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COVID-19 mRNA BNT162b2 vaccine safety and antibodies level among healthcare workers at Centre Hospitalier du Nord

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ABSTRACT
Studying the levels of the anti-spike protein receptor-binding domain (S-RBD) antibodies as well as the vaccine safety is very important to evaluate the protection level against the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2) infection and to motivate individuals to receive the vaccine. In this study, we evaluate the effect of the mRNA BNT162b2 vaccine using the EUROIMMUN anti-SARS-CoV-2 ELISA (IgG) for the measurement. We detected the IgG class antibodies to SARS-CoV-2 in the human serum, or plasma, of 217 eligible participants aged >18 years, recruited between March and June 2021. These participants were divided into 2 groups: the first group consisted of 149 participants without prior infection, while the second group included 68 participants who had recovered from symptomatic and asymptomatic COVID-19 infections. All the adverse effects were minor local or systematic reactions such as local pain, asthenia, body ache, muscle pain and headache. The level of the adverse effects increased following the second vaccine dose. The adverse effects were higher in participants with previous symptomatic SARS-CoV2 infection (p=0.020). This was due to the presence of anti-S-RBD IgG levels before the vaccination. Moreover, the adverse effects were higher in females than males after the first dose (p=0.025) and the second dose (p=0.01). As for the anti-S-RBD IgG levels, they were all positive at the end of the second dose. The anti-S-RBD IgG levels 21 days after the vaccination dose were higher than the pre-vaccination levels (p=0.000) and they were higher in previously infected participants before getting the first dose (p=0.000). Our results show a good antibody response at the end of the two mRNA BNT162b2 vaccine doses in both previously infected and not infected participants. Moreover, our study highlighted the minor adverse effects reported following each dose.

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INTRODUCTION

The coronavirus, also known as COVID-19, is a continuing pandemic of coronavirus that was initially discovered in Wuhan, China, at the end of December 2019. The Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2) was to blame for the pandemic. Coronaviruses belong to the Coronavirinae subfamily of the Coronaviridae family, and there are four genera in the subfamily: Alpha coronavirus, Beta coronavirus, Gamma coronavirus, and Delta coronavirus. The SARS-CoV2 genome is a single-stranded positive-sense viral RNA with a nucleocapsid protein that is larger than any other RNA virus's genome. The capsid outside the genome is created by the nucleocapsid protein (N) and the genome is further packed by an envelope that is made up of three structural proteins: membrane protein (M), spike protein (S), and envelope protein (E) (Brian & Baric, 2005; Centers for Disease Control and Prevention, 2020; Hosseini et al., 2020; Logunov et al., 2021; Platto, Wang, Zhou, & Carafoli, 2020)

SARS-CoV-2 is transmitted to oral and respiratory mucosal cells via respiratory droplets from infected patients. The virus, which has a single-stranded RNA genome, replicates and spreads to the lower airways where it can cause severe pneumonia. The Spike-converting enzyme 2 (ACE2) interaction leads to Spike cleavage in the prefusion state by the proteases TMPRSS-2/furin. (Boopathi et al., 2020; Brian & Baric, 2005; Centers for Disease Control and Prevention, 2020; Funk, Laferrière, & Ardakani, 2020; Hosseini et al., 2020; Logunov et al., 2021; Platto et al., 2020). The coronavirus causes fever, dry and persistent cough, fatigue, anosmia/dysgeusia, loss of appetite, and dyspnea. However, a variety of other symptoms may occur including headaches, sore throat, myalgia, rigors, intestinal discomfort/diarrhea, ocular manifestations, and other symptoms. In severe cases, hypoxia and respiratory distress may occur, necessitating hospitalization, and some patients may require supplemental oxygen and ventilator support as a result of respiratory distress. (Funk et al., 2020).

Currently, researchers have identified many COVID-19 treatments, such as antibodies derived from convalescent plasma drawn from previously infected patients or monoclonal antibodies that can bolster a patient's immune system ahead of its own antibodies. Furthermore, many antivirals such as Remdesivir, Hydroxychloroquine, and Lopinavir have been subject of numerous research projects. In addition, steroids like dexamethasone are used to treat the worst effects of COVID-19 by suppressing the body's own immune response. A variety of other treatments for COVID-19 has been tried, but none has been proven to be effective. (Chodosh & Maldarelli, 2020; Joshi et al. 2021; Libster et al. 2021; Matthay & Thompson, 2020; Self et al. 2020). This virus infected 209,876,613 cases until August 21, 2021, and resulted in more than 4,400,284 deaths due to its complications (World Health organization, 2021b). Global efforts sparked a race to develop a safe and effective vaccine against this virus. Currently, more than seven vaccines have been approved for emergency use. COVID-19 vaccinations have been widely distributed in recent months, raising hopes that the pandemic's end is near.

Objectives

The purpose of this study was to assess anti-S-RBD IgG levels of COVID-19 mRNA BNT162b2 (Pfizer-BioNTech) vaccine recipients with or without previous SARS-CoV-2 infection before receiving the first dose, before getting the second dose, and 21 days after getting the second dose. Moreover, this study aims to assess the safety of this vaccine for the healthcare workers at the Centre Hospitalier du Nord (CHN). The main objectives of our project are to study the antibodies level and the safety of the COVID-19 mRNA BNT162b2 vaccine among the healthcare workers at CHN during the period between March 2021 and June 2021.

METHODS

Study design and participants

This single-center study was conducted at one Lebanese University Hospital, the CHN. Following their consent, all CHN healthcare workers were recruited and enrolled in this study. From March to June 2021, we

recruited 329 participants older than 18 years, of which 217 were eligible and/or accepted to participate in this study. The 112 were rejected either because they refused to sign the consent or they stopped working at the hospital. The participants were divided into two groups: 149 who had never been infected before and 68 who had recovered from COVID-19, as determined by a positive real-time reverse transcription-polymerase chain reaction, primarily using a nasopharyngeal swab and in accordance with international guidelines. The recovered patients developed asymptomatic (n=33) and symptomatic (n=35) forms of the COVID-19. None of these participants was hospitalized due to the infection.

The anti-S-RBD IgG levels of each participant were tested based on three different intervals. The first testing was done upon arrival at the vaccination center and before receiving the first dose of the Pfizer-BioNTech vaccine (Pfizer Inc., New York, NY; BioNTech SE, Mainz, Germany). The second test was done 21 days after receiving the first dose and directly before getting the second dose of the Pfizer-BioNTech vaccine and the third test was done 21 days after receiving the second dose. An online field-tested survey developed by the team targeting the vaccine beneficiaries was shared after receiving the first dose and the second dose to record the demographical and clinical information of each participant including the needed information in case of COVID-19 infection (duration, symptoms and treatment) and the adverse effects due to the vaccination (Figure 1).

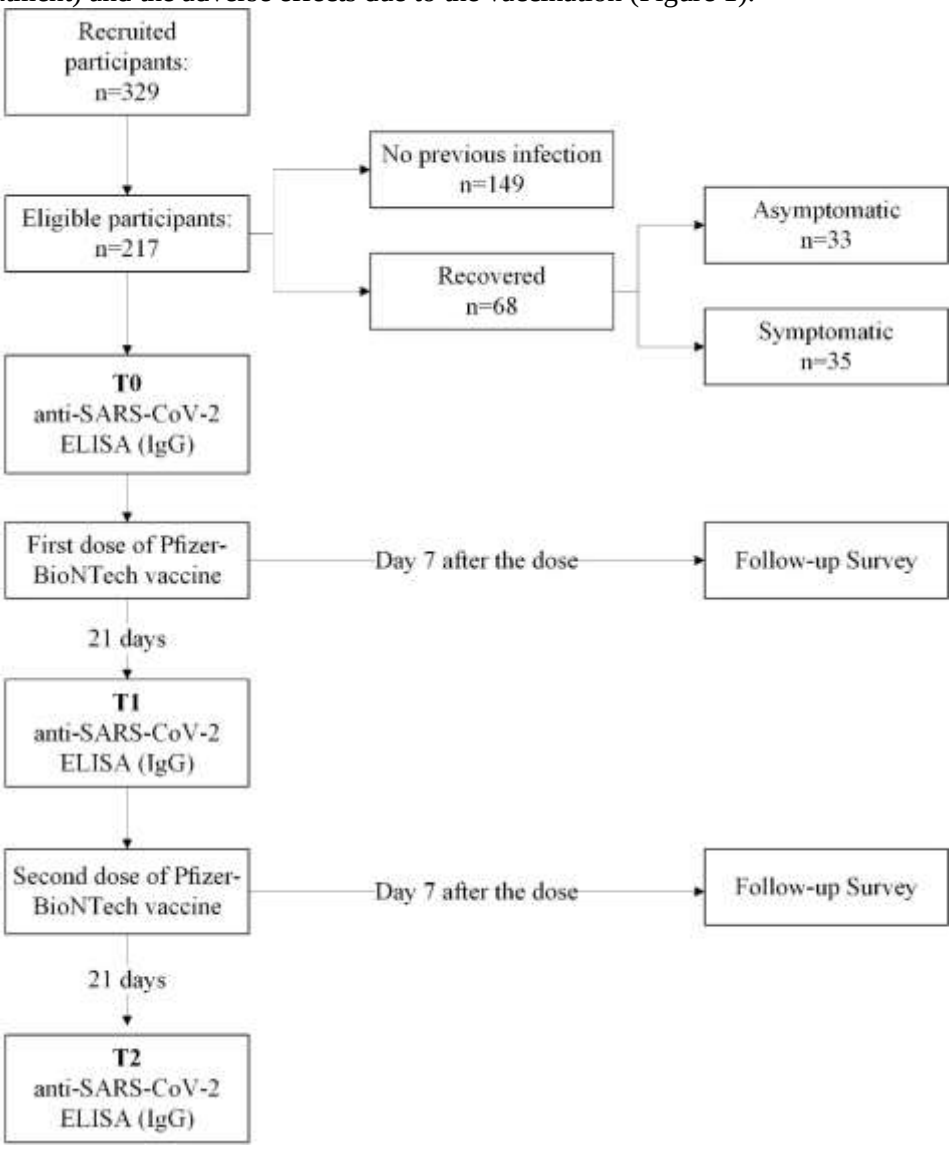

Figure 1. Study design

This figure summarizes the study design. It shows that 329 participants were recruited where 217 were accepted to participate in this study. The eligible participants were divided into 2 groups: previously infected and not infected. Three serology tests were done for these participants before getting their first vaccine dose, 21 days after getting their first dose and 21 days after getting their second dose. A follow-up survey was shared seven days after each dose to track the occurrence of any side effects.

Statistical analysis

The statistical analysis was performed using the Statistical Package for Social Science (SPSS) software v20.0. The T-test, χ^2 and Mc Nemar test were used to study the correlations between the different parameters used in this study. Data on demographic status, medical history, serology levels before and after each dose, vaccine adverse effects after each dose and the occurrence of the adverse effects were analyzed using descriptive statistics. For qualitative variables, the results were presented as percentages, while quantitative variables were presented as a minimum, maximum, mean, and standard deviation (SD). The Mc Nemar test was used to study the antibodies level before and after the first vaccination dose. The independent sample t-test was used to study the association between the participants' weight and age with the COVID-19 infection occurrence. Finally, the χ^2 was used to study the association between the:

- Gender and the vaccine side effects vaccine post-dose 1 and 2
- COVID-19 previous symptomatic and asymptomatic infection and the vaccine side effects
- COVID-19 previous symptomatic and asymptomatic infection and the antibodies level before the first dose
- Side effects post-dose 1 and the initial antibodies level before the first dose
- Antibodies level post-dose 1 and the side effects post-dose 2
- Occurrence of adverse effects after dose 2 and the serology levels 21 days after dose 1
- Anti-S-RBD IgG levels before the vaccination and 21 days after receiving the first dose
- Influence of age or weight on the occurrence of the SARS-CoV2 infection

The research team studied the anti-S-RBD IgG levels before and after the vaccination in non-infected and recovered patients. Moreover, we investigated the systemic and local side effects after each dose.

Biochemical analysis

The serum anti-S-RBD IgG levels were determined using fresh samples obtained after centrifuging whole blood collected in dry tubes for 15 minutes at 3500 rpm at room temperature. The EUROIMMUN anti-SARS-CoV-2 ELISA (IgG) was used for the measurement, which is an enzyme-linked immunosorbent assay designed for the quantitative detection of IgG class antibodies to SARS-CoV-2 in human serum or plasma. The unit of measurement used is in accordance with the most recent World Health Organization (WHO) notification (Notice WHO Standard (20/136) Unit Conversion—RN21040201).

RESULTS AND DISCUSSION

Following the recruitment of 329 subjects, 217 (139 females and 78 males) were eligible to be included in our study as previously described. The mean age was 38.87 years (SD 10.73) and ranged between 21 and 64 years. The majority of our demographic was Lebanese (n=210). The non-Lebanese (n=7) were either Palestinian (n=6) or Syrian (n=1). As for the medical history of our participants, 41% (n=90) are suffering from at least one non-communicable chronic disease (NCCD) (Table 1)

Table 1. Types of NCCD that our participants are suffering from

Types of NNCD	Group 1
Diabetes	14.4%
High blood pressure	20%

Cardiovascular diseases	13.3%
Respiratory problems	4.4%
Cancer	1.1%
Obesity	11.1%
Low immunity	2.2%
Autoimmune diseases	3.3%
Organ transplant	1.1%
Allergy	48.9%

The development of adverse effects after receiving the first dose was reported in 69.6% (n= 151) of the cases in both groups (with or without previous infection) where 66% (n=45) of the previously infected participants reported having at least one side effect. After receiving the first dose, the most common side effect was the local pain (84.8%) followed by the headache (29.1%), body ache (29.1%) and muscle pain (27.8%) (Table 2). The occurrence time of these adverse effects was between 4h and 7 days. The most common time of occurrence of these effects was 12-24 hours after receiving the first dose (28.1%) (Table 3) (Centers for Disease Control and Prevention, 2021; Menni et al., 2021; Pfizer-BioNTech, 2021; Venkatakrishnan et al., 2021; World Health Organization, 2021; World Health organization, 2021)

However, the development of adverse effects after receiving the second dose was reported in 83% (n=169) of the cases in both groups (with or without previous infection). Noting that 13 participants didn't answer this question. After receiving the second dose, the most common side effect was the local pain (75.7%) followed by asthenia (56.2%), body ache (56.2%), headache (42.0%), and muscle pain (46.7%) (Table 2). The most common time of occurrence of these effects was 24-48 hours after receiving the first dose (34.6%) (Table 3). These adverse effects are identical to the side effects reported by the WHO, by the Center for Disease Control and Prevention (CDC) and by the Pfizer/BioNTech company (Centers for Disease Control and Prevention, 2021; Menni et al., 2021; Pfizer-BioNTech, 2021; Venkatakrishnan et al., 2021; World Health Organization, 2021; World Health Organization, 2021).

Table 2. Adverse effects reported after receiving the first and the second vaccine doses

Adverse effects	Post dose 1	Post dose 2
Local pain	84.4%	75.7%
Hand numbness	11.3%	14.2%
Local redness	7.9%	13.8%
Hyperthermia	6.6%	27.8%
Headache	29.1%	42.0%
Body ache	29.1%	56.2%
Asthenia	24%	56.2%
Muscle pain	27.8%	46.7%
Chest pain	1.3%	4.8%
High blood pressure	2.0%	3.0%
Simple rash	2.0%	1.8%
Rash all the body	0.0%	0.6%
Fainting	0.0%	1.2%
Anaphylactic choc	0.0%	0.6%
Dyspnea	2.6%	6.5%
Breathing difficulty	2.0%	4.7%
Nausea vomiting	7.3%	13.6%
Diarrhea	2.6%	10.1%
Abdominal pain	5.3%	8.9%
Tachycardia	6.6%	6.5%
Dizziness	7.3%	10.1%
Airways obstruction/Tongue edema	0.0%	0.6%
Hospital admission/ER	0.0%	1.8%

Table 3. Occurrence time of the adverse effects post dose 1 and 2

Time	Post dose 1	Post dose 2
< 4 hours	9.7%	3.7%
4-12 hours	24.4%	30.4%
12-24 hours	28.1%	34.6%
24-48 hours	4.1%	7.8%
48 hours - 4 days	2.3%	0.5%
4 - 7 days	0.9%	0.9%

According to the model adopted in this study, the anti-S-RBD IgG levels were tested before getting the first dose, 21 days after getting the first dose and 21 days after getting the second dose. The level of these antibodies in 72% of our participants was negative before getting their first dose while 26% were positive and 2% were borderline (Table 4). The positive serology levels were between 36 and 2000 (Table 5). When we studied the serology levels of those who recovered from the virus, we were able to identify anti-S-RBD IgG in the serum of more than 82% of these participants (Tables 6 and 7). According to the studies done, Anti-spike S1 receptor-binding domain antibodies against SARS-CoV-2 persisted several months after infection. Therefore, positive serology was identified in participants who were previously infected with the SARS-CoV-2. Our results were confirmed by the previously published data (Bavaro et al., 2021; Shah et al., 2021).

As a second stage in our study, the anti-S-RBD IgG levels were tested 21 days after receiving the first vaccine dose. The positivity level indicating the presence of the antibodies went from 25.8% to 96.3%. Only 1.9% (n=4) of the participants' serology were negative and less than 1.8% (n=4) were borderline (Table 4). 21.3% of the participants were able to reach a serology level of more than 3840 for the serology anti-Spike IgG (Table 5). As for those who have been infected with the virus and after studying their serology levels 21 days after the first mRNA vaccine dose, we realized that the response was high. 82.4% of individuals who already had SARS-CoV-2 infections reported high antibody titers and neutralization activity (more than 2001 UI/ml) after the first dose of the mRNA vaccine (Tables 6 and 7). Our results confirm the previously achieved results. According to a study recently published "SARS-CoV-2 vaccines for all but a single dose for COVID-19 survivors", COVID-19 survivors might only need one dose of mRNA vaccine. Increasing our sample size is needed to confirm our results within all of the Lebanese population. However, due to the emerging variants, a recent study on the delta variant revealed the importance of receiving both vaccine shots, due to the challenges posed by mutations (Bavaro et al., 2021; Shah et al., 2021).

Finally, we tested the anti-S-RBD IgG levels of our participants 21 days after receiving the second vaccine dose. All the serology levels of our participants were positive (Table 4). They were able to create a high response toward the two doses of the mRNA vaccine (Table 5). Recently the Pfizer and BioNTech submitted their initial data to the Food and Drug Administration (FDA) that supports delivering a third booster dose 8 months apart from the second dose to ensure better safety from the emerging variants (Bavaro et al., 2021; Berkeley, 2021; Liu et al., 2021; Shah et al., 2021).

Table 4. Anti S-RBD IgG results before the vaccination and 21 days post dose 1 and 2 within all the participants

Serology results	T0: Before the vaccination	T1: 21 days post dose 1	T2: 21 days post dose 2
Negative (0-25 BAU/ml)	71.9%	1.9%	0%
Borderline (26-35 BAU/ml)	2.3%	1.8%	0%
Positive (>35 BAU/ml)	25.8%	96.3%	100%

Table 5. Anti S-RBD IgG results before the vaccination and 21 days post dose 1 and 2 within all the participants

Serology results-Intervals		T0: Before the vaccination	T1: 21 days post dose 1	T2: 21 days post dose 2
Negative	0-25	71.9%	1.9%	0%
Borderline	26-35	1.9%	1.9%	0%
Positive	36-100	11.2%	9.0%	0%
	101-300	9.3%	21.8%	0%
	301-500	2.9%	14.2%	1.0%
	501-2000	2.8%	19.9%	19.0%
	2001-3840	0%	10.0%	30.0%
	>3840	0%	21.3%	50.0%

Table 6. Anti S-RBD IgG results before the vaccination and 21 days, post dose 1 within the recovered participants

Serology results	T0: Before the vaccination	T1: 21 days post dose 1
Negative (0-25 BAU/ml)	10.3%	0%
Borderline (26-35 BAU/ml)	7.3%	0%
Positive (>35 BAU/ml)	82.4%	100%

Table 7. Anti S-RBD IgG results before the vaccination and 21 days post dose 1, within the recovered participants

Serology results-Intervals		T0: Before the vaccination	T1: 21 days post dose 1
Negative	0-25	10.3%	0%
Borderline	26-35	7.3%	0%
Positive	36-100	35.4%	0%
	101-300	29.4%	1.5%
	301-500	8.8%	1.5%
	501-2000	8.8%	13.9%
	2001-3840	0.0%	24.6%
	>3840	0.0%	58.5%

By using this anti-S-RBD IgG response model, including both groups (with or without a previous SARS-CoV2 infection), we studied the association between the occurrence of adverse effects and gender. The association between the side effects post-dose 1 and gender turned out to be statistically significant ($p=0.025<0.05$) (Figure 2) as well as post-dose 2 ($p=0.01<0.05$) (Figure 3). When we compared our results to previously published studies, our results for the CHN healthcare workers showed similar findings. There are different conceivable clarifications for the incongruities in adverse effects between males and females. Concurring to a later evaluation of vaccine-induced hormonal resistance, women have expanded immunological reactogenicity, making them more resistant to irresistible infections. Moreover, this increments the chance of antagonistic occasions. These sex-based contrasts can be credited to hormonal, hereditary, and microbial reactions, centered on the work of sex hormones and

immunological reactions. In other investigations, the relation between estrogen and flu antibodies has been recommended to advance resistance where lifted estrogen levels has been related to queasiness and spewing, the two most common side effects. In other studies, the interactions between estrogen and flu vaccines have been proposed to boost immunity, and elevated estrogen levels have been linked to nausea and vomiting, the two most common side effects. In addition to biological factors, there are theories for sex-based disparities that are related to differences between men and women in how they feel pain and interact with the healthcare system. Enlarging our sample size and taking into account an equal distribution of male and female patients would aid in the confirmation of our findings (Akau, 2021; Fischinger, Boudreau, Butler, Streeck, & Alter, 2019; Gee, 2021).

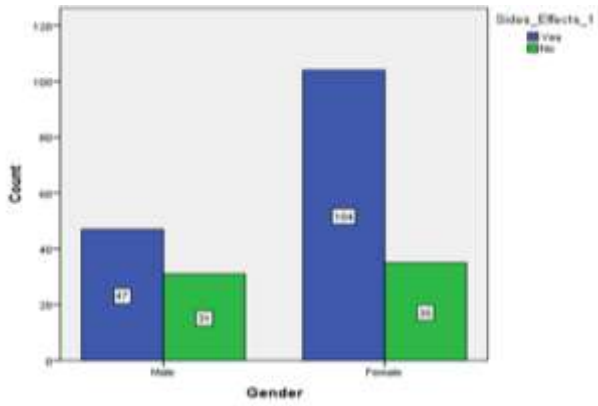

Figure 2. Association between the sides effects post-dose one and Gender

This figure represents the relation between the side effects occurrence post-dose 1 and the gender. From those who answered this question, 57 out of 78 males suffered from side effects up to 7 days after receiving the first vaccine dose while 107 out of 139 suffered from side effects.

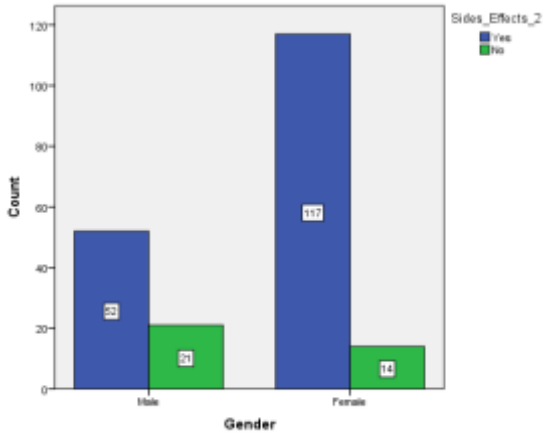

Figure 3. Association between the sides effects post-dose two and Gender

This figure represents the relation between the side effects occurrence post-dose 2 and the gender. From those who answered this question, 52 out of 73 males suffered from side effects up to 7 days after receiving the first vaccine dose while 107 out of 131 suffered from side effects.

However, we were unable to find an association between all the previously infected cases, with or without symptoms, and the occurrence of side effects ($p=0.371>0.05$) (Figure 4). These results don't match the results identified in previous studies. According to a study published in April 2021, COVID-19 infections in the past were linked to a higher likelihood of self-reported adverse effects after vaccination with BNT162b2/Pfizer. Our results

could be due to the fact that many previous COVID-19 infections were asymptomatic (Raw, Kelly, Rees, Wroe, & Chadwick, 2021). Therefore, we selected only the symptomatic cases and we performed a second analysis. Among the participants who had a previous SARS-CoV2 infection, we were able to find a significant relationship between the symptomatic cases (n=33) and the occurrence of adverse effects after receiving the first vaccine dose ($p=0.020<0.05$) (Figure 5). When we compared our results to previously published studies, our results within the CHN healthcare workers showed similar findings. According to a study published in April 2021, SARS-CoV2 infections in the past were linked to a higher likelihood of self-reported adverse effects after vaccination with BNT162b2/Pfizer (Monforte et al., 2021; Raw et al., 2021).

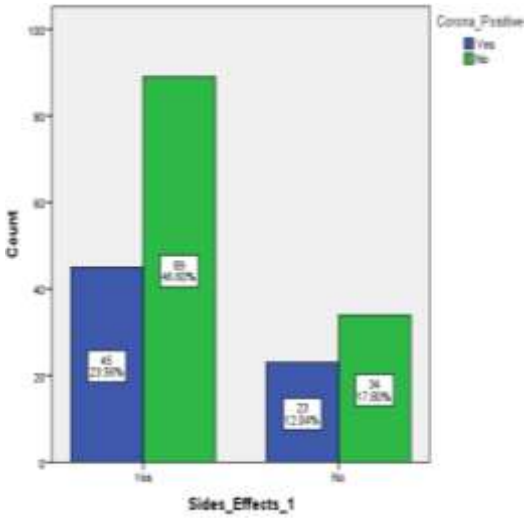

Figure 4. Association between the previous symptomatic and asymptomatic infection and the occurrence of side effects post-dose one

This figure represents the relation between the side effects occurrence post-dose 1 within the patients who have recovered from the coronavirus. From those who have recovered from symptomatic and asymptomatic COVID-19 infection, 45 out of 68 participants suffered from side effects up to 7 days after receiving the first vaccine dose while 23 didn't suffer from any side effects.

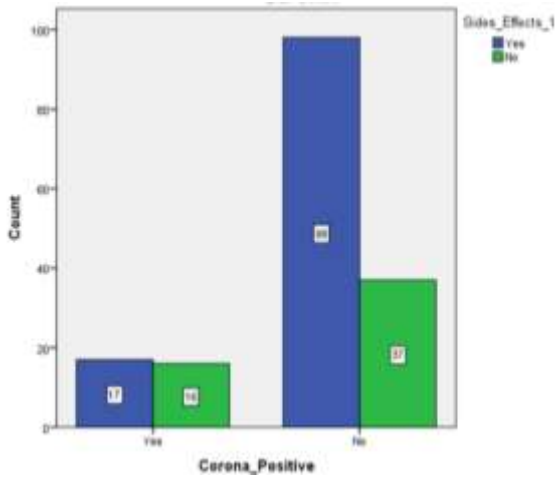

Figure 5. Association between the previous symptomatic infections and the occurrence of side effects post-dose one

This figure represents the relation between the side effects occurrence post-dose 1 within the patients who have recovered from a symptomatic COVID-19 infection. From those who have recovered from a symptomatic COVID-19 infection, 17 out of 33 participants suffered from side effects up to 7 days after receiving the first vaccine dose while 16 didn't suffer from any side effects.

In addition, we were able to find an association between the group of participants who were previously infected by the SARS-CoV2, with or without symptoms, and the anti-S-RBD IgG levels before receiving the first vaccine dose (T0) ($p=0.000<0.05$) (Figure 6). Compared to previously published studies, our results for the CHN healthcare workers showed similar findings. Many studies found that neutralizing antibody levels were higher 7 to 10 days after a single dose in previously infected people than they were 7 to 10 days after the second dose in people who had never been infected (Naaber et al., 2021; Wise, 2021).

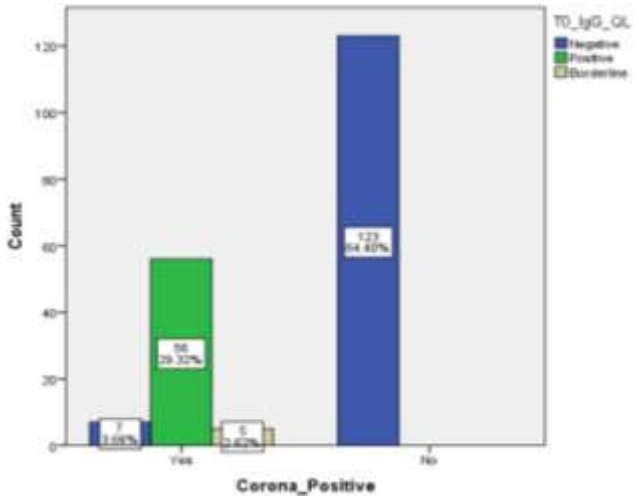

Figure 6. Association previous infection by the SARS-CoV2, with or without symptoms, and the anti-S-RBD IgG levels before receiving the first vaccine dose (T0)

The serology levels of the participants who have recovered from the COVID-19 infection before receiving their first vaccine dose was positive in 56 cases out of 68 cases, while the serology was borderline in five cases and negative in the other seven cases.

The number of participants who suffered from adverse effects post-dose two increased. 94.6% of those who have suffered from adverse effects after receiving their second dose had positive serology levels 21 days after receiving the first dose. However, we were unable to find a significant relationship between the occurrence of adverse effects after dose 2 and the serology levels 21 days after dose 1 ($p=1.000>0.05$) (Figure 9). The second dose of the COVID-19 vaccine, according to the studies, will most likely have more severe side effects (Centers for Disease Control and Prevention, 2021; Curley, 2021). However, one South Korean study found that the side effects of the Covid-19 vaccine were unrelated to antibody formation. The severity of side effects following vaccination has nothing to do with antibody formation. As a result, expanding the sample and recruiting additional participants who have recovered from SARS-C0V2 will be able to confirm the results (Hyun-tai, 2021).

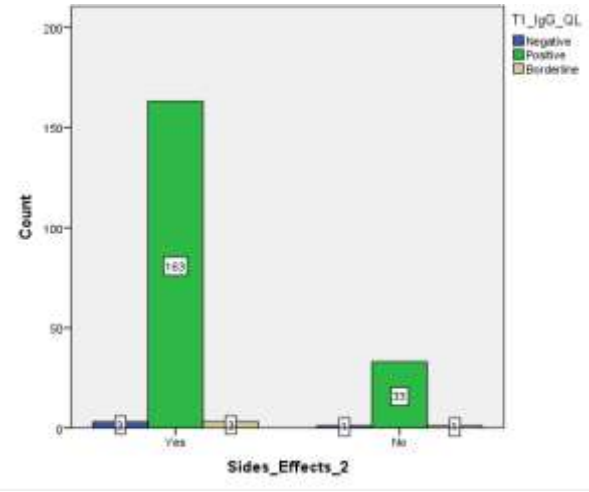

Figure 1. Association between the occurrences of adverse effects after dose 2 and the serology level 21 days after dose 1

The serology levels of the participants 21 days after receiving their first vaccine dose was positive in 169 cases. One-hundred and sixty three out of these 169 cases suffered from adverse effects up to 7 days after receiving their second dose.

Using the Mc Nemar test to study the effect of the levels of antibodies before and after the first vaccination dose, we were able to find a significant association between the IgG before the vaccination and 21 days after receiving the first dose; this association turned out to be statistically highly significant ($p=0.000<0.05$) (Figure 8). These results are similar to the results identified in previous studies. However, there is a strong immune response to the RBD region of the spike protein after receiving both vaccine doses (Naaber et al., 2021).

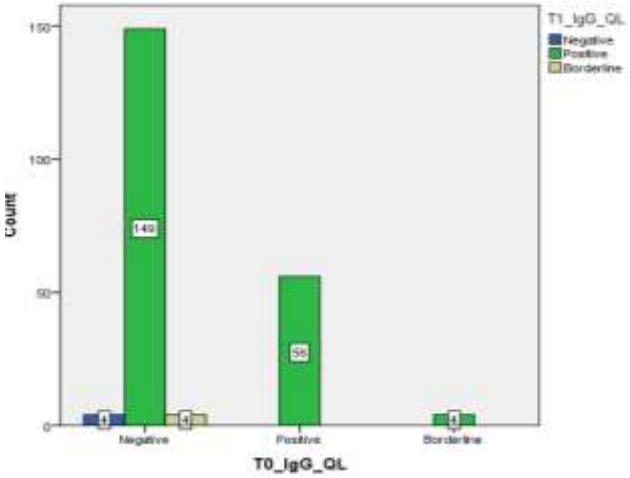

Figure 8. Difference between the IgG before the vaccination and 21 days after receiving the first dose

This figure represents the difference between the serology level before and after receiving the first vaccine dose. The serology level of 157 participants out of the 217 participants was negative before getting the first dose, while it was positive in 56 cases and borderline in 4 cases. The serology level of 149 participants out of the 157 negative cases became positive after receiving the first dose.

The research team was unable to find an association between the influence of age (p=0.171>0.05) or weight (p=0.799>0.05) on the SARS-CoV2 infection. According to our results, age does not influence the COVID-19 infection. When we compared our results to previously published studies, we were unable to find a similar study. The age result could be explained by the fact that the oldest of our participants was only 64 years old. This is why expanding the sample and increasing the number of participants over the age of 64 is required to confirm the findings in the Lebanese population (Centers for Disease Control and Prevention, 2021; Cunningham et al., 2021; Maragakis, 2020). Obesity, according to the studies, puts people at a higher risk of contracting SARS-CoV2, as well as having poorer progression and higher rates of hospitalization. Obesity has been linked to a more severe COVID-19 infection and death in an increasing number of reports. Before repeating the analysis and comparing the Lebanese population results with the previously published results, it is recommended to increase the sample size and take into account hormonal and genetic factors (Dietz & Santos-Burgoa, 2020; Kwok et al., 2020; Sattar, McInnes, & McMurray, 2020).

CONCLUSION AND RECOMMENDATION

According to the WHO, more than 4,543,716,443 vaccine doses were delivered to date worldwide (World Health Organization, 2021). Many researchers are currently working on evaluating the current vaccines' effect as well as the vaccine's adverse effects. Based on these results, vaccination strategies could be adjusted and could encourage the yet unvaccinated to get their doses.

The research team was able to highlight the local and systematic adverse effects that occurred after the vaccination. They were mainly minor reactions such as local pain, asthenia, body ache, muscle pain, and headache. These side effects started 4 hours after the vaccination and didn't last more than 7 days. An association between the side effects and gender was identified (p=0.025) where the adverse effects increased in women more than in men. Moreover, we found an association between the occurrence of the adverse effect after receiving the first dose and the participants with previous symptomatic infection (p=0.020). However, this relation was not found in all the participants of the study (p=0.799). Finally, we were unable to find an association between the anti-S-RBD IgG levels before the vaccination and the occurrence of the adverse effects in all the participants (p=0.703) or between the anti-S-RBD IgG levels after receiving the first dose and the occurrence of the adverse effects in all the participants (p=0.703). As for the antibody response after the mRNA BNT162b2 COVID-19 vaccine administration, this study found a large response. All the participants were able to create a high antibody level 21 days after receiving their second vaccine dose. An association was found between the anti-S-RBD IgG levels before the vaccination and the participants with symptomatic and asymptomatic infection (p=0.000). According to the result, we didn't find an association between the presence of chronic diseases and the infection (p=1.483), the COVID-19 infection and the age (p=0.171), or weight (p=0.799).

Further investigations after increasing the sample size and taking into consideration recruiting additional symptomatic recovered participants and an equal distribution between males and females are needed in order to confirm these results to then be able to generalize them over the healthcare workers in Lebanon.

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REFERENCES

Akau, K. (2021). Sex and gender and COVID-19 vaccine side effects. https://medicine.yale.edu/news-article/sex-and-gender-and-covid-19-vaccine-side-effects/

Bavaro, D.F., Laghetti, P., Milano, E., Brindicci, G., Volpe, A., Lagioia, A. & Monno, L. (2021). Anti-spike S1 receptor-binding domain antibodies against SARS-CoV-2 persist several months after infection regardless of disease severity. *Journal of Medical Virology, 93*(5), 3158-3164. doi:10.1002/jmv.26878

Berkeley, L.J. (2021, July 8,). Pfizer says it is developing a covid booster shot to target the highly transmissible delta variant. https://www.nbcchicago.com/news/business/money-report/pfizer-says-it-is-developing-a-covid-booster-shot-to-target-the-highly-transmissible-delta-variant/2550362/

Boopathi, S., Poma, A.B. & Kolandaivel, P. (2020). Novel 2019 coronavirus structure, mechanism of action, antiviral drug promises and rule out against its treatment. *Journal of Biomolecular Structure and Dynamics*, 1-10.

Brian, D.A. & Baric, R.S. (2005). Coronavirus genome structure and replication. *Coronavirus Replication and Reverse Genetics*, 1-30.

Centers for Disease Control and Prevention. (2020). COVID-19 and your health. https://www.cdc.gov/coronavirus/2019-ncov/vaccines/faq.html

Centers for Disease Control and Prevention. (2021). COVID-19 risks and vaccine information for older adults. https://www.cdc.gov/aging/covid19/covid19-older-adults.html

Centers for Disease Control and Prevention. (2021). Possible side effects after getting a COVID-19 vaccine. https://www.cdc.gov/coronavirus/2019-ncov/vaccines/expect/after.html

Centers for Disease Control and Prevention. (2021). Reactions and adverse events of the pfizer-BioNTech COVID-19 vaccine. *Cdc*, https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/reactogenicity.html

Chodosh, S. & Maldarelli, C. (2020) The verdict on hydroxychloroquine is in. https://www.popsci.com/story/health/hydroxychloroquine-covid-19-treatment/

Cunningham, J.W., Vaduganathan, M., Claggett, B.L., Jering, K.S., Bhatt, A.S., Rosenthal, N. & Solomon, S.D. (2021). Clinical outcomes in young US adults hospitalized with COVID-19. *JAMA Internal Medicine, 181*(3), 379-381.

Curley, B. (2021). Second dose of COVID-19 vaccine has stronger side effects. Retrieved from https://www.healthline.com/health-news/heres-why-your-second-dose-of-covid-19-vaccine-will-likely-have-stronger-side-effects

Dietz, W. & Santos-Burgoa, C. (2020). Obesity and its implications for COVID-19 mortality. *Obesity (Silver Spring), 28*(6), 1005.

Fischinger, S., Boudreau, C.M., Butler, A.L., Streeck, H. & Alter, G. (2019). (2019). Sex differences in vaccine-induced humoral immunity. Paper presented at the *Seminars in Immunopathology, 41*(2) 239-249.

Funk, C.D., Laferrière, C. & Ardakani, A. (2020). A snapshot of the global race for vaccines targeting SARS-CoV-2 and the COVID-19 pandemic. *Frontiers in Pharmacology, 11*, 937.

Gee, J. (2021). First month of COVID-19 vaccine safety monitoring—United states, december 14, 2020–January 13, 2021. *MMWR.Morbidity and Mortality Weekly Report, 70*

Hosseini, E.S., Kashani, N.R., Nikzad, H., Azadbakht, J., Bafrani, H.H. & Kashani, H.H. (2020). The novel coronavirus disease-2019 (COVID-19): Mechanism of action, detection and recent therapeutic strategies. *Virology, 551*, 1-9.

Hyun-tai, S. (2021). 'Covid-19 vaccine side effects irrelevant to antibody formation'. http://www.koreabiomed.com/news/articleView.html?idxno=11254

Joshi, S., Parkar, J., Ansari, A., Vora, A., Talwar, D., Tiwaskar, M. & Barkate, H. (2021). Role of favipiravir in the treatment of COVID-19. *International Journal of Infectious Diseases, 102*, 501-508. doi:https://doi.org/10.1016/j.ijid.2020.10.069

Kwok, S., Adam, S., Ho, J.H., Iqbal, Z., Turkington, P., Razvi, S. & Syed, A.A. (2020). Obesity: A critical risk factor in the COVID-19 pandemic. *Clinical Obesity, 10*(6), e12403.

Libster, R., Pérez Marc, G., Wappner, D., Coviello, S., Bianchi, A., Braem, V. & Polack, F.P. (2021). Early high-titer plasma therapy to prevent severe covid-19 in older adults. *N Engl J Med*, doi:10.1056/NEJMoa2033700

Liu, J., Liu, Y., Xia, H., Zou, J., Weaver, S.C., Swanson, K.A. & Muik, A. (2021). BNT162b2-elicited neutralization of B. 1.617 and other SARS-CoV-2 variants. *Nature*, 1-5.

Logunov, D.Y., Dolzhikova, I.V., Shcheblyakov, D.V., Tukhvatulin, A.I., Zubkova, O.V., Dzharullaeva, A.S. & Erokhova, A.S. (2021). Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: An interim analysis of a randomised controlled phase 3 trial in russia. *The Lancet*,

Maragakis, L.L. (2020). Coronavirus and COVID-19: Younger adults are at risk, too. *Johns Hopkins Medicine*,

Matthay, M.A. & Thompson, B.T. (2020). Dexamethasone in hospitalised patients with COVID-19: Addressing uncertainties. *The Lancet Respiratory Medicine, 8*(12), 1170-1172.

Menni, C., Klaser, K., May, A., Polidori, L., Capdevila, J., Louca, P. & Spector, T.D. (2021). Vaccine side-effects and SARS-CoV-2 infection after vaccination in users of the COVID symptom study app in the UK: A prospective observational study. *The Lancet Infectious Diseases, 21*(7), 939-949. doi:10.1016/S1473-3099(21)00224-3

Monforte, A. d., Tavelli, A., Perrone, P.M., Za, A., Razzini, K., Tomasoni, D.Marc & hetti, G. (2021). Association between previous infection with SARS CoV-2 and the risk of self-reported symptoms after mRNA BNT162b2 vaccination: Data from 3,078 health care workers. *EClinicalMedicine, 36*, 100914.

Naaber, P., Adamson, A., Sepp, E., Tserel, L., Kisand, K. & Peterson, P. (2021). Antibody response after COVID-19 mRNA vaccination in relation to age, sex, and side effects.

Pfizer-BioNTech. (2021). Pfizer-BioNTech COVID-19 vaccine overview and safety. Retrieved from https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/Pfizer-BioNTech.html

Platto, S., Wang, Y., Zhou, J. & Carafoli, E. (2020). History of the COVID-19 pandemic: Origin, explosion, worldwide spreading. *Biochemical and Biophysical Research Communications*, doi:https://doi.org/10.1016/j.bbrc.2020.10.087

Raw, R.K., Kelly, C., Rees, J., Wroe, C. & Chadwick, D. (2021). Previous COVID-19 infection, but not long-COVID, is associated with increased adverse events following BNT162b2/pfizer vaccination. *The Journal of Infection*,

Sattar, N., McInnes, I. B. & McMurray, J.J. (2020). Obesity is a risk factor for severe COVID-19 infection: Multiple potential mechanisms. *Circulation, 142*(1), 4-6.

Self, W. H., Semler, M.W., Leither, L.M., Casey, J.D., Angus, D.C., Brower, R.G. & Filbin, M.R. (2020). Effect of hydroxychloroquine on clinical status at 14 days in hospitalized patients with COVID-19: A randomized clinical trial. *Jama, 324*(21), 2165-2176.

Shah, J., Liu, S., Potula, H., Bhargava, P., Cruz, I., Force, D. & Ramasamy, R. (2021). IgG and IgM antibody formation to spike and nucleocapsid proteins in COVID-19 characterized by multiplex immunoblot assays. *BMC Infectious Diseases, 21*(1), 1-8.

Venkatakrishnan, A.J., Kumar-M, P., Silvert, E., Garcia-Rivera, E., Szenk, M., Suratekar, R. & Soundararajan, V. (2021). Female-male differences in COVID vaccine adverse events have precedence in seasonal flu shots: A potential link to sex-associated baseline gene expression patterns. *MedRxiv*, https://www.medrxiv.org/content/10.1101/2021.04.01.21254798v1

Wise, J. (2021). Covid-19: People who have had infection might only need one dose of mRNA vaccine.

World Health Organization. (2021). Coronavirus disease (COVID-19): Vaccines safety. https://www.who.int/news-room/q-a-detail/coronavirus-disease-(covid-19)-vaccines-safety

World Health Organization. (2021). Side effects of COVID-19 vaccines. *Who*, https://www.who.int/news-room/feature-stories/detail/side-effects-of-covid-19-vaccines
World Health Organization. (2021). WHO coronavirus (COVID-19) dashboard. https://covid19.who.int