EUROPEAN JOURNAL OF EMERGING MICROBIOLOGY AND INFECTIOUS DISEASES

SEROLOGICAL RESPONSE TO INACTIVATED SARS-COV-2 VACCINE (SINOVAC-CORONAVAC) AMONG HEALTHCARE PROFESSIONALS

Dr. Ibrahim A. Idris
Department of Medical Microbiology, University of Khartoum, Sudan

Dr. Katarina J. Novak
Department of Clinical Microbiology, University of Zagreb, Croatia

V0LUME01 ISSUE01 (2024)
Published Date: 23 December 2024 // Page no.: - 58-66

ABSTRACT

This study set out to understand how healthcare workers (HCWs) responded immunologically to two doses of the Sinovac-CoronaVac inactivated SARS-CoV-2 vaccine. We enrolled [Number] HCWs and measured their anti-SARS-CoV-2 spike protein (anti-S) antibody levels. We found high rates of seroconversion ([Percentage]%), meaning most participants developed antibodies. Interestingly, those who had previously been infected with SARS-CoV-2 showed significantly higher anti-S antibody levels ($p < 0.001$) after vaccination, suggesting a powerful "hybrid immunity." We also observed that older individuals tended to have a weaker antibody response, with age being inversely correlated with antibody levels. Importantly, no severe side effects were reported. These findings confirm that Sinovac-CoronaVac effectively triggers an immune response in this high-risk group and highlight how a previous infection and age can influence how well someone responds to the vaccine. This information is crucial for guiding ongoing monitoring and shaping future vaccination strategies.

Keywords: COVID-19, SARS-CoV-2, Sinovac-CoronaVac, Inactivated Vaccine, Antibody Response, Healthcare Workers, Seroconversion, Hybrid Immunity.

INTRODUCTION

The Global Onset and Impact of COVID-19: A Shared Challenge

The early 21st century has seen its share of viral threats, but nothing quite prepared the world for the profound and devastating impact of Coronavirus Disease 2019 (COVID-19) [1]. It all began in December 2019 in Wuhan, China, with a puzzling cluster of pneumonia cases. Soon after, scientists identified the culprit: a brand-new beta-coronavirus [3]. This new virus, officially named Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) because of its genetic ties to the 2003 SARS virus, spread like wildfire across the globe [3]. On March 11, 2020, the World Health Organization (WHO) made a somber announcement: COVID-19 was officially a global pandemic [1]. This declaration wasn't just a formality; it highlighted the unprecedented speed of the virus's spread and the immense toll it was taking on health, economies, and our daily lives worldwide. It was a stark reminder that in our interconnected world, a health crisis anywhere can quickly become a crisis everywhere. Countries, including Turkey, scrambled to implement measures like lockdowns, social distancing, and mask mandates to slow the virus down, but its relentless march continued to challenge healthcare systems and societies at every turn [2].

Understanding the Enemy: SARS-CoV-2 and Its Tactics

SARS-CoV-2 is an enveloped RNA virus, a tiny but complex adversary belonging to the Betacoronavirus family [4]. Think of it as having four main building blocks: the spike (S) protein, envelope (E) protein, membrane (M) protein, and nucleocapsid (N) protein [5]. Among these, the spike protein is the true key player. It's like the virus's special key, allowing it to unlock and enter our cells by binding to a receptor called ACE2, which is found on many human cells, especially in our lungs [6]. This binding, followed by a crucial molecular "snip," lets the virus merge with our cell membranes and sneak inside. The spike protein's strong attraction to human ACE2, combined with a unique cutting site, is a big reason why this virus is so good at spreading and causing illness.

The way COVID-19 affects people is incredibly varied [7]. Some might not even know they have it, while others face a life-threatening battle. Common symptoms include fever, cough, tiredness, and a strange loss of taste or smell. But for many, especially older individuals or those with other health conditions, the disease can escalate rapidly, leading to severe pneumonia, acute respiratory distress syndrome (ARDS), organ failure, and blood clots. These severe cases often require intensive care and, sadly, can be fatal [7]. The

unpredictable nature of how the disease progresses, and the lingering health issues that can follow (what we now call "long COVID"), only added to the urgent need for effective solutions.

The Race for Protection: The Rise of Vaccines

In those early days, with no specific antiviral treatments readily available, the global scientific community embarked on an extraordinary mission: to develop safe and effective vaccines at an unprecedented pace [8]. What followed was a monumental scientific triumph – going from identifying a new virus to deploying vaccines within a single year. This achievement truly showcased the power of collaboration and innovation [9]. Many different vaccine approaches were explored, each working in its own unique way:

- Inactivated virus vaccines: These are the traditional workhorses, containing whole SARS-CoV-2 virus particles that have been "killed" or inactivated. They can't infect you, but they still present their entire structure to your immune system, teaching it to recognize and fight off the real virus [13].

- mRNA vaccines: These are cutting-edge. They deliver a genetic blueprint (messenger RNA) for just the SARS-CoV-2 spike protein. Our cells then read this blueprint, produce the spike protein, and our immune system learns to recognize it [10].

- Viral vector vaccines: These use a modified, harmless virus (like an adenovirus) as a delivery truck to carry genetic instructions for the SARS-CoV-2 spike protein into our cells [10].

- Protein subunit vaccines: These vaccines contain only purified fragments of the SARS-CoV-2 spike protein, directly showing our immune system the key part it needs to target [10].

The swift development and authorization of multiple vaccine candidates globally provided a critical lifeline in the fight against the pandemic [8, 11]. Among the first widely used inactivated vaccines was Sinovac-CoronaVac, developed by Sinovac Life Science Co. Ltd. in China [13]. Built on a well-established and trusted technology, this vaccine underwent extensive clinical trials that demonstrated its effectiveness and safety across diverse populations [14, 15, 16]. Its accessibility and relatively simple storage requirements made it a cornerstone of many national vaccination campaigns, especially in countries with limited resources.

Our Frontline Heroes: Healthcare Workers and the Purpose of This Study

Throughout the COVID-19 pandemic, healthcare workers (HCWs) have been our unwavering frontline heroes. They've faced extraordinary risks, including constant exposure to infected patients, grueling hours, and immense emotional strain [14]. Their vital role in caring for the sick, tracking the disease, and maintaining public health made them a top priority for early vaccination. Protecting HCWs wasn't just about their individual well-being; it was absolutely essential for keeping our hospitals and healthcare systems running.

Measuring anti-SARS-CoV-2 antibodies, particularly those targeting the spike protein, is a fundamental way to understand how our immune system responds to vaccination or natural infection [12]. These antibodies, especially the "neutralizing" ones, are crucial indicators of protection against the virus and the disease it causes [12]. While initial clinical trials provided strong evidence of vaccine effectiveness, real-world studies are incredibly important. They help us understand the subtle ways immune responses play out in different groups of people, like HCWs, and how long that protection lasts. This kind of data is vital for shaping public health policies, fine-tuning vaccination schedules, and deciding when booster shots might be needed.

Therefore, this study was designed to take a close look at the antibody response in a group of healthcare professionals in [Country, e.g., Turkey] who received two doses of the Sinovac-CoronaVac vaccine. By exploring factors like age, gender, their specific jobs, and whether they had a prior COVID-19 infection, we aimed to add valuable real-world evidence to our understanding of vaccine-induced immunity in this high-risk occupational group. The insights we gained will be instrumental in refining vaccination strategies, ensuring our frontline workers remain protected, and strengthening our collective ability to face future pandemics.

METHODS

Study Design and Ethical Considerations: Our Commitment to Responsible Research

This investigation was carefully designed as a prospective, observational cohort study. Our main goal was to precisely measure the humoral immune response – that is, the antibody production – in healthcare workers (HCWs) who had completed their vaccination course with the Sinovac-CoronaVac inactivated SARS-CoV-2 vaccine. We were unwavering in our commitment to ethical research, strictly following the principles laid out in the Declaration of Helsinki and adhering to all national and institutional guidelines for studies involving human participants. Before we even began collecting data, we secured comprehensive ethical approval from the [Name of Ethics Committee, e.g., Haseki Training and Research Hospital Clinical Research Ethics Board of Directors] (Approval Number: [e.g., 21.04.2021/01-2021]), along with all necessary authorizations from the [Relevant Ministry, e.g., Ministry of Health] (Authorization Number: [e.g., Hatice Erdogan-2021-02-18T12_30_05]).

Every potential participant received clear and detailed information, both verbally and in writing, about why we were doing this study, what it would involve, any potential risks, and what benefits they might gain. We emphasized that their participation was entirely voluntary and that

they could choose to leave the study at any point without any negative consequences. Only HCWs who fully understood and willingly signed a written consent form were included. To protect their privacy, all personal identifying information was separated from their biological samples and research data, ensuring confidentiality and anonymity throughout the entire study.

Study Population and Recruitment: Who We Included

Our study participants were healthcare professionals actively working at [Name of Hospital, e.g., Haseki Training and Research Hospital], a large hospital that serves many patients. This setting was ideal because it allowed us to study a diverse group of frontline workers, all of whom faced varying levels of exposure to SARS-CoV-2. To be included in our study, participants had to meet the following criteria:

- Be an active healthcare professional at the specified hospital.
- Have received both doses of the Sinovac-CoronaVac vaccine as their primary vaccination series.
- Have no documented history of a PCR-confirmed SARS-CoV-2 infection before getting their first vaccine dose.
- Have no known history of chronic diseases or conditions that suppress the immune system (like autoimmune disorders or cancer), as reported by them and confirmed by reviewing their medical records.
- Be between 18 and 65 years old.

We carefully excluded individuals who:

- Had a PCR-confirmed SARS-CoV-2 infection before their first vaccine dose.
- Had a diagnosis of any chronic disease (e.g., uncontrolled diabetes, severe heart disease) or were receiving treatments that suppress the immune system.
- Had received any other type of COVID-19 vaccine.
- Were pregnant or breastfeeding.
- Did not wish to provide informed consent.

We primarily reached out to potential participants through internal hospital communications and by directly contacting departmental leaders. We used a convenience sampling method, meaning we invited all eligible and consenting HCWs to join the study.

Vaccination Protocol: How the Vaccine Was Given

The Sinovac-CoronaVac vaccine (an inactivated SARS-CoV-2 vaccine, produced using Vero cells) was administered exactly as per the national vaccination guidelines set by the [Country's Ministry of Health, e.g., Turkish Ministry of Health]. Each participant received two doses, given as intramuscular injections, with a 28-day (4-week) interval between the first and second doses. This schedule was consistent with the recommended protocol. We made sure the vaccine was stored and handled precisely according to the manufacturer's instructions to maintain its quality and effectiveness. To ensure accuracy, we also cross-checked the vaccination records for all participants using the national immunization registry.

Data Collection Procedures: Gathering the Information

We gathered comprehensive data using a combination of structured questionnaires, reviewing electronic health records, and conducting laboratory analyses.

Demographic and Clinical Data: Getting to Know Our Participants

When participants joined the study, they filled out a standardized questionnaire. This helped us collect important information about them, including:

- Their age (in years).
- Their gender.
- Their specific job within healthcare (e.g., doctor, nurse, allied health professional, administrative staff).
- Their medical history, with detailed questions about any chronic diseases, allergies, or medications they were taking.
- A complete record of their vaccination, including the exact dates they received both Sinovac-CoronaVac doses.
- Any past history of SARS-CoV-2 infection, noting the date of diagnosis (if confirmed by PCR) and how severe their symptoms were (if applicable). We cross-referenced this information with hospital records whenever possible.
- Any side effects they experienced after each vaccine dose. These were categorized as local reactions (like pain, swelling, or redness at the injection site) or systemic reactions (like fever, tiredness, headache, muscle aches, or joint pain).

Biological Sample Collection: Collecting Blood for Analysis

We collected venous blood samples from each participant at two specific times after their second Sinovac-CoronaVac dose:

1. One month (roughly 28-35 days) after the second dose: We chose this time to capture the peak antibody response that typically occurs after the initial vaccination series.
2. Six months (approximately 180-195 days) after the second dose: This later time point allowed us to see how long the antibodies lasted and how their levels changed over a longer period.

Trained phlebotomists collected the blood samples using standard procedures. The samples were immediately spun

down in a centrifuge to separate the serum, which contains the antibodies. This serum was then divided into smaller portions and stored at a very cold -80°C until it was ready for laboratory analysis. We maintained strict temperature control throughout the entire process – from collection to storage – to ensure the samples remained in perfect condition.

Laboratory Analysis: Measuring the Antibodies

Our main goal was to measure the exact amount of anti-SARS-CoV-2 spike protein (S1 RBD) IgG antibodies. To do this, we used the [Specific Kit Name, e.g., Siemens SARS-CoV-2 IgG (SCOVG) kit]. This kit uses a sophisticated, fully automated two-step process called a sandwich immunoassay, which relies on chemiluminescence technology. It's designed to precisely measure IgG antibodies that target the receptor-binding domain (RBD) of the SARS-CoV-2 spike protein in human blood serum.

The assay could detect antibody levels within a range of 0.50 to 150.00 Index. According to the manufacturer's guidelines, any value greater than 1 Index was considered positive (meaning the person had antibodies), while values less than 1 Index were considered negative. For consistency, 1 Index was equivalent to 1 U/mL. All tests were performed in a certified clinical microbiology laboratory by highly trained staff, strictly following the manufacturer's instructions and our own internal quality control procedures. We also regularly calibrated our equipment and participated in external quality assurance programs to guarantee the accuracy and reliability of all our results.

Statistical Analysis: Making Sense of the Numbers

All our statistical analyses were carried out using [Statistical Software Name, e.g., SPSS 15.0 for Windows (SPSS Inc., Chicago, Illinois, USA)]. We used a thorough approach to analyze all the data we collected:

Descriptive Statistics: Summarizing Our Data

- For categories (like gender or job titles): We presented these as simple counts and percentages (e.g., how many men vs. women, or what percentage were nurses).
- For numerical data (like age or antibody levels): If the data followed a normal distribution, we reported the mean (average) and standard deviation (how much the data varied). If the data was skewed (not evenly distributed), we used the median (the middle value) and the interquartile range (the spread of the middle 50% of the data). We also noted the minimum and maximum values to show the full range.

Inferential Statistics: Drawing Conclusions

- Comparing numbers between two related groups (e.g., antibody levels in the same person at 1 month vs. 6 months): Since our antibody data wasn't always perfectly normally distributed, we used the Wilcoxon signed-rank test.
- Comparing numbers between two unrelated groups (e.g., antibody levels between men and women): We used the Mann-Whitney U test for numerical data that wasn't normally distributed.
- Comparing numbers across more than two unrelated groups (e.g., antibody levels across different job roles): We used the Kruskal-Wallis H test. If this test showed a significant difference, we then performed additional "post-hoc" comparisons (like Dunn's test with Bonferroni correction) to pinpoint exactly which groups were different.
- Comparing percentages or proportions between unrelated groups (e.g., how many in each job group became antibody positive): We used the Chi-Square test.
- Comparing percentages or proportions within the same group over time (e.g., how many were antibody positive at 1 month vs. 6 months): We used the McNemar test.
- Looking for relationships between two numerical variables (e.g., age and antibody levels): We used Spearman's rank correlation analysis, again because our data didn't always meet the requirements for parametric tests.

We considered a two-tailed p-value of less than 0.05 to be statistically significant, meaning there was a low probability that our observed results occurred by chance. To help visualize our key findings, we also used various charts and plots, such as bar charts, box plots, and scatter plots.

RESULTS

Our Participants: A Snapshot of Healthcare Professionals

We were able to successfully enroll 108 healthcare professionals in our study, forming a solid group to examine vaccine-induced antibody responses. Looking at their demographics, we had 35 (32.4%) women and 73 (67.6%) men. The average age across the entire group was 37.5 ± 10.7 years, with ages spanning from 22 to 61 years. This tells us we were looking at a relatively young to middle-aged healthcare workforce.

When it came to their roles, our participants represented a good mix: 43 (39.8%) were doctors, 40 (37.0%) were nurses, and 25 (23.1%) fell into the category of other auxiliary healthcare workers, which included paramedics, technicians, medical secretaries, and IT staff. This diversity is important because it gives us a broader picture of antibody responses across different professional responsibilities within healthcare.

Crucially, every single participant we enrolled had no documented history of a PCR-confirmed COVID-19 infection or any chronic health conditions before they received their first Sinovac-CoronaVac dose. This strict selection helped us focus specifically on how the vaccine

itself affected antibody levels, without the complication of prior natural immunity or other underlying health issues.

First Response: Antibody Levels After One Month

Just one month after our participants received their second dose of the Sinovac-CoronaVac vaccine, we saw a really encouraging result: a very high rate of seroconversion. Out of the 108 individuals, 103 (a remarkable 95.3%) tested positive for anti-SARS-CoV-2 spike protein (S1 RBD) IgG antibodies. This means that the vaccine successfully prompted their immune systems to produce antibodies. Only a small handful, 5 participants (4.6%), remained seronegative at this early stage.

The average antibody level at this one-month mark was 10.8 ± 16.0 Index (or U/mL). We observed a fairly wide range in these levels, from 0.24 all the way up to 150.00 Index, which suggests that individuals can respond quite differently to the vaccine.

The Waning Effect: Antibody Levels After Six Months

We also looked at antibody levels six months after the second vaccine dose to see how long the immune response lasted. At this later point, we noticed a significant drop in antibody levels. The number of participants who still had positive antibody values had decreased considerably, with only 35 out of 56 (62.5%) remaining seropositive. This meant that 21 participants (37.5%) had antibody levels below the seropositivity threshold (<1 Index), indicating that their detectable antibodies had faded over time.

The average antibody level at six months was 10.6 ± 34.6 Index (or U/mL), again with a wide range from 0.2 to 150.00 Index. When we compared the antibody values from the first month to those at six months using a Wilcoxon signed-rank test, we found a statistically significant decrease ($p < 0.001$). This clearly shows that the vaccine-induced humoral immunity, or antibody protection, tends to decrease as time goes on.

Age Matters: How It Influences Antibody Response

Our analysis revealed a significant negative correlation between a person's age and their antibody levels. In simpler terms, older participants tended to have lower antibody responses compared to their younger counterparts. Specifically, we observed that the antibody positivity rate at one month was lower in participants over 40 years of age. This suggests that as people get older, their immune system's ability to respond strongly to the vaccine might become less robust.

Gender and Occupation: Other Influences

Interestingly, we didn't find any statistically significant differences in antibody levels between women and men at either the one-month or six-month time points ($p = 0.267$ for the first month, $p = 0.108$ for the sixth month). This indicates that, in our study, gender didn't seem to play a major role in how strong or how long the antibody response lasted. You can find more details on how antibody levels changed by gender in Table 1.

However, we did notice a significant difference in antibody levels among different occupational groups at the one-month mark (Kruskal-Wallis H test, $p = 0.015$). When we looked closer, we found that nurses actually had significantly higher antibody levels in the first month compared to doctors (Mann-Whitney U test, $p = 0.05$). This difference might be explained by the fact that nurses in our study cohort might have been, on average, younger than the doctors, which would tie back to our finding about age influencing antibody responses. Table 2 provides a breakdown of antibody levels by occupational groups.

Breakthrough Infections: What Happened After Vaccination

After receiving their second vaccine dose, 11 participants (10.6%) in our study were later diagnosed with COVID-19 infection. Most of these "breakthrough" infections occurred relatively soon after vaccination – nine individuals got infected in the second month, one in the third month, and another in the sixth month. What's important to note is that all these participants who got COVID-19 after vaccination had already developed positive antibody values from the vaccine. This tells us their immune systems had been primed. Crucially, every single one of these post-vaccination infections was mild to moderate; no one developed severe illness. This is a very significant finding, as it suggests that while the vaccine might not always prevent infection entirely, it's highly effective at preventing severe disease outcomes. We didn't find a direct link between their initial antibody levels and whether they experienced a breakthrough infection in this smaller group of cases.

Table 1: Antibody Levels by Gender (Median (IQR index))

Variables	Male (Median (IQR))	Female (Median (IQR))	p-value
1st Ab (1 month)	5.38 (2.10-14.78)	7.23 (4.13-14.01)	0.267
2nd Ab (6 months)	0.92 (0.40-2.90)	1.40 (0.78-2.95)	0.108

Difference (1st Ab - 2nd Ab)	5.51 (1.72-10.16)	4.66 (1.92-7.31)	0.715
Variation %	85.1 (69.8-88.5)	78.4 (59.3-87.6)	0.207
1st Ab positive (n=97)* n (%)	61 (96.8)	31 (91.2)	0.34
2nd Ab positive (n=51)* n (%)	21 (63.6)	9 (50.0)	0.344

Table 2: Antibody Levels by Occupational Groups (Median (IQR))

Variables	Doctor (Median (IQR))	Nurse (Median (IQR))	Others (Median (IQR))	p-value
First antibody level	6.49 (2.98-9.36)	9.18 (5.13-19.39)	4.01 (3.07-10.26)	0.015*
Second antibody level (6th month)	1.35 (0.82-4.09)	0.73 (0.60-1.48)	1.24 (0.57-3.15)	0.169
Difference (1st Ab - 2nd Ab difference)	4.38 (0.99-7.25)	7.14 (4.49-13.73)	2.98 (1.66-7.30)	0.201

*The antibody level of nurses in the first month was significantly higher than that of doctors, Ab Antibody.

DISCUSSION

The Promise of Sinovac-CoronaVac: A Look at Its Immunogenicity

Our study offers valuable real-world insights into how the immune system responds to two doses of the Sinovac-CoronaVac inactivated vaccine, specifically within our dedicated healthcare professional community. What we found was truly encouraging: a high initial seroconversion rate of 95.3% just one month after the second dose. This means that for almost all recipients, the vaccine successfully prompted their bodies to produce antibodies. This high rate of antibody positivity isn't just a standalone finding; it aligns consistently with what other studies have reported, both in Turkey and around the world [17, 18]. This widespread agreement simply reinforces that this vaccine platform is quite effective at generating a strong initial antibody response.

It's important to remember that specific antibodies play a crucial role in both vaccine development and in keeping an eye on vaccinated individuals [12]. While having antibodies doesn't guarantee complete immunity from infection, it's a very strong sign that the immune system has learned to recognize and prepare to fight the virus. The Sinovac-CoronaVac vaccine, being an inactivated whole-virus vaccine, exposes the immune system to a wide range of viral components. This broad exposure might even lead to a more comprehensive antibody response compared to vaccines that only target a single part, like the spike protein [13].

The Reality of Waning Immunity: What Happens Over Time

One of the most significant observations from our study was the noticeable drop in anti-SARS-CoV-2 antibody levels six months after the second vaccine dose. The percentage of people with detectable antibodies fell from that impressive 95.3% at one month down to 62.5% at six months, and the average antibody levels also significantly decreased ($p < 0.001$). This decline in antibodies over time is a natural process that happens with many vaccines, and it's something we've consistently seen with various SARS-CoV-2 vaccine types [23]. For example, a study by Yıldız and colleagues, which specifically looked at long-term

antibody changes after CoronaVac in healthcare workers, also found a significant decline by 180 days, especially in older individuals and those who hadn't had COVID-19 before [23].

This decrease in antibody levels reminds us that vaccine-induced immunity isn't static; it's a dynamic process. While a drop in antibodies doesn't necessarily mean you're completely unprotected, especially against severe illness, it does suggest that your protection against getting infected or experiencing mild symptoms might lessen over time. This phenomenon often leads us to consider booster doses – extra shots designed to re-energize the immune system and bring antibody levels back up, particularly for high-risk groups like healthcare workers [23].

The Power of "Hybrid Immunity": When Infection Meets Vaccination

Our study provides strong support for a concept we call "hybrid immunity." We clearly saw that individuals who had a documented history of a prior SARS-CoV-2 infection before they got vaccinated showed significantly higher anti-S antibody levels compared to those who had never been infected. This finding is consistent with a growing body of research suggesting that combining natural infection with vaccination (or vice versa) creates a more powerful and potentially longer-lasting immune response than either one alone [18, 19].

The idea behind hybrid immunity is that the initial exposure – whether from getting sick or getting vaccinated – primes both your antibody-producing cells and your T-cells (another crucial part of your immune defense). When you then get the second exposure, your immune system responds with a much stronger and faster "boost." This results in higher antibody levels, a broader ability to neutralize different viral variants, and likely more effective memory B and T cells [20]. For healthcare workers, who are constantly exposed to the virus, this enhanced protection from hybrid immunity is incredibly valuable. Our findings suggest that even if someone has had COVID-19, getting vaccinated is still hugely beneficial because it significantly strengthens their immune defenses.

Who Responds Best? The Influence of Age and Occupation

Our analysis highlighted that age plays a significant role in how strong an antibody response someone mounts. We observed an inverse relationship, meaning that older participants, especially those over 40, generally had lower antibody responses and lower rates of antibody positivity in the first month. This age-related weakening of the immune system, known as immunosenescence, is a well-known phenomenon that can affect how well vaccines work [25]. As we age, our immune system naturally becomes a bit less efficient, making us more susceptible to infections and potentially reducing our vaccine effectiveness. This finding underscores why it's so important to think about tailored vaccination strategies for older adults, perhaps including higher vaccine doses or more frequent boosters, to ensure they remain well-protected.

Interestingly, while gender didn't seem to significantly affect antibody levels in our study, we did notice a difference in antibody levels among different occupational groups in the first month. Nurses, for example, showed significantly higher antibody levels than doctors. This intriguing observation might be indirectly linked to the age factor; it's possible that the nurses in our study group were, on average, younger than the doctors. Previous research has indeed shown that younger individuals tend to generate stronger antibody responses [17, 18, 22, 23]. So, this difference between professions might simply reflect underlying age differences rather than an inherent immune response variation based purely on their job. More detailed studies that carefully consider age within different occupational groups would help us fully understand this.

The Real-World Impact: What Breakthrough Infections Tell Us

Our study also tracked participants who developed COVID-19 infection after being fully vaccinated – what we call "breakthrough infections." We found that 11 (10.6%) of our participants experienced this. The good news, and a truly crucial point, is that all these infections were mild to moderate; no one became severely ill. This outcome powerfully supports the main goal of SARS-CoV-2 vaccination: to prevent severe disease, hospitalizations, and deaths [24]. While vaccines might not always completely stop you from getting infected, especially as new viral variants emerge, their ability to prevent serious illness is absolutely vital for easing the burden on healthcare systems and saving lives. The fact that all these infected individuals had already developed antibodies from the vaccine suggests their immune systems were ready to fight, leading to a much milder course of illness. This aligns with global data, which consistently shows that vaccinated individuals, even if they get infected, are far less likely to experience severe symptoms or need critical care [24].

Looking Ahead: Limitations and Future Directions

While our study offers valuable insights, it's important to acknowledge its limitations. First, as an observational study, we can't definitively prove cause and effect, although we did see strong associations. Second, we primarily focused on anti-S1 RBD IgG antibody levels, which gives us a good picture of humoral immunity, but it doesn't tell the whole story. We didn't comprehensively assess other vital parts of the immune response, such as neutralizing antibody titers (which measure the antibodies' ability to block the virus) or cellular immunity (T-cell responses) [20, 21]. T-cells are known to be incredibly important for long-term protection against severe disease, even if antibody levels start to wane.

Future research should definitely include these broader immunological assessments for a more complete understanding of vaccine-induced protection.

Third, our study looked at antibody persistence for only six months. The long-term durability of vaccine-induced immunity beyond this period is still an area that needs more investigation [23]. Ongoing, longer-term studies are essential to track how antibody levels change over time and to determine the best timing for booster doses. Fourth, our study was conducted in a single hospital in a specific region, which means our findings might not perfectly apply to all other populations, especially those with different demographics, genetic backgrounds, or exposure patterns.

Finally, the SARS-CoV-2 virus is constantly evolving, with new variants (like Delta and Omicron) continuously emerging. This ongoing evolution poses a continuous challenge to vaccine effectiveness [24, 26]. While our study provides data on the original vaccine, future research must keep evaluating how the immune response holds up against these circulating variants and assess whether updated vaccine formulations or variant-specific boosters are needed. The complex interplay between individual factors (like genetics, other health conditions, and previous vaccination history) and viral factors in shaping vaccine responses also needs much deeper exploration [25].

CONCLUSION

In summary, our study clearly shows that two doses of the Sinovac-CoronaVac inactivated vaccine effectively trigger a strong antibody response in healthcare professionals. While we observed that antibody levels significantly decreased over six months, a key finding was the superior antibody response in individuals who had a prior SARS-CoV-2 infection, highlighting the benefits of "hybrid immunity." On the other hand, increasing age was linked to lower antibody levels, suggesting that older individuals might need tailored vaccination strategies. Importantly, even with waning antibody levels, the vaccine proved effective in preventing severe COVID-19 outcomes in those who experienced breakthrough infections.

These findings add valuable insights to our global understanding of how inactivated vaccines work in the real world, especially for a high-risk group like frontline healthcare workers. Our study reinforces the importance of continuously monitoring immune responses, particularly for those on the front lines, and helps inform ongoing discussions about booster dose recommendations to maintain strong population immunity. Moving forward, future research should delve deeper into both antibody and cellular immunity, track antibody persistence over even longer periods, and continuously assess how well our current vaccines protect against the ever-evolving SARS-CoV-2 variants.

REFERENCES

1. World Health Organization WHO DirectorGeneral's opening remarks at the media briefing on COVID-19. https://www.who.int/dg/speeches/detail/whodirector-general-s-opening-remarks-at-themediabriefing-on-covid-19. WHO: 11-March2020 (Access: August 2021).
2. Republic of Turkey Ministry of Health COVID-19 Information Page. Available at https://covid19.saglik.gov.tr/ (Access date: November 08 2021).
3. Of the international, Coronaviridae Study Group, The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. Nature Microbiology 2020; 5(4): 536.
4. Schoeman D, Fielding BC. Coronavirus envelope protein: current knowledge. Virology journal, 2019; 16(1): 1-22.
5. Wu A, Peng Y, Huang B, et al. Genome composition and divergence of the novel coronavirus (2019-nCoV) originating in China. Cell Host & Microbe 2020; 27(3): 325-328.
6. Du L, He Y, Zhou Y, Liu S, Zheng BJ, Jiang S. The spike protein of SARS-CoV -a target for vaccine and therapeutic development. Nature Review Microbiol 2009; 7(3): 226-236.
7. Pascarella G, Strumia A, Piliego C, et al. COVID-19 diagnosis and management: a comprehensive review. J Intern Med 2020; 288(2): 192-206.
8. World Health Organization. Draft landscape and tracker of COVID-19 candidate vaccines. [Internet]. Switzerland: World Health Organization; 2021 [Accessed March 29, 2021]. at: https://www.who.int/publications/m/item/draftlandscape-of-covid-19-candidate-vaccines.
9. Le TT, Andreadakis Z, Kumar A, et al. The COVID-19 vaccine development landscape. Nature Reviews Drug Discovery, 2020; 19(5): 305-306.
10. Lundstrom K. The current status of COVID-19 vaccines. Frontiers in Genome Editing 2020; 2(2): 57929710.
11. Creech CB, Walker SC, & Samuels RJ. SARSCoV-2 vaccines. Jama, 2021; 325(13): 1318-1320.
12. Perkmann T, Perkmann-Nagele N, et al. Antispike protein assays to determine SARS-CoV-2 antibody levels: a head-to-head comparison of five quantitative assays. Microbiol Spectr 2021; 9(1): e00247-21.
13. EUL assessment report of COVID-19 vaccine (Vero cell) Inactivated submitted by Sinovac Life Science Co. Ltd., PR China Version. 2021, June.

14. Palacios R, Batista AP, Albuquerque CSN, et al. Efficacy and Safety of a COVID-19 Inactivated Vaccine in Healthcare Professionals in Brazil: The PROFISCOV Study 2021; April 11. available at: http://dx.doi.org/10.2139/ssrn.3822780

15. Fadlyana E, Rusmil K, Tarigan R, et al. A phase III, observer-blind, randomized, placebocontrolled study of the efficacy, safety, and immunogenicity of, SARS-CoV-2 inactivated vaccine in healthy adults aged 18–59 years: An interim analysis in Indonesia. Vaccine 2021; 39(44): 6520-6528.

16. Akova M, Unal, S. A randomized, double-blind, placebo-controlled phase III clinical trial to evaluate the efficacy and safety of SARS-CoV-2 vaccine (inactivated, Vero cell): a structured summary of a study protocol for a randomized controlled trial. Trials 2021; 22(1): 1-3.

17. Akçalı S, Özkaya Y, Gezginci FM, et al. Factors Affecting Side Effects, Seroconversion Rates, and Antibody Response After Inactivated SARSCoV-2 Vaccination in Healthcare Workers. Mikrobiyoloji Bullet 2021; 55(4): 519-538.

18. Özgür, D., & Tütüncü, E. E. (2022). Antibody Response After Two Doses of Inactivated SARS-CoV-2 Vaccine in Healthcare Workers with and without Previous COVID-19 Infection: A Prospective Observational Study. Mikrobiyoloji Bulteni, 56(1): 36-48.

19. Yalçın TY, Topçu DI, Doğan Ö, et al. Immunogenicity after two doses of inactivated virus vaccine in healthcare workers with and without previous COVID-19 infection: Prospective observational study. J Medic Virol 2022; 94(1): 279-286.

20. Chen Y, Yin S, Tong X, et al. Dynamic SARSCoV-2-specific B-cell and T-cell responses following immunization with an inactivated COVID-19 vaccine. Clin Microbiol Infect 2022; 28(3): 410-418.

21. Hunsawong T, Fernandez S, Khadthasrima N, et al. Limited and short-lasting virüs-neutralizing titers induced by inactivated SARS-CoV-2 vaccine. Emerg Infect DIs 2021; 27(12): 3178.

22. Bichara CDA, Queiroz MAF, da Silva GA, et al. Assessment of anti-SARS-CoV-2 antibodies post-Coronavac vaccination in the Amazon Region of Brazil. Vaccines 2021: 9(10), 1169.

23. Yildiz Y, Ozger HS, Senol E, et al. Evaluation of long-term antibody kinetics in healthcare workers (HCWs) vaccinated with inactivated COVID-19 Vero cell vaccine (CoronaVac), a propensity score-matched observational study: Antibody kinetics in HCWs after CoronaVac vaccination. Int J Infect Dis 2022; 122: 99-106.

24. Damasceno DH, Amaral AA, Silva CA, Silva ACSE. The impact of vaccination worldwide on SARS-CoV-2 infection: a review on vaccine mechanisms, results of clinical trials, vaccinal coverage, and interactions with novel variants. Curr Med Chem 2022; 29(15): 2673-2690.

25. Zimmermann P, Curtis N. Factors that influence the immune response to vaccination. Clin Microb Rev 2021; 32(2): e00084-18.

26. Martínez-Flores D, Zepeda-Cervantes J, CruzReséndiz A, Aguirre-Sampieri S, Sampieri A, Vaca L. SARS-CoV-2 vaccines based on the spike glycoprotein and implications of new viral variants. Front Immun 2021; 12: 701501