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Investigating the Clinical Course of COVID-19 and its Relationship with Vaccine Administration

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Abstract

Background: Assessing and monitoring the clinical progression of COVID-19 can provide valuable insights for developing effective treatment protocols and improving patient stability after discharge. This study aims to assess the clinical course of COVID-19 patients and their association with the administration of recommended vaccines.

Objectives: Investigating the clinical course of COVID-19 and its relationship with vaccine administration.

Methods: A cross-sectional study was conducted on 140 patients with COVID-19 who were discharged from Vasei Hospital, Sabzevar, Iran, between February and July 2022. Participants were selected via convenience sampling. A researcher-developed questionnaire was used to evaluate recovery progress at 4 and 12 weeks' post-discharge. Data were analyzed using SPSS v.24 with a significance level of 0.05.

Results: The administration of recommended vaccine doses showed a significant relationship with the recovery rate at the second follow-up (12 weeks, P = 0.026), but not at the first follow-up (4 weeks). A significant relationship was found between the PCR test result at the second period and the recovery rate at the first follow-up (P = 0.002), but not at the second follow-up (P = 0.51).

Conclusion: The study findings indicate that vaccination impacts both immunity levels and the long-term recovery of patients with COVID-19.

Keywords: Clinical Efficacy, Complications, Functional Recovery, Viral Disease, COVID-19, Vaccines.

1. Background

The global COVID-19 pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), presented significant obstacles to diagnostics and treatments worldwide (1). The clinical spectrum of COVID-19 ranges from asymptomatic infection to symptoms such as fever, fatigue, weakness, severe viral

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pneumonia requiring hospitalization, and, in some cases, death (2). Early diagnosis often relies on symptoms such as fever, cough, and loss of smell or taste, which can help identify individuals who need diagnostic testing (1).

According to Carfì et al., many patients still exhibited symptoms like persistent fatigue, muscle weakness, and psychological impairments after a 6-week follow-up (3). De Graaf et al. (2021) found that a majority of patients experienced varying degrees of psychological disorders, suggesting that identifying prevalent post-recovery symptoms is key to improving future management (4). Struyf et al. concluded that the diagnostic accuracy of individual symptoms is generally poor. Symptoms such as a sore throat or coryza alone do not justify PCR testing (5).

Patients with severe symptoms requiring ventilator support and prolonged hospitalization often experience lingering symptoms indicative of incomplete recovery. Research indicates that SARS-CoV-2 can damage the lungs, heart, and brain, increasing the risk of long-term complications (6). Persistent post-discharge symptoms may include fatigue, dyspnea, cough, cognitive disturbances, and psychological disorders (7).

The virus causes not only acute respiratory problems but also long-term damage to the alveoli (8). Salehi et al. revealed that even mild COVID-19 can cause permanent heart muscle damage, increasing the future risk of heart failure (9). Furthermore, the risk of neurodegenerative diseases and stroke is elevated in patients with COVID-19 (10).

Casas-Rojo et al. substantiated the impact of COVID-19 on various organ systems, including the nervous, cardiovascular, digestive, and ocular systems. The susceptibility of these systems varies among individuals, leading to divergent symptomatic presentations during infection and post-recovery (11). It is crucial to emphasize the significance of monitoring the clinical progression and post-discharge care of patients. Some studies have utilized post-discharge data to devise specialized treatment protocols (12). However, many of these protocols lack World Health Organization approval (13). Therefore, the growing research focus on this issue highlights the importance of post-discharge patient follow-up and clinical assessment (14).

The manifestations of COVID-19 can persist following discharge and often overlap with those of other illnesses. Due to the diverse and variable severity of these symptoms, comprehensive studies are needed to delineate the disease profile and establish effective management strategies. Monitoring and managing the progression of COVID-19 from infection to discharge can provide valuable insights for developing evidence-based treatment algorithms and recommendations to ensure patient stability and well-being. This study aimed to investigate the clinical course of patients with COVID-19 and its association with the administration of recommended vaccines.

2. Objective

Investigating the clinical course of COVID-19 and its relationship with vaccine administration.

3. Methods

Study Design and Participants

This cross-sectional study was conducted at a treatment center affiliated with Sabzevar University of Medical Sciences from February to July 2022. The study involved the following steps.

3.1 Participant Recruitment

A sample of 140 patients diagnosed with COVID-19 was estimated based on Huang's study (15) with a 95% confidence level and a precision of 0.07. Participants were selected using convenience sampling. Eligibility criteria included individuals over 18 years of age, with a PCR-confirmed diagnosis of COVID-19, who required hospitalization. Individuals with a

history of drug addiction or smoking (cigarettes/hookah) were excluded.

$$n = \frac{pq\left(z_{1-\alpha/2}\right)^2}{d^2} = \frac{0.76 * 0.24 \times (1.96)^2}{0.07^2} = 144$$

3.2. Instrument Development

The investigation utilized a researcher-developed tool. The development and validation process involved the following steps:

Item Identification: An extensive literature review was conducted in Web of Science, PubMed, Scopus, and Google Scholar up to December 2023 to identify signs and symptoms of COVID-19. A preliminary checklist was created, and duplicate items were removed.

Delphi Survey: A two-round Delphi survey was conducted with a panel of experts to validate the checklist. The panel comprised 10 Ph.D. nursing faculty members, five infectious disease specialists, five internal medicine specialists, two respiratory disease specialists, and five critical care nurse practitioners. Experts were required to have a minimum of three years of relevant experience and complete the checklist.

The final checklist comprised two sections: 1) Demographic information (age, gender, occupation, education, etc.), and 2) Recovery of symptoms (respiratory, fever, digestive, anosmia, and anxiety-related symptoms).

3.3. Data Collection

Before commencing the study, written telephone consent was obtained from all participants under the supervision of the university's ethics committee. Data collection took place during the COVID-19 outbreak through semi-structured telephone interviews conducted by trained, blinded interviewers to minimize bias. Patient recovery and clinical progress were evaluated using the self-report checklist at two stages: 4 and 12 weeks post-discharge.

3.4. Statistical Analysis

Data were analyzed using SPSS v.24. Categorical variables are reported as frequencies (percentages), and continuous variables as means ± standard deviations. The relationship between variables was examined using the chi-square test, with a significance level set at $P < 0.05$.

4.Result

This cross-sectional study involved a two-stage follow-up of 140 patients with COVID-19. The mean age was 45 ± 13.45 years (range: 22-97), with 75 males (53.6%) and 65 females (46.4%). Most participants were employed (67.14%). The mean duration of symptom stability was 6 ± 2.32 days, and the mean hospitalization duration was 16 ± 6.23 days. The most frequent hospitalization duration was 5 days (24.4%). Most patients (78.1%) reported no quarantine before hospitalization. After hospitalization, 52.6% were not quarantined, while the most frequent quarantine duration was 7 days (12.6%). The time from vaccination to infection ranged from 1 to 340 days, with the highest frequency at 60 days (18.6%). Symptoms most commonly appeared on the third day (19.9%). Most patients (92.6%) completed their treatment, and 16.8% received oxygen therapy at home. Demographic details are presented in Table 1.

Table 1. Frequency distribution of patients' demographic characteristics

Variable		Number Frequency (%)
Level of education	Illiterate	68 (48.9)
	Below a high school diploma	50 (36.0)
	High school diploma	14 (10.1)
	Academic education	8 (5.0)
Caregiver at home	Nurse	7 (5.1)
	Family member	129 (94.2)
	None	1 (0.7)
Marital status	Single	86 (61.42)
	Married	54 (38.57)
Type of nutrition	Regular	54 (38,57)
	Diabetic	22 (15.71)
	Low salt, low fat	22 (15.71)
	High protein	12 (8.58)
	Low protein	7 (5.01)
	Low salt	13 (9.28)
	Low fat	10 (7.14)
vaccination	Yes	88 (62.85)
	No	52 (37.15)
The frequency of the patient's infections	One time	89 (63.57)
	Two times	31 (22.15)
	>three times	20 (14.28)
Oxygen therapy at home	Yes	68 (48.9)
	No	72 (51.1)

At the 4-week follow-up, the time to recovery since symptom onset ranged from 10 to 120 days, with peaks at 30 and 40 days. At the 12-week follow-up, 38.1% of patients felt another follow-up was needed. The recovery time ranged from 7 to 90 days, with the most frequent report of 20 days. A comparison of patient conditions at 4 and 12 weeks is shown in Table 2.

Table 2. Comparison of follow-ups scheduled 4 and 12 weeks after discharge

Variable	Severity of symptoms	4-week follow-up	12-week follow-up
Degree of recovery	Complete (no symptoms)	64(60.4)	76 (80.8)
	Moderate (less than three initial symptoms)	38 (35.8)	17 (18.1)
	Poor (3-5 initial symptoms)	2 (1.9)	1 (1.1)
	No recovery (Over five symptoms)	2 (1.9)	0
Repeated PCR test	Positive	1 (6.7)	3 (75.0)
	Negative	14 (93.3)	1 (25.0)
Adherence to the recommendations of the health care provider (traditional medicine, etc.)	Yes	92 (84.4)	41 (83.7)
	No	17 (15.6)	7 (14.3)

Vaccination status showed a significant relationship with the recovery rate at the 12-week follow-up (P = 0.026), but not at the 4-week follow-up (Table 3).

Table3. The relationship between vaccination and the recovery rate in the first and second follow-ups (4 and 12 weeks after discharge)

Vaccination/recovery in the second follow-up			Complete (no symptoms)	Moderate (less than three initial symptoms)	Poor (3-5 initial symptoms)	Chi-square test
			Number (percentage)	Number (percentage)	Number (percentage)	
4-week follow-up	Vaccination	Yes	55(58.5)	37(39.4)	2 (2.1)	P = 0.094
		No	7 (100.0)	0 (0.0)	0 (0.0)	
12-week follow-up	Vaccination	Yes	69 (81.2)	15(17.6)	1 (1.2)	P = 0.62
		No	4 (66.7)	2 (33.3)	0 (0.0)	

There was no significant relationship between the type of vaccine received (first, second, or third dose) and recovery rate at either follow-up (Table 4).

Table 4. The relationship between vaccination and the recovery rate at the first and second follow-ups (4 and 12 weeks after discharge)

Vaccination/Recovery rate in the first and second follow-ups			Complete (no symptoms) Number (percentage)	Moderate (less than three initial symptoms) Number (percentage)	Poor (3-5 initial symptoms) Number (percentage)	Chi-square test
4-week follow-up	Vaccination	None	3 (100.0)	0 (0.0)	0 (0.0)	P =0.437
		First dose	2 (40.0)	3 (60.03)	0 (0.0)	
		Second dose	25 (67.6)	12(34.4)	0 (0.0)	
		Third dose	28 (53.8)	22(42.3)	2 (3.8)	
12-week follow-up	Vaccination	None	2 (66.7)	1 (33.3)	0 (0.0)	P = 0.026
		First dose	4 (66.7)	1 (16.7)	1 (16.7)	
		Second dose	25 (83.3)25	5 (16.7)	0 (0.0)	
		Third dose	40 (81.6)	9 (18.4)	0 (0.0)	

The results of the chi-square test showed that at the first and second follow-ups (4 and 12 weeks after discharge), there was no significant relationship between the recovery rate and the type of vaccine received for the first, second, and third doses (Table 5).

Table 5: The relationship between recovery rate and the type of vaccine received in the first, second, and third doses at the first and second follow-ups (4 and 12 weeks after discharge)

Recovery rate /Type of vaccine received for the first dose at the first and second follow-ups			Complete (no symptoms) Number (percentage)	moderate(less than 3 initial symptoms) Number (percentage)	Poor (3-5 initial symptoms) Number (percentage)	Chi square test
4-week follow-up	Type of vaccine for the first dose	AstraZeneca	9 (52.9)	8 (47.1)	0 (0.0)	P = 0.894
		Bharat	1 (100.0)	0 (0.0)	0 (0.0)	
		Sinopharm	39 (61.9)	22(34.9)	2 (3.2)	
		Barkat	3 (42.9)	4 (57.1)	0 (0.0)	
		Unspecified	3 (50.0)	3 (50.0)	0 (0.0)	
12-week follow-up	Type of vaccine for the first dose	AstraZeneca	9 (75.0)	3 (25.0)	0 (0.0)	P = 0.456
		Bharat	1 (100.0)	0 (0.0)	0 (0.0)	
		Sinopharm	52(86.7)	7 (11.7)	1 (1.7)	
		Barkat	4 (66.7)	2 (33.3)	0 (0.0)	
		Unspecified	3 (50.0)	3 (50.0)	0 (0.0)	
Type of vaccine for the second dose						
4-week follow-up	Type of vaccine for the second dose	AstraZeneca	0 (52.9)	8 (47.1)	0 (0.0)	P = 0.816
		Bharat	1 (100.0)	0 (0.0)	0 (0.0)	
		Sinopharm	38 (63.3)	20 (33.3)	2 (3.3)	
		Barkat	3 (42.9)	4 (57.1)	0 (0.0)	
		Unspecified	3 (50.0)	2 (40.0)	0 (0.0)	
12-week follow-up	Type of vaccine for the second dose	AstraZeneca	(75.0)9	3 (25.0)	0 (0.0)	P = 0.242
		Bharat	0 (0.0)	0 (0.0)	0 (0.0)	
		Sinopharm	49 (87.5)	7 (12.5)	0 (0.0)	
		Barkat	4 (66.7)	2 (33.3)	0 (0.0)	
		Unspecified	3 (60.0)	2 (40.0)	0 (0.0)	
Type of vaccine for the third dose						
4-week follow-up	Type of vaccine for the third dose	AstraZeneca	3 (37.5)	5 (62.5)	0 (0.0)	P = 0.859
		PastoCovac	1(100.0)	0 (0.0)	0 (0.0)	
		Sinopharm	19 (55.9)	13 (38.2)	2 (5.9)	
		Barkat	3 (50.0)	3 (50.0)	0 (0.0)	
		Unspecified	3 (75.0)	1 (25.0)	0 (0.0)	
12-week follow-up	Type of vaccine for the third dose	AstraZeneca	5 (71.4)	52(28.6)	0 (0.0)	P = 0. 898
		PastoCovac	1 (100.0)	0 (0.0)	0 (0.0)	
		Sinopharm	28 (84.8)	5 (15.2)	0 (0.0)	
		Barkat	4 (80.0)	1 (20.0)	0 (0.0)	
		Unspecified	3 (75.0)	1 (25.0)	0 (0.0)	

5. Discussion

Patients who develop severe COVID-19 often face persistent clinical and psychological manifestations, even after recovery. Remote follow-up can be a valuable tool for managing these patients (16). This study followed the clinical course of COVID-19 patients in Sabzevar, Iran, between February and July 2022, using a self-report method to explore the relationship between vaccination and symptom improvement at 4 and 12 weeks post-discharge.

The results indicated that more than 80% of patients attained full recovery 12 weeks after discharge. This recovery rate is encouraging and appears higher than that reported in earlier studies. In a cohort study, Huang et al. found that 76% of patients recovered from COVID-19 reported fatigue or muscle weakness at least 6 months after discharge (15).

Other studies from China by Zhao et al. and Liang et al. also followed up with patients 3 months after discharge (17, 18). The relatively high recovery rate at 12 weeks in our study may reflect the combined impact of vaccination and the dominance of less virulent variants, such as Omicron, during the 2022 study period—factors not present in earlier studies from 2020 (19).

Nevertheless, the results also showed that COVID-19 is associated with persistent symptoms, as some patients had not recovered completely even 3 months after discharge. Liang et al. (2020) in China reported a recovery rate of 90.1% after 3 months (18), which is 10.7% higher than the rate observed in the present study. This variation could be related to methodological differences, such as self-report versus paraclinical assessment. Furthermore, a comprehensive systematic review has since confirmed that a significant proportion of survivors experience at least one persistent symptom at 12 months, with fatigue and weakness remaining among the most common, underscoring the long-term nature of this health burden (20).

Several studies substantiate that older adults, men, people of Black ethnicity, individuals with obesity, smokers, and patients with diabetic, cardiovascular, or renal diseases, as well as those with hypertension, are at higher risk of hospitalization due to COVID-19 (21, 22). Our findings are consistent with this, as we found that underlying diseases and old age, followed by addiction and smoking, were the most frequent risk factors for hospitalization.

In the present study, the most common initial symptoms in hospitalized patients were pulmonary involvement, fever and chills, body pain, and shortness of breath. It differs from other studies that have reported fever and cough to be the most common complaints (23). This variation could be due to differences in guidelines adopted by various countries, based on available resources, or to different viral strains. The influence of different strains could not be compared in this study because we did not have access to reference laboratory data to determine the prevalent strain. Indeed, the symptom profile of COVID-19 has evolved with the emergence of new variants; for instance, the Omicron variant, which was dominant globally in 2022, is associated with a lower prevalence of classic symptoms, such as loss of smell, and a different constellation of initial complaints, which could explain the observed differences (24).

Because a considerable portion of severe COVID-19 cases occur in older adults with underlying diseases, medication safety is essential for this group. In this context, most countries have explored the potential of herbal and traditional medicine to manage the pandemic. A systematic review by Nguyen et al. demonstrated that integrating traditional Chinese medicine with conventional medicine improved symptoms in patients with COVID-19 (25). In the present study, many patients had frequently used complementary and traditional medications before hospitalization.

Likewise, studies conducted in Ethiopia suggest that half of the study population had used herbal medications to treat COVID-19 (26). Similarly, in our study, patients frequently followed traditional medicine recommendations during the two follow-up stages (4 and 12 weeks). Traditional herbal medications are popular and enjoy strong social support in Iran (27). Although delayed, the national guidelines in Iran (Version 11, released in December 2021) incorporated preventive recommendations and complementary treatments from traditional medicine to diagnose and treat COVID-19 through outpatient and inpatient services (28). The global interest in traditional medicine for COVID-19 is also reflected in WHO's ongoing efforts to evaluate evidence-based traditional therapies, acknowledging their widespread use and the need for robust clinical data to guide practice (29).

Men and illiterate individuals had the highest frequency among patients with COVID-19. Consistent with our results, numerous researchers have highlighted that men are more susceptible to severe COVID-19 infections, and they have confirmed the role of literacy in preventing and mitigating this disease (21, 30).

Sun et al. have stressed the positive role of family support in caring for patients during a pandemic, as well as in promoting their health during hospitalization and after discharge (31). Family-based management has been suggested as an effective strategy for improving risk perception (32). In the present study, over 90% of patients were cared for by family members, indicating strong family support and emotional ties within the studied population. This finding is crucial, as social support has been identified as a protective factor against poor mental health outcomes, such as post-traumatic stress disorder and anxiety, in patients recovering from COVID-19 (33).

According to the CDC (Centers for Disease Control and Prevention), receiving an updated dose of the COVID-19 vaccine protects against severe disease, hospitalization, and death (34). Heftdal et al., investigating the relationship between COVID-19 incidence and positive PCR tests in Denmark, showed that individuals who received two doses of the COVID-19 vaccine were at a lower risk of infection after an 8-month follow-up (35). In line with these findings, our results showed a significant relationship between vaccination and the recovery rate at the 12-week follow-up. Emerging evidence suggests that explicit vaccination may be associated with a reduced risk of developing Long COVID. A meta-analysis found that vaccination before SARS-CoV-2 infection was associated with a significantly lower risk of persistent symptoms, providing a biological plausibility for our observed association between vaccination and improved recovery (36).

Strengths and Limitations

One of the strengths of this study is that data collection took place during the COVID-19 outbreak using semi-structured interviews conducted over the phone. A key limitation is the reliance on patient self-reports to confirm recovery, rather than using diagnostic tests and radiological images. While self-report is a limitation, it is noteworthy that patient-reported outcomes are increasingly recognized as essential endpoints in Long COVID research, as they capture the symptom burden that matters most to the patient (37). Studying the recovery course of emerging diseases can help provide valuable information for managing healthcare services and developing more effective responses to a pandemic.

6. Conclusion

This cross-sectional study demonstrated that vaccination influences immunity and long-term recovery in patients with COVID-19. Given the substantial number of individuals affected, monitoring the clinical progression of the disease is crucial. Our findings, derived from a systematic follow-up of patients'

recovery and vaccination status, contribute to this understanding. A key limitation was the reliance on patient self-reports rather than diagnostic tests to confirm recovery. Nonetheless, the results of this study can help health authorities implement preventive measures and formulate strategies for controlling infectious diseases. Furthermore, these insights can inform public health policies aimed at improving population health outcomes.

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Availability of data and materials: Data is provided within the manuscript.

Conflicts of interests: The authors declare no competing interests.

Consent for publication: Not applicable.

Ethics approval and consent to participate: This study was approved by the Ethics Committee of Sabzevar University of Medical Sciences (IR.MEDSAB.REC.1400.136) and was assigned the project code 400124. All methods were performed in accordance with the relevant guidelines and regulations. Participants were selected via convenience sampling from Vasei Hospital, which served as the sole COVID-19 center in Sabzevar. Before data collection, the study's purpose was thoroughly explained to all potential participants. Informed written consent was obtained verbally via telephone, a procedure approved by the ethics committee, and all participant questions were addressed.

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Author contributions: Conceptualization; A D M GH, H Y, M KSH, and R Z; Data curation; F B, B K, E S, Formal analysis; Investigation; Software; E N; Roles/Writing - original draft; A D M GH, H Y, F B, R Z and E S, review & editing; A D M GH, H Y, F B.

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