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Original Article

Evaluation of COVID-19 vaccination status and immune response among staff at Shahid Motahari Hospital, Urmia, 2021

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Abstract

***Background & Aims*:** The Ministry of Health and Treatment implemented vaccination as one of the primary strategies to control the coronavirus disease 2019 (COVID-19) pandemic. Given their critical role in treatment and disease control, healthcare workers were prioritized for vaccination. This study aims to assess the vaccination status and level of immunity against COVID-19 among healthcare workers at Shahid Motahari Hospital in Urmia, Iran, in 2021.

***Materials & Methods*:** A cross-sectional study was conducted with 150 volunteer healthcare workers at Shahid Motahari Hospital. Venous blood samples were collected to measure severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) neutralizing antibodies using the ELISA method. Data analysis was performed using version 16 of SPSS software.

***Results*:** The participants had a mean age of 37.5 years, with 47.3% being male. A significant 98% of the participants were vaccinated against COVID-19. The predominant vaccines administered were Sputnik V (72%), AstraZeneca (54%), and Sinopharm (27%). The mean level of SARS-CoV-2 neutralizing antibodies was significantly higher in vaccinated individuals compared to unvaccinated individuals (p = 0.001). There was no significant difference in antibody levels between male and female participants (p = 0.67). A positive correlation was observed between the number of vaccine doses received and the level of neutralizing antibodies (R = 0.207).

***Conclusion*:** Vaccination with the mentioned vaccines, whether administered singly or in combination, effectively increased serum antibody levels, providing sufficient protection against COVID-19 for healthcare workers. To maintain immunity levels among healthcare workers and protect against emerging strains of the virus, it is essential to administer booster doses.

***Keywords*:** COVID-19, Immunity level, Iran, Healthcare workers, Vaccination

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Introduction

The coronavirus disease 2019 (COVID-19) pandemic, which originated in China in December 2019, rapidly spread worldwide, leading to considerable mortality and extensive economic and social disruption (1). The disease is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus, a single-stranded RNA virus belonging to the Coronaviridae family, genus Betacoronavirus. Various structural components of the virus, including the envelope, membrane, spike, and nucleocapsid proteins, serve as antigens (2). The spike protein, which enables the virus to attach to the Angiotensin-Converting Enzyme 2 (ACE2) receptor on host cell surfaces, facilitating viral entry and infection, is composed of two subunits: S1 and S2 (3). The S1 subunit contains the Receptor Binding Domain (RBD), which directly binds to the ACE2 receptor on the host cell surface (2, 3).

Following viral infection, the host immune system produces various antibodies against these antigens, particularly the spike protein, which contributes to immune defense against the virus (4). Research indicates that antibodies targeting different regions of the spike protein vary in their efficacy in conferring immunity (4, 5). Specifically, only those antibodies that neutralize the interaction between the spike antigen and the ACE2 receptor are crucial for providing resistance against the disease (5). These are known as neutralizing antibodies.

Research has demonstrated that the generation of antibodies targeting the RBD of the S1 subunit of the spike protein can block the attachment of the virus to the ACE2 receptor on the host cell surface, serving as a marker of immunity against SARS-CoV-2 (4, 5). Elevated titers of these antibodies have been observed in the serum of individuals who have recovered from COVID-19, further substantiating their role in conferring immunity.

The transfusion of serum from individuals who have recovered from COVID-19 to patients with severe manifestations of the disease has been linked to clinical improvement, likely due to the presence of neutralizing antibodies in the serum of recovered individuals (6). Consequently, testing for the presence of these antibodies in the serum of both recovered and vaccinated individuals is routinely employed to assess the body's immunity against COVID-19 (7). A higher titer of neutralizing antibodies indicates superior vaccine efficacy in stimulating the immune system and enhances the body's preparedness for future exposure to the virus.

Healthcare workers are pivotal in preventing and treating diseases, particularly during epidemics. Beyond implementing preventive measures and developing and disseminating vaccines, their dedicated service during the COVID-19 pandemic significantly contributed to controlling the disease and mitigating both human and economic losses (8). Despite the prioritization of healthcare workers for protection and early vaccination, a considerable number of these individuals succumbed while serving patients (9). Even with multiple doses of vaccines, it remains crucial to ensure the immunity of healthcare workers against COVID-19. Doing so is vital for maintaining the workforce that provides direct patient care and for being prepared to tackle future epidemics involving new strains of the virus (10).

This study aimed to evaluate the immunity levels of healthcare staff at Shahid Motahari Hospital in Urmia, Iran, by measuring serum levels of anti-COVID-19 neutralizing antibodies. Given that hospital staff are at a higher risk of exposure and infection with COVID-19 compared to other healthcare workers, this assessment is particularly crucial.

Materials & Methods

This cross-sectional study was conducted in Urmia, Iran, during the summer of 2021. After obtaining informed consent, venous blood samples were collected from volunteer staff at Shahid Motahari Hospital within the hospital laboratory's blood collection department. Following centrifugation, the serum samples were separated and stored at -20°C until analysis.

The enzyme-linked immunoassay (ELISA) kit from Pishtaz Teb Company, designed for the quantitative measurement of SARS-CoV-2 neutralizing antibodies in human serum, was utilized in this study. In this assay,

the wells of the ELISA plate are coated with the RBD antigen. According to the kit instructions, standards and participant serum samples were added to the wells simultaneously with Horseradish peroxidase-conjugated (HRP-conjugated) ACE-2. If SARS-CoV-2 neutralizing antibodies were present in the serum, these antibodies would bind to the antigens at the bottom of the wells, preventing the conjugate from binding to the RBD coated in the wells.

After washing away the unbound material, a color solution was added to the wells. Subsequently, a stop solution was added, and the optical absorbance of the standards and samples was measured at 450 nm wavelength, with a reference filter at 630 nm, using an ELISA reader. The serum level of neutralizing antibodies was then calculated. In this method, the intensity of the color produced is inversely proportional to the level of neutralizing antibodies in the serum.

Statistical Analysis

Descriptive statistics of the study variables, including absolute and relative frequencies, means, standard deviations, and standard errors, were calculated and reported. The independent t-test and the Tukey post-hoc test were utilized to analyze the mean level of neutralizing antibodies across different groups. To examine the relationship between the levels of SARS-CoV-2 neutralizing antibodies and the number of vaccine doses received, Spearman's correlation coefficient was employed. Data analysis was conducted using SPSS version 16 software. It is noteworthy that throughout all stages of analysis, a significance level of 0.05 was considered for rejecting the null hypothesis.

Results

This study included 150 employees from various departments of Shahid Motahari Hospital in Urmia, with a mean age of 37.5 years. Their demographic details are outlined in Table 1.

Table 1. Demographic information of the participants in the study

Variable type		Number (percent)	Total number (n)
	Gender	Male 71 (47.3%), Female 79 (52.7%)	150
Vaccination status	Vaccinated	148 (98.7%)	150
	Unvaccinated	2 (1.3%)	
Number of vaccine doses	Two doses	35 (23.3%)	148
	Three doses	111 (74.0%)	
	Four doses	2 (1.3%)	
Vaccine type	Sputnik V	4 (2.7%)	148
	AstraZeneca	80 (54.1%)	
	Sinopharm	40 (27.0%)	
	Sputnik V-AstraZeneca	15 (10.1%)	
	Sinopharm-AstraZeneca	9 (6.1%)	

The study found that the level of SARS-CoV-2 neutralizing antibodies was significantly higher in vaccinated healthcare workers compared to their unvaccinated counterparts (p = 0.001). No significant difference was observed in the mean level of SARS-CoV-2 neutralizing antibodies between male and female workers at Shahid Motahari Hospital in Urmia (p = 0.67). The level of neutralizing antibodies increased with the number of vaccine doses received, demonstrating a positive correlation between the number of vaccinations and the antibody level (R = 0.207). Although healthcare workers who received four doses of the vaccine exhibited higher antibody levels compared to those who received fewer doses, the difference was not statistically significant (p = 0.081) (Table 2).

Table 2. Results of statistical analysis of the relationship between different variables and the level of neutralizing antibodies

Variable		Number (Percent)	Mean ± SD	*P* value
Gender	Male	71 (47.3%)	73.41 ± 68.11	0.67
	Female	79 (52.7%)	91.40 ± 74.11	
Vaccination status	Vaccinated (148)	88.41 ± 79.10		0.001
	Unvaccinated (2)	75.10 ± 34.10		
Number of vaccine doses	Two doses (35)	69.38 ± 12.00		0.081
	Three doses (111)	96.42 ± 78.90		
	Four doses (2)	47.40 ± 13.10		

Relationship Between Neutralizing Antibody Levels and Vaccine Types

This study examined the correlation between the level of neutralizing antibodies and the type of vaccine administered to healthcare workers at Shahid Motahari Hospital in Urmia, Iran. The lowest and highest levels of SARS-CoV-2 neutralizing antibodies were detected in individuals who received the Sputnik vaccine (29.87 ± 19.32 U/ml) and those who received the Sputnik-AstraZeneca combination vaccine (47.38 ± 0.49 U/ml), respectively.

Statistical analysis revealed that the level of neutralizing antibodies in workers vaccinated with the Sputnik vaccine was significantly lower than those vaccinated with the AstraZeneca, Sputnik-AstraZeneca combination, and Sinopharm-AstraZeneca combination vaccines ($p < 0.05$). However, there was no significant difference in neutralizing antibody levels between the Sputnik vaccine group and the Sinopharm vaccine group ($p = 0.075$). Additionally, no significant differences were observed in the levels of neutralizing antibodies between workers vaccinated with the Sinopharm vaccine and other groups, or among the groups receiving combination vaccines ($p > 0.05$) (Figure 1).

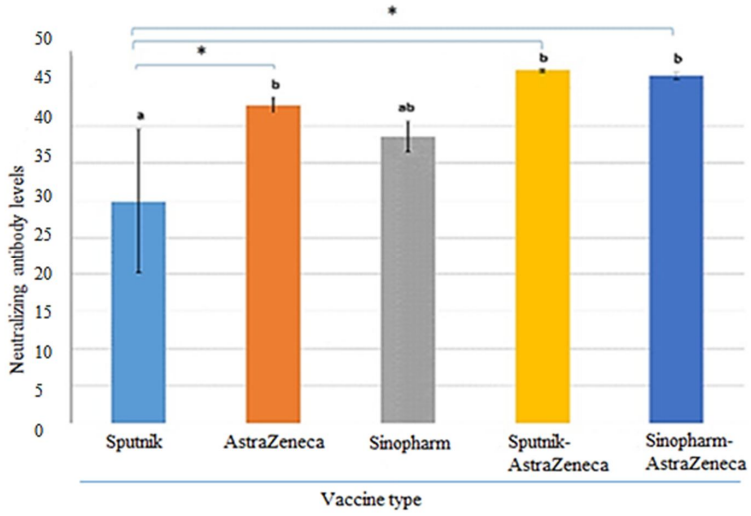

Fig. 1. Comparison of mean levels of neutralizing antibodies in vaccinated workers at Shahid Motahari Hospital, Urmia, Iran, by vaccine type

As illustrated, the mean level of neutralizing antibodies in workers vaccinated with the Sputnik vaccine is significantly lower than in those vaccinated with the AstraZeneca, Sputnik-AstraZeneca combination, and Sinopharm-AstraZeneca combination vaccines ($p < 0.05$).

Discussion

The present study revealed that the vaccination coverage among healthcare workers was highly effective. Out of the 150 employees surveyed, 98.7% were vaccinated against SARS-CoV-2, while 1.3% remained unvaccinated. The reluctance of some healthcare workers to receive vaccination, despite being a small percentage, poses a risk to both themselves and their patients, potentially accelerating the spread of the disease (11-13). Therefore, identifying and vaccinating these individuals is crucial for controlling the COVID-19 pandemic.

A diverse range of high-quality vaccines was administered to a substantial number of employees. The vaccines included Sputnik V (72.7%), AstraZeneca (54.1%), Sinopharm (27%), a combination of Sputnik-AstraZeneca (10.1%), and a combination of Sinopharm-AstraZeneca (6.1%). These vaccines were administered in varying doses: two doses (23.3%), three doses (74%), and four doses (1.3%). The types and percentages of vaccines used in this study were somewhat similar to those reported by Pourakbari et al. However, in their study, the highest percentage of injections was for the Sputnik vaccine, and the COVAXIN vaccine was also included in their vaccination program, which was not administered to the staff at Motahari Hospital (14).

These findings demonstrate that, despite the rapid spread of the disease and the initial challenges faced by the medical community, the implementation of effective policies ensured the availability and use of diverse vaccines in appropriate doses across various treatment centers.

The results of this study indicate that protective immunity was effectively established in vaccinated individuals, with 100% of those vaccinated developing neutralizing antibodies against the RBD of SARS-CoV-2. Additionally, the level of antibodies increased with the number of vaccine doses received. Consistent with the findings of Sammartino et al. in Italy (15) and Jacot et al. (16), the study confirmed that neutralizing antibodies are well established after the third dose of the vaccine.

In the following, the findings affirm the efficacy of vaccination as a preventive measure in controlling infectious diseases and underscore the high quality of the vaccines used.

In the present study, the majority of employees (74%) had received three doses of the vaccine. However, the level of neutralizing antibodies was also significantly high in those who had received two doses, with no significant difference observed between these groups (Table 2). This result aligns with the study by Dinc et al. (17), which reported 99.2% immunogenicity, but differs from the study by Pourakbari et al. (14), which reported a 74% prevalence of neutralizing antibodies. The discrepancies in results could be attributed to variations in the number of doses administered, the type of vaccine used, and the timing of blood sample collection, with Pourakbari et al.'s study seemingly conducted closer to the time of vaccination.

In the current study, the highest antibody titer was observed in individuals who received the combination of Sputnik-AstraZeneca vaccines, while the lowest titer was noted in those who received the Sputnik vaccine. A study by Adjobimey et al. (18) with a different combination of vaccines found that Moderna produced the highest titer, whereas Sinopharm resulted in the lowest titer among vaccinated individuals. Contrarily, a study by Claro et al. in 2022 demonstrated that the Sinopharm vaccine was effective in inducing long-term immunity (19).

The discrepancy in these results may be attributed to the varying numbers of individuals vaccinated with Sputnik across the studies. This highlights the importance of considering the sample size and specific vaccine combinations when comparing the efficacy of different vaccines in inducing neutralizing antibodies.

The immunity conferred by COVID-19 vaccines is estimated to last approximately 6 to 12 months. This

duration can be extended by administering booster doses, which also contribute to the establishment of effective herd immunity over time. However, the comparative degree and potential of vaccine-induced immunity versus natural immunity remain not fully understood (20).

Based on the study's findings, it is recommended to administer regular vaccinations to employees at six-month intervals. This approach will help maintain a safe level of immunity against COVID-19 among healthcare workers, ensuring their continued protection and readiness to handle future outbreaks.

The current study found no significant difference in the mean levels of SARS-CoV-2 neutralizing antibodies between female and male employees of Shahid Motahari Hospital in Urmia ($p > 0.05$). This result contrasts with the findings of a study by Dimeglio et al. in 2021, conducted on healthcare workers at a university hospital in southern France, which reported lower neutralizing antibody titers in female employees compared to males (21). There is no credible scientific evidence suggesting a negative impact of female gender on humoral immune responses, including the immune response against SARS-CoV-2 antigens. Therefore, these contradictory findings could be attributed to differences in study design, vaccine type, and the number of doses administered.

Vaccination with the aforementioned vaccines, whether administered singly or in combination, has effectively protected healthcare workers against COVID-19 by sufficiently increasing serum antibody levels for preventive safety. To sustain employee immunity levels and protect against new virus strains, booster dose injections are deemed necessary.

Conclusion

The present study demonstrated that vaccination of hospital staff has a positive impact on increasing the levels of anti-SARS-CoV-2 antibodies. Given the importance of maintaining the health of healthcare personnel in the face of disease outbreaks, it is recommended that vaccination programs be pursued continuously and rigorously to support the health of staff and, consequently, the health of patients. These findings can serve as a basis for health decisions and policy-making regarding vaccination in healthcare facilities.

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Author's Contributions

Conceptualization was carried out by Maryam Taavon and Vahid Tanhaei Marand. Methodology was designed by Maryam Taavon, Vahid Tanhaei Marand, and Sadegh Feizollahzadeh. Data collection was conducted by Maryam Taavon. Data analysis was performed by Maryam Taavon and Sadegh Feizollahzadeh. Writing of the original draft was done by Sadegh Feizollahzadeh. Writing - review and editing was undertaken by Sadegh Feizollahzadeh. Visualization was handled by Maryam Taavon and Vahid Tanhaei Marand. Supervision was provided by Vahid Tanhaei Marand. Project administration was overseen by Vahid Tanhaei Marand. Ethics approval was granted by Maryam Taavon. Literature review was conducted by Maryam Taavon, Vahid Tanhaei Marand, and Sadegh Feizollahzadeh. Validation was carried out by Maryam Taavon, Vahid Tanhaei Marand, and Sadegh Feizollahzadeh.

Data Availability

The data supporting these findings are available from the corresponding author upon reasonable request.

Conflict of Interest

The authors have no conflict of interest in this study.

Ethical Statement

The code of ethics for this article is IR.IAU.URMIA.REC.1401.048.

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