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Comprehensive Evaluation of COVID-19 Vaccines Antibody Response Among Healthcare Professionals: A Multi-Center Study in Iran

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Abstract

Background: The coronavirus disease 2019 (COVID-19) vaccines are very good at protecting individuals from serious illness, needing hospital care, and dying from different strains of the virus. However, vaccines might not completely prevent individuals from catching and spreading the virus, and this might depend on some personal factors.

Objectives: To find out the immune response of COVID-19 vaccines, this cross-sectional study conducted within June 2021 to May 2023 assessed different types of COVID-19 vaccine antibody responses among healthcare professionals and their associations with demographic factors and comorbidity risk factors.

Methods: This descriptive-analytical study was conducted on recruited healthcare professionals from Sina, Imam Khomeini Complex, 501 AJA, Baqiayatallah, and Firoozgar hospitals in Tehran, Iran. The vaccines whose antibody response was investigated in this study are Sinopharm® (China), AstraZeneca® (United Kingdom), Sputnik® (Russia), and Covaxin® (India). Anti-spike, anti-receptor-binding domain (RBD), and anti-neutralizing immunoglobulin G (IgG) were evaluated by commercial kits according to instructions.

Results: This study involved 1 029 healthcare workers who were over 18 years old. The average age was 41.48 ± 9.9 years, and 602 (58.5%) of them were male. The vaccines they received were Sputnik V (392 or 38.16%), AstraZeneca (335 or 32.61%), Baharat (45 or 4.3%), and Sinopharm (255 or 24.82%). The Covaxin and AstraZeneca vaccines increased both anti-RBD and anti-neutralizing IgG Ab levels; however, the Sinopharm vaccine increased only the latter. The Sputnik vaccine was the least effective. Gender and diabetes influenced the antibody levels, but age did not.

Conclusions: This study revealed the substantial effectiveness of COVID-19 vaccines in generating robust antibody responses among healthcare professionals. All four vaccine types, Sinopharm, AstraZeneca, Sputnik, and Covaxin, elicited significant antibody responses in over 70% of participants, highlighting the crucial role of vaccination in building defense against COVID-19.

Keywords: COVID-19 Vaccines, Antibody Response, Immune Activation

1. Background

The fight against the coronavirus disease 2019 (COVID-19) pandemic requires widespread vaccination efforts. Vaccines are essential in reducing the spread of the virus and preventing severe illness and fatalities. By preparing the immune system to recognize and fight

against the virus, vaccines provide critical defense against infection and can lessen the severity of symptoms (1).

Extensive efforts have been made to develop and distribute effective vaccines. The COVID-19 vaccines have shown remarkable effectiveness in preventing severe disease, hospitalization, and death linked to specific variants. Although vaccines can reduce the risk of infection and mild cases of COVID-19, their ability to completely stop virus transmission varies and can be influenced by individual factors (1, 2).

Most importantly, vaccines have consistently demonstrated their ability to significantly reduce hospitalization rates and alleviate severe illness, even in emerging variants, such as the Delta variant (2). Achieving complete herd immunity might be challenging; however, widespread vaccination coverage among adults can pave the way for a return to normalcy (1). Additionally, vaccines have been shown to expedite recovery from infections and reduce the likelihood of virus transmission (3). In summary, vaccines are crucial in managing COVID-19 transmission and lessen its impact on healthcare systems, economies, and communities (1, 4).

Four primary types of COVID-19 vaccines have been developed, each utilizing distinct mechanisms of action. Understanding how each vaccine type works is crucial for appreciating their unique roles in the fight against COVID-19. All these vaccines have proven effective in reducing symptomatic COVID-19 cases, severe disease, and deaths (4).

Assessing the levels of antibodies induced by COVID-19 vaccines provides valuable insights into the immune response triggered by different vaccine types. Multiple investigations have consistently shown robust immune responses in individuals after COVID-19 vaccination (5, 6). Understanding the effectiveness of vaccines and antibody profiles is vital in our collective efforts to combat the pandemic and create a healthier future.

2. Objectives

To find out the immune response of COVID-19 vaccines, this comprehensive cross-sectional study was conducted to assess different types of COVID-19 vaccine efficacy and antibody responses among healthcare professionals and their associations with demographic factors and comorbidity risk factors.

3. Methods

3.1. Study Design

This cross-sectional study within June 2021 to May 2023 was conducted with the authorization of the Ethics Committee of the Iran University of Medical Sciences, Tehran, Iran. The study was assigned registration number IR.IUMS.FMD.REC.1400.570.

3.2. Participants

After informing the medical staff of the hospitals in question, we recruited volunteer healthcare professionals (over 18 years of age) for this study who met certain criteria, including providing written informed consent, having no history of immunosuppression (either drug-related or disease-related), having no recent history of COVID-19, and having received their first and second doses of the COVID-19 vaccine regularly with a similar commercial brand and at least 4 weeks prior to participating obtained second dose but not more than 2 months ago.

Sampling was conducted within June 2021 to May 2023. The participants were employed at Sina, Imam Khomeini Complex, 501 AJA, Baqiayatallah, and Firoozgar hospitals in Tehran, Iran. To collect samples, staff nurses took 10 mL of venous blood. The serum was then separated from the whole blood sample through centrifugation and stored in a freezer at -20°C until the blood collection was completed, following the instructions provided in the assay kit package insert.

3.3. COVID-19 Vaccines

The vaccines whose antibody response was investigated in this study are Sinopharm® (China), AstraZeneca® (United Kingdom), Sputnik® (Russia), and Covaxin® (India).

3.4. Laboratory Analysis

To conduct an assay for anti-neutralizing antibodies (Abs), anti-spike Abs, and receptor-binding domain (RBD) Abs, the quantitative Pishtaz Teb ELISA kits were employed according to the manufacturer's instructions (7-9).

These ELISA kits include the Q-SARS-CoV-2-anti-RBD IgG ELISA kit (PT-QCoV-2-anti-RBD IgG-96), designed to identify anti-RBD IgG in human serum samples, the Q-SARS-CoV-2-anti-spike (PT-QCoV-2-anti-spike IgG-96), Q-SARS-CoV-2-anti-neutralizing (PT-SARS-CoV-2 NTAb 96), and Q-SARS-CoV-2-anti-neutralizing ELISA kits, developed to quantitatively measure anti-spike, anti-RBD, and anti-neutralizing immunoglobulin G (IgG) in human serum samples.

3.5. References Range

Due to the manufacturer's instructions (7-9), the anti-RBD IgG Ab concentration $\geq$ 5 RU/mL was considered positive; this cut-off for anti-spike IgG and anti-neutralizing IgG Abs were $\geq$ 8RU/mL and $\geq$ 2.5RU/mL, respectively.

3.6. Statistical Analysis

The data were assessed using SPSS software (version 27.0). Mean and standard deviation presented continuous variables; however, numbers and percentages represented categorical data. Variables showing significant differences initially underwent binary logistic regression for additional analysis. This subsequent analysis aimed to associate independent factors (vaccine types, demographic data, previous history of COVID-19 infection, and comorbidity risk factors) with antibody levels as the dependent variable. Outcomes were presented as a 95% confidence interval (CI) and odds ratio (OR). A significance level of $P < 0.05$ determined statistical significance.

4. Results

4.1. Participants' Characteristics

A total of 1 029 healthcare professionals over 18 years participated in this study. All participants were employed at selected hospitals in Tehran, Iran. The demographic features of the participants are shown in Table 1.

Table 1. Characteristics of Study Participants (n = 1029) [a]

Characteristics	Total Participants (n = 1 029)
Age (y)	41.48 ± 9.9
Gender	
Male	602 (58.5)
Female	427 (41.49)
Vaccine type	
Sputnik V	392 (38.16)
AstraZeneca	335 (32.61)
Baharat	45 (4.3)
Sinopharm	255 (24.82)
Past medical history	
COVID-19 history	831 (80.75)
Diabetes mellitus	14 (1.3)
Hypertension	20 (1.94)
Cardiovascular disease	8 (0.77)
Hyperthyroidism	22 (2.1)
Hypothyroidism	1 (0.09)
Asthma	4 (0.38)
Migraine	7 (0.6)
History of drug allergy	2 (0.19)
Seasonal allergy	48 (4.66)
Hospitalization due to COVID-19 before vaccination	16 (1.55)
Reinfection with COVID-19 after vaccination	
Sputnik	38 (9.69)
AstraZeneca	33 (9.85)
Baharat	7 (15.55)
Sinopharm	12 (4.70)
Vaccination history	
COVID-19 vaccine	1029 (100)
Influenza vaccine	873 (84.83)
Pneumococcal vaccine	35 (3.40)

Abbreviations: DM, diabetes mellitus; HTN, hypertension; CVD, cardiovascular disease; COVID-19, coronavirus disease 2019.
[a] Values are presented as mean ± SD or No. (%).

4.2. Antibody Responses

The results of assessing antibody responses after COVID-19 vaccination were quite interesting. The levels of anti-neutralizing antibodies, anti-spike antibodies, and anti-RBD antibodies showed significant variation among the participants in the study. The total population of receivers of Sputnik (38.16%) and AstraZeneca (32.61%) vaccines were the most prevalent in the present study. The analyzed serum samples showed a positive antibody presence in over 70% of the cases. Table 2 provides further details on these results.

4.3. Association of Antibody Levels with Independent Factors

A binary logistic regression analysis examined the correlation between antibody levels and various independent factors, such as vaccine types, demographic characteristics, and comorbidity risk factors. In this analysis, the Sputnik vaccine was considered the reference as it accounted for a higher percentage of injections. To evaluate the variables, we first carried out a chi-square test for each parameter and only included the results that showed a correlation in the model. The study's outcome was presented as ORs with 95% CIs, with the results detailed in Table 3.

The analysis revealed that recipients of the Covaxin vaccine had a statistically significant increase in anti-RBD IgG Ab levels, compared to the reference Sputnik vaccine. In contrast, age had an inverse relationship with the antibody level (OR = 0.998, CI = 0.98-1.01, P = 0.94), although it was not statistically significant.

Regarding anti-spike IgG Ab levels, AstraZeneca and Covaxin vaccines showed a significant increase, compared to the reference Sputnik vaccine, and there was a direct relationship with gender (OR = 1.24, CI = 0.83-1.76, P = 0.31) and diabetes (OR = 0.9, CI = 0.18-4.31, P = 0.89). On the other hand, COVID history (OR = 0.64, CI = 0.07, CI =

Table 2. Antibody Levels Among Study Participants [a]

Variables	Anti-RBD IgG Ab Level (RU/mL)		Anti-spike IgG Ab Level (RU/mL)		Anti-neutralizing IgG Ab Level (RU/mL)	
Vaccine type	> 5	< 5	> 8	< 8	> 2.5	< 2.5
Sputnik	304 (77.55)	88 (22.45)	295 (75.25)	44 (11.22)	316 (80.61)	76 (19.39)
AstraZeneca	282 (84.18)	53 (15.82)	246 (73.43)	34 (10.15)	240 (71.64)	94 (28.06)
Covaxin	29 (64.44)	13 (28.89)	24 (53.33)	11 (24.44)	22 (48.88)	23 (51.11)
Sinopharm	183 (71.76)	72 (28.23)	159 (62.35)	45 (17.64)	172 (67.45)	83 (32.55)
Total	798 (77.55)	226 (21.96)	724 (70.35)	134 (13.02)	750 (72.89)	276 (26.82)

[a] Values are presented as No. (%).

Table 3. Association of Antibody Levels with Independent Factors

Variables	Positive Anti-RBD IgG Ab			Positive Anti-spike IgG Ab			Positive Anti-neutralizing IgG Ab		
	Sig.	OR	95% CI	Sig.	OR	95% CI	Sig.	OR	95% CI
Vaccine type									
Sputnik (reference)									
AstraZeneca	0.076	0.721	0.50 - 1.35	0.003	0.49	0.31 - 0.79	< 0.001	0.535	00.36 - 0.77
Baharat	< 0.001	0.469	0.31 - 0.7	0.002	0.46	0.28 - 0.75	0.25	0.81	0.56 - 1.16
Sinopharm	0.751	1.121	0.55 - 2.27	0.26	1.5	0.7 - 3.46	0.016	2.31	1.17 - 2.32
Comorbidity factors									
Age	0.769	0.998	0.98 - 1.01	NA	NA	NA	0.94	0.999	0.98 - 1.01
Gender	NA	NA	NA	0.31	1.24	0.83 - 1.76	NA	NA	NA
DM	NA	NA	NA	0.89	0.9	0.18 - 4.31	NA	NA	NA
Previous history of COVID-19	NA	NA	NA	0.07	0.64	0.39 - 1.05	0.004	1.65	1.17 - 2.32
Influenza vaccine	NA	NA	NA	0.39	0.77	0.42 - 1.39	< 0.01	2.35	1.64 - 3.38

Abbreviations: DM, diabetes mellitus; HTN, hypertension; CVD, cardiovascular disease; COVID-19, coronavirus disease 2019.

0.39-1.05) had an inverse relationship; nevertheless, none of the relationships was statistically significant.

The present study showed that anti-neutralizing IgG Ab levels significantly increased in recipients of the AstraZeneca vaccine, compared to the reference. Older age (OR = 0.99, CI = 0.98-1.01, P = 0.94) had an inverse relationship, which was not statistically significant. However, the history of previous COVID-19 infection (OR = 1.65, CI = 1.17 - 2.32, P = 0.004) and influenza vaccination (OR = 2.35, CI = 1.64-3.38, P < 0.01) had a direct relationship with the increase in the antibody level, which was statistically significant. This finding means that in AstraZeneca recipients, previous COVID-19 infection increased the level of anti-neutralizing IgG Ab up to 65 times, compared to Sputnik recipients. Additionally, having a history of influenza vaccination increased the antibody level 135 times, compared to the Sputnik group.

Finally, the anti-neutralizing IgG Ab level of Sinopharm vaccine recipients was significantly higher than the antibody level of the reference vaccine. Sinopharm produced anti-neutralizing IgG Ab more than two times (OR = 2.31, CI = 1.17 - 2.32, P = 0.016), compared to Sputnik.

5. Discussion

The primary finding of the present study reveals the remarkable effectiveness of COVID-19 vaccines in generating robust antibody responses among healthcare professionals. The current multi-center investigation focused on four distinct vaccine types, namely Sinopharm, AstraZeneca, Sputnik, and Covaxin. The results demonstrated that all these vaccines elicited significant antibody responses, with more than 70% of the participants exhibiting positive antibody levels. This overarching observation underscores the pivotal role of vaccination in stimulating immune responses and building defense against COVID-19 (10).

A notable aspect of the findings of the current study lies in the differential impact of vaccine types on antibody

levels. Each vaccine type triggered unique responses with distinct antibody profiles. The data showed that recipients of Covaxin exhibited significantly higher levels of anti-RBD IgG antibodies than the reference Sputnik vaccine. Additionally, AstraZeneca and Covaxin recipients displayed significantly elevated levels of anti-spike IgG antibodies, compared to Sputnik. Furthermore, the study revealed that recipients of AstraZeneca and Sinopharm vaccines had significantly higher levels of anti-neutralizing IgG antibodies than the reference vaccine. These variations in antibody profiles emphasize the importance of considering vaccine type when evaluating immune responses.

Intriguingly, the present analysis identified several factors that influence changes in antibody levels following COVID-19 vaccination. Age played a role in shaping the immune response, as Zhou's report (11), with an inverse relationship observed in the context of anti-RBD IgG antibodies. The presence of comorbidities, such as diabetes and a history of previous COVID-19 infection, also appeared to impact the levels of anti-spike IgG antibodies and anti-neutralizing IgG antibodies (12). However, it is important to note that these relationships were not consistently statistically significant. The data suggest that individual characteristics can have varying effects on antibody responses; therefore, it is essential to consider the interplay of these factors.

Remarkably, we identified that anti-neutralizing IgG antibody levels were the least affected by covariate factors, with the history of previous COVID-19 infection and influenza vaccination showing statistically significant associations with increased antibody levels. This finding underscores the resilience of anti-neutralizing IgG antibodies in responding to various influences and highlights their potential as an important component of immunity against COVID-19 (13).

It is important to acknowledge the limitations of the present study. There are some publications from Iran reporting the side effects and efficacy of different vaccines among healthcare workers and other individuals (14-16). This study evaluated the effectiveness of the most common COVID-19 vaccine in Iran via antibody level assessments, which was not reported in previous Iranian studies, and COVID-19 vaccine side-effect differences were not mentioned in the current study (14-16). Although the findings of the present study provide valuable insights into vaccine efficacy and antibody responses, they are based on a specific population of healthcare professionals and specific vaccines. Further research is needed to assess the generalizability of these findings to larger populations and to consider additional vaccines and variants.

5.1. Conclusions

Notably, each vaccine type resulted in distinct antibody profiles. Covaxin recipients showed significantly higher anti-RBD IgG antibodies, highlighting the vaccine's effectiveness in generating this response. AstraZeneca and Covaxin led to elevated anti-spike IgG antibodies. Anti-neutralizing IgG antibody levels varied, with AstraZeneca and Sinopharm recipients having significantly higher levels of Abs. According to the findings of the current study, all vaccines trigger specific antibody responses, targeting key viral components, such as the spike protein and RBD. Positive antibody levels indicated sensitive and effective immune responses. The results shed light on the crucial role of vaccines in combating the pandemic and offer insights into optimizing vaccination strategies. The present multi-center study demonstrated that different vaccine types induce distinct antibody profiles, and individual factors, such as age and comorbidities, affect these responses. Notably, anti-neutralizing IgG antibodies appear to exhibit resilience against covariate factors, potentially playing a pivotal role in long-term immunity against COVID-19. These insights contribute to the ongoing efforts to combat the pandemic and underline the importance of vaccination in safeguarding public health.

Footnotes

Authors' Contribution: Study concept and design: Fatemeh Beiraghdar and Mahin Jamshidi Makiani; acquisition of the data: Parisa Kianpour, Sayed Alireza Nadji, Babak Jahangiri, Mohammad Hadi Karbalaie Niya, Atabak Najafi, Reza Pourfallah, Reza Mourtami, Mahdi Chahabi, and Mina Nouri; analysis and interpretation of the data: Zahra Panahi, Sayed Alireza Nadji, and Mina Nouri; drafting of the manuscript: Parisa Kianpour and Reza Pourfallah; critical revision of the manuscript for important intellectual content: Sajad Sahab Negah, Mohammad Hadi Karbalaie Niya, Fatemeh Beiraghdar, and Mahin Jamshidi Makiani; statistical analysis: Zahra Panahi, Babak Jahangiri, and Reza Mourtami; administrative, technical, and material support: Sajad Sahab Negah, Atabak Najafi, and Mahdi Chahabi; study supervision: Fatemeh Beiraghdar and Mahin Jamshidi Makiani.

Conflict of Interests: The authors have no conflict of interest.

Data Availability: The dataset presented in the study is available on request from the corresponding author during submission or after publication.

Ethical Approval: The present study was conducted with the authorization of the Ethics Committee of the Iran University of Medical Sciences. The present study was assigned registration number IR.IUMS.FMD.REC.1400.570.

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Informed Consent: Written informed consent was obtained.

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