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The perspective of Iranian patients with multiple sclerosis on the third dose of COVID-19 vaccine

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Keywords
Multiple Sclerosis; COVID-19; Vaccination; Patient Preference; Iran

Abstract

Background: Now that the majority of the population has been immunized with two-dose vaccines, debates over the third booster dose have been raised. We studied the viewpoint of cases with multiple sclerosis (MS) on this matter.

Methods: In a cross-sectional study, a google form containing questions about participants' characteristics, the history of coronavirus disease 2019 (COVID-19) infection and vaccination, and opinions on the third dose was designed.

Results: Of 1067 responders, only 16 (1.5%) were not vaccinated at all. The most used vaccine type was Sinopharm BBIBP COVID-19 vaccine (BBIBP-CorV) (n = 1002, 93.9%). Generally, 58 (5.4%) cases were hospitalized due to COVID-19. Of those with full vaccination, 134 (13.3%) got COVID-19 infection after the second dose. Only 13 participants (1%) did not agree with the third dose, while 564 (53.0%) believed that a booster dose was needed. Of all, 488 (45.7%) declared that they did not have a final idea and would follow the instructions by the experts. A significant association was found between not receiving the first two doses and not believing in the third dose (P = 0.001). 692 patients declared their reasoning for the importance of the third dose. All the cases who thought the administered vaccine was not efficient enough had received Sinopharm BBIBP-CorV. Those who got infected after full vaccination were more uncertain about the efficacy of the vaccine [odds ratio (OR): 2.6, 95% confidence interval (CI): 1.6-4.2].

Conclusion: It seems that the majority of the Iranian patients with MS expect the authorities to administer a third booster dose, especially if scientifically validated.

Introduction

Vaccination against coronavirus disease 2019 (COVID-19) has brought hope for ending the pandemic. Now that a substantial proportion of the population has been immunized with two-dose vaccines, debates over the third booster dose have been raised. It is of note in immune-compromised patients.[1]

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Studies have shown that the third dose can promote immune responses in some initial vaccine non-responders.[2] Cases with multiple sclerosis (MS) were among the first vaccinated groups in Iran, many of whom are under treatment with immune-modulator or immunosuppressing agents. Now, with the third dose in perspective, controversy about the best policy is highlighted. One important factor in designing protocols is to investigate the patients' attitudes toward the subject. Here, we studied the viewpoint of Iranian cases with MS on this matter.

Materials and Methods

Patients: The participants were among members of the Telegram groups of Iranian patients with MS. The members were patients with established demyelinating diseases diagnosed or treated in different parts of Iran. Those with diagnoses rather than definite MS [radiologically isolated syndrome (RIS), clinically isolated syndrome (CIS), neuromyelitis optica spectrum disorders (NMOSD), myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), chronic relapsing inflammatory optic neuritis (CRION), and transverse myelitis] were excluded. All others who filled in the questionnaire were included.

Study design: In a cross-sectional study, a google form containing questions about demographic data [age, gender, education (with or without an academic degree), employment (employed or unemployed), marital status, and place of residence] and MS disease characteristics [MS type: relapsing-remitting MS (RRMS), secondary progressive MS (SPMS), or primary progressive MS (PPMS), MS duration (time from the first presentation till now), the need for aid in walking, pointing to the Expanded Disability Status Scale (EDSS) higher or lower than 6, and disease-modifying treatment (DMT)] was designed. There were also questions about the history of COVID-19 infection (its severity and relation to the vaccination timing) and vaccination (number of received doses and vaccine type). Finally, the participants were asked about their opinions of the third dose (if it was needed and their reason for the idea). To make sure of the data validity about MS type and EDSS, every participant had to enter their National MS Registry Code. These two variables were compared with the data in the registry system.

The questionnaire was reviewed by two MS experts and two patients. The final version was made available in Telegram groups of Iranian patients with MS, from September 28 to October 2, 2021.

Applicable descriptive analysis was performed for quantitative [mean ± standard deviation (SD)] and qualitative (number, percentage) data. Univariate logistic regression was used to evaluate the relationship between outcome measure (attitudes toward the booster dose) and basic characteristics [age, gender, education, employment, place of residence, marital status, MS type (progressive or not), disability scale, MS duration], and also the history of COVID-19 infection, vaccination, and losing a close relative due to COVID-19. Analysis was performed via SPSS software (version 26, IBM Corporation, Armonk, NY, USA). Two-tailed P-value less than 0.05 was considered significant.

Ethical considerations: The study protocol was approved by the Ethics Committee of Tehran University of Medical Sciences, Tehran, Iran, by Institutional Review Board (IRB) code of "IR.TUMS.NI.REC.1400.012".

Results

A total of 1115 patients viewed the form and 1067 responders filled it out. The basic characteristics of the included group are summarized in table 1.

The majority of the responders (n = 1010, 94.7%) had been fully vaccinated. Thirty-seven (3.5%) had received the first dose. Only 16 (1.5%) were not vaccinated at all. The most used vaccine type was Sinopharm BBIBP COVID-19 vaccine (BBIBP-CorV) (n = 1002, 93.9%). Generally, 58 (5.4%) cases were hospitalized due to COVID-19. Of those with full vaccination, 134 (13.3%) got COVID-19 infection after the second dose. Those who claimed to have lost a close relative counted for 374 (35.1%).

Only 13 participants (1.0%) did not agree with receiving the third dose. While 564 (53.0%) believed that a booster dose was needed, 488 (45.7%) declared that they did not have a final idea and would follow the instructions by the experts. Of all, 692 patients declared their reasoning for the importance of the third dose (Table 2).

There was no significant relation between rejecting the idea of the third dose and any basic characteristic (age, gender, education, employment, place of residence, marital status, MS type, MS duration, EDSS). Only a significant association was found between not receiving the first two doses and not believing in the third dose (P = 0.001) (Table 3).

Table 1. The basic characteristics of the participants

Variable	Value
Age (year)	37.2 ± 8.7
Gender	
Women	823 (77.1)
Men	232 (21.7)
Education	
Without academic degree	257 (24.1)
With academic degree	805 (75.4)
Employment	
Unemployed	578 (54.2)
Employed	479 (44.9)
Place of residence	
Rural areas	13 (1.2)
Urban areas	1043 (97.7)
Marital status	
Married	632 (59.2)
Not married (single, divorced, deceased partner)	429 (40.1)
MS type	
RRMS	831 (77.9)
SPMS	168 (15.7)
PPMS	67 (6.3)
EDSS	
< 6	960 (89.9)
≥ 6	100 (9.4)
MS duration (year)	9.1 ± 6.3
MS medication	
Interferon beta-1A (intramuscular)	116 (10.9)
Interferon beta-1A (subcutaneous)	64 (6.0)
Interferon beta-1B	16 (1.5)
Glatiramer acetate	64 (6.0)
Fingolimod	145 (13.6)
Dimethyl fumarate	149 (14.0)
Teriflunomide	30 (2.8)
Natalizumab	31 (2.9)
Rituximab	361 (33.8)
Ocrelizumab	38 (3.6)
Cyclophosphamide	0 (0)
Mitoxantrone	2 (0.2)
Azathioprine	7 (0.7)
Mycophenolate mofetil	2 (0.2)
Cladribine	1 (0.1)

Data are presented as mean ± standard deviation (SD) and number (percent) for quantitative and qualitative data, respectively.
MS: Multiple sclerosis; RRMS: Relapsing-remitting multiple sclerosis; SPMS: Secondary progressive multiple sclerosis; PPMS: Primary progressive multiple sclerosis; EDSS: Expanded Disability Status Scale

No association was found between this outcome measure and the prior history of COVID-19 in the patients or their families.

Analyzing the related factors to believing in the inefficacy of the administered vaccine, EDSS > 6, male gender, not having an academic degree, COVID-19 infection after full vaccination, and hospitalization due to COVID-19 showed significant relation in univariate analysis (P = 0.200).

Table 2. The distribution of the patients' reasoning for the necessity of the third dose

The reasoning	n (%)*
The administered vaccine is not strong enough	156 (22.5)
New mutations have emerged	257 (37.1)
The time has passed from the second dose, so the immunity is decreased	307 (44.4)
MS cases are at more risk of severe COVID-19 due to their disease	238 (34.4)
MS cases are at more risk of severe COVID-19 due to their drugs	302 (43.6)

*The proportion was calculated relative to 692 responders to the question; all the cases who thought the administered vaccine was not efficient enough had received Sinopharm BBIBP COVID-19 vaccine (BBIBP-CorV).
MS: Multiple sclerosis; COVID-19: Coronavirus disease 2019

Entering them in the final model, using the forward conditional method, male gender, not having an academic degree, and COVID-19 infection after full vaccination remained significant (Table 4). The results of the same approach for the other reasons, "new mutations need further doses of the vaccine" and "time has passed since the first two doses, so there is a need for a booster dose", are also summarized in table 4. None of the variables were found to be significantly related to the answer "patients with MS are at higher risk of severe COVID-19 due to their disease" and "patients with MS are at higher risk of severe COVID-19 due to their DMTs" (P > 0.050).

Discussion

Now that various vaccines are being approved for the third dose, especially for immunocompromised cases,[3] this study highlights the viewpoint of the MS population on the third dose vaccination. Only a minority was completely against the idea, of whom two cases had not been vaccinated at all. Considering the small sample size of the patients disapproving the booster dose limits the generalizability of this finding.

Table 3. Cross-tabulation of vaccination status in relation to belief in the third dose

	Not believing in the third dose	Believing in the third dose
Not vaccinated	2	14
Got vaccinated (one or two doses)	11	1036

Table 4. Multivariate analysis of related factors to the rationales for the necessity of the third dose

Rationale	Variable	OR (95% CI)	P
The administered vaccine is inefficient	Male gender	2.0 (1.3-3.1)	0.001
	No academic degree	2.4 (1.4-4.3)	0.002
	COVID-19 infection after full vaccination	2.6 (1.6-4.2)	< 0.001
New mutations need further doses of the vaccine	Progressive MS	0.5 (0.3-0.7)	0.001
	Employed	1.4 (1.1-2.0)	0.038
	Married	0.6 (0.5-0.9)	0.006
Time has passed since the first two doses, so there is a need for a booster dose	Progressive MS	0.5 (0.3-0.9)	0.021
	No academic degree	2.3 (1.4-3.9)	0.002
	Prior history of COVID-19 infection	0.5 (0.4-0.8)	0.004

OR: Odds ratio; CI: Confidence interval; MS: Multiple sclerosis; COVID-19: Coronavirus disease 2019

A previous study in Iran showed that about 33% of patients with MS did not agree with vaccination [they were either unsure (28%) or disagreed (8%)].[4] While about a year later, another study demonstrated that only 7% had not received vaccination.[5] Tracking United States (US) surveys also shows that the rate of vaccine hesitancy has decreased over time among patients with MS, probably due to providing more information to the patients.[6]

In a report by Neely and Scacco, the objection against booster doses was minor among American adults. Education, race, and trust in the health care system are found to be game-changing factors.[7] Surveys in the US and other parts of the world discovered similar altering socioeconomic factors.[6,8-10] In our study, education was associated with the reason for considering a booster dose. In another study from Iran, lower education was noticed to be associated with higher COVID-19 vaccine hesitancy in general among patients with MS.[5]

Unlike some other reports,[11-13] doubt about the vaccine efficacy was not a dominant concern in our study. Those who got infected after full vaccination were more uncertain about the efficacy of the vaccine, as predicted. Although this study is about the third dose, and the mentioned issue is not that prevalent, it seems important to assure the population, especially men and those with lower education levels. Discussing the results of research comparing BBIBP-CorV (Sinopharm) with other vaccines[14,15] could be beneficial. Finally, it is crucial to insist on the efficacy of all approved vaccines in preventing severe COVID-19 and mortality, regardless of their efficacy in antibody production.[16]

Patients with progressive MS seem less worried about the new mutations and the time that has passed since the first two doses. The possible rationale behind this finding is unclear to us at the moment. However, there should be more emphasis on repeated vaccination in this group as there are more possible disabilities and older age.

It seems that unemployed married cases cared less about new mutations. It could be suggested that this group may have less exposure to the outside crowds; thus, they are less obsessed with the newly emerging virus mutations.

Participants with a history of prior COVID-19 infection appear to be less concerned about the time-lapse from the initial doses. This could be linked to their belief that the infection itself may have strengthened their immune response but needs further verification.

Conclusion

It is clear that the society of Iranian patients with MS is not against the third booster dose. Even the majority expects the authorities to administer it, especially if scientifically validated.

Conflict of Interests

The authors declare no conflict of interest in this study.

Acknowledgments

None.

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