Vaccination Coverage in Patients with Idiopathic Inflammatory Central Nervous System Demyelinating Diseases at Siriraj hospital, a Single-Center Experience

Onpawee Sangsai[1], Tatchaporn Ongphichetmetha[1], Malinee Chunsangchan[1], Sasitorn Siritho[1,2*] and Jiraporn Jitprapaikulsan[1]

[1]Siriraj Neuroimmunology Center, Division of Neurology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, 10700, Thailand

[2]Bumrungrad International Hospital, Bangkok 10110, Thailand

Corresponding Author*
Sasitorn Siritho
Siriraj Neuroimmunology Center, Division of Neurology, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, 10700,
Thailand
Fax: (66) 2411-1103

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Abstract

Introduction: Individuals with Idiopathic Inflammatory Central Nervous System Demyelinating Diseases have an elevated risk for infection. Vaccination is key to reducing infection.

Objective: This study aimed to determine vaccination coverage, the adverse effects of vaccination, and general vaccination knowledge in the patients.

Methods: A single-center cross-sectional study in the Multiple Sclerosis Clinic at Siriraj Hospital, Thailand, was performed using the designed questionnaires.

Results: Of 100 participants, 90% were female, with a mean (SD) age of 46.2 (12.9). Overall, all received compulsory vaccine coverage. For optional vaccines, the coverage was lower-than-expected, with rates of 3%, 4%, and 3% for human papilloma virus, pneumococcal, and zoster vaccine, respectively. Only 28% of participants received the 2021/2022 seasonal influenza vaccine. The only factor associated with the uptake of the influenza vaccination was the participants' health coverage. By asking questions to evaluate general vaccination knowledge, two questions related to vaccination and immuno-suppressive agents received the highest percentage of 'not sure' responses.

Conclusion: Vaccination coverage was lower than expected among Thai CNS-IIDDs patients, both for optional and seasonal influenza vaccines. Vaccination in these groups of patients should be encouraged to prevent potential infections.

Keywords: Vaccination • Idiopathic inflammatory central nervous system • Demyelinating diseases • multiple sclerosis • Neuromyelitis optica spectrum disorder • NMOSD • MOGAD

Introduction

Idiopathic Inflammatory Central Nervous System Demyelinating Diseases (CNS-IIDDs) encompass Multiple Sclerosis (MS), Neuromyelitis Optica Spectrum Disorder (NMOSD), and Myelin Oligodendrocyte Glycoprotein Antibody Disease (MOGAD).

Treatment in CNS-IIDDs mainly relates to Immunosuppressive (ISs) or Disease-Modulating agents (DMDs) aiming at reducing neuroinflammation. On the other hand, those agents increase the risk of infection among patients [1]. The retrospective study reported the overall rate of infection in MS patients receiving infused, injectable, and oral medications of 37.3%, 36.8%, and 38.7%, respectively, with sinusitis, upper respiratory tract infection, and upper urinary tract infection being the leading infection causes [2]. A recent randomized control trial also showed an increased risk of infection, particularly lower respiratory tract infection and herpes virus infections, in MS patients taking fingolimod [3]. According to the retrospective cohort study, patients with MS were more likely to be hospitalized and die of influenza than individuals without MS [4]. Although immunization would be a key to reduce the infection rate in susceptible patients, it is overlooked and needs more attention.

Different countries vary in vaccine requirements for young healthy children, such as the Bacillus Calmette and Guerin (BCG) is a mandatory vaccine in Thailand. Also, most Asian countries, including Thailand, offer obligatory vaccination against Japanese Encephalitis. According to the Thai Expanded Program on Immunization (EPI), the compulsory vaccination includes BCG, hepatitis B, diphtheria-tetanus-pertussis; oral polio, MMR, Japanese Encephalitis (JE), HIB vaccine and optional vaccines are varicella, human papillomavirus, hepatitis A, pneumococcal, meningococcal, zoster, and influenza vaccine [5]. A recent systematic review and updated practice guideline on immunization in MS recommend that patients with MS follow all local vaccine standards and receive the influenza vaccination annually, and clinicians should counsel MS patients about treatment-specific vaccination guidance according to prescribing information [6]. Likewise, The Royal College of Physicians of Thailand (RCPT) recommends annual influenza vaccine uptake, particularly for patients receiving ISs [5]. In the past decade, the Thai FDA has approved more DMD/ISs to use in CNS-IIDDs, and those agents need particular pre-vaccination guidelines regarding specific drug use. Few studies have evaluated immunization in patients with MS, usually focused on the influenza vaccine. In Canada, fewer than 40% of MS patients received the influenza vaccine in 2015 [7]. In North America, 74.1% of study participants received the seasonal influenza vaccine. The compulsory and optional vaccine uptake was also lower than desired in the MS population compared with public health recommended targets. They also assessed patients' attitudes about vaccination and reported misconceptions about immunization safety in the context of MS [8]. In Italy, the study sharing a real-world, single-center experience was conducted. They reported that before new therapy started, 87.1% of the MS patients completed immunization, including meningococcal, pneumococcal conjugated, and haemophilus influenza B vaccines [9]. Since 2019, the COVID-19 pandemic has drawn people's attention to the importance of vaccination. Several studies about COVID-19 vaccination in MS patients have emerged. Achiron et al. proved the safety of the COVID-19 BNT162b2 vaccine for MS patients. They found no significant increased risk of relapse activity after vaccination [10]. For NMOSD and MOGAD, fewer studies on immunization currently exist. A study from China suggested that it was safe to provide NMOSD patients

receiving ISs/DMD inactivated or viral protein vaccines. In contrast, all live vaccines were prohibited in patients receiving ISs/DMD [11].

In Thailand, the vaccination uptake in patients with CNS-IIDDs has not been reported. We aimed to determine lifetime coverage of compulsory and optional vaccines, including seasonal influenza, COVID-19 vaccine, adverse effects from vaccination, and general vaccination knowledge in CNS-IIDDs patients at our center.

Materials and Methods

Using our questionnaires, we conducted a single-center, retrospective, cross-sectional study in the Multiple Sclerosis and Related Disorders Clinic at Siriraj Hospital, a university-based hospital in Thailand, in May 2022.

Participants

We consecutively recruited patients who were routinely follow-up at the Multiple Sclerosis and Related Clinic at Siriraj Hospital. The experienced coordinator asked patients to self-answer the designed questionnaire. They were included if they

- were at least 18 years of age,
- fulfilled diagnostic criteria for each specific CNS-IDDS regarding MS [12], NMOSD [13], MOGAD [14], acute transverse myelitis [15], or idiopathic or recurrent optic neuritis including Chronic Relapsing Inflammatory Optic Neuropathy (CRION) [16].

They were excluded if they refused to take the questionnaire or could not provide information about vaccination. The study's protocol was approved by the Siriraj Institutional Review Board (200/2564). All patients had written informed consent.

Questionnaires

We created a survey questionnaire containing 6 main categories: basic information, lifetime vaccination uptake, influenza vaccination uptake, previous side effects from vaccination, general knowledge about vaccination, and COVID-19 vaccination. Most questions were closed-ended questions with yes/no questions or multiple choice. All patients were asked by the same experienced coordinator to self-answer the designed questionnaire. For those with visual impairment, the coordinator also helped them mark the answer on the questionnaire. The questionnaire took approximately 3 minutes-7 minutes to complete.

The questionnaire included age, gender, education level, region of residence, average monthly income, health coverage, and underlying diseases or previous health problems. We categorized age group as <35, 35-50, 50-65, or >65 years old. Education level was categorized as below junior high school or junior high school and above. We classified the region of residence into Bangkok metropolis and vicinity and others. Average monthly income was reported as <20,000 baht, 20,000 baht-50,000 baht, and >50,000 baht. We categorized health coverage as Universal Coverage (UC), Social Security (SS), Civil Servant Medical Benefits (CSMB), State enterprise, or self-pay. The underlying disease was recorded as "yes" with the disease name or "no." For detail about the participants' diseases, we re-viewed each participant's diagnosis and current treatment from our hospital's electronic medical record.

Participants reported whether they had ever received vaccines for any of the following: hepatitis A, hepatitis B, pneumococcal, varicella, zoster, Measles-Mumps-Rubella (MMR), tetanus, rabies, HIB, Human Papilloma (HPV), meningococcal, Tdap vaccine, both inside and outside Siriraj hospital, where responses were yes or no. For the influenza vaccine, we mainly focused on the most recent season 2021/2022 influenza vaccine, to assess current behaviors. To evaluate recent trends in influenza vaccine coverage, we needed data on influenza vaccination from 2016 to 2020. We also obtained information about previous side effects of vaccination. Understanding of vaccination was tested using the seven questions we designed to evaluate general knowledge about vaccination in the participants. The responses were yes, no, or not sure. For the COVID-19 vaccine, participants reported whether they had received any COVID-19 vaccine, which platforms of vaccine and their possible side effects. For those who had not received the COVID-19 vaccine, we asked if they wished to get vaccinated and their opinions about the COVID-19 vaccine.

Statistical analysis

We performed statistical analysis on PASW Statistics for Windows version 18.0 (SPSS Inc., Chicago, IL, USA). Mean and standard deviation was reported for normally distributed continuous variables and median and interquartile range for skewed data. Categorical variables were reported as percentages. We also evaluated factors associated with influenza vaccination uptake using Pearson's chi-squared statistics. The evaluated factors included gender, age group, education level, region of residence, average monthly income, and health coverage. P-value<0.05 indicated statistical significance.

Results

Participants characteristics

One hundred participants were recruited, with 90% being female. The mean age of 46 (SD 18 years-69 years). The third quarter was junior high school and above. Most of the participants lived in Bangkok's metropolis (67%). Up to 74% had an average monthly income of less than 20,000 baht. Health coverage was SS (30%), UC (28%), State enterprise (17%), CSMB (10%), respectively. Only 15% of the participants were self-pay.

The most recruited participants were NMOSD (56%), followed by MS (30%), MOGAD (6%), idiopathic or relapsed TM (6%), and idiopathic or recurrent ON (2%), respectively. All received at least one agent of either ISs or DMD. 69% of the participants had concomitant diseases (Table 1).

Table. 1 Clinical and demographic characteristics of participants.

Parameters	Participants (n = 100)
Age at the time of survey (years), mean (SD)	46.2 (12.9)
Female, n	90
Diagnosis, n	
Neuromyelitis optica spectrum disorder	56
Multiple sclerosis	30
Myelin oligodendrocyte glycoprotein antibody disease	6
Idiopathic or relapsed transverse myelitis	6
Idiopathic or recurrent optic neuritis	2
Education level, n	
Below junior high school	25
Junior high school and above	75
Region of residence, n	
Bangkok metropolis and vicinity	67
Others	33
Average monthly income (baht), n	
< 20,000	74
20,000-50,000	20
> 50,000	6
Health coverage, n	
Universal Coverage (UC)	28
Social security (SS)	30
Civil Servant Medical Benefits (CSMB)	10
State Enterprise	17
Self-pay	1
Underlying disease, n	
Yes	31
No	69
Immunosuppressive or immunomodulatory agents status, n	100

Vaccination coverage

All compulsory vaccine coverage, including hepatitis B, MMR, tetanus, and haemophilus influenzae B, were 100%. For optional vaccines, the most commonly received were rabies (12%), followed by varicella (5%), pneumococcal (4%), HPV (3%), zoster (3%), and Tdap (3%). None received the meningococcal and hepatitis A vaccines (Figure 1).

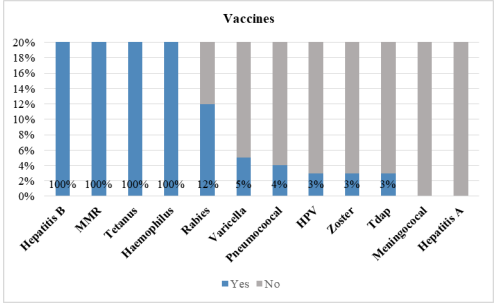

Figure 1. Prior compulsory and optional vaccines exposure in Thai patients with demyelinating diseases.

The influenza vaccine coverage increased after 2017, but after the pandemic of COVID-19, the influenza vaccination seemed to drop slightly (Figure 2a). All influenza vaccine exposure was less than a third in the past 5 years. Only 28% received the seasonal influenza vaccine during 2021-2022. Of those, 36.4% were older than 65 years, 25.9% were 50 years-65 years of age, 28.9% were 35 years-50 years, and 23.5% were <35 years of age (Figure 2b).

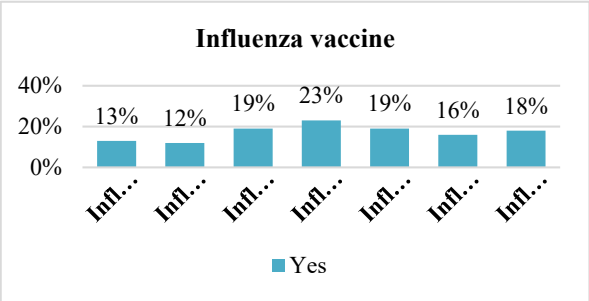

Figure 2a. Frequency of the influenza vaccine coverage during 2016-2022.

Nearly a third (27%) of the participants experienced vaccination-related side effects, including local site injection reaction (22%), low-grade fever (9%), myalgia (4%), and chills (3%). Only 1% of the participant had a severe allergic reaction. Using Pearson's chi-squared statistics, the participants' health coverage was the only factor related to influenza vaccination coverage.

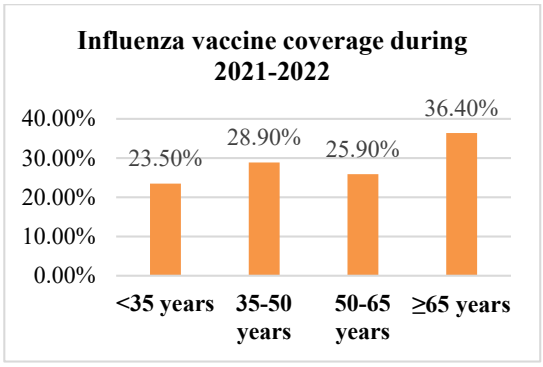

Figure 2b. Frequency of the 2021-2022 influenza vaccine coverage stratified by age.

General vaccination knowledge

We also asked questions regarding general knowledge about vaccination. The response rates were true, false, and not sure. More than 80% of the participants know that there are live-attenuated and inactivated vaccines, and vaccination can reduce the severity of pliable infectious diseases accordingly. Also, only a third convinces that vaccination could prevent infectious diseases. 56% know that the influenza vaccine should be vaccinated annually. Surprisingly, most do not seem aware that a live-attenuated vaccine could not be given to patients receiving an ISs, and ISs could reduce the effectiveness of vaccines (Table 2).

Table 2. General vaccination knowledge and responses.

Vaccination could reduce the severity of vaccine-preventable infection	Participants (n = 100)
True	89
False	3
Not sure	8
There are a live-attenuated vaccine and an inactivated vaccine	
True	84
False	7
Not sure	9
The live-attenuated vaccine could not be given to patients receiving an immunosuppressive drug	
True	40
False	19
Not sure	41
Immunosuppressants could reduce the effectiveness of vaccines	
True	40
False	19
Not sure	41
The influenza vaccine should be given annually	
True	56
False	19
Not sure	25
The influenza vaccine can cause flu illness	
True	38
False	39
Not sure	23

COVID-19 Vaccination

91% received the COVID-19 vaccination. Among the five COVID-19 vaccine platforms; CoronaVac (Sinovac), ChAdOx1 nCoV-19 (AstraZeneca), BBIBP-CorV (Sinopharm), BNT162b2 nCoV-19 (Pfizer), and mRNA-1273 SARS-CoV-2 (Moderna), the most commonly received was ChAdOx1 nCoV-19 (54%), followed by BNT162b2 nCoV-19 (39%), CoronaVac (25%), BBIBP-CorV (17%), and mRNA-1273 SARS-CoV-2 (13%). Of the remaining 9 percent who did not get vaccinated, of whom 55% did not want to get vaccinated.

Among all the participants receiving the COVID-19 vaccine, a leading side effect was local site injection reactions (60.4%), followed by flu-like symptoms. In general, the COVID-19 side effects did not last longer than a few days after injection. We will report the detail of COVID-vaccination in CNS-IIDDs elsewhere separately.

Discussion

This cross-sectional study of vaccination coverage in CNS-IIDDs in a single center showed that the compulsory vaccine coverage was 100%; however, the frequency of the optional vaccine was lower than expected, mostly less than 30%. The seasonal influenza vaccination has persisted low in the past five years, especially during the pandemic of COVID-19. The achievement (91%) is reached for the mandatory COVID-19 vaccine campaign in the country during the pandemic of COVID-19.

Our study showed that all participants received compulsory vaccines according to Thai EPI guidelines, including MMR, HIB, and hepatitis B. The coverage is much more than 74.1%, 88.5%, and 32.3% of those reported in North America, respectively [8]. Our participant, whose mean age was 46.2 years, was born after the WHO EPI launching, while the participants in the North American study, whose mean age was 61.8 years, were born before the recommendation came out. This reason possibly resulted in an increasing vaccination after establishing the WHO EPI in 1974 [17].
For optional vaccines, the coverage differs by study region. The North American study reported 61.2% of pneumococcal and 41.2% of zoster vaccination coverage [8], while those in the Italian study were 86.7%, respectively [9]. Our study showed surprisingly lower-than-expected rates of 3%, 4%, and 3% for HPV, pneumococcal, and zoster vaccination coverage, respectively.

We then focus on Varicella-Zoster Virus (VZV) vaccination. RCPT recommended completing the varicella vaccination course before starting ISs if the screening VZV-IgG antibody is negative. Also, the Thai Clinical Practice Guidelines for MS and NMOSD mandate screening VZV serostatus before initiating any DMTs or ISs [18], and it is re-quired to have vaccination with proven immunity before starting any DMTs for MS, such as fingolimod, cladribine, alemtuzumab, etc. [19].

The low immunization in this optional vaccination coverage might be explained by the negligence of both participants and medical personnel and by the collateral effect of the COVID-19 pandemic. The participants' economic status might also affect their decision for immunization, especially for high-cost vaccine such as varicella and zoster vaccine. There should be a high alarm for underrate vaccination, especially in the specialist clinic susceptible to varicella infection.

The North American study revealed that the 2019/2020 seasonal influenza vaccination coverage ranged from 59.1% among MS patients aged 18-24 to 79.9% for those aged older than 65 years, and factors including postsecondary education and higher household income were associated with the influenza vaccination [8]. Compared with our Thai study, only 28% of participants received the 2021/2022 seasonal Influenza vaccine. The only

factor associated with influenza vaccination was a type of health coverage, CSMBs. Although the influenza vaccination rate was higher than in the previous study in 2012, which was 15.2% among the population with chronic diseases [20], it was far from expected. However, we could see an increasing influenza vaccination rate from 2016 to 2019, then a drop-down during 2019 and 2020, perhaps delayed or omitted vaccination during the COVID- 19 outbreak. Healthcare providers and policymakers should focus on the low seasonal influenza vaccination rate in Thailand. Also, the annual influenza vaccination campaign and education about the efficacy of vaccination, in particular patients in need, should be done.

Similar to the North American study, our study showed the most common adverse reaction after vaccination was an injection site reaction with pain, followed by fever 22% vs. 9% [8]. For the SARS-CoV-2 vaccination, the vaccination rate was 91% up until May 2022. The viral vector-based platform, ChAdOx1 nCoV-19, was our participants' most widely used vaccine (54%), followed by BNT162b2 nCoV-19 (39%), similar to a previous Thai study in 2021 [21]. Of those, 60.4% developed pain at the injection site, followed by fever and headache, but none showed a severe adverse reaction. Among the 9% who did not receive COVID-19 vaccination, 55.5% did not get vaccinated because of doubtfulness in vaccine efficacy.

Our study was the first study on vaccination among Thai CNS demyelinating diseases. Although, there were several limitations. Firstly, this study had a small sample size. Secondly, Thai has no personnel vaccination book; all vaccination documents are retained where the vaccination occurred, so we collected the information by asking the participants. Recall bias may appear in this process.

Conclusions

In summary, the present study showed that vaccination was lower than expected among patients with CNS-IIDDs, both for optional and seasonal influenza vaccines. Without vaccination coverage, patients have an increased risk for possibly preventable infections. Vaccination in these groups of patients should be encouraged. Medical personnel may play a significant role in guiding patients about the importance of immunization and education about each specific vaccination needed in different conditions.

Reference

1. Wijnands, José Maria Andreas, et al. "Disease-modifying drugs for multiple sclerosis and infection risk: a cohort study." *J. Neurol. Neurosurg. Psychiatry* 89.10 (2018): 1050-1056.
2. Swart, Elizabeth CS, et al. "Infection incidence and management in multiple sclerosis patients after initiating disease-modifying therapy." *Mult. Scler. Relat. Disord.* 56 (2021): 103285.
3. Zhao, Zhao, et al. "Incidence and risk of infection associated with fingolimod in patients with multiple sclerosis: a systematic review and meta-analysis of 8,448 patients from 12 randomized controlled trials." *Front. Immunol.* 12 (2021): 611711.
4. Montgomery, Scott, J. Hillert, and S. Bahmanyar. "Hospital admission due to infections in multiple sclerosis patients." *Eur. j. neurol.* 20.8 (2013): 1153-1160.
5. The Royal College of Physicians of Thailand. "Recommended adult and elderly immunization schedule". 2011
6. Farez, Mauricio F., et al. "Practice guideline update summary: Vaccine-preventable infections and immunization in multiple sclerosis: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology." *Neurology* 93.13 (2019): 584-594.
7. Marrie, Ruth Ann, et al. "Uptake of influenza vaccination among persons with inflammatory bowel disease, multiple sclerosis or rheumatoid arthritis: a population-based matched cohort study." *Can. Med. Assoc. Open Access J.* 9.2 (2021): E510-E521.
8. Marrie, Ruth Ann, et al. "Uptake and attitudes about immunizations in people with multiple sclerosis." *Neurol.: Clin. Pract.* 11.4 (2021): 327-334.
9. Sbragia, Elvira, et al. "Vaccinations in patients with multiple sclerosis: a real-world, single-center experience." Human Vaccines & Immunotherapeutics 18.6 (2022): 2099171.
10. Achiron, Anat, et al. "COVID-19 vaccination in patients with multiple sclerosis: what we have learnt by February 2021." *Mult. Scler. J.* (2021): 135245852110034.
11. Cai, Haobing, et al. "Vaccination in neuromyelitis optica spectrum disorders: Friend or enemy?." Mult. Scler. Relat. Disord. 58 (2022): 103394.
12. Thompson, Alan J., et al. "Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria." *Lancet Neurol.* 17.2 (2018): 162-173.
13. Wingerchuk, Dean M., et al. "International consensus diagnostic criteria for neuromyelitis optica spectrum disorders." *Neurology* 85.2 (2015): 177-189.
14. López-Chiriboga, A. Sebastian, et al. "Association of MOG-IgG serostatus with relapse after acute disseminated encephalomyelitis and proposed diagnostic criteria for MOG-IgG–associated disorders." *JAMA neurol.* 75.11 (2018): 1355-1363.
15. Transverse Myelitis Consortium Working Group*. "Proposed diagnostic criteria and nosology of acute transverse myelitis." Neurology 59.4 (2002): 499-505.
16. Kidd, D., et al. "Chronic relapsing inflammatory optic neuropathy (CRION)." Brain 126.2 (2003): 276-284.
17. Keja, Ko, et al. "Expanded programme on immunization." *World health stat. q., Rapp. trimest. stat. sanit. mond.* 41.2 (1988): 59-63.
18. Brownlee, Wallace, et al. "Treating multiple sclerosis and neuromyelitis optica spectrum disorder during the COVID-19 pandemic." *Neurology* (2020).
19. Manouchehrinia, Ali, et al. "Prevalence of a history of prior varicella/herpes zoster infection in multiple sclerosis." *J. neurovirology* 23 (2017): 839-844.
20. Owusu, Jocelynn T., et al. "Seasonal influenza vaccine coverage among high-risk populations in Thailand, 2010–2012." *Vaccine* 33.5 (2015): 742-747.
21. Sirikalyanpaiboon, May, et al. "COVID-19 vaccine acceptance, hesitancy, and determinants among physicians in a university-based teaching hospital in Thailand." *BMC infect. dis. 21* (2021): 1-12.

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