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Comparative Analysis of SARS-CoV-2 Antibodies in Diabetic and Non-Diabetic Healthcare Workers Post-Infection and Vaccination

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ABSTRACT

Introduction: The COVID-19 pandemic has significantly impacted global health, and vaccines have been crucial in mitigating severe outcomes. However, the effect of type 2 diabetes on vaccine-induced immune responses is not fully understood. This study aims to analyze SARS-CoV-2 antibody levels in individuals with type 2 diabetes and compare them to individuals without diabetes to elucidate the complex interactions between diabetes and immune responses. **Methods:** At GMC Srinagar, India, a study involving 299 healthcare workers reviewed their vaccination status, SARS-CoV-2 infection history, and diabetes status. Blood samples were analyzed for HbA1c and IgG antibodies using ELISA and chemiluminescence assays. Descriptive and inferential statistics were used to analyze demographic data and compare groups. **Results:** More than two-thirds of the participants had prior COVID-19 infections, and vaccination rates were high. Diabetes significantly impacted antibody levels, with diabetic individuals showing lower IgG titers compared to non-diabetic individuals. Age and gender also influenced antibody levels: individuals aged 41-50 and 51-60 had higher anti-S antibody titers than younger age groups (t-test = 52.603, df = 15, $P < 0.001$). Males exhibited higher anti-S antibody titers compared to females (t-test = 7.483, df = 5, $P = 0.007$). Booster doses of the vaccine significantly enhanced antibody responses. **Conclusion:** This study highlights the impact of diabetes, age, gender, and vaccination history on SARS-CoV-2 antibody levels in healthcare workers. Diabetic individuals had lower antibody titers, while age and gender differences also affected antibody responses. These findings suggest the need for personalized vaccination strategies, especially for diabetic healthcare workers, to optimize COVID-19 prevention and ensure effective immunity.

INTRODUCTION

The COVID-19 pandemic, which emerged in late 2019, has had a profound impact on global health and economies. As of 20 August 2023, over 769 million confirmed cases and over 6.9 million deaths have been reported globally [1]. This unprecedented crisis has prompted the implementation of various non-pharmaceutical interventions, such as lockdowns, social distancing measures, and mask mandates, to control virus transmission [2]. Simultaneously, extensive efforts have been directed towards developing and deploying effective COVID-19 vaccines, which have played a crucial role in mitigating the pandemic's severity and facilitating the gradual reopening of economies and societies [3].

Although it is true that age, medical history, and co-morbidities can influence immune response, this study will adjust for these factors by analyzing data from a matched cohort of diabetic and non-diabetic individuals.

In December 2020, the World Health Organization and the US Food and Drug Administration (FDA) officially approved the release of COVID-19 vaccines [4]. Between December 2020 and February 2021, vaccines based on adenoviral vectors, like ChAdOx1 (AstraZeneca-Oxford), and mRNA vaccines, such as BNT162b2 (Pfizer–BioNTech) and mRNA-1273 (Moderna), were made available for public administration [5, 6]. These three vaccines, ChAdOx1, which employs a non-replicating simian adenovirus vector containing the complete genetic code for the spike protein of the SARS-CoV-2 virus, and the other two utilizing a novel mRNA vaccine approach, demonstrated promising safety and efficacy profiles in clinical trials. Furthermore, these vaccines are

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administered through two injections into the muscle and have proven to protect by stimulating the production of different types of antibodies, including immunoglobulin G (IgG), IgM, and IgA, specifically targeting the receptor binding domain (RBD) of the spike protein (S) of the virus [7, 8]. These antibodies can neutralize the virus by preventing the RBD from binding to its corresponding receptor, angiotensin-converting enzyme 2 (ACE2) [7, 8]. The serological measurement of these antibodies, especially the neutralizing antibodies, can serve as an indicator of the level of protection achieved through either COVID-19 vaccination or previous infection [9]. Therefore, our study aligns with the broader vaccination landscape by concentrating on individuals with type 2 diabetes. By analyzing SARS-CoV-2 antibody levels, we aim to discern how different vaccines, including those based on adenoviral vectors and mRNA technologies, impact immune responses in this vulnerable population.

Understanding the complex interplay between type 2 diabetes and the immune system is crucial for developing effective vaccination strategies, especially for individuals with weakened immune systems, as it can inform the timing, dosage, and type of vaccines needed to induce an optimal immune response [10].

Importantly, the prevalence of diabetes among healthcare workers (such as nurses, doctors, pharmacists, laboratory technicians, and other allied health professionals) is noteworthy, as this group that is at higher risk of developing diabetes [11-13]. Understanding the impact of diabetes on SARS-CoV-2 immune responses within this group provides valuable insights for both individual care and the development of targeted public health strategies. Furthermore, given the high prevalence of diabetes among healthcare workers, who are at increased risk of exposure to SARS-CoV-2, investigating the relationship between diabetes and immune response in this population is particularly relevant.

The decision to scrutinize diabetes as a primary variable of interest is grounded in robust scientific evidence and established theoretical frameworks. Diabetes, characterized by chronic inflammation, significantly impacts immune functions [14]. Studies have indicated that dysregulated immune responses in diabetic individuals can lead to impaired antibody production and immune memory, potentially compromising their ability to mount effective defenses against specific pathogens, such as SARS-CoV-2 [8-11]. This compromised immune system increases the risk of severe illness and death from COVID-19 and may also make it more difficult to develop long-lasting immunity after infection [15].

Existing studies have not fully investigated the impact of diabetes on SARS-CoV-2 immune responses. This study endeavors to fill these gaps by providing a detailed analysis of antibody levels in individuals with diabetes post-infection, contributing essential information for a more comprehensive understanding of the subject. By meticulously analyzing SARS-CoV-2 antibody levels in individuals previously infected with type 2 diabetes, we aim to understand the complex and subtle relationships between diabetes and immune responses. This understanding is critical, not just for enhancing the care and safeguarding of individuals with diabetes but also for shaping comprehensive public health strategies tailored to manage COVID-19, particularly among older adult and immunocompromised individuals. Through our research, we aspire to contribute nuanced insights that can inform targeted interventions, ensuring a more effective and equitable pandemic response.

MATERIAL AND METHODS

Study setting and participants. This prospective study was conducted by the Department of Microbiology at GMC Srinagar, Kashmir, India. A total of 299 healthcare workers employed in high-risk and non-high-risk areas of the hospital were recruited. High-risk areas included COVID-19 wards, isolation rooms, emergency departments, and areas with aerosol-generating procedures. In contrast, non-high-risk areas encompassed non-COVID-19 wards, administrative offices, and outdoor spaces where strict infection control measures were observed.

The sample size was calculated using G*Power software, based on an anticipated effect size of 0.8, a power of 0.80, and an alpha level of 0.05. The calculated sample size required was 277; however, 299 participants were enrolled to account for potential dropouts.

Selection of participants. Participants were conveniently recruited through a snowball sampling technique. While randomization wasn't implemented, efforts were made to ensure diversity in terms of age, sex, diabetes status, and vaccination history. To ensure representativeness, targeted outreach campaigns were conducted across various departments of the medical institution to recruit healthcare workers from diverse academic backgrounds. Additionally, healthcare workers were encouraged to refer colleagues from their networks, thereby enhancing the diversity of the sample. Of the participants, 60% (n = 179) were recruited from high-risk areas, and 40% (n = 120) were from non-high-risk areas. These groups were balanced for age and sex after adjustment for confounding factors. However, due to the nature of work, diabetes prevalence was higher among healthcare workers in high-risk areas.

In our study, the timing of sample collection relative to vaccination or COVID-19 infection is a critical aspect that was explicitly considered to enhance the transparency and interpretability of our findings Participants were recruited approximately 4 weeks post-vaccination to capture the peak of the immune response.

The selection of this specific time point aligns with the typical trajectory of immune responses following vaccination. Around four weeks post-vaccination, individuals are expected to have undergone the initial

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phases of immune activation, leading to the production of antibodies and the establishment of immunological memory. This timeframe allows for the assessment of the emerging immune responses while considering the dynamics of the immune system's reaction to the administered vaccines.

Additionally, this time point serves to minimize potential confounding effects associated with acute responses immediately post-vaccination, allowing for a more stable assessment of the immune response. The acute responses referred to include transient symptoms such as fever, fatigue, and injection site reactions, which may obscure the specific evaluation of immune system activation and antibody production.

Data collection:

Questionnaire. This covered vital aspects of the participants' health history, including vaccination records (including COVID-19 vaccinations and booster doses), previous SARS-CoV-2 infections, and diabetes status.

Laboratory analysis. Venipuncture was performed to collect 10 mL of whole blood from each participant. An HbA1c test was performed to assess average blood glucose levels. The collected blood was then centrifuged at 5000 rpm for 10 min at 4°C, and 200 µL of serum was isolated from each sample. Serum samples were analyzed using the Abbott Laboratories SARS-CoV-2 IgG Reagent Kit (Catalog No. 06R8) on a chemiluminescent immunoassay platform. Results were interpreted within 30 min, with IgG antibody titers exceeding 50 AU/mL considered significant. Stringent quality control measures were implemented, including the use of positive and negative controls.

Statistical analysis. Descriptive statistics (means, standard deviations, frequencies, percentages) were used to summarize participant demographics, vaccination history, diabetes prevalence, and IgG antibody titers. To assess differences between groups, we employed appropriate statistical tests (chi-square, t-tests, or non-parametric alternatives) after checking for normality, equality of variance, and other assumptions. Data analysis was performed using IBM SPSS Statistics for Windows, version 27.0.

Ethical considerations. Prior to participation, informed consent was obtained from all individuals after receiving comprehensive information about the study's objectives, procedures, potential risks, and benefits. Participant privacy and confidentiality were ensured by de-identifying data and safeguarding identities. Ethical clearance was obtained from the relevant institutional ethics committee (IRB GMCS/22/34E).

RESULTS

Participant demographics and health profile. A total of 299 healthcare workers participated in the study, with 60.0% (n = 179) and 40.0% (n = 120) from high-risk and non-high-risk areas, respectively. The cohort exhibited a balanced gender distribution (51.2% males and 48.8% females). The majority of participants were in the 41-50 year age group (32.1%) or the 21-30 year age category (27.1%). Doctors (33.8%) and technicians (18.7%) represented the most prominent professional categories. Most participants (65.2%) had a history of SARS-CoV-2 infection. Overall, 73.6% of participants were vaccinated, and 20.7% had received booster doses. The prevalence of diabetes among the participants was 27.4%. The vast majority of participants (98.3%) exhibited a positive SARS-CoV-2 antibody titer [defined as an index value $\geqslant$ 1.00; negative: < 0.80; equivocal: 0.80 – 0.99]. Additionally, most participants (73.6%) showed normal HbA1c levels (Table 1).

Association between diabetes status and immune response. A comparison of anti-S antibody titer levels between participants with and without diabetes revealed a statistically significant difference (t-test = -28.082, P < 0.001). Participants with diabetes exhibited a mean anti-S antibody titer of 0.27 AU/mL, while those without diabetes had a mean titer of 6109.0826 AU/mL. This substantial difference in antibody titers suggests a potential impact of diabetes on the immune response to SARS-CoV-2 infection.

Further analysis revealed that the majority of participants (98.3%) had an Anti-S antibody titer above the cut-off of 50.0, indicating a robust humoral response to SARS-CoV-2 infection. In contrast, a small proportion of participants (1.7%) had antibody titers below the cut-off, suggesting a possible decline in antibody levels over time or an underlying immune deficiency. The cutoff value of 50.0 AU/mL was established based on recommendations from assay manufacturers or established guidelines in the field of serology. These recommendations often consider factors such as assay sensitivity, specificity, and the desired balance between false-positive and false-negative results (Table 2).

The analysis revealed a significant difference in antibody titers between participants with and without diabetes (P < 0.001). Specifically, individuals with diabetes exhibited a lower mean antibody titer compared to those without diabetes, with a mean difference of -6109.0826 AU/mL (95% confidence interval [CI]: -6877.184 to -5340.981). This finding suggests that diabetes may modulate the humoral immune response to SARS-CoV-2 infection or vaccination (Table 3).

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Table 1. Demographic and health characteristics of the study population

Variable	Frequency/Percentage, n (%)
Gender	
Male	153 (51.2)
Female	146 (48.8)
Total	299 (100.0)
Age group, years	
21-30	81 (27.1)
31-40	65 (21.7)
41-50	96 (32.1)
51-60	57 (19.1)
Professional category	
Doctor	101 (33.8)
Administrative	17 (5.7)
Technician	56 (18.7)
Orderly	62 (20.7)
Nurse	19 (6.4)
Others	44 (14.7)
History of SARS-CoV-2 infection	
No	104 (34.8)
Yes	195 (65.2)
Vaccinated	
No	79 (26.4)
Yes	220 (73.6)
Booster received	
No	237 (79.3)
Yes	62 (20.7)
Diabetes status	
No	217 (72.6)
Yes	82 (27.4)
Anti-S antibody titer	
Negative	5 (1.7)
Positive	294 (98.3)
HbA1c groups	
Normal	220 (73.6)
Pre-diabetes	39 (13.0)
Diabetes	40 (13.4)

Table 2. Group statistics for anti-S antibody titer based on diabetes status

Diabetes Status	Anti-S Antibody Titer, AU/mL	N	Mean, AU/mL	SD, AU/mL
No	≥ 50.0	294	0.27	0.446
Yes	< 50.0	5	0.40	0.548

Table 3. One-sample test results for status (diabetes) and anti-S antibody titer

Variable	*P*-value	Mean difference	95% confidence interval	
			Lower	Upper
Status (diabetes)	<0.001	-.726	-0.782	-.0.675
Anti-S Ab titer	<0.001	6109.0826	5340.981	6877.184

Table 4 describes the association between gender, age group, professional category, and diabetes status with anti-S antibody titer among healthcare workers. The prevalence of diabetes was significantly different across age groups ($P < 0.001$), with the highest prevalence among participants aged 51–60 years (54.4%) and the lowest prevalence among those aged 21–30 years (6.2%). While there were notable differences in diabetes prevalence by gender and professional category, these differences did not reach statistical significance (gender: $P = 0.076$; professional category: $P = 0.028$). Males had a slightly higher prevalence of diabetes (29.4%) compared to females (25.3%). The highest prevalence of diabetes among professional categories was observed in administrative staff (41.2%), while the lowest prevalence was among doctors (21.8%).

There were no significant differences in the prevalence of negative anti-S antibody titer between males and females ($P = 0.33$) or across age groups ($P = 0.124$). However, a significant difference in the prevalence of negative anti-S antibody titers was found among professional categories ($P = 0.025$), with the highest prevalence among technicians (3.6%) and the lowest prevalence among doctors (0.0%).

These findings suggest that age is a significant factor influencing the prevalence of diabetes among healthcare workers. Additionally, professional category appears to be associated with the prevalence of negative anti-S antibody titers. Further research is needed to investigate the underlying mechanisms and potential implications for immune responses to SARS-CoV-2 infection.

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Table 4. Association of diabetes status and anti-S antibody titer with demographic and professional characteristics

Gender	**Status of diabetes**			***P*-value**
	No	**Yes**	**Total**	
Male	108 (70.6)	45 (29.4)	153 (100.0)	0.076
Female	109 (74.7)	37 (25.3)	146 (100.0)	
Total	217 (72.6)	82 (27.4)	299 (100.0)	
Gender	**ANTI-S antibody titer**			***P*-value**
	Negative	**Positive**	**Total**	
Male	5 (3.3)	147 (96.7)	152 (100)	0.33
Female	0 (0)	146 (100)	146 (100)	
Total	5 (1.7)	293 (98.3)	298 (100)	
Age group	**Status of diabetes**			***P*-value**
	No	**Yes**	**Total**	
21-30	76 (93.8)	5 (6.2)	81 (100.0)	<0.001*
31-40	53 (81.5)	12 (18.5)	65 (100.0)	
41-50	62 (64.6)	34 (35.4)	96 (100.0)	
51-60	26 (45.6)	31 (54.4)	57 (100)	
Total	217 (72.6)	82 (27.4)	299 (100.0)	
Age group	**ANTI-S antibody titer**			***P*-value**
	Negative	**Positive**	**Total**	
21-30	1 (1.2)	80 (98.8)	81 (100.0)	0.124
31-40	1 (1.6)	63 (98.4)	64 (100.0)	
41-50	1 (1.0)	95 (99.0)	96 (100.0)	
51-60	2 (3.5)	55 (96.5)	57 (100.0)	
Total	5 (1.7)	293 (98.3)	298 (100.0)	
Professional category	**Status of diabetes**			***P*-value**
	No	**Yes**	**Total**	
Doctor	79 (78.2)	22 (21.8)	101 (100.0)	0.028*
Administrative	10 (58.8)	7 (41.2)	17 (100.0)	
Technician	39 (69.6)	17 (30.4)	56 (100.0)	
Orderly	39 (62.9)	23 (37.1)	62 (100.0)	
Nurse	15 (78.9)	4 (21.1)	19 (100.0)	
Others	35 (79.5)	9 (20.5)	44 (100.0)	
Total	217 (72.6)	82 (27.4)	299 (100.0)	
Professional category	**ANTI-S Antibody Titer**			***P*-value**
	Negative	**Positive**	**Total**	
Doctor	0 (0.0)	100 (100)	100 (100.0)	0.025*
Administrative	0 (0.0)	17 (100)	17 (100.0)	
Technician	2 (3.6)	54 (96.4)	56 (100.0)	
Orderly	1 (1.6)	61 (98.4)	62 (100.0)	
Nurse	0 (0.0)	19 (100)	19 (100.0)	
Others	2 (4.5)	42 (95.5)	44 (100.0)	
Total	5 (1.7)	293 (98.3)	298 (100.0)	

**P*-value < 0.05 is considered statistically significant at 95% CI

Influence of prior infection and vaccination on immune response. Table 5 presents the association between diabetes status and past SARS-CoV-2 infection, vaccination status, and booster dose receipt among healthcare workers. The prevalence of past SARS-CoV-2 infection was not significantly different between participants with and without diabetes (P = 0.100). However, there was a significant difference in vaccination status between these groups (P < 0.001). Specifically, a higher proportion of participants without diabetes (86.1%) were vaccinated compared to those with diabetes (67.7%). The prevalence of booster receipt was not significantly different between participants with and without diabetes (P = 0.118).

There was no significant difference in the prevalence of negative anti-S antibody titer between participants with and without a history of SARS-CoV-2 infection (P = 0.115). This finding might be influenced by factors such as variations in the severity of prior infections, differences in the timing of antibody testing relative to infection onset, and the interplay of host immune responses with comorbidities or other underlying factors. Similarly, there was no significant difference in the prevalence of vaccination status between participants with negative and positive anti-S antibody titer (P = 0.389). Although a slightly higher proportion of participants with negative anti-S antibody titers were vaccinated (98.7%) compared to those with positive titers (98.2%), this difference was not statistically significant. The prevalence of booster receipt was not significantly different between participants with negative and positive anti-S antibody titer (P = 0.411).

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These findings suggest that while diabetes status appear to influence the immune response, prior SARS-CoV-2 infection, vaccination status, and booster dose receipt may not be strong predictors of negative anti-S antibody titers in this cohort of healthcare workers. However, further research is needed to investigate these relationships more comprehensively and explore potential contributing factors.

Table 5. Comparative analysis of health parameters based on past SARS-CoV-2 history, vaccination, and booster dose status

H/o SARS-CoV-2 in past	Status of diabetes			*P*-value
	No	Yes	Total	
No	77 (74.0)	27 (26.0)	104 (100.0)	
Yes	140 (71.8)	55 (28.2)	195 (100.0)	0.100
Total	217 (72.6)	82 (27.4)	299 (100.0)	
H/o SARS-CoV-2 in past	**ANTI-S antibody titer**			***P*-value**
	Negative	**Positive**	**Total**	
No	0 (0.0)	104 (100)	104 (100.0)	
Yes	5 (2.6)	189 (97.4)	194 (100.0)	0.115
Total	5 (1.7)	293 (98.3)	298 (100.0)	
Vaccinated	**Status of diabetes**			***P*-value**
	No	**Yes**	**Total**	
No	68 (86.1)	11 (13.9)	79 (100.0)	
Yes	149 (67.7)	71 (32.3)	220 (100.0)	<0.001*
Total	217 (72.6)	82 (27.4)	299 (100.0)	
Vaccinated	**ANTI-S antibody titer**			***P*-value**
	Negative	**Positive**	**Total**	
No	1 (1.3)	78 (98.7)	79 (100.0)	
Yes	4 (1.8)	215 (98.2)	219 (100.0)	0.389
Total	5 (1.7)	293 (98.3)	298 (100.0)	
Booster received	**Status of diabetes**			***P*-value**
	No	**Yes**	**Total**	
No	174 (73.4)	63 (26.6)	237 (100.0)	
Yes	41 (70.7)	17 (29.3)	58 (100.0)	0.118
Total	215 (72.9)	80 (27.1)	295 (100.0)	
Booster received	**ANTI-S antibody titer**			***P*-value**
	Negative	**Positive**	**Total**	
No	3 (1.3)	233 (98.7)	236 (100.0)	
Yes	1 (1.7)	57 (98.3)	58 (100.0)	0.411
Total	4 (1.4)	290 (98.6)	294 (100.0)	

**P*-value < 0.05 is considered statistically significant at 95% CI

The distribution of anti-S antibody titer levels. The results revealed a notable variation in antibody titer levels, with the majority of participants (51.8%) exhibiting antibody titers ranging from 2001 to 10000 units/mL. This indicates that a substantial proportion of healthcare workers mounted a robust humoral response to SARS-CoV-2 infection. However, a small percentage of participants (1.7%) displayed antibody titers below 50 units/mL, suggesting a potential decline in antibody levels over time or the presence of an underlying immune deficiency. Additionally, 22.1% of participants exhibited antibody titers between 501 and 2000 AU/mL, which could potentially indicate a waning immune response in some individuals. These findings underscore the importance of monitoring antibody levels among healthcare workers to ensure optimal protection against SARS-CoV-2 reinfection. A statistically significant difference in antibody titer levels was observed among the different titer ranges ($P = 0.006$) (Table 6).

Table 6. Comparative analysis of antibody levels among study participants (vaccinated and non-vaccinated)

Antibody titer (AU/mL)	Frequency, n (%)	*P*-value
0-49	5 (1.7)	
50-500	16 (5.4)	
501-2000	66 (22.1)	
2001-10000	155 (51.8)	0.006*
10001-20000	42 (14.0)	
>20000	15 (5.0)	
Total	299 (100.0)	

**P*-value < 0.05 is considered statistically significant at 95% CI

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Table 7. Comparative analysis of anti-S antibody titer groups across various demographic and health categories

	Anti-S AB titer groups						Total	*P*-value
Age group	**0-49**	**50-500**	**501-2000**	**2001-10000**	**10001-20000**	**>20000**		
21-30	1	11	25	37	4	3	81	-
	1.2%	13.6%	30.9%	45.7%	4.9%	3.7%	100.0%	
31-40	1	3	19	35	6	1	65	
	1.5%	4.6%	29.2%	53.8%	9.2%	1.5%	100.0%	
41-50	1	1	17	58	14	5	96	
	1.0%	1.0%	17.7%	60.4%	14.6%	5.2%	100.0%	
51-60	2	1	5	25	18	6	57	
	3.5%	1.8%	8.8%	43.9%	31.6%	10.5%	100.0%	
Total	5	16	66	155	42	15	299	
	1.7%	5.4%	22.1%	51.8%	14.0%	5.0%	100.0%	
	Anti-S AB titer groups						**Total**	***P*-value**
Gender	**0-49**	**50-500**	**501-2000**	**2001-10000**	**10001-20000**	**>20000**		
Male	5	8	37	77	21	5	153	0.007*
	3.3%	5.2%	24.2%	50.3%	13.7%	3.3%	100.0%	
Female	0	8	29	78	21	10	146	
	0.0%	5.5%	19.9%	53.4%	14.4%	6.8%	100.0%	
Total	5	16	66	155	42	15	299	
	1.7%	5.4%	22.1%	51.8%	14.0%	5.0%	100.0%	
	Anti-S AB titer groups						**Total**	***P*-value**
Professional category	**0-49**	**50-500**	**501-2000**	**2001-10000**	**10001-20000**	**>20000**		
Doctor	0	5	20	54	15	7	101	-
	0.0%	5.0%	19.8%	53.5%	14.9%	6.9%	100.0%	
Administrative	0	1	4	8	3	1	17	
	0.0%	5.9%	23.5%	47.1%	17.6%	5.9%	100.0%	
Technician	2	4	10	29	10	1	56	
	3.6%	7.1%	17.9%	51.8%	17.9%	1.8%	100.0%	
Orderly	1	2	17	33	7	2	62	
	1.6%	3.2%	27.4%	53.2%	11.3%	3.2%	100.0%	
Nurse	0	1	3	9	3	3	19	
	0.0%	5.3%	15.8%	47.4%	15.8%	15.8%	100.0%	
Others	2	3	12	22	4	1	44	
	4.5%	6.8%	27.3%	50.0%	9.1%	2.3%	100.0%	
Total	5	16	66	155	42	15	299	
	1.7%	5.4%	22.1%	51.8%	14.0%	5.0%	100.0%	
	Anti-S AB titer groups						**Total**	***P*-value**
H/o SARS-CoV-2 in past	**0-49**	**50-500**	**501-2000**	**2001-10000**	**10001-20000**	**>20000**		
No	0	10	25	56	9	4	104	0.011*
	0.0%	9.6%	24.0%	53.8%	8.7%	3.8%	100.0%	
Yes	5	6	41	99	33	11	195	
	2.6%	3.1%	21.0%	50.8%	16.9%	5.6%	100.0%	
Total	5	16	66	155	42	15	299	
	1.7%	5.4%	22.1%	51.8%	14.0%	5.0%	100.0%	
	Anti-S AB titer groups						**Total**	***P*-value**
Vaccinated	**0-49**	**50-500**	**501-2000**	**2001-10000**	**10001-20000**	**>20000**		
No	1	11	23	39	3	2	79	<0.001
	1.3%	13.9%	29.1%	49.4%	3.8%	2.5%	100.0%	
Yes	4	5	43	116	39	13	220	
	1.8%	2.3%	19.5%	52.7%	17.7%	5.9%	100.0%	
Total	5	16	66	155	42	15	299	
	1.7%	5.4%	22.1%	51.8%	14.0%	5.0%	100.0%	
							Total	***P*-value**
Booster received	**0-49**	**50-500**	**501-2000**	**2001-10000**	**10001-20000**	**>20000**		
No	3	15	57	125	25	12	237	0.002*
	1.3%	6.3%	24.1%	52.7%	10.5%	5.1%	100.0%	
Yes	1	1	8	28	17	3	58	
	1.7%	1.7%	13.8%	48.3%	29.3%	5.2%	100.0%	
Total	4	16	65	153	42	15	295	
	1.4%	5.4%	22.0%	51.9%	14.2%	5.1%	100.0%	

*P-value < 0.05 is considered statistically significant at 95% CI

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Notable disparities were observed in anti-S antibody titer levels across different age groups (t-test = 52.603, df = 15, $P < 0.001$). Specifically, participants aged 41-50 and 51-60 years exhibited higher antibody titers compared to younger age groups. Gender-based differences were observed in anti-S antibody titers (t-test = 7.483, df = 5, $P = 0.007$), with males displaying significantly higher antibody titers compared to females. Furthermore, significant variation in antibody titers was observed among professional categories (t-test = 18.693, df = 25, $P < 0.001$), with doctors having significantly higher titers compared to other professional categories.

Participants with a history of SARS CoV-2 infection exhibited significantly higher antibody titers (t-test = 12.226, df = 5, $P = 0.011$) compared to those without a history of infection. Vaccinated individuals showed significant variation in antibody titers (t-test = 26.741, df = 5, $P < 0.001$). Those vaccinated had notably higher antibody titers compared to non-vaccinated individuals. Participants who received a booster dose had significantly higher antibody titers (t-test = 15.820, df = 5, $P = 0.002$) compared to those without a booster dose (Table 7).

DISCUSSION

Our study reveals intriguing gender-specific variations in SARS-CoV-2 antibody responses among healthcare workers. Specifically, the higher antibody responses observed in males compared to females align with studies indicating hormonal and genetic influences on immune response [16, 17]. This finding highlights the need to explore the underlying mechanisms, potentially involving hormonal fluctuations, genetic predispositions, or differences in immune cell activation pathways [18, 19]. For example, several studies have indicated the role of sex hormones in modulating immune responses, which could potentially influence antibody production [20, 21]. The higher antibody responses in males could be attributed to the immunomodulatory effects of sex hormones, including estrogen and testosterone [22, 23]. These findings align with previous research emphasizing gender-specific variations in COVID-19 outcomes and immune responses [24-26].

Age-related differences in antibody titers illuminate the impact of age on immune responses. While the study did not find statistically significant trends within specific age brackets, the higher antibody titers observed in older age groups, particularly those aged 41-50 and 51-60, suggest a cumulative effect of prolonged virus exposure. This finding aligns with previous studies that indicate stronger and more diverse immune responses in older individuals due to repeated encounters with pathogens [27, 28]. However, the complex nature of age-related immune responses is likely influenced by factors such as comorbidities, prior infections, and overall health status [29, 30]. Further investigations are necessary to explore these factors and their impact on immune responses [29, 30].

Our results highlight the critical role of vaccinations in potentially mitigating diabetes risks and enhancing antibody responses. Recent studies have emphasized the protective effects of vaccinations against diabetes, as evidenced by the reduced prevalence of diabetes among vaccinated individuals [31, 32]. Additionally, individuals who received vaccinations, particularly those who also received booster doses, had significantly higher antibody responses, underscoring the importance of robust vaccination strategies. However, further research is needed to understand why booster doses did not significantly influence diabetes prevalence in this study. This investigation should include a comprehensive exploration of potential factors, such as differences in vaccine types, dosages, and individual immune responses [32].

Variations in antibody titers across professional categories emphasize the diverse risks faced by healthcare workers. For example, doctors, who are directly involved in patient care, exhibit substantially higher antibody titers, which likely reflects their elevated exposure levels. This finding aligns with previous research highlighting the heightened vulnerability of frontline healthcare professionals [33, 34]. Moreover, the disparities observed within professional categories suggest a nuanced interplay of factors, including exposure duration, working conditions, and individual immune responses. This complexity underscores the importance of tailored interventions and workplace safety measures for different healthcare roles [35].

This study provides an important understanding of the interplay between demographic factors and immune response to SARS-CoV-2 infection and vaccination. These findings have significant implications for public health strategies. For example, tailoring vaccination efforts based on specific demographic factors, such as gender, age, and profession, could potentially enhance immune responses among healthcare workers, thereby strengthening their defenses against SARS-CoV-2. One approach to achieving this goal would be to implement targeted vaccination campaigns designed for different demographic groups, such as offering vaccination clinics at specific times and locations convenient for different age groups and professions.

Furthermore, this study highlights the need for comprehensive research that considers the complex interplay of factors influencing immune response, including genetic predispositions, environmental factors, and socioeconomic variables. Such research could leverage electronic health records to identify individuals with specific risk factors and offer tailored healthcare interventions. For example, individuals identified as having genetic predispositions or socioeconomic factors that may negatively impact their immune response could be prioritized for personalized vaccination schedules or immune-boosting interventions. This approach would provide a more holistic understanding of the factors

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influencing immune responses and facilitates the development of personalized healthcare approaches.

This study, while offering valuable insights into antibody responses among healthcare workers, has several limitations. First, its single-center design and non-randomized sampling may limit generalizability and introduce bias. Second, relying solely on IgG antibodies, without considering the timing of sample collection relative to infection or vaccination, provides a limited view of immune response. Third, the study does not address potential confounders, such as underlying health conditions or lifestyle factors, nor does it explore the mechanisms behind the observed variations in antibody titers related to demographic factors. These limitations highlight the need for more robust, multi-center studies that incorporate a wider range of immune markers and account for potential confounding variables to better understand the complex interplay of demographics and immune response to SARS-CoV-2.

This study provides valuable insights into the complex interplay of demographic factors, immune responses, and vaccination efficacy among healthcare workers. Specifically, the observed disparities and trends in SARS-CoV-2 antibody levels, diabetes prevalence, and vaccination responses pave the way for more targeted interventions and further research initiatives designed to address the challenges faced by healthcare workers during the COVID-19 pandemic. Ultimately, this work provides a foundation for optimizing public health strategies and developing personalized healthcare approaches.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest associated with this manuscript.

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