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Multiple Sclerosis and Related Disorders

COVID-19 vaccine hesitancy in Iranian patients with multiple sclerosis

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ABSTRACT

Background: World Health Organization (WHO) mentioned COVID-19 vaccination as the safest way to eradicate this pandemic. In the meantime, vaccine hesitancy (a delay in accepting or rejecting the vaccine despite the availability of vaccination services) is a barrier. Hence, we studied this obstacle in the Iranian multiple sclerosis (MS) population.

Objective: MS patients eligible for vaccination were asked to complete a google form survey. Demographic information, MS disease-related factors, flu vaccination history, COVID-19 vaccination history, cause of vaccination refusal, past history of COVID-19 infection, and their compliance with public health guidelines after vaccination were recorded.

Results: 1479 patients participated in this study. 6.9% of participants have not received the vaccination. Sinopharm was the most commonly used vaccine (92.9%). Vaccine hesitancy was associated with young age, lower education, unemployment, negative flu vaccination history, no previous episode of COVID-19 infection, less concern about COVID-19, and the expectation of not getting infected with the virus after vaccination. Participants mentioned concerns about the side effects of the vaccines as the most prevalent cause of avoiding vaccination (58.0%). Patients' concern of SARS-CoV-2 significantly decreased after vaccination (p-value < 0.001).

Conclusion: Our findings in this study elucidate that a minor group of patients with MS has vaccine hesitancy, which may expose them to more severe COVID 19. The treating physicians should ask the history of vaccination and try to persuade such patients with scientific knowledge transformation. The long-term consequences of not being vaccinated should be clarified to such patients especially those who are receiving immunosuppressive agents.

1. Introduction

Severe Acute Respiratory Syndrome Corona Virus 2(SARS-CoV-2) which resulted in Coronavirus disease 2019 (COVID-19) is an infectious disease and then has rapidly become a worldwide pandemic (Gralinski and Menachery, 2020).

World Health Organization (WHO) mentioned COVID-19 vaccination as the safest way to eradicate COVID 19 pandemic (2022a).

Certain patients who have underlying diseases may be more susceptible to viral infections. Patients with multiple sclerosis (MS) who need immunomodulatory or immunosuppressive medications comprise one category (Zheng et al., 2020). National Multiple Sclerosis Society (NMSS) guideline on COVID-19 recommended that these patients should receive the COVID-19 vaccine at once it becomes available (2022b). Furthermore, adults with advanced MS, older age, or other

comorbidities (such as diabetes, obesity, cardiovascular disease, pregnancy) are at higher risk for severe infection, so they should get vaccinated sooner (Dror et al., 2020).

However, doubts about receiving the vaccine are a barrier to COVID-19 vaccination (Dror et al., 2020).

Vaccine hesitancy means a delay in accepting or rejecting the vaccine despite the available vaccination services. This doubt varies according to place, time and vaccines. It is associated with many factors such as satisfaction, comfort, and trust in vaccines (MacDonald, 2015).

There is inaccurate information about vaccines on social media. Companies are widely criticized for not dealing with this misinformation (Wardle and Singerman, 2021).

Vaccine hesitancy was studied before the pandemic. Diem et al. (2021) investigated pneumococcal vaccination refusal and Ziello et al. (2021) reported about influenza vaccine hesitancy both in persons with

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MS. The results could predict the possible challenges for the SARS-CoV-2 vaccination.

Ehde et al. (2021) investigated willingness to get COVID-19 vaccination among adults with MS. They found its association with higher awareness of one's risk of infection with COVID-19 and a higher level of education. Safety concerns were also found as the main cause for SARS-CoV-2 vaccine hesitancy in the study by Yap et al. (2021). To our knowledge, no report from Iran was published so far.

Understanding the frequency and related determinants of vaccine hesitancy will aid policymakers in gaining a better understanding of intervention barriers and developing strategies to overcome them.

The current study aimed to provide evidence on the effect of vaccines on patients' concerns about COVID-19, and the prevalence of compliance with public health guidelines after vaccination among Iranian MS patients.

2. Methods

In this observational study, a questionnaire was designed and approved by two MS experts.

It was piloted on five patients. The final google form was made available in online groups of MS patients in Iran from September 28 to November 22, 2021.

Participants' demographic information (age, sex, education, employment status), MS disease-related factors (MS type, current disease-modifying treatment (DMT), and disease severity), flu vaccination history in the last five years, their belief about the effects of DMT on vaccine efficacy, COVID-19 vaccination history, their reason for vaccination refusal, type and time of the first COVID-19 vaccine dose, history of COVID-19 infection, their concerns about COVID-19, their expectations of vaccine efficacy and their compliance with public health guidelines after vaccination were recorded.

High-efficacy drugs include fingolimod, natalizumab, rituximab, ocrelizumab, azathioprine, mycophenolate, and cyclophosphamide.

Disease severity was assessed by expanded disability status scale (EDSS) (who were able to walk without any aid (EDSS < 6), who needed aid for walking (EDSS ≥ 6)).

COVID-19 was diagnosed by an infectious disease specialist or internist based on a positive reverse transcription polymerase chain reaction (RT-PCR), clinical symptoms and signs, or computed tomography (CT) scan results.

The concern about COVID-19 scale ranged from 1 to 10 (1 the least, 10 the most concern)

Descriptive statistics were reported as mean $\pm$ standard deviation (SD) and proportion for quantitative and qualitative variables, respectively. Binary logistic regression methods were used to determine the possible factors associated with vaccine hesitancy. The Wilcoxon rank-sum test was performed to determine the link between patients' pre- and post-vaccination complaints. Statistical significance was defined as a *p-value* less than 0.05. IBM® SPSS® version 26 was used for analyses.

Sensitivity analysis was performed by redefining vaccine hesitancy excluding those with claims of missed appointment and inability to present in vaccination centers as the reasons for not getting vaccinated.

3. Results

Among 1517 participants, eight duplicated cases, 25 cases with neuromyelitis optica spectrum disorder (NMOSD), and five cases under 18 years of age were excluded. The basic characteristics of the remaining 1479 participants are presented in Table 1.

Among 1479 participants 1377(93.1%) were vaccinated (111 (7.5%) first dose, 1266 (85.6%) both doses). 102 (6.9%) have not received vaccination. Sinopharm was the most common vaccine (92.9%), followed by AstraZeneca (3.2%), Sputnik (1.4%), COVIran Barekat (1.2%), and others (1.2%). 638 (46.3%) of vaccinated patients obtained their vaccines in the first four months of the vaccination program.

Table 1
Basic characteristics of the participants.

Variables	*
Age (year)	37.2 ± 8.8
Gender	
Female	1182 (79.9)
Male	297 (20.1)
Education	
High school	406 (27.5)
College	704 (47.6)
Postgraduate	369(24.9)
Employment status	
Employed	635 (42.9)
Unemployed	844 (57.1)
MS type	
Non progressive	1113 (75.3)
Progressive	278 (18.8)
Unknown	88 (5.9)
EDSS	
Unassisted ambulation	1325 (90.4)
Assisted ambulation	141 (9.6)
MS treatment	
High efficacy	747 (51.4)
Others	705 (48.6)
Past COVID-19 infection	
No	1052 (71.5)
Yes	420 (28.5)
Concern about COVID-19	6.56 (4-10)
Vaccine expectation	
Less severe COVID-19 infection	1089 (73.7)
Not getting infected with COVID-19 after vaccination	389 (26.3)
Belief about the effects of DMT on vaccine efficacy	
No effect	1057 (71.5)
Decreased efficacy	422 (28.5)
Flu vaccination history	
Negative	1082 (73.5)
Positive	391 (26.5)

*Quantitative variables are presented as mean ± SD, whereas qualitative variables are reported as number (%) and categorical variables as median (IQR).

Concern about the side effects of vaccines was the most prevalent cause of avoiding vaccination (58.0%), followed by belief in the ineffectiveness of the vaccines (15%), not having options for vaccine type (15%), mistrust in vaccination generally (14%), no vaccination appointments (4%), inability to present in vaccination centers (4%) and others (17.0%). The other reasons include pregnancy, COVID-19 infection, and traveling.

Patients with vaccine hesitancy were younger (*p-value* = 0.012). Moreover, it was significantly associated with lower education, unemployment, no flu vaccination history, no previous episode of COVID-19 infection, less coronavirus concern, the expectation of not getting infected with the virus after vaccination which are presented in Table 2. Whereas high efficacy DMT (*p-value* = 0.066) and female gender (*p-value* = 0.055) were significant in univariate regression but not significant in the final multivariate model.

137 of 1266 completely vaccinated patients (10.9%) experienced COVID-19 infection after their second dose. Furthermore, 46/1377 (3.3%) who received at least one dose of vaccine were infected by COVID-19 after their first dose.

Table 2
Associations between vaccine hesitancy and basic patients' characteristics.

Variable	B	Exp (B)	*p-value*
Age	032	1.032	.012
Education	-508	602	.035
Employment status	-617	539	.021
Past COVID-19 infection	-813	444	< .001
Concern about COVID-19	100	1.105	.002
Flu vaccination history	-743	476	.017
Vaccine expectation	983	2.672	< .001

Exp (B): exponentiation B which is an estimation of odds ratio (OR).

193/1377 (14.0%) of vaccinated patients had decreased compliance with health guidelines after vaccination.

The effect of getting vaccinated on decreasing the score of concerns about coronavirus was significant (*p-value* < 0.001).

3.1. Sensitivity analysis

After excluding those who did not get vaccinated in terms of missed appointment and inability to present in vaccination centers from the vaccine hesitant group, age (*p-value* = .016), female gender (*p-value* = .037), unemployment (*p-value* = .012), past COVID-19 infection (*p-value* < .001), less concern about coronavirus (*p-value* = .004), no flu vaccination history (*p-value* = .046), expectation of not getting infected with the virus after vaccination (*p-value* < .001), and high efficacy DMT (*p-value* = 0.031) remained significantly associated with the outcome measure.

4. Discussion

This is the first report of vaccine hesitancy relevant factors besides investigating the effect of vaccination on patients' concerns, and their compliance with public health guidelines.

Our study indicated that (6.9%) of the patients with MS had not received vaccination which was less than vaccine hesitancy in adults with multiple sclerosis in the United States (20.3%) (Ehde et al., 2021). Vaccine-hesitant cases frequently expected of not getting infected with the virus after vaccination. Besides they were less concerned about the virus and had not been infected with SARS-CoV-2 before. This may be related to the assumption that vaccines should prevent infection completely. It also appears this group thinks if they have not been infected in the past, they will not experience it in the future. Moreover, they have fewer concerns about this pandemic. As a point of reference, a research found that healthcare workers who are not involved with or caring for COVID-19 positive patients seem to be more vaccine-hesitant and have less worries, which is consistent with our results (Dror et al., 2020).

Additionally, we discovered that vaccination hesitation was connected with educational level in MS patients. It is in agreement with the results of a previous US study that indicated more willingness to receive the vaccine in higher-level education patients and higher concern of COVID-19 infection (Ehde et al., 2021). But it was the only factor that was not associated after sensitivity analysis which was predictable, because a lower academic degree may lead to lower insight for checking social media and web-based appointments for vaccination.

Besides, Xiang et al. (2021) exhibited an association of vaccine willingness with higher educational level and prior influenza vaccine acceptance. Unsurprisingly, there is a negative association between past flu vaccination history and COVID-19 vaccine hesitancy in our study. Past history of vaccination in general impacts future decision-making concerning vaccination (Diem et al., 2021; Uhr and Mateen, 2021; Wu et al., 2021).

A meta-analysis demonstrated that males had a considerably greater risk of COVID-19-related complications and mortality (Galbadage et al., 2020), which may result in increased uptake of COVID-19 vaccinations. In our study, females were more vaccine-hesitant (OR: 2.053, *p-value* = 0.055) which stayed significant in sensitivity analysis (*p-value* = .037). Younger adults conceive they are less likely to be hospitalized because of COVID-19 or to die from it than older cases (Diem et al., 2021). This issue may explain our findings that vaccine hesitancy was more frequent at a younger age.

Patients who were currently taking a high-efficacy DMT were more averse to vaccination. According to one research, some high-efficacy DMTs, such as rituximab, an immunosuppressive medication, increased the incidence of COVID-19 side effects (Simpson-Yap et al., 2021). As a result, they may become more concerned about the vaccine's adverse effects on their body.

In general, the greatest vaccine-hesitant respondents' concern was about the possible vaccine side effects which are confirmed by other studies (Yap et al., 2021; Ehde et al., 2021; Xiang et al., 2021; Uhr and Mateen, 2021). Therefore, informing the patients about vaccine safety sounds necessary. The treating physicians should give information about the long-term consequences of COVID-19 to the concerned patients.

The research showed that vaccinated patients were substantially less worried about COVID-19, and as a result, 14.0% of vaccinated patients (193/1377) lowered their compliance with public health norms after immunization. This reduction may explain why 137 of 1266 patients who were completely vaccinated (10.9%) experienced COVID-19 infection after their second dose. WHO mentioned COVID-19 vaccination does not provide 100% protection. However, it is more effective against serious illness and fatalities (2022c). Especially with the emergence of omicron, a new variant of COVID-19 that spread much faster (2022d), CDC announced the importance of wearing a mask in public, vaccination, and boosters (2022e).

The most important limitation of the current study lies in the fact that vaccine-hesitant patients might not feel like participating in this web-based survey. It may promote to the bias of lower rate of vaccine-hesitancy in this study compared to other countries.

5. Conclusion

It is critical to comprehend the causes and essential aspects that contribute to vaccine rejection. Our findings in this study identified some at-risk groups (younger adults, those with less education, those who are unemployed, those with a negative flu vaccination history, those who have never had an episode of COVID-19 infection, those who are less concerned about COVID-19 infection, and those who expect not to become infected following vaccination). These patients' doctors should persuade them to obtain immunizations. Neurologists should inform vaccine-hesitant MS patients about COVID-19 long-term consequences and highlight how common vaccination was to eradicate some previous pandemics. They can also mention some studies indicated no significant difference in the rates of COVID-19 vaccine side effects informed among those with neuroinflammatory diseases and control groups (Epstein et al., 2021).

Additional appropriate information about the vaccine safety, potential self-limited vaccine side effects, how it works to defend against severe illness is also required. Advertising text or voice message reminders may be influential.

CRediT authorship contribution statement

Naghmeh Abbasi: Data curation, Formal analysis, Investigation, Writing – original draft, Writing – review & editing. **Fereshteh Ghadiri:** Methodology, Data curation, Formal analysis, Investigation, Writing – original draft, Writing – review & editing. **Abdorreza Naser Moghadasi:** Data curation, Investigation, Writing – review & editing. **Amirreza Azimi:** Data curation, Investigation, Validation. **Samira Navardi:** Data curation, Investigation, Validation. **Hora Heidari:** Data curation, Investigation, Validation. **Maryam Karaminia:** Data curation, Investigation, Validation. **Mohammad Ali Sahraian:** Conceptualization, Project administration, Resources, Supervision, Validation, Writing – review & editing.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.msard.2022.103723.

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