZD1222/ChAdOx1-S) during the study duration .

With reference to the comparison between the vaccinated and non-vaccinated groups, there is no difference that can be considered statistically significant between the vaccinated and non-vaccinated subjects as regard sex, and comorbidities. But there is a statistically significant difference in the vaccination rates between working and non-working people.

Unlikely, **Alnemari et al.** [15] revealed that the sociodemographic characteristics of vaccinated and unvaccinated groups (age, gender, comorbidities) significantly differed (p-value <0.001). Also, **Sayeed et al.** [12] found that even though the non-vaccinated COVID-19 cases, despite being young (with a mean age of 60 vs. 65 years and p-value < 0.0001), had fewer comorbidities (63.9% vs. 77.2%, OR:0.52, 95% CI: 0.39–0.68, and p-value < 0.0001) and a greater probability of severe COVID-19 at the time of admission to the hospital (61.8% vs. 48.7%, OR:1.7, 95% CI: 1.35–2.16, and p-value < 0.0001) than the vaccinated cases. **Ruiz et al.** [16] and **Epaulard et al.**[17] showed similar trends in their studies in Spain and France, respectively.

With reference to re-infection characteristics among the reinfected group, the present study detected that among the included subjects, 59 of them reported COVID-19 re-infection 14.75%. Re-infection was diagnosed by symptoms in 57.6% and based on clinical diagnosis in 20.33%, while only 22.03% were confirmed by PCR test. The number of re-infections was once in 72.88% and twice or more in 20.33%. Time period between vaccination and re-infection; 23.40% were in the vaccine effective period (6 months), 38.30% were after the vaccine effective period (>6 months), while, 38.30 % of subjects did not recall the date of reinfection. Four subjects need readmission to the hospital, and only one needs admission to the ICU.

A systemic review and meta-analysis detected that a total of 118 reinfected patients were included in 50 studies. Patients often presented with overt symptoms upon reinfection [18]. Two case reports were reported on patients who had been vaccinated before reinfection. One patient developed reinfection 10 days after the first dose but did not report the vaccine type [19].Another patient developed reinfection 13 days after the first dose of the Pfizer vaccination was administered [20].

Description of vaccinated group: In comparison between reinfected and not reinfected patients, there is no statistically significant difference between vaccinated re-infected and vaccinated not re-infected subjects as regard to age, sex, job, and comorbidities. Reinfection after vaccination was more frequent in working than non-working subjects.

A cohort study by **Lewis et al.** [21] in the state of Rhode Island found that the probability of re-infection within 9 months of recovering from a primary COVID-19 infection was roughly 2% in the general non-vaccinated population, but 10% in long-term congregate care (LTCC) workers and 13% in LTCC residents. Upon the completion of the primary vaccination series after recovery from a previous COVID-19 infection, 62% of the general population and 49% of the workers and residents of LTCC facilities experienced vaccine effectiveness, This showed that vaccination was associated with significant advantages for preventing re-infection after recovering following a prior COVID-19 infection, with the vaccination reducing the risk for all subpopulations by almost half. Among LTCC residents and employees, for whom the probability of reinfection at 9 months after primary infection among those who remained unvaccinated was at least 5-fold greater than in the general population (10%-13% vs 2%), this is a particularly notable finding [22].

Description of vaccinated group: comparison between reinfected and not reinfected patients, There is no statistically significant difference between reinfected vaccinated and non-reinfected vaccinated subjects as regard to vaccination type and the type of booster doses. There is no statistically significant difference between incomplete, full-vaccinated, and vaccinated subjects with booster doses subjects as regard to reinfection and hospitalization frequency.

Quattrocchi et al. [23] conducted a case-control study that matched, which revealed that 44,227 laboratory confirmed COVID-19 infections were detected in Cyprus between June and August 2021. Of these, 93 (0.2%) were re-infections (cases), which were matched to 186 individuals confirmed with a single case of COVID-19 infection (controls). In contrast to 12.9% and 32.8% of controls, 7.5% and 8.6% of cases, correspondingly, had received a partial and full vaccination. Throughout the investigation period, nine patients were admitted to hospitals; of these, eight belonged to the control group and one to the cases group (4.3% vs. 1.1%; P = 0.151).

In Comparison between the vaccinated and non-vaccinated groups, there is no statistically significant variation between the vaccinated and non-vaccinated subjects as regard reinfection and hospitalization frequency, although the reinfection rate among the vaccinated group was 13.82% and that among non-vaccinated group was 20.00%. The duration of hospital admission during re-admission ranged between 5-7 days (6 days for non-vaccinated

persons and a mean value of 6 ± 1 day for vaccinated persons).

The relative risk between the vaccinated and non-vaccinated people was statistically insignificant (RR = 1.08, 95% CI 0.76–1.534, and p = 0.66), according to a cohort study by **Rahman et al.** [24] **.** The study also found that 37 (38.5%) of full-dose vaccinated individuals and 96 (36.1%) of non-vaccinated individuals were infected. In addition, the relative risk between those who received a complete dosage of vaccinations and those who only received a single dose was not statistically significant. The mean time intervals between the full dose vaccination date and the COVID-19 positive test date were 65.1 (median 66.0, IQR: 51.3–82.0) days. In a retrospective cohort analysis, 354 out of 83,356 vaccinated patients experienced reinfection (2.46 cases per 100,000 people per day), while 2168 out of 65,676 non-vaccinated patients experienced it (10.21 cases per 100,000 people per day) [25].

People who experienced an infection at the end of the first vaccination series showed stronger protection against reinfection than people who had not received any vaccinations, according to a previous case-control study of residents of Kentucky [26]. A larger cohort study conducted in the United Kingdom has revealed similar outcomes [27]. Also, the main finding of the meta-analysis done by **Flacco et al.** [28] was the significant reduction of the risk of hospitalization due to severe COVID-19 that was observed among the vaccinated subjects, either receiving one or more doses.

Conclusion

Although our results revealed no statistically significant difference between the vaccinated and unvaccinated groups regarding the reinfection rate. But, it may show a piece of evidence that COVID-19 vaccination plays an important clinical role in reducing the severity of COVID-19 infection.

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None declared

Competing interests

None declared

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