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Safety and Effectiveness of the Pfizer-BioNTech COVID-19 Vaccine among Health Staff in Sulaimani City, Iraq: A Prospective Cohort Study

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Abstract

A cohort study was conducted among 210 health staff members in Sulaimani city to assess the safety and effectiveness of the Pfizer-BioNTech vaccine. They were divided into two groups: vaccinated and unvaccinated. The vaccinated group received two doses of the Pfizer vaccine, while the unvaccinated group did not receive any vaccines during this study. Vaccine reactogenicity was assessed using a self-report form. Whereas vaccine immunogenicity was assessed by testing the anti-receptor binding domain IgG (anti-RBD IgG) antibody. Several adverse effects were observed with each dose. The most frequent adverse effects were pain at the inoculation site, tiredness, myalgia and fever. The average adverse effects per person in the first and second doses were 5.3 (SD 3.3) and 6.3 (SD 3.5) respectively (p = 0.005). The immunized group's anti-RBD IgG antibody levels were greatly improved after taking the first and second doses (32.50 and 44.92 binding antibody units (BAU)/mL respectively). After eight months of taking the two doses, the antibody level dropped to 17.00 BAU/mL. This study indicates that the vaccine can be safe and effective for enhancing antibody production.

Keywords: Anti-RBD IgG antibody, COVID-19, Effectiveness, Pfizer vaccine, Safety.

سلامة وفعالية لقاح Pfizer–BioNTech COVID–19 بين العاملين في المجال الصحي في مدينة السليمانية ، العراق: دراسة حشدية

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الخلاصة:

تم إجراء دراسة حشدية على 210 من العاملين في المجال الصحي في مدينة السليمانية لتقييم سلامة وفعالية لقاح Pfizer–BioNTech. تم توزيع عينات الدراسة المذكورة انفا على مجموعتين: ملقحة وغير ملقحة. تلقت المجموعة الملقحة الجرعتين الأولى والثانية من لقاح فايزر ، ولم تتلق المجموعة غير الملقحة أي لقاحات خلال فترة الدراسة. تم تقييم الاثار الجانبية اللقاح باستخدام استمارة تقرير ذاتي. تم تقييم مناعة اللقاح عن طريق اختبار الجسم المضاد (anti–RBD IgG antibody). لوحظت العديد من الآثار الجانبية مع كل

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جرعة. كانت الآثار الجانبية الأكثر شيوعًا هي الألم في موقع التلقيح ، والتعب ، والألم العضلي ، والحمى. كان معدل الآثار الجانبية لكل شخص في الجرعتين الأولى والثانية 5.3 (SD 3.3) و 6.3 (SD 3.5) ، على التوالي ($p= 0.005$). ازدادت مستويات الأجسام المضادة (anti−RBD IgG antibody) بشكل كبير في المجموعة الملقحة بعد اخذ الجرعتين الأولى والثانية (32.50 و 44.92 وحدة / مل ، على التوالي). بعد ثمانية أشهر من اخذ جرعة الثانية ، انخفض تركيز الأجسام المضادة إلى 17.00 وحدة / مل. تشير هذه الدراسة إلى أن اللقاح آمن وفعال في تعزيز إنتاج الأجسام المضادة.

Introduction

At the end of 2019, pneumonia from an unidentified source occurred in Wuhan, China. In the first month of 2020, the etiological agent was identified as the new coronavirus. The virus's genetic sequence became obtainable within a month. The disease was diagnosed as COVID-19, caused by SARS-CoV-2 which spread worldwide. In the third month of 2020, the WHO declared that the disease had developed from an outbreak to a pandemic [1]. A report by the WHO on February 28th, 2023 showed that the number of cases and deaths were 758,390,564 and 6,859,093 respectively [2].

A worldwide vaccination campaign policy to prevent virus transmission and achieve community immunity was adopted [3]. Active immunization became the cornerstone of international healthcare policies against COVID-19 [4]. The Moderna and Pfizer–BioNTech, the first COVID-19 vaccines, became accessible in the USA. At the end of 2020, they were approved as a double-dose series, with a four-week interval for Moderna and a three-week interval for Pfizer–BioNTech [5]. In June 2021, WHO accepted several COVID-19 vaccines, including Moderna, Pfizer, BBIBP-CorV, CoronaVac, AstraZeneca, and Johnson and Johnson [6]. Up to February 25th, 2023 exactly 13,226,873,459 doses of the vaccine had been given [2].. WHO COVID-19 guidelines provided high-priority categories that included essential personnel and workers to guarantee the continuity of important services such as food, water, and electricity supply; individuals who were more likely to come into contact with the virus and spread it; and those at a higher risk of complications and death due to infection [7].

The Pfizer-BioNTech vaccine was the only mRNA-based vaccine approved against an infectious disease such as SARS-CoV-2. Many adverse effects were apprehended following immunization due to immune response [8]. Although there was no proof that the COVID-19 vaccination was a cause of mortality; only a small number of people suffered from anaphylaxis after immunization with the Moderna and Pfizer vaccines [9]. Concerns over the possibility that COVID-19 vaccines could have diminished efficacy against emerging virus strains increased with the incidences of mutation in SARS-CoV-2. However, the Pfizer vaccine demonstrated high levels of neutralizing antibodies against all risky variants examined to date [10].

At the time of this current study, limited clinical data about the effectiveness and adverse effects of COVID-19 vaccines was available in Sulaimani city, Iraq. This research was, therefore, conducted to assess the safety and effectiveness of the Pfizer vaccine among health staff working in public hospitals and health centres in Sulaimani city.

Materials and Methods

This prospective cohort study was done between April 25th, 2021, and July 15th, 2022, in Sulaimani city, Iraq. Convenience sampling method was employed to select the respondents. The study population comprised all health staff who had not received COVID-19 vaccines. They worked in public hospitals and health centres in Sulaimani city. They were eligible for vaccination without contraindication to take the Pfizer vaccine.

Inclusion Criteria

Vaccinated Group

Health staff members were eligible and were prepared to take two doses of 30 μg of the Pfizer vaccine intramuscularly, with a 21-day gap between doses. They donated five mL of blood at four specified times.

Unvaccinated Group

The health staff members were qualified to take the COVID-19 vaccine but did not intend to do so during the study period. They donated three mL of blood at four specified times.

Exclusion Criteria

Individuals who (1) had previously received the COVID-19 vaccine; (2) had an acute febrile illness at the time of participation; (3) had a history of allergic reactions to the vaccine ingredients; (4) their anti-RBD-IgM antibody test was positive at the time of participation; and (5) had received convalescent plasma against SARS-CoV-2 in the past four months were excluded from participation.

Ethical Considerations

This study was carried out in accordance with the Declaration of Helsinki's guidelines [11] and the recommendations of the Research Ethics Committee of the College of Health and Medical Technology-Sulaimani Polytechnic University. The study was approved by the scientific committee of the College of Health and Medical Technology-Sulaimani Polytechnic University (Ethics Committee Certificate of Approval; number 40 on April 18th, 2021). Before the participants took part, they were asked to sign the written consent forms.

Data Collection

A total of 210 health staff participated in the current study. Of those, 110 respondents were in the vaccinated group and 100 individuals were in the unvaccinated group. Face-to-face interviews were conducted to collect data from the participants. Following each dose of the vaccine, the respondents were given a self-report form to evaluate any local effects (such as swelling, redness, itching, axillary lymphadenopathy, pain at the inoculation site, and tightness in the injected limb) and systemic reactions (such as tiredness, headache, chest pain, myalgia, arthralgia, fever, chills, dyspnoea, diarrhoea, nausea, vomiting, and allergic reactions), as well as grades of adverse effects (Grade 1: Mild, does not affect daily works. Grade 2: Moderate, impact on daily activities. Little or no therapy is required. Grade 3: Severe, obstacles to daily activities, and need for treatment. Grade 4: Serious, usually requiring hospitalization) [12] that could happen within a week after vaccination.

Laboratory Tests

Blood samples were drawn four times in the vaccinated group; an hour before receiving the first dose (first sample), an hour before getting the second dose (second sample), four weeks after receiving the second dose (third sample), and eight months following the second dose (fourth sample).

In the unvaccinated group, blood samples were also collected four times: the first sample was drawn on the first day of participation, and the second and third samples were drawn after three and seven weeks of participation, respectively. The fourth sample was drawn eight months after the second blood sample was collected. The following tests were performed:

- The Anti-RBD*IgM antibody test was carried out only for the first blood sample.
- The Anti-RBD IgG antibody test was done for all blood samples.

- A complete blood count (CBC) test was carried out for the vaccinated group's first, second, and third blood samples.

* Refers to antibodies that act against the receptor binding domain (RBD) of the virus spike protein [13].

A VIDAS instrument with an enzyme-linked fluorescence assay (ELFA) technique was used to measure anti-RBD IgG and IgM antibodies by using the VIDAS® SARS-COV-2 IgG kit and the VIDAS® SARS-COV-2 IgM kit manufactured by BioMérieux SA. The test value's interpretation of the findings is: <1.00 (negative) and >1.00 (positive) [14]. This technique was used to monitor antibody responses in participants by quantitatively measuring anti-RBD IgG antibody levels. CBC was calculated using a Swelab Lumi haematology analyser. The antibody tests were performed at the laboratory of the Ali Naji Health Center, and CBC tests were done at the laboratory of the Allergy and Asthma Center. Both centers belonged to the General Directorate of Health in Sulaimani City.

Statistical Analysis

SPSS version 22 was used for data analysis. Analytical and descriptive methods were used in this study. The analytical technique included an independent-sample t-test employed to compare the means of two separate samples, and ANOVA was conducted to compare more than two means. The descriptive approach involved calculating mean and standard deviation (SD), percentages, and frequencies. The association between categorical variables was examined using the chi-square test (χ2-test). A p-value ≤ 0.05 was considered significant.

Results

The participants had negative anti-RBD IgM antibody test results and did not receive any COVID-19 vaccines at the time of participation. The mean ages of the vaccinated and unvaccinated were 39.7 (SD 10.6) years and 39.1 (SD 12.5) years respectively. The body mass index (BMI) of the vaccinated and unvaccinated groups were 26 (SD 4.0) and 26.2 (SD 3.3) respectively. These differences were insignificant ($P > 0.05$).

The Vaccine Adverse Effects

The adverse effects per person following the first and second doses were 5.3 (SD 3.3) and 6.3 (SD 3.5) respectively ($P = 0.005$). Overall, the occurrence of side effects increased after the second dose, but these increases were not significant ($p > 0.05$), except for insomnia (p= 0.023) (Figures 1 and 2).

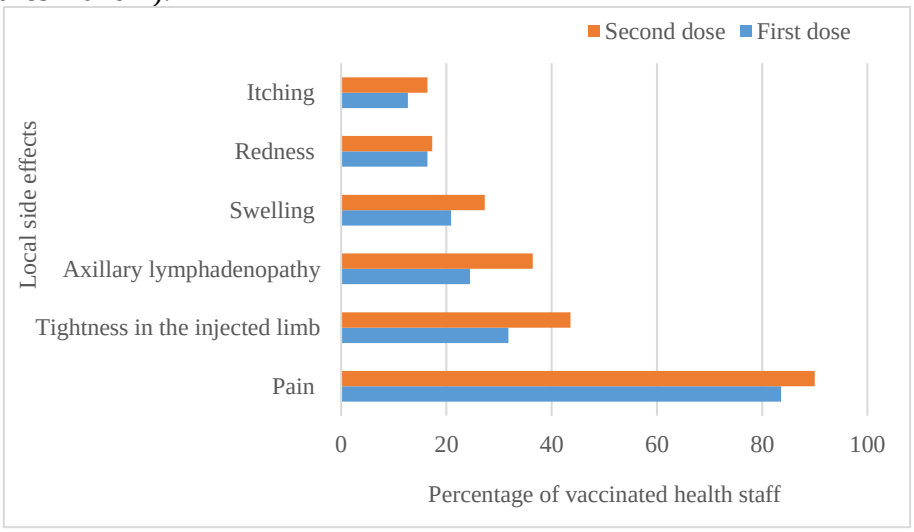

Figure 1: Local side effects following the first and second doses (n=110).

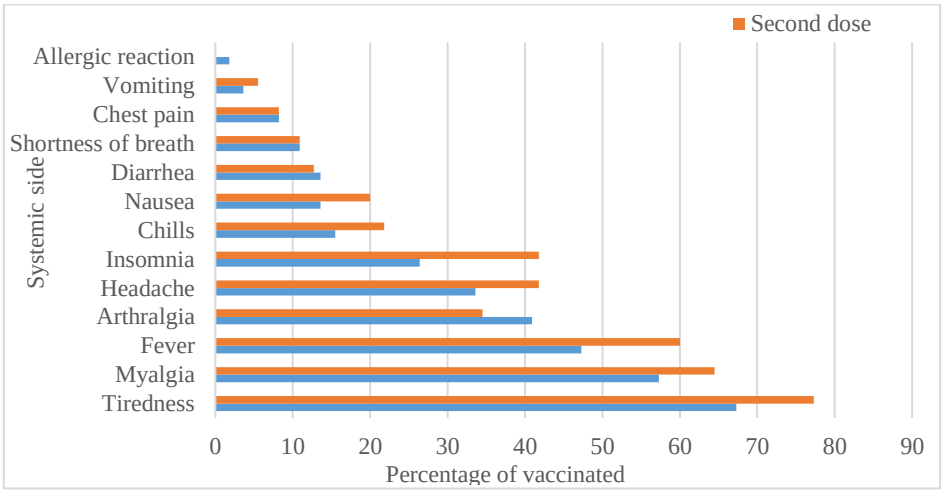

Figure 2: Systemic side effects following the first and second doses (n=110).

The results revealed no significant differences between the first and second doses regarding the vaccine's adverse event grades (p = 0.09) (Figure 3).

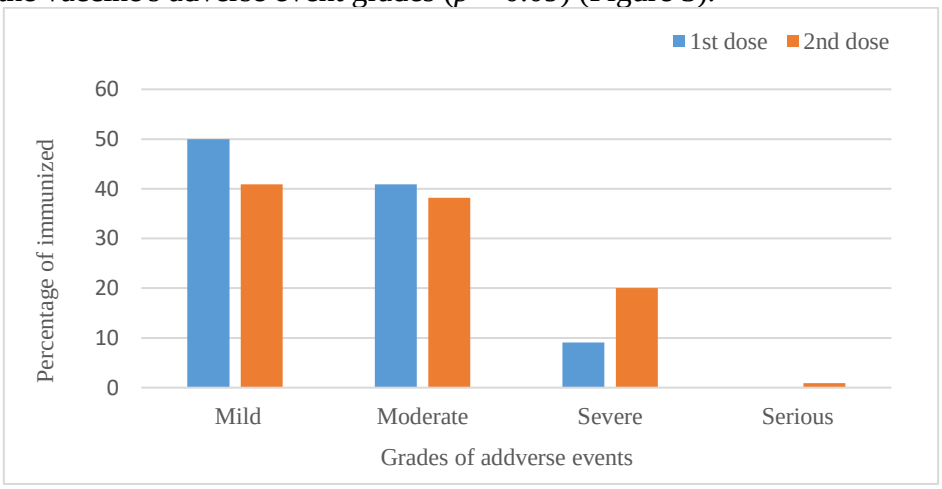

Figure 3: Grades of adverse events after the first and second doses (n=110).

Blood Parameters

A CBC test was performed three times for immunized individuals before receiving the vaccine and after taking the first and second doses. No significant differences were found between the means of the blood parameters ($p > 0.05$) (Table 1).

Table 1: Comparison between blood parameters in relation to the testing times (n=110).

Blood Parameter	Mean			*p*-value	Pairwise Comparison *P*-value		
	1st test	2nd test	3rd test		1st test vs† 2nd test	1st test vs 3rd test	2nd test vs 3rd test
Total WBCs*/µL	6790	6750	6858	0.866	1.000	1.000	1.000
Neutrophil/µL	3920	3796	3862	0.398	0.542	1.000	1.000
Lymphocyte/µL	2322	2393	2415	0.519	1.000	0.824	1.000
Monocyte/µL	313	317	324	0.844	1.000	1.000	1.000
Eosinophil/µL	183	196	202	0.177	0.656	0.204	1.000
Basophil/µL	55	55	60	0.180	1.000	0.299	0.360
Platelet/µL	245214	246796	250617	0.712	1.000	1.000	1.000
Hemoglobin (gm/dL)	14.19	13.89	14.10	0.336	0.448	1.000	0.959

*White blood cells
†Versus

Anti-RBD IgG Antibody Levels

Concerning the antibody produced in the participants, when the anti-RBD IgG antibody levels were compared between the vaccinated and unvaccinated groups, the difference in the first test was insignificant ($p = 0.075$). In contrast, in the second, third and fourth tests, it was highly significant ($p < 0.001$) (Table 2).

Antibody levels highly increased in the immunized individuals after receiving each dose; these increases were significant ($p < 0.001$). Eight months following receiving the second dose, the results of all the tests were positive. However, the antibody levels decreased by nearly 2.64 times. In the unvaccinated group, the antibody levels largely remained the same without experiencing any significant changes ($p = 0.340$) (Table 2).

Table 2: A comparison of anti-RBD IgG antibody levels between groups at four-time points

Group	Mean				*p*-value	Pairwise Comparison *p*-value					
	1st test	2nd test	3rd test	4th test		1st test vs 2nd test	1st test vs 3rd test	1st test vs 4th test	2nd test vs 3rd test	2nd test vs 4th test	3rd test vs 4th test
Vaccinated (n=110)	3.67	32.50	44.92	17.00	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Unvaccinated (n=100)	3.07	2.89	2.88	2.37	0.340	1.000	1.000	0.482	1.000	1.000	1.000

Regarding the vaccinated group, 52% of them had been previously infected with SARS-CoV-2. Individuals who had contracted the infection, showed a stronger immune response after both doses than the uninfected participants ($p < 0.05$). Respondents who had never been infected with the virus, showed a stronger immune response following the second dose than the first dose ($p < 0.001$) (Figure 4).

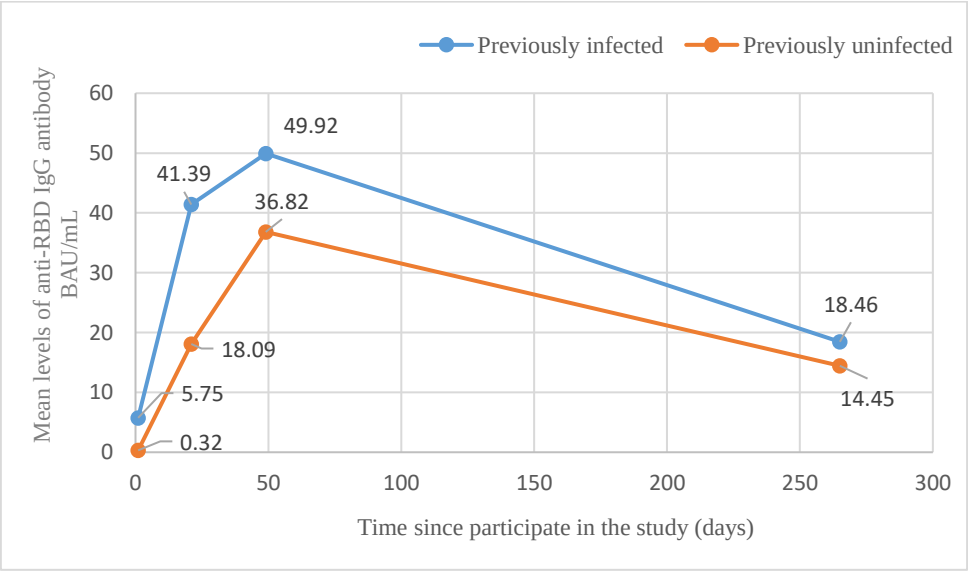

Figure 4: Anti-RBD IgG antibody levels in the vaccinated individuals at four-time points in relation to a prior infection with SARS-CoV-2

To evaluate the impact of individuals' characteristics on the levels of anti-RBD IgG antibody produced after receiving the first and second doses of the Pfizer vaccine, the anti-RBD IgG antibody levels in relation to the participants' characteristics were compared at

four-time points. The results indicated that the differences in anti-RBD IgG antibody levels in relation to respondents' characteristics were insignificant (P > 0.05) (Table 3).
Table 3 shows a comparison of the anti-RBD IgG antibody levels of immunized individuals in relation to their characteristics at four different time points.

Table 3: Anti-RBD IgG antibody's mean levels in relation to demographic characteristics

Characteristics	No. (%)	Mean of 1st test	*p*-value	Mean of 2nd test	*p*-value	Mean of 3rd test	*p*-value	Mean of 4th test	*p*-value
Gender									
Male	47 (42.7)	3.51	0.306	34.78	0.291	45.62	0.866	17.23	0.948
Female	63 (57.3)	3.79		30.79		44.40		16.82	
Age Group									
≤35	64 (58.2)	3.37	0.474	31.02	0.498	45.20	0.490	17.33	0.241
>35	46 (41.8)	3.89		33.56		44.72		16.80	
BMI									
≤24.99	50 (45.5)	3.36	0.877	29.95	0.524	44.39	0.891	16.76	0.868
>24.99	60 (54.5)	3.93		34.62		45.36		17.19	
Blood Group									
A	34 (30.9)	3.85	0.939	31.31	0.933	44.15	0.793	16.62	0.926
AB	13 (11.8)	3.05		34.06		47.59		17.52	
B	19 (17.3)	3.86		33.41		44.65		17.00	
O	44 (40.0)	3.64		32.55		44.84		17.17	

Discussion

Vaccination is expected to have temporary systemic and localized adverse effects as a result of the immune response and injury at the inoculation area [1, 8, 15]. Both intrinsic and extrinsic factors can influence the immunogenicity and reactogenicity of vaccinations in a certain individual. Among these factors are host characteristics such as sex, age, weight, ethnicity, health status, and prior immunity, in addition to vaccine factors such as the composition of the vaccine, site, and route of administration [16]. In the current study, the occurrence of side effects per individual following the second dose was noticeably greater than following the first dose. These findings are in accordance with the three studies were conducted in Poland, South Korea and the Czech Republic [17, 18, 19]. Another study reported that the frequency of most systemic side effects increased after the second dose [19, 20]. In addition, a study was carried out in Saudi Arabia among individuals aged between 12 to 18 years to assess the adverse effects of the Pfizer vaccine, indicating that the incidence of adverse effects was more common after the second dose [21].

The current study revealed that pain at the vaccinated location, tiredness, myalgia and fever were high after both doses. These findings are in accordance with those of a survey was done in Iraq [22]. A study displayed that pain at the vaccination area, tiredness, myalgia, and headache were common adverse effects following both vaccine doses [23]. Likewise, an active surveillance study and two cross-sectional studies reported that the highest side effects were pain at the inoculation site, fatigue and headache [19, 20, 24].

The number of health staff with insomnia increased significantly after the second dose. This result parallels the finding of an active survey [20]. In addition, another study showed that the vaccine decreased sleep quality [25]. Only 1.8% of the recipients suffered from

allergies after the first dose and none of them had allergies after the second dose. The findings of a study indicated that allergic reaction was uncommon after immunization with the Pfizer vaccine which reduced after the second dose [26].

Regarding the grades of adverse events, grade 3 highly increased after the second dose. This result is consistent with that of a survey conducted at a medical school [27]. Similarly, a study reported that grade 3 was highly increased following the second dose [28]. Additionally, a study that was carried out among Jordanian people who were immunized with COVID-19 vaccines, reported that the severity of the adverse events was more common after the second dose [29]. The results of the current study indicated that none of the participants entered the hospital after taking the first dose and only one individual was hospitalized after taking the second dose. These results agree with those of another study was conducted among healthcare workers [25].

Regarding haematological parameters, there were no remarkable differences in the total number of WBCs, lymphocytes, monocytes, eosinophils, basophils, neutrophils, platelets and haemoglobin before and after receiving the vaccine. A study performed in Saudi Arabia to evaluate haematological parameters in a population immunized with the Pfizer vaccine,. observed that there were no significant changes in the blood film and complete blood count before and after receiving the vaccine [30]. The findings of another study indicated that the occurrence of thrombocytopenia, leukopenia, as well as neutropenia very rarely happened after getting the Pfizer vaccine [31].

Overall, the level of anti-RBD IgG antibodies following the second dose was significantly greater than the first dose, and there were no remarkable differences between males and females in relation to the levels of the antibodies. These results are similar to those of a study that was carried out in the United States of America [32]. The present study found that the anti-RBD IgG antibody levels were not associated with age, BMI, or blood groups. These results are consistent with those of a study conducted on large populations of healthcare workers [33]. Participants with a prior history of SARS-CoV-2 infection demonstrated a significantly stronger immune response in producing the antibodies after three weeks of receiving the first dose, at a level close to that observed after the second dose. Similarly, two studies indicated that people with pre-existing immunity after receiving a single dose, their IgG antibody reached a level similar to this observed in individuals without pre-existing immunity after getting two doses [34, 35]. In contrast, respondents with the seronegative developed low-level anti-RBD IgG antibody after receiving single dose. Similarly, another study reported that one dose of the vaccine induced the production of small amounts of neutralizing antibodies in adolescents without pre-existing immunity [36].

After the first and second doses, high levels of anti-RBD IgG antibodies were observed in the respondents who had previously contracted the infection. These findings are in accordance with the results of other studies [37, 38, 39]. The current study observed significant antibody levels following the second dose in individuals without a history of SARS-CoV-2 infection. This result is similar to that of a study was conducted in Belgium [40].

After eight months of taking two doses, all results of the anti-RBD IgG antibody tests were positive, but their levels had reduced. A study demonstrated that the effectiveness of Pfizer's two-dose regimen reached a top level after two months of the first dose and fell after seven months [41]. Similarly, another study that was conducted in Poland displayed that the vaccine was effective after 7–9 months of receiving two doses [33].

The levels of anti-RBD IgG antibody at eighth-month post-immunization were remarkably higher in persons who had previously contracted the infection than individuals who did not have a history of the disease. This result agrees with that of a study done among healthcare workers in Poland [42]. A separate study showed that the levels of IgG antibody following ten months of getting two doses of the Pfizer vaccine remained proportionately high, especially in individuals with a prior history of the disease [43].

Conclusion

The Pfizer vaccine was safe but had some common temporary side effects. The vaccine did not induce any notable changes in the numbers of leukocytes or thrombocytes. Strong immune responses occurred following the one dose in individuals with pre-existing immunity and after two doses in participants without pre-existing immunity. The vaccine produced significant levels of anti-RBD IgG antibody in adults following a month of getting two doses, and after eight months, the antibodies remained in the blood. The level of the antibodies steadily decreased with time. The antibodies produced were unaffected by gender, age, BMI or blood group.

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