Original Research Article

COVID-19 Vaccine Hesitancy in Systemic Lupus Erythematosus – Experience From a Tertiary Care Rheumatology Centre in South India

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International Archives of Integrated Medicine, Vol. 9, Issue 6, June, 2022.
Available online at http://iaimjournal.com/
ISSN: 2394-0026 (P) **ISSN: 2394-0034 (O)**
Received on: 25-6-2022 **Accepted on:** 30-6-2022
Source of support: Nil **Conflict of interest:** None declared.

How to cite this article: Sreenath S, Nagendran R, Vinoth S, P S Arul Rajamurugan, T N Tamilselvam. COVID-19 Vaccine Hesitancy in Systemic Lupus Erythematosus – Experience From a Tertiary Care Rheumatology Centre in South India. IAIM, 2022; 9(6): 12-20.

Abstract

Background: Patients with rheumatological diseases like SLE are at an increased risk of COVID-19 infection and hence should be prioritized for vaccination. Vaccine hesitancy is a major hindrance in achieving herd immunity against COVID-19. In this study, we aim to determine the COVID-19 vaccination rate in our SLE population and the factors associated with vaccine hesitancy.

Materials and methods: We conducted an interview-based cross-sectional study on patients >18 years attending the lupus clinic of our Institute. Questionnaires were used to collect demographic details, disease status, vaccination-related data, and information regarding attitude and beliefs about COVID-19 vaccination. Descriptive statistics were used for analysis.

Results: Of the 584 patients studied, the vaccination rate was 67%, and there was vaccine hesitancy of 21%, and vaccine resistance of 12%. Non-vaccination was strongly associated with older age, rural living, unemployment, and in patients with anti-phospholipid antibodies, prior stroke, prior COVID-19 infection, and those who were currently using corticosteroids. The major reasons for vaccine hesitancy were fear of worsening lupus, fear of side effects, and religious reasons. We also came to know about various misconceptions regarding COVID vaccination prevalent among SLE patients under our follow-up causing them to opt against the vaccine. The vaccine-hesitant group may rethink

their decision if there is proper reassurance and guidance from their treating physician or if more friends and family members start accepting vaccines.

Conclusions: Vaccine hesitancy is a major problem in our group of SLE patients keeping the vaccination rates low. The reasons for vaccine hesitancy must be looked into and addressed to improve the vaccination rates and thereby achieve herd immunity. Proper guidance from the treating rheumatologist was reported as the major factor which may encourage the vaccine-hesitant population to opt in for the vaccination.

Key words

Vaccination, COVID-19, Systemic Lupus Erythematosus, Vaccine hesitancy.

Introduction

Patients with Systemic Autoimmune Rheumatological Diseases (SARD) like Systemic Lupus Erythematosus (SLE) are likely to be at increased risk for SARS–CoV-2 infection, hospitalization, and worse outcomes [1]. Because of this increased risk, international rheumatology associations do recommend that patients with rheumatological diseases should be prioritized for vaccination before the non-prioritized general population of similar age and sex [2]. Other than hypersensitivity to vaccine components, there are no known additional contraindications to COVID-19 vaccination for AIIRD patients.

Our centre is a tertiary care Apex institute for Rheumatology, catering to patients all across Tamil Nadu and other southern states of India. We conduct Lupus Specialty clinic every Saturday to focus on and address the needs and impart special care to SLE patients who usually follow up once every month. A very extensive campaign for COVID-19 vaccination has been going on in India ever since COVID-19 vaccines – Covaxin (BBV152) [3], Covishield [4] followed by Sputnik V became available. During our regular lupus specialty clinic, we were surprised to note that a large number of SLE patients under our follow-up are still unvaccinated. As described by WHO, vaccine hesitancy is a "delay in acceptance or refusal of safe vaccines despite availability of vaccine services" [5]. Vaccine hesitancy is one important factor that might drastically slow down the race to achieving herd immunity, especially among our patient population [6]. This study aimed to look at that problem in detail and assess the factors which determine vaccine hesitancy and vaccine resistance in our group of SLE patients. We aimed at identifying factors that determine the decision regarding vaccination and the general attitude/perceptions/beliefs towards it.

Materials and methods

This was an interview-based cross-sectional study conducted among patients with Systemic Lupus Erythematosus who were being followed up in the Lupus Specialty Clinic of the Institute of Rheumatology, Madras Medical College, Chennai from February 2022 to May 2022. Ethical committee clearance was obtained from the institution's ethical committee. No funding was obtained for the study. This study included consecutive patients above 18 years of age who attended the Lupus Specialty Clinic and were under regular follow-up with good compliance. All patients were given detailed information about the purpose, the nature of the data collected, and how the data will be used for academic or research purposes. Informed written consent was obtained from all participants.

The questionnaire included questions intended to collect demographic details, information about the disease status, current medications, and vaccination status. In unvaccinated patients, questions were asked about the possible reasons for not receiving vaccines, the likelihood of them receiving vaccines in the future, and the factors that determine their decisions regarding vaccination. The Questionnaire was administered in vernacular language by a resident doctor who

is fluent in the language and their responses were recorded. The data about duration of illness, organ systems involved, comorbidities, current medications, and history of previous covid infection were collected from the patients themselves and by going through the treatment records and follow-up book.

In Tamil Nadu, only three COVID-19 vaccines were widely available for the general population at the time of the study – ChAdOx1 nCoV-19 (Covishield), BBV152 (COVAXIN), and Sputnik V. Patients who have received at least one dose of any of these vaccines were considered as vaccinated. Among the unvaccinated, when they were asked whether their vaccine decision is likely to change, those who answered 'definitely not' were considered to be vaccine-resistant. Those who answered 'may change' or 'likely to change' were considered vaccine-hesitant. Among those who were not vaccinated, questions were asked to find out the likely reasons or factors which may cause them to change their mind if at all, in the future.

We used descriptive statistics to study the data. For the demonstration of the data, we used Mean values with standard deviations (SDs) (mean ± SD) or median with range. Categorical variables were presented as counts and percentages. To analyse the significance, the Chi-square test and Fisher's exact test were used. A value of $P < 0.05$ was taken as significant. For statistical analysis, we used IBM SPSS statistics software version 22.0 (Armonk, NY: IBM Corp.)

Results

A total of 584 patients who were willing to participate in the study were included. Among them, 392 were vaccinated (67.12%) with at least one dose of the three available vaccines in Tamil Nadu. 192 were unvaccinated (32.87%). The demographic details of both vaccinated and unvaccinated groups are shown in **Table - 1**. Those who were unvaccinated were of slightly older age (38.9 ± 9.36 years) than those who were vaccinated (32.5 ± 9.85 years), were mostly from rural areas of Tamil Nadu and were unemployed or not working at present due to illness. There was no statistically significant difference between both groups in terms of gender, educational status, and socioeconomic class. P-value <0.05 were considered significant.

The systemic lupus erythematosus disease duration, organ involvement, other co-morbidities, prior covid infection, and medication details of the study population are detailed in **Table - 2**. On analysis, the decision to not get vaccinated was more in those with antiphospholipid antibodies (p-value <0.001), lung disease (p-value <0.001), stroke (p-value 0.01), psychiatric illness (p-value 0.04) and in those taking corticosteroids (p-value 0.003), mycophenolate mofetil (p-value 0.002) and aspirin (p-value <0.001). The decision of not getting vaccinated was found to be more in those with a history of COVID-19 infection.

The unvaccinated group was asked whether their decision regarding vaccines is likely to change. Those who answered 'definitely not' were considered to be Vaccine Resistant. Those who answered 'may change' or 'likely to change' were considered Vaccine Hesitant. Of the total study population 12% were found to be vaccine-resistant and 21% to be vaccine-hesitant (**Figure - 1**).

Those who were unvaccinated were asked questions to know the possible reasons that would have made them move towards a decision to not get vaccinated. 46% of the unvaccinated were afraid that their disease will worsen after vaccination and 36% were afraid of the possible side effects. About 28% of them had strong religious/spiritual reasons for not getting vaccinated or had family/friends advising against vaccination. Other reasons mentioned by the study population are illustrated in (**Figure - 2**).

Among the vaccine-hesitant group, we asked them what could be the possible factors that might make them change their decision and opt for getting vaccinated (**Figure - 3**). More than

52% reported that reassurance from their treating doctor will make them rethink their decision. 35% reported that they may also feel safer in getting vaccinated once more family members and friends take vaccines and share their experiences. 26% said that they may feel confident and are likely to take the vaccines soon after their current disease state improves.

Table - 1: Demographic characteristics of the study population according to their vaccination status.

	Vaccinated (%) N=392	**Unvaccinated (%) N=192**	**P value**
Gender			0.651
Male	14 (3.57)	8 (4.17)	
Female	378 (96.42)	184 (95.83)	
Age (years)	32.5 ± 9.85	38.9 ± 9.36	0.003
Area Living In			<0.001
Rural	131 (33.42)	151 (78.65)	
Urban	261 (66.58)	41 (21.35)	
Education			0.41
No formal education	14 (3.57)	14 (7.29)	
Primary School	74 (18.88)	82 (42.71)	
High School/ Higher Secondary	148 (37.75)	40 (20.83)	
Graduate	102 (26.02)	30 (15.62)	
Postgraduate	54 (19.78)	26 (13.54)	
Employment			0.031
Employed	107 (27.29)	21 (10.94)	
Not employed	145 (36.99)	69 (35.94)	
Student	72 (18.37)	8 (4.17)	
Retired	26 (6.63)	20 (10.42)	
Not working at present due to illness	42 (10.71)	74 (38.54)	
Socio-Economic Class			0.663
Upper class	16 (4.08)	12 (6.25)	
Upper Middle Class	101 (25.76)	44 (22.92)	
Middle Class	142 (36.22)	70 (36.46)	
Lower Middle Class	116 (29.59)	38 (19.79)	
Lower Class	17 (4.34)	28 (14.58)	

Figure - 1: Vaccine resistance and vaccine hesitance among the study population.

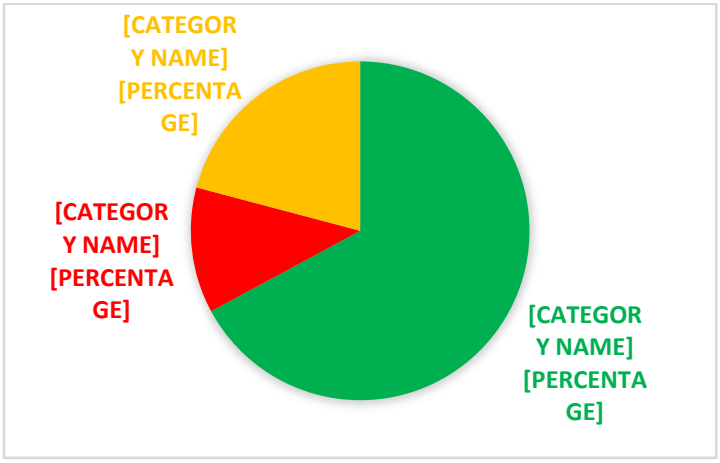


Table - 2: Clinical characteristics and medication details of the study population according to their vaccination status.

	Vaccinated (%) N=392	**Unvaccinated (%) N=192**	**P value**
Disease Duration			0.354
<5 years	138 (35.20)	77 (40.10)	
5-10 years	154 (39.28)	35 (18.23)	
>10 years	100 (25.51)	80 (41.66)	
Organ Systems Involved			
Musculoskeletal	362 (92.35)	156 (81.25)	0.06
Mucocutaneous	224 (57.14)	160 (83.33)	0.34
Respiratory System	88 (22.45)	60 (31.25)	0.46
Renal	142 (36.22)	102 (53.12)	0.73
Nervous system	101 (25.76)	41 (21.35)	0.68
Gastrointestinal	29 (7.39)	25 (13.02)	0.06
Cardiovascular	98 (25.00)	66 (34.37)	0.056
Antiphospholipid antibodies	54 (13.77)	160 (83.33)	<0.001
Haematological	112 (28.57)	85 (44.27)	0.23
Co-morbidities			
Diabetes	124 (31.63)	44 (22.92)	0.09
Hypertension	120 (30.61)	38 (19.79)	0.75
Heart Disease	112 (28.57)	42 (21.88)	0.65
Lung disease	45 (11.48)	43 (22.39)	<0.001
Liver Disease	20 (5.10)	16 (8.33)	0.34
Stroke	28 (7.14)	41 (21.35)	0.01
Psychiatric Illness	22 (5.61)	26 (13.54)	0.04
History of TB/Hep B/Hep C	16 (4.08)	6 (3.12)	0.47
Current Medications			
Steroids	288 (73.47)	122 (82.30)	0.003
HCQ/Chloroquine	334 (85.20)	180 (93.75)	0.4
Methotrexate	88 (22.45)	36 (18.75)	0.34
Azathioprine	132 (33.67)	36 (18.75)	0.65
Cyclophosphamide	26 (6.63)	22 (11.46)	0.42
Mycophenolate Mofetil	142 (36.22)	98 (51.04)	0.002
Cyclosporine/Tacrolimus	10 (2.55)	14 (7.29)	0.5
Rituximab	10 (2.55)	8 (4.17)	0.62
Aspirin/Acitrom	126 (32.14)	92 (47.92)	<0.001
Others	110 (28.06)	44 (22.92)	0.45
Prior Covid Infection			<0.001
Yes	56 (14.28)	54 (28.12)	
No	336 (85.71)	138 (71.87)	

Among those who have taken the vaccine, we asked them about the various factors which may have motivated them to get vaccinated. Around 58% of the vaccinated group thought they were at a higher risk of getting the infection and 56% did not want to get the infection and hence opted for vaccination. Other factors which motivated them are illustrated in **Figure - 4**.

Figure - 2: Reasons given by unvaccinated group for deciding not to get vaccinated.

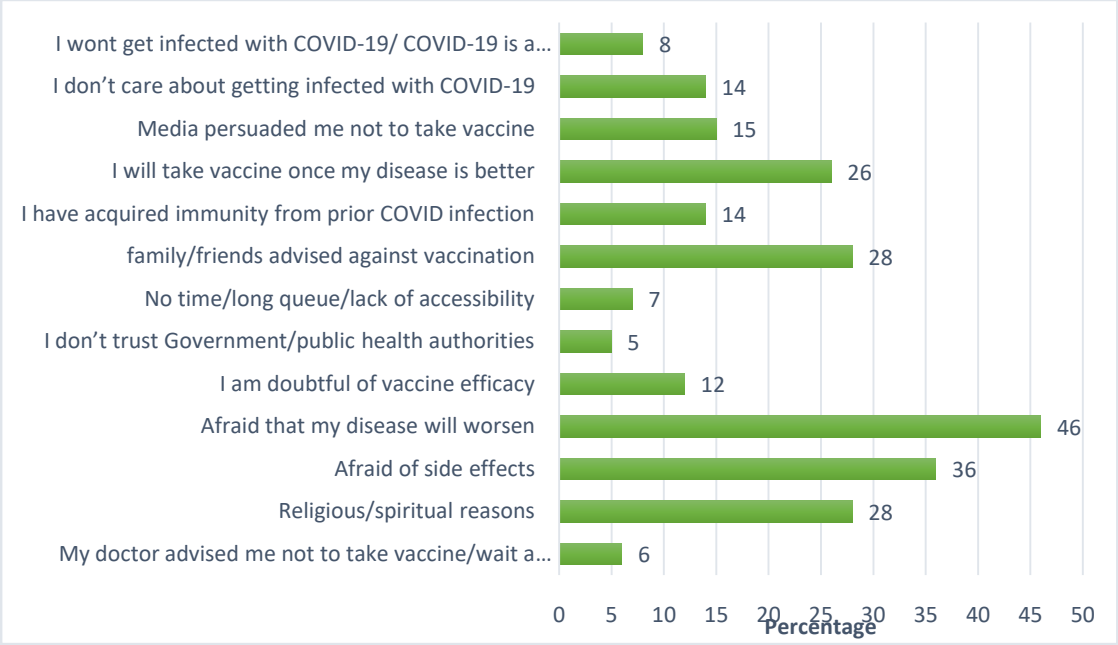


Figure - 3: Factors which are likely to influence the unvaccinated group to change their decisions and get vaccinated.

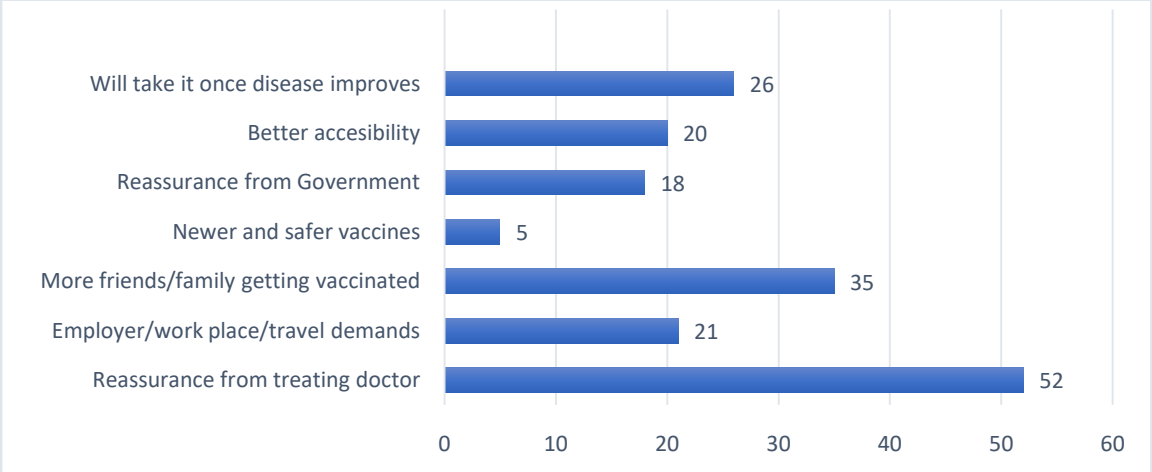
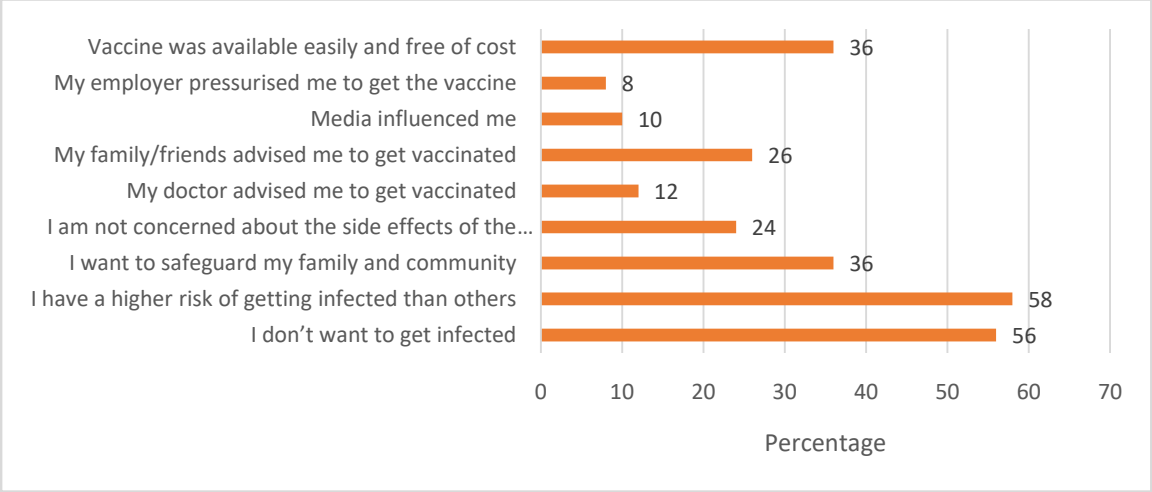


Figure - 4: Factors which motivated the vaccinated group.



Discussion

Among our SLE patients, we had only a 62.17% of vaccination rate which explicitly showed a definite lacuna in our efforts to promote vaccination. Those who were unvaccinated were slightly older than those who were vaccinated. This could be reflective of the general apprehension and fear of vaccination and side effects among elderly people with more co-morbidities. The majority of our patient population comes from the rural areas of Tamil Nadu where the vaccination campaigns may not be as strong as it is in urban areas. So it was not surprising to find that majority of those who did not get vaccinated were those from rural areas and were unemployed or not working at present due to illness. In a study from Brazil [7], among 908 patients with autoimmune rheumatological diseases, the vaccine-hesitant patients were predominantly female, of lower socioeconomic status, and less educated than non-hesitant patients. But in our study, we found no role played by factors like gender, educational status, and socioeconomic class in decisions about getting vaccinations. We also found that the decision to not get vaccinated was more in those with anti-phospholipid antibodies, lung disease, stroke, and psychiatric illness and in those taking corticosteroids, mycophenolate mofetil, and aspirin. But In a multivariable model, (odds ratio [OR], 95% confidence interval [CI]), current use of corticosteroids (OR: 2.24, 95% CI: 1.56–4.43), presence of antiphospholipid antibodies (OR: 2.32, 95% CI: 1.42–6.3) and history of stroke (OR: 2.35, 95% CI: 1.31–4.38) were the only factors which remained independently associated with higher odds of COVID-19 vaccine hesitancy (all $p < 0.05$). In a similar study about vaccine hesitancy in a predominantly black population from the United States of America [8], there were no differences in disease activity, damage, or medication use, except for more glucocorticoid use in the vaccine-hesitant group. History of prior covid infection was found to be a significant factor in vaccine hesitancy in our study. Prior COVID-19 infection would have made many of them think that they have acquired immunity naturally and hence the hesitancy.

On evaluating the responses about factors that influenced their decision to not get vaccinated, we found that about half of the patients were worried about their disease worsening after vaccination, and about one-third were concerned about the vaccine's side effects. An alarmingly high number, around one-third of the unvaccinated group either had strong religious or spiritual reasons or their friends/families were demotivating them about vaccination. Around one-fourth of the unvaccinated group were receptive and were planning to get vaccinated once their disease condition improves. We also found that only a small number of people cited lack of accessibility or mistrust of Government/Public health authorities as to the reason for avoiding vaccination. This shows the reasonable efficiency with which the public health system and the vaccine drives are ongoing. The role of media cannot be neglected as around 15% feel media had a huge influence on their decision. 8% had misbeliefs that they won't get infected with COVID-19 and 14% believed that they have acquired complete immunity from COVID-19 from their prior infection. Patients with autoimmune rheumatic diseases were initially suspected to have less robust immune responses, but studies have shown that they have adequate protective antibodies post COVID-19 disease, at rates similar to that in healthy controls [9]. Also, in patients who have previously had COVID-19, a single dose of vaccine provided a higher humoral response than did two doses of vaccine in infection-naive patients [10]. There lies the importance of talking to the patient to impart proper ideas/knowledge and to guide them out from misconceptions.

About 12% of the study group responded that they are unlikely to change their decision of not getting vaccinated (vaccine-resistant) and most of them were those with religious/spiritual reasons. 21% suggested that they may change or are likely to change their decision (vaccine-

hesitant). More than half of the vaccine-hesitant group reported that they are likely to get vaccinated if they receive firm assurance and guidance from their doctor. More than one-third feel they may get vaccinated once more friends and family also chose to do the same. About one-fifth of the vaccine-hesitant group are likely to change their decisions if there are workplace/travel demands necessities. Only about 5% were apprehensive about the currently available vaccines and demanded newer safer vaccines for them to change their decision. A better reassurance and proper guidance from the treating physician and support from family, friends, and religious institutions need to be strengthened to close the deficiencies in vaccination and to motivate the unvaccinated to rethink their decision.

The most important motivating factor for the group who got vaccinated was the fear of getting infected with COVID-19 as they thought they were at higher risk of getting infected (58%) and the intention of safeguarding their kith and kin (36%). Even though 36% of the vaccinated group were motivated by the easy access to free-of-cost vaccines provided by the Government, about 20% of the unvaccinated group feel that still better accessibility to vaccines may make them rethink their decision.

Conclusion

More than one-third of our lupus patients are still unvaccinated. And around one-third of the unvaccinated lupus population are strongly resistant to the idea of vaccination. The decision to not get vaccinated was found to be strongly associated with older age, rural living, and unemployment. In our population, gender, educational status, and socioeconomic class do not play a significant role in vaccination decisions. The most important motivating factor for the group who got vaccinated was the fear of getting infected with COVID-19 as they thought they were at higher risk of getting infected and the intention of safeguarding their kith and kin. Vaccine hesitancy was found to be more in those with anti-phospholipid antibodies, prior stroke, prior history of COVID-19 infection, and those who were currently using corticosteroids. The major reasons for vaccine hesitancy as reported by the patient population were fear of worsening lupus, fear of side effects, and religious reasons. There are many misconceptions among our patients - few of them think they are unlikely to get infected whereas others think they have acquired complete immunity after a natural COVID-19 infection. Two-thirds of our unvaccinated group are vaccine-hesitant but may rethink their decision if there is proper reassurance and guidance from their treating physician or if more of their friends and family members start accepting vaccines. There is also a need to strengthen the public health care system regarding vaccination and provide better accessibility to the free-of-cost vaccine. Religious groups and media have reasonable say in vaccination decisions of our patients and they also need to be given proper information and guidance about the need for good vaccination rates, especially among our patients.

Acknowledgement

The authors would like to thank the patients who participated and cooperated with our study.

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