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Original Article

Evaluation of willingness to obtain of Covid 19 vaccine in patients with multiple sclerosis

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Abstract: Introduction: Assessing vaccine willingness and understanding sources of vaccine hesitancy in individuals with multiple sclerosis (MS) helps healthcare providers approach patients more effectively while respecting their autonomy to encourage coronavirus disease 2019 (COVID-19) vaccination. Materials and Methods: A descriptive-analytical cross-sectional study using a researcher-made checklist was conducted on MS patients referred to Neshat Clinic of Hamadan during the years 2020-2021. The checklist contained questions about demographic information, MS phenotype, duration of illness, expanded disability status scale (EDSS) score, and COVID-19 vaccination status. The expanded disability status scale (EDSS) is the most commonly used instrument for measuring disability in patients with multiple sclerosis (MS). The EDSS scale ranges from 0 to 10 in increments of 0.5 units, denoting advanced points of disability. Results: Based on the results, 20 individuals (10%) were in the vaccine non-acceptance group, while 181 individuals (90%) were in the vaccine acceptance group. A significant number of relapsing and remitting (RR) type MS patients (90.7%) and all primary progressive (PP) type MS patients (100%) accepted the vaccine. In comparison, vaccine non-acceptance in the secondary progressive (SP) group was relatively higher (20.7%) compared to other types of MS, and this difference was significant ($P < 0.05$). Additionally, there was a statistically significant relationship between the history of COVID-19 and vaccine acceptance ($P < 0.05$). Conclusion: The study results demonstrated a high rate of COVID-19 vaccine acceptance among MS patients. MS phenotype, previous infection experiences, and other influences allow for COVID-19 vaccine acceptance among MS patients. This information can improve health programs and communication strategies for COVID-19 and future possible infectious disease vaccination in individuals with MS.

Keywords: Vaccination, vaccine acceptance, coronavirus disease 2019, multiple sclerosis

Introduction

One of the main and most important global strategies to control the coronavirus epidemic is vaccination which is currently the most effective way to control infectious diseases, especially those at high-risk patients. In addition to providing health and reducing mortality, vaccination leads to a reduction of medical costs, consumption of drugs, and economic problems. Immunization programs are successful only when there is a high level of acceptance and coverage in these programs [1, 2]. To achieve this, the acceptance of the coronavirus disease 2019 (COVID-19) vaccine and the confidence to vaccinate people are critical [3]. In general, the acceptance and demand for vaccines in different societies have a complex nature, which can be different depending on the time, place, and behavioral beliefs of the members of the society. The results of the studies indicate that the people of the society may avoid the vaccination recommended by the health system due to the prevailing misconceptions and lack of belief in the effectiveness and trust of the vaccine [4]. People with multiple sclerosis (MS) may be especially concerned about the effects of the vaccine because of the nature of the immune system of those with MS and the modulating treatment of this disease. Some studies report weak side effects post-vaccination in MS patients [5]. A meta-analysis by Stefanou in 2023 found MS relapses in 1.9% of MS patients after SARS-CoV-2 vaccines [6]. Also, a prospective, multi-center cohort study in 2023 reported local side effects and flu-like symptoms in

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19.2% of vaccinated MS patients following vaccination [7]. Moreover, it has been reported that upper respiratory tract infections can double the risk of recurrence [8], and infection-related relapses can be more neurologically damaging [9]. Therefore, measures to prevent infection are essential for people with MS.

Studies have investigated the public's opinion about the vaccination program before the vaccine's introduction [10]. Therefore, assessing vaccine willingness and understanding the sources of vaccine hesitancy in people with MS will help providers more effectively approach patients to encourage COVID-19 vaccination while respecting patient autonomy. The main objective of our study was to evaluate the willingness to receive the COVID-19 vaccine among MS patients and investigate the possible association with demographic, clinical, and psychosocial factors.

Methods

Study design and patients

A cross-sectional study was carried out on 201 patients with multiple sclerosis (MS). To conduct this study, a checklist made by a researcher was used to collect information on patients with multiple sclerosis who were referred to the Neshat Clinic in Hamadan City, Iran, and had a registered case related to the disease before the period of 2020-2021. This checklist contains questions about demographic information (age, gender, marital status, education level, etc.), disease status (type of MS; relapsing-remitting or progressive, etc.), duration of MS disease from first symptom, expanded disability status scale (EDSS), type of MS medication, and patient's COVID-19 vaccination status. To calculate the sample size, according to Serrazina et al.'s study, 80.9% of patients were willing to receive the COVID-19 vaccine [11]. Therefore, taking into account the Type 1 error level equal to 0.05 and the accuracy of the test equal to 0.08, a sample size of 140 people was obtained, and 201 samples were studied to reduce the error. This study was approval by the ethics committee of Hamadan University of Medical Sciences (IR.UMSHA.REC.1401.912).

Inclusion and exclusion criteria

Patients with MS symptoms with ages 18 or older whose illness were confirmed by a neurologist and who were willing to participate in this study. The exclusion criteria were the presence of other diseases and unwillingness to complete the questionnaire.

Qualitative demographic data collection in the studied groups (accepting the vaccine and not accepting the vaccine)

The demographic information (gender, marital status, education level), disease status (type of MS; relapsing-remitting or progressive), duration of MS disease from first symptom, the type of MS medication, and the patient's COVID-19 vaccination status were obtained from the questionnaire and medical records of the patients. The vaccination willingness was determined by those willing to receive the vaccine and the number of those who already recieved the COVID-19 vaccine.

Quantitative demographic data collection in the studied groups (accepting the vaccine and not accepting the vaccine)

Quantitative demographic information, including age and years of illness, was obtained from the patient's medical records. The scoring was based on the neurologist's diagnosis that was recorded in the patient's medical records. EDSS stages 1.0 to 4.5 were given to patients with MS who were able to walk without any support while those with stages of 5.0 to 9.5 were expressed with poor gait.

Data analysis

The demographic information was presented as a table to describe the data. Statistical analysis was performed by SPSS software version 22 using an independent t-test. The results were reported as mean ± standard deviation (SD), and $P < 0.05$ was considered statistically significant to analyze all data.

Results

Comparison of the qualitative demographic data between the studied groups (accepting the vaccine and not accepting the vaccine)

According to the results of this study, which was conducted on patients with MS, (10%) 20 patients did not receive any vaccine dose, (3%) 6 patients received one dose, (29.9%) 60 patients received two doses, and (57.2%) 115

Table 1. Comparison of the frequency of qualitative demographic variables between two groups (accepting the vaccine and not accepting the vaccine)

Variable		Frequency (%)			*p*-value
		Total	Vaccine accepting	Not accepting the vaccine	
Gender	Female	126 (62.7)	111 (88.1)	15 (11.9)	0.230
	Male	75 (37.3)	70 (93.3)	5 (6.7)	
Education Status	Below School	43 (21.4)	40 (39.0)	3 (7.0)	
	High School	101 (50.2)	93 (92.1)	8 (7.9)	0.217
	University degree	57 (28.4)	48 (84.2)	9 (15.8)	
Marital Status	Unmarried	53 (26.4)	44 (83.0)	9 (17.0)	0.046*
	Married	148 (73.6)	137 (92.6)	11 (7.4)	
MS Treatment Compliance	No	17 (8.5)	17 (100.0)	0 (0.0)	0.152
	Yes	184 (91.5)	164 (89.1)	20 (10.9)	
MS Phenotype	PP	21 (10.4)	21 (100.0)	0 (0.0)	
	RR	151 (75.1)	137 (90.7)	14 (9.3)	0.047*
	SP	29 (14.4)	23 (79.3)	6 (20.7)	
	0	98 (48.8)	81 (82.7)	17 (17.3)	
Coronavirus Frequency	1	79 (39.3)	76 (96.2)	3 (3.8)	
	2	17 (8.5)	17 (100.0)	0 (0.0)	0.007*
	3	7 (3.5)	7 (100.0)	0 (0.0)	

RR: relapsing and remitting type of MS patients, PP: primary progressive type of MS patients, SP: secondary progressive type of MS patients. *p<0.05.

people received three vaccine doses. Based on this data, it can be concluded that more than half of the subjects in the present study received all three vaccine doses. A large percentage of participants (39.3%) used Ritoximab, followed by InFB1 (16.4%), Fingolimod (12.9%), Natalizumab (9%), GA (9%), Teriflunomide (7%), Teczifuma (3%), Azathioprine (1.5%), respectively. In the following, we grouped the people who did not receive any dose of the vaccine and the people who received at least one dose of the vaccine as people who accepted the vaccine, then using the chi-square test, we compared qualitative demographic characteristics in these two groups. The results of this comparison are summarized in **Table 1**. In total (10%) 20 of the studied people were in the group of not accepting the vaccine and (90%) 181 were in the group of accepting the vaccine. According to the results of **Table 1**, 126 (62.7%) of the studied subjects were female, and only 75 (37.3%) were male. Most women (88.1%) and most men (93.3%) accepted the vaccine, and there was no significant difference between the two groups of men and women in terms of vaccine acceptance (*p*-value = 0.230). In general, a very large percentage of the studied subjects had continued treatment for MS (91.5%), and most of the people who had continued treatment (89.1%) had received the vaccine; that is, they had injected at least one of the three doses. In the present study, most people (75.1%) had MS-type RR. A vast number of people with MS type RR (90.7%) and also all people with MS type PP (100%) accepted the vaccine, but the non-acceptance of the vaccine in the SPMS group was relatively more than other types of MS (20.7%) which showedthis difference was statistically significant (*p*-value < 0.05). Almost half of the people (48.8%) were not infected with a coronavirus at all, (39.3%) were infected once, (8.5%) were infected twice, and (3.5%) were infected three times. However, 100% of people who have been infected with coronavirus two or three times accepted the vaccine, but (17.3%) of those who have never been infected did not. The relationship between the number of times of contracting coronavirus and acceptance of the vaccine is statistically significant was *p*-value = 0.007.

Comparison of the quantitative demographic data between the studied groups (accepting the vaccine and not accepting the vaccine)

In **Table 2**, the mean and standard deviation of the quantitative variables were presented sep-

Table 2. Comparison of quantitative demographic variables between two groups (accepting the vaccine and not accepting the vaccine)

Variables	Mean ± Standard Deviation (SD)			*p*-value
	Total	Vaccine accepting	Not accepting the vaccine	
Age	40.86 ± 9.807	40.78 ± 10.170	41.55 ± 5.643	0.741
Years of Illness	8.38 ± 6.194	8.50 ± 6.491	7.30 ± 1.838	0.411
EDSS	1.930 ± 2.007	1.892 ± 1.881	2.275 ± 2.957	0.420

EDSS: expanded disability scale score.

arately for acceptance/non-acceptance of the vaccine and were compared using the t-test. Based on the results of this table, the average age in the group that did not accept the vaccine was higher than the other group (41.55 ± 5.643). Still, this difference was not statistically significant (*p*-value = 0.741). Also, in the patients who accepted the vaccine, the average duration of the disease (8.50 ± 6.491) was longer than the other group, and this difference was also not significant (*p*-value = 0.411). In addition, the average scale of extensive disability in people who did not accept the vaccine (2.275 ± 2.957) was higher than the patients who accepted the vaccine.

In the current study, the variables related to the reason for not receiving the vaccine and receiving the vaccine after the recommendation had a high percentage of missing observations (87.1% missing for each of these two variables), which could have caused bias in the analyses. Therefore, these two variables were not analyzed.

Discussion

The study showed only 10% of patients had not received any dose of the COVID-19 vaccine which seems to be a low number. This is similar to a study conducted in the United States of America (USA), where the rate of reluctance to get vaccinated against COVID-19 in multiple sclerosis patients was 15.4% [12]. Also, a systematic review and meta-analysis in 2022 reported that more than 66% of MS patients were willing to get the vaccine against COVID-19 [13]. In a multicenter study by Nabavi et al. in Iran on 892 multiple sclerosis patients, the willingness to receive the Covid-19 vaccine in these patients was 86% [14]. Our study showed no significant relationship between vaccine acceptance rates in multiple sclerosis patients. However, in Hung et al.'s study, no significant relationship was observed between the status of patients and the rate of acceptance of the COVID-19 vaccine which is in line with the results of our study [16]. One of the reasons for not observing a significant relationship in our study is the small sample size, especially in connection with patients who did not accept the vaccine, which affected the power of the study and prevented the observation of a significant relationship. The difference in study methodology and the way of controlling confounding variables in different studies can also justify this difference in the results between studies. Our study showed no significant relationship between vaccine acceptance and non-acceptance rate in multiple sclerosis patients.

In our study, although the willingness to vaccination was higher in men, this difference was not statistically significant. However, in previous studies, males' willingness to get vaccinated was statistically significant than that of women [16, 17].

In line with the results of the present study, in the study of Xiang et al. in China, no significant relationship was observed between the age of patients and the degree of willingness to carry out the COVID-19 vaccination [15]. Also, similar to the result obtained in the study, in the multicenter study conducted in Iran by Nabavi et al., increasing the age of the patients and the duration of the disease did not have a significant effect on the acceptance of the vaccine in patients with multiple sclerosis [14]. Contrary to the results of our study, the study conducted by Serrazina et al. in Europe [11] and Uhr et al. in America [18], a significant relationship was observed between the age of patients and the willingness to carry out the COVID-19 vaccination. Also, according to the results from a study of the Poland adult population in 2021, the highest percentage of people who were unwilling to get the vaccine against COVID-19 were young people aged 18-34 because they were worried about its side effects [19]. While in a

study by Salimi et al in 2021, Marital status did not have a significant effect on the rate of vaccine acceptance, so that it was reported as 12.79% for singles and 84.76% for married people [20], in the present study, married people had a higher acceptance rate for the Covid-19 vaccination than single people.

In the current study, 100% of patients with the PP phenotype accepted the vaccine, significantly more than the RR and SPMS phenotypes. Individuals with different MS phenotypes may have different levels of disease severity and extent of damage to the nervous system. Individuals with more severe phenotypes may be more willing to accept the vaccine because they experience more injury and complications from the disease.

In the study by Ghadiri, which is in line with our results, EDSS had no significant impact on the studied groups [21].

Among the limitations of the current study was the small sample size in the discussion of vaccine non-acceptance, which reduces the determination between variables on vaccine acceptance. The impact of economic, social, and cultural factors has not been considered in this study, which can be considered another limitation of the study. In addition, three issues of confidence, complacency, and constraints are involved in vaccine hesitance [22]. However, Health believes that the most motivating factor for the COVID-19 vaccination in the general population is the medical doctor's recommendation [23].

Conclusion

In conclusion, the study results showed that the rate of acceptance of the COVID-19 vaccine in multiple sclerosis patients in Hamadan was high. Factors such as the type of MS phenotype, previous experiences of the disease, and the marital status of people with MS affect the acceptance of the COVID-19 vaccine in patients with multiple sclerosis. This information can help to improve health programs and inform about the vaccination of COVID-19 in people with MS.

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Disclosure of conflict of interest

None.

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