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Perioperative SARS-CoV-2 screening and comparison of immunoglobin values: a retrospective study

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ABSTRACT

Aims: The SARS-CoV-2 pandemic has posed significant challenges to perioperative management, particularly in the context of preoperative screening and immune response evaluation. Various methods, including polymerase chain reaction (PCR) tests, immunoglobulin (Ig) level assessments, chest X-rays, and computerized tomographies, have been employed to mitigate risks. This study aims to explore the differences in immune responses, particularly Ig levels, between vaccinated and non-vaccinated individuals undergoing surgery during the pandemic.

Methods: During the study period, data from 656 patients who underwent elective or urgent surgery were collected. Among these, only 86 patients had complete and reliable data on vaccination status and immunoglobulin G (IgG) and immunoglobulin M (IgM) levels. Patients with missing or incomplete information were excluded. The final 86 patients were grouped as follows: non-vaccinated and non-infected (NVNI), non-vaccinated but previously infected (NVI), and individuals who received two doses of the Biontech mRNA vaccine (B). The study compared IgG and IgM levels among these three groups.

Results: Patients in group B were significantly older than those in groups NVNI and NVI (mean age: 43.5±13.0 years vs. 30.0±13.2 years and 38.0±18.8 years, respectively; $p<0.05$). Ig G levels were highest in group B (median: 4641.2 AU/ml, IQR: 13137±14502), followed by group NVI (median: 345.5 AU/ml, IQR: 3236±8082), and were lowest in group NVNI (median: 2.4 AU/ml, IQR: 4.1±5.5) ($p<0.05$ for all comparisons). Similarly, Ig M levels were significantly higher in group B (median: 0.38 AU/ml, IQR: 0.91±1.40) than in groups NVI (median: 0.28 AU/ml, IQR: 0.61±0.93) and NVNI (median: 0.05 AU/ml, IQR: 0.18±0.29) ($p<0.05$), while there was no significant difference in Ig M levels between groups NVI and NVNI ($p>0.05$).

Conclusion: Vaccination enhances the immune response, leading to significantly higher IgG levels compared to non-vaccinated individuals, regardless of prior infection. However, some vaccinated individuals did not achieve protective antibody levels. Further research is needed to assess the clinical implications of these findings.

Keywords: Perioperative screening, SARS-CoV-2, immunoglobulin levels, vaccination

INTRODUCTION

The emergence of SARS-CoV-2 in December 2019 marked a pivotal moment in global health, as the virus rapidly spread from Wuhan, China, to become a worldwide pandemic. By October 2021, COVID-19 had infected over 238 million people and caused nearly 4.9 million deaths globally, posing unprecedented challenges to healthcare systems and medical professionals.[1-3] Among the many challenges faced during the pandemic, the management of perioperative care, particularly for patients undergoing elective or urgent surgeries, became a critical issue. The lack of robust data on preoperative screening and the immune response to SARS-CoV-2 created significant dilemmas for anesthesiologists and surgeons, leading to the adoption of various diagnostic tools, including thoracic CT scans, lung X-rays, PCR testing, and laboratory markers such as lymphopenia, eosinopenia, and C-reactive protein (CRP) levels.[4-8]

The rapid development and deployment of SARS-CoV-2 vaccines, including the Pfizer/BioNTech mRNA vaccine (BNT162b2), ushered in a new era in pandemic management. These vaccines were authorized under emergency use protocols, utilizing rolling review regulatory tools to expedite their assessment and distribution.[9] Despite the success of vaccination programs, questions remain regarding the durability and efficacy of immune responses, particularly in terms of immunoglobulin G (IgG) and immunoglobulin M (IgM) levels, which are critical indicators of antiviral immunity. While prior infection and vaccination have been shown to elicit antibody responses, the correlation between antibody levels and protective immunity remains a subject of ongoing research.[10-12]

Previous studies have provided valuable insights into the immune responses elicited by SARS-CoV-2 infection and vaccination. However, these studies often face limitations, such as small sample sizes, heterogeneity in vaccine types, and variability in the timing of antibody measurements.[13-15] Additionally, there is a lack of comprehensive data on the comparative immune responses in surgical patients, particularly in the context of perioperative care. This gap in the literature highlights the need for further research to better understand the relationship between vaccination status, prior infection, and perioperative immune responses.

In this retrospective study, we aimed to address these limitations by investigating the differences in IgG and IgM levels among patients with varying vaccination and infection histories. Our goal was to provide a clearer understanding of how these factors influence perioperative immune status, thereby contributing to improved preoperative risk assessment and management strategies for surgical patients during the COVID-19 pandemic.

METHODS

The Study Design And Oversight

This study is a retrospective analysis designed to evaluate perioperative SARS-CoV-2 screening and Ig levels in patients undergoing elective and urgent surgeries. The study protocol was reviewed and approved by the Institutional Review Board (IRB) of a university-affiliated special hospital, and ethical approval was obtained from the Scientific Research Ethics Committee of Şehit Prof. Dr. İlhan Varank Training and Research Hospital. (Date: 18.09.2024, Decision No: 2024/279). Informed consent was obtained from each participant during the preoperative anesthetic evaluation. All data were collected, stored, and analyzed in accordance with the ethical guidelines and privacy policies of the IRB and the Declaration of Helsinki.

The Study Population

A total of 656 patients who underwent elective or urgent surgeries between July and December 2021 were initially included in this study. Various perioperative parameters were evaluated, including age, vaccine type, PCR results, IgG and IgM levels, American Society of Anesthesiologists (ASA) scores, operative time, postoperative complications, and prior COVID-19 infection history.

To ensure a homogeneous study population and enable meaningful statistical comparisons, we applied strict inclusion and exclusion criteria. Although data were initially collected from 656 patients who underwent elective or urgent surgery between July and December 2021, not all of them were eligible for the final analysis.

A large proportion of patients (n=540) had received vaccine types other than two doses of the Biontech mRNA vaccine. This group included patients who were vaccinated solely with non-Biontech vaccines (e.g., Sinovac or AstraZeneca), as well as those who had received mixed regimens involving Biontech and other brands (e.g., two doses of Sinovac followed by one dose of Biontech). These patients were excluded to avoid confounding effects from different vaccine combinations and to ensure a consistent immunological comparison.

Additionally, in some urgent surgical cases, patients were taken to the operating room without sufficient time to complete preoperative Ig testing. As a result, 20 patients with missing or incomplete data regarding vaccination status or antibody levels were excluded.

Another 10 patients who received mixed vaccine regimens (e.g., one dose of Biontech and one dose of another brand) were also excluded to preserve the clarity of group definitions. After applying these exclusion criteria, 86 patients remained eligible for analysis.

The final assessed patients was divided into three groups based on vaccination and infection history. The non-vaccinated, non-infected (NV-NI) group consisted of 22 patients who had never received a COVID-19 vaccine and had no prior SARS-CoV-2 infection. The non-vaccinated, infected (NV-I) group included 25 patients who had not been vaccinated but had a documented history of SARS-CoV-2 infection. The Biontech Vaccinated (B) group comprised 39 patients who had received two doses of the Biontech mRNA vaccine, regardless of their prior infection status.

This classification allowed for a comparative analysis of immune responses by assessing IgG and IgM levels across these distinct patient groups, providing valuable insights into the impact of vaccination and prior infection on perioperative immune status.

This research was carried out at a university-affiliated private hospital, which catered to a heterogeneous patient demographic during the COVID-19 pandemic. The healthcare facility delivered comprehensive medical services to both domestic and international patients, encompassing a wide range of surgical and perioperative interventions.

Analytical testing was performed using the ARCHITECT i1000 system (Abbott Laboratories), which utilizes a chemiluminescent microparticle immunoassay (CMIA) for the quantitative detection of antibodies in serum samples. The ARCHITECT system calculates the mean chemiluminescence value from triplicate measurements of the calibrator (C) and stores this value for subsequent calculations. Sample results (S) are determined by dividing the sample chemiluminescence by the calibrator value.

In this study, we quantitatively measured IgG antibodies targeting the S1 subunit of the viral spike (S) protein and IgM antibodies directed against the nucleocapsid (N) protein using a commercially available Abbott kit. Following the manufacturer's guidelines, IgG antibody levels were considered positive at concentrations ≥50.0 AU/ml (arbitrary units per milliliter). For IgM antibodies, results were classified as positive if the index value was ≥1.1 AU/ml.

Statistical Analysis

The data analyses were conducted using IBM SPSS Statistics for Windows, Version 28.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were expressed as mean (±standard deviation), median (minimum–maximum), frequency (percentage), or ratio, as appropriate. The normality of the data distribution was evaluated using the Kolmogorov-Smirnov test. For comparisons involving independent quantitative variables, non-parametric tests such as the Kruskal-Wallis test and Mann-Whitney U test were employed. Categorical variables were analyzed using the chi-square test. A p-value of <0.05 was considered statistically significant.

In this study, the SPSS 28.0 program (IBM SPSS Statistics for Windows, Version 28.0; IBM Corp.) was utilized for all statistical analyses. Data were summarized using means, standard deviations, minimum and maximum values, medians, frequencies, and ratios, as appropriate. Continuous variables were presented as mean (±standard deviation), while categorical variables were expressed as numbers (percentages) or ratios. The Kolmogorov-Smirnov test was applied to assess the distribution of variables. For the analysis of quantitative independent data, the Kruskal-Wallis and Mann-Whitney U tests were used, whereas the chi-square test was applied for qualitative independent data. Statistical significance was defined as a p-value <0.05.

RESULTS

A total of 656 patients who underwent elective or urgent surgeries between July and December 2021 were initially included in this study. After applying exclusion criteria—such as incomplete data or vaccination with regimens other than two doses of the Biontech mRNA vaccine—the final analysis was conducted on 86 patients. These patients were categorized into three groups based on their vaccination and infection history: non-vaccinated and non-infected (NV-NI, n=22), non-vaccinated but previously infected (NV-I, n=25), and individuals who received two doses of the Biontech mRNA vaccine (group B, n=39). The demographic and immunological characteristics of these groups are presented in Table 1. An overview of the patients' demographic and immunological data across the study groups is provided in Table 2.

The overall mean age of the study population was 38.42±SD years, and the mean ASA score was 1.22±SD. Only two patients tested positive for SARS-CoV-2 via PCR and underwent emergency surgery due to life-threatening conditions. The mean operative time was 86.7±SD minutes.

In group B (n=39), the median IgG level was 4641.2 AU/ml, while the median IgM level was 0.38 AU/ml. The median age in this group was 43.0 years. Despite receiving two doses of the vaccine, five patients had IgG levels below the seropositivity threshold of 50 AU/ml.

A total of 47 patients (7%) had not received any vaccination. Among them, 25 patients had a documented history of SARS-CoV-2 infection (group NV-I), with a median IgG level of 345.5 AU/ml and a median IgM level of 0.28 AU/ml. The median age in this group was 38.0 years, and only one patient had an IgG level below 50 AU/ml.

The remaining 22 patients were neither vaccinated nor previously infected (group NV-NI). In this group, the median IgG level was 2.4 AU/ml, and the median IgM level was 0.05 AU/ml. All patients in this group had IgG levels below 50 AU/ml. The median age in group NV-NI was 30.0 years.

The age of patients in group B was significantly higher (p<0.05) compared to both the NVİ and NV-Nİ groups. Additionally, the age of patients in the NVİ group was significantly higher (p<0.05) than that of the NV-Nİ group (Table 1).

Regarding IgG levels, group B demonstrated significantly higher values (p<0.05) compared to both the NVİ and NV-Nİ groups. Furthermore, IgG levels in the NVİ group were significantly higher (p<0.05) than those in the NV-Nİ group (Table 1).

For IgM levels, group B exhibited significantly higher values (p<0.05) compared to the NVİ and NV-Nİ groups. However, no significant difference (p>0.05) in IgM levels was observed between the NVİ and NV-Nİ groups (Table 1).

A significant positive correlation (r=0.450) was observed between immunoglobulin M (IgM) and immunoglobulin G (IgG) levels (Figure 1).

A significant positive correlation (r=0.388) was observed between age and IgG levels. A significant positive correlation (r=0.105) was found between age and IgM levels (Figure 2). The correlation of IgG and IgM levels with age is detailed in Figure 3.

Among the study participants, seven patients (1%) had received two doses of the BioNTech vaccine and one dose of the Sinovac vaccine. Five patients (0.7%) had received two doses of BioNTech and two doses of Sinovac. Twenty-seven patients (4%) were administered two doses of Sinovac, while seven patients (1%) received three doses of Sinovac. Fifty-seven patients (8%) had been vaccinated with one dose of BioNTech. Additionally, thirty-nine patients had received two doses of Sinovac and one dose of BioNTech; within this group, one patient exhibited an IgG level below 50 AU/ml.

Other vaccination profiles included one patient with two doses of the Pfizer vaccine, one patient with one dose of the AstraZeneca vaccine, one patient with one dose of the Sputnik vaccine, and three patients with two doses of the Moderna vaccine. One patient had received the Janssen vaccine. Five patients were administered one dose of Sinovac, and within this group, one patient also had an IgG level below 50 AU/ml.

Table 1. Evaluation of age distribution and serum immunoglobulin G and M levels between the groups

			NV-NI	NV+INF	B	p
Age	Mean±SD		27.8±13.2	34.4±18.8	43.5±13.0	0.001[K]
	Median		30.0	38.0	43.0	
Age	0-18 age	n %	6 27.3%	5 20.0%	0 0.0%	0.003[X²]
	19-44 age	n %	14 63.6%	1 52.0%	21 53.8%	
	45≤ age	n %	2 9.1%	7 28.0%	18 46.2%	
IgG	Mean±SD		4.1±5.5	3236±8082	13137±14502	0.000[K]
	Median		2.4	345.5	4641.2	
IgM	Mean±SD		0.18±0.29	0.61±0.93	0.91±1.40	0.000[K]
	Median		0.05	0.28	0.38	

[K] Kruskal-wallis (Mann-whitney u test)/[X²] Chi-square test, NV-NI: Non-vaccinated and non-infected, B: Biontech vaccinated, IgG: Immunoglobulin G, IgM: Immunoglobulin M, SD: Standard deviation

Table 2. Evaluation of the age characteristics between the groups

		Min-max	Median	Mean±SD/n %
Age (years)		2.0-81.0	37.0	36.9±16.2
Age (years)	0-18 age			11 12.8%
	19-44 age			48 55.8%
	45≤ age			27 31.4%
IgG (Au/ml)		0.0-40000	595.2	6899.2±12106.6
IgM (Au/ml)		0.00-6.00	0.20	0.64±1.11
Non vaccinated-non infected				22 25.6%
Non vaccinated+infected				25 29.1%
2 doses of Biontech				39 45.3%

Min: Minimum, Max: Maximum, SD: Standard deviation, IgG: Immunoglobulin G, IgM: Immunoglobulin M

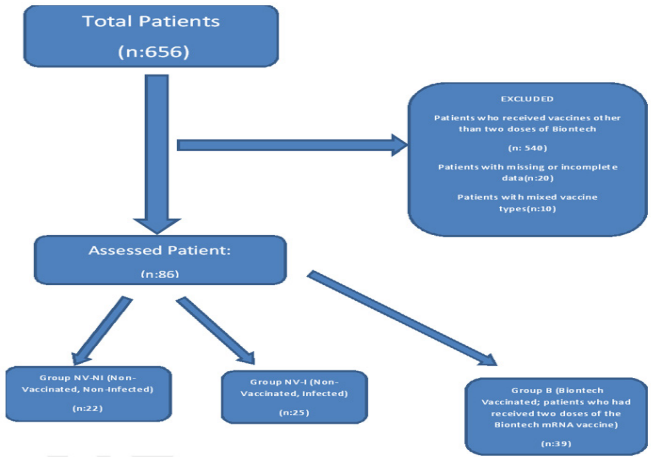

Figure 1. Flow diagram

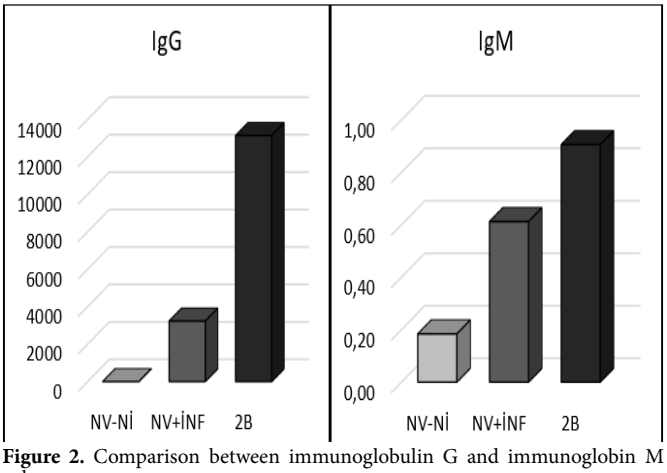

Figure 2. Comparison between immunoglobulin G and immunoglobin M values
NV-NI: Non-vaccinated and non-infected, B: Biontech vaccinated

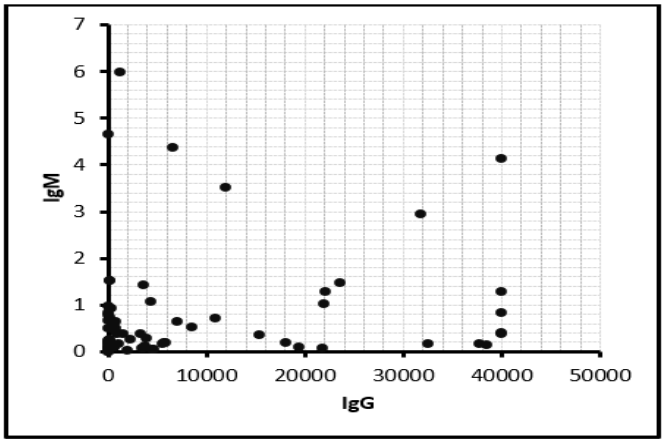

Figure 3. Correlation of immunoglobulin G and immunoglobulin M values with age

Overall, we identified seven patients (1% of the total study population) who did not achieve protective IgG levels (≥50 AU/ml) despite being vaccinated.

DISCUSSION

Our study aimed to evaluate differences in immune responses between vaccinated and non-vaccinated populations by measuring Ig levels. Identifying predictive immune response factors, such as Ig values which is critical for assessing various medical challenges and assisting physicians in anticipating clinical outcomes. We compared quantitative Ig levels across three groups admitted to the surgical residency unit between July and December 2021. Our findings demonstrated that vaccination elicits a stronger immune response, resulting in higher IgG levels compared to non-vaccinated individuals and non-vaccinated-infected groups.

One patient, who was PCR-positive and unvaccinated, was admitted for an emergency cesarean section under spinal anesthesia. Tragically, the patient passed away 43 days post-operation. Another patient, who had received two doses of Sinovac and one dose of BioNTech, contracted COVID-19 one month after surgery. Additionally, a patient with two doses of BioNTech and a negative PCR test was diagnosed with COVID-19 based on thoracic CT findings post-operation. Another patient, also vaccinated with two doses of BioNTech, was diagnosed with pulmonary tuberculosis two months after surgery.

An unvaccinated patient was diagnosed with COVID-19 after three months of her operation but recovered. Another

patient, who had received two doses of Sinovac and one dose of BioNTech, developed COVID-19 one month after surgery and required intensive care admission but eventually recovered.

While antibody levels alone are not the sole indicators of immunity, they correlate with antiviral immunity. However, numerous factors can influence this response, including ethnicity, age, body-mass index (BMI), vaccine type, sex, prior infection history, infection severity, time since vaccination, and profession. For instance, healthcare professionals tend to produce higher and more sustained Ig levels.[11-19]

In our study, IgG levels in group B were significantly higher ($p<0.05$) than in the NVİ and NV-Nİ groups. Furthermore, IgG levels in the NVİ group were significantly higher ($p<0.05$) than in the NV-Nİ group. These observations align with findings by Angyal et al.[21], who reported that individuals vaccinated after COVID-19 infection exhibited 6.8-fold higher antibody responses and 5.9-fold higher T-cell responses after the first dose of the BNT162b2 vaccine compared to those without prior infection.

The age of patients in group B was significantly higher ($p<0.05$) than in the NVİ and NV-Nİ groups, and the age of patients in the NVİ group was significantly higher ($p<0.05$) than in the NV-Nİ group. This age difference may contribute to the observed disparity in antibody responses between groups. Similar findings were reported by De Giorgi et al.[22] and Robbiani et al.[23], who noted that age enhances immune responses. In our study, a significant positive correlation was observed between IgG ($r=0.388$) and IgM ($r=0.105$) levels and age.

Rapid development of SARS-CoV-2-specific IgM has been associated with a milder disease course, whereas delayed IgM elevation is often observed in severe cases.[23] However, the data on IgM development remain inconsistent. Some studies report that a subset of patients never develop IgM, and in some cases, IgG production precedes IgM.[24] For instance, one study found that approximately 50% of inactivated vaccine recipients did not develop IgM after the first dose of the BNT162b2 vaccine.[25]

In our study, the IgM seroconversion rate was 28% in group B after two doses of the BioNTech vaccine. Wei et al.[27] identified 5.1% of participants as non-responders after one dose of BNT162b2, defined as those who did not produce sufficient Igs. In our study, the non-responder rate was 12.8% in group B.

Limitations

This study has several limitations. First, we only evaluated surgical patients or those undergoing diagnostic or therapeutic procedures under anesthesia. Second, the time since vaccination was not consistently recorded. Third, prior infection status in the vaccinated population was not accounted for. Finally, our sample size was limited. Despite these limitations, we believe our findings contribute valuable insights into understanding immune responses during the pandemic era.

CONCLUSION

In conclusion, the findings of this study demonstrate that vaccination elicits a stronger immune response, resulting in higher IgG levels compared to non-vaccinated individuals and non-vaccinated-infected groups. However, as medical professionals, we recognize the need for further research to better understand immune responses, factors influencing COVID-19 severity, and the underlying reasons for increased disease severity. Future studies should investigate additional variables that may impact clinical outcomes, such as pregnancy, vitamin deficiencies, and heavy metal toxicities. It is also important to note that, despite vaccination, some individuals may not achieve protective antibody levels, highlighting the complexity of immune responses and the need for personalized approaches to vaccination and disease management.

ETHICAL DECLARATIONS

Ethics Committee Approval

Ethical approval was obtained from the Scientific Research Ethics Committee of Şehit Prof. Dr. İlhan Varank Training and Research Hospital. (Date: 18.09.2024, Decision No: 2024/279).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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