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RESEARCH ARTICLE OPEN ACCESS

The Efficacy and Safety of Heterologous Immunization with Pfizer-BioNTech (Pfizer) to Individuals Who Have Completed A Primary Vaccination Schedule with Sinopharm (BBIBP-CorV)

Nawfal R. Hussein[1], Warveen L. Abdulkareem[2], Narin A. Rasheed[3]* and Mohammed Rashid Ameen[3]

[1]Department of Biomedical Sciences, College of Medicine, University of Zakho, Zakho, Kurdistan Region, Iraq.
[2]Department of Internal Medicine, Azadi Teaching Hospital, Duhok, Kurdistan Region, Iraq .
[3]Department of Medical Laboratory Technology, College of Health and Medical Technology Shekhan, Duhok Polytechnic University, Duhok, Kurdistan Region, Iraq.

Abstract

The aim of this study was to examine the effectiveness and potential adverse reactions when providing a different Pfizer-BioNTech booster shot to 235 volunteers who had previously received the BBIBP-CorV Sinopharm primary vaccination series. Between February and December 2022, a questionnaire-based cross-sectional study was conducted in Duhok, located within the Kurdistan Region of Iraq. The individuals included in the study were adults aged 18 and above, who had received a Pfizer-BioNTech booster shot following the completion of a two-dose vaccination regimen with Sinopharm (BBIBP-CorV). The findings revealed that among those vaccinated with BBIBP-CorV, there were breakthrough infections at a rate of 4.26%, and no significant correlation was identified between post-vaccination infections and factors such as demographics or medical history. Furthermore, individuals who had a Pfizer booster dose experienced breakthrough infections at a rate of 5.73%, and similarly, no link was discovered between this rate and demographic or medical factors. Additionally, the study uncovered that participants commonly experienced side effects, primarily consisting of mild effects at the injection site. The study implies that both the Sinopharm and Pfizer vaccines demonstrate satisfactory safety profiles. It also suggests that giving a heterologous booster dose to individuals who have finished their primary vaccination with the BBIBP-CorV vaccine offers a significant level of protection against infection.

Keywords: COVID-19, Healthcare Workers, Sinopharm, Pfizer, Duhok, Iraq

***Correspondence:** narin.rasheed@gmail.com

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INTRODUCTION

In the last two decades, our planet has experienced three major epidemics caused by different species of coronaviruses.[1,2] Among these, the highly contagious viral disease known as Coronavirus Disease 2019 (COVID-19) is caused by SARS-CoV-2, which has both respiratory and extra-respiratory symptoms of differing levels of clinical severity.[3]

The World Health Organization (WHO) declared COVID-19 a pandemic on March 11th, 2020. Subsequently, this highly contagious virus has had a devastating impact on an enormous number of individuals worldwide. As of August 2023, the global death toll resulting from COVID-19 has about 7 million.[4-6] Besides, public health and social measures (PHSM), enormous worldwide efforts have been undertaken to contain the pandemic with the innovation of numerous safe and efficacious COVID-19 vaccines. Mass vaccination has become the fundamental weapon in slowing down the ongoing pandemic and has effectively decreased infection, severe disease, and death.[3,7-10] As the WHO declared on 1st of August 2023 that about thirteen billion and half of doses of vaccines were administered during the pandemic6. Despite the availability of vaccines, there has been increasing incidence of breakthrough infections as a result of waning immune responses brought about by age-associated immunosenescence, effects of sex-specific hormones, serostatus, and comorbidities.[11-13] However, breakthrough infections among fully vaccinated people challenge the successful achievement of immunization. The occurrence of breakthrough infections is mainly attributed to the waning of vaccine immunity over time and the continuous emergence of novel variants of COVID-19 that have the potential to bypass immunity[14-16] and have a huge impact to COVID-19 diagnosis in approach to treatment and vaccination.[17] To address these issues, Several countries, including Iraq, are considering administering booster doses in their vaccination programs, with studies showing higher protection after boosting doses.[10,18,19] Furthermore, several studies have concluded that mixing vaccine types, including heterologous boosters, is well-tolerated with stronger immune responses.[19-21] However, more data is needed to further highlight the safety concerns and effectiveness of heterologous boosters, and subsequently guide policymakers to optimize the selection of booster vaccine types. The immunization advisory committee in Iraq has allowed fully vaccinated individuals to take an additional dose from one of the present vaccines in Iraq: Pfizer-BioNTech, Sinopharm (BBIBP-CorV), and Oxford-AstraZeneca (ChAdOx1 nCoV-19). The current study aimed to investigate the safety and effectiveness of boosting Pfizer-BioNTech following primary COVID-19 vaccination with Sinopharm (BBIBP-CorV) in Duhok city, Kurdistan region, Iraq.

MATERIALS AND METHODS

Study Design and Questionnaire

A questionnaire-based cross-sectional study was carried out between February and December 2022 in Duhok city, Kurdistan Region of Iraq. The target subjects were adults aged 18 years and older who took a booster dose from Pfizer-BioNTech after initial two-dose vaccination with Sinopharm (BBIBP-CorV). Potential participants were contacted by phone calls and invited to participate in the study. Those who agreed to participate were interviewed and information was obtained using a standardized questionnaire. A total of 235 subjects were recruited, including healthcare workers (HCW). The questionnaire form consisted of two sections. The first section entailed questions on demographic data (age, sex, and occupation), concomitant chronic diseases, and history of PCR-confirmed COVID-19 infection before vaccination, including its date and severity. The second section was dedicated to the vaccines, the date of the first two doses of Sinopharm (BBIBP-CorV) and the booster dose of Pfizer-BioNTech, local and systemic reactions after each vaccine dose, IgG level within the first month following the completion of Sinopharm vaccine regimen and history of breakthrough infection that happen during the initial three months following the completion of Sinopharm vaccine regimen and the additional booster shot of Pfizer-BioNTech, including the date and severity of infection. Subjects who did not give consent, contracted infection before the completion of Sinopharm vaccine regimen, and whose anti-SARS-

CoV-2 IgG levels were not tested two weeks after the completion of Sinopharm vaccine regimen were excluded from the study.

Participants

The study participants were healthcare workers from Duhok Governorate. A total of 235 volunteers participated in the study, but Individuals who have had a recent COVID-19 before vaccination within the past six months were excluded. Additionally, volunteers who were with suspected infection, were pregnant, had recent coagulopathy, or any confirmed or suspected autoimmune or immunodeficiency disease, and were infected after the first dose of Sinopharm were also excluded. The age group was 21 years and above. The study participants were monitored for a total of 104 days, which included a 14-day

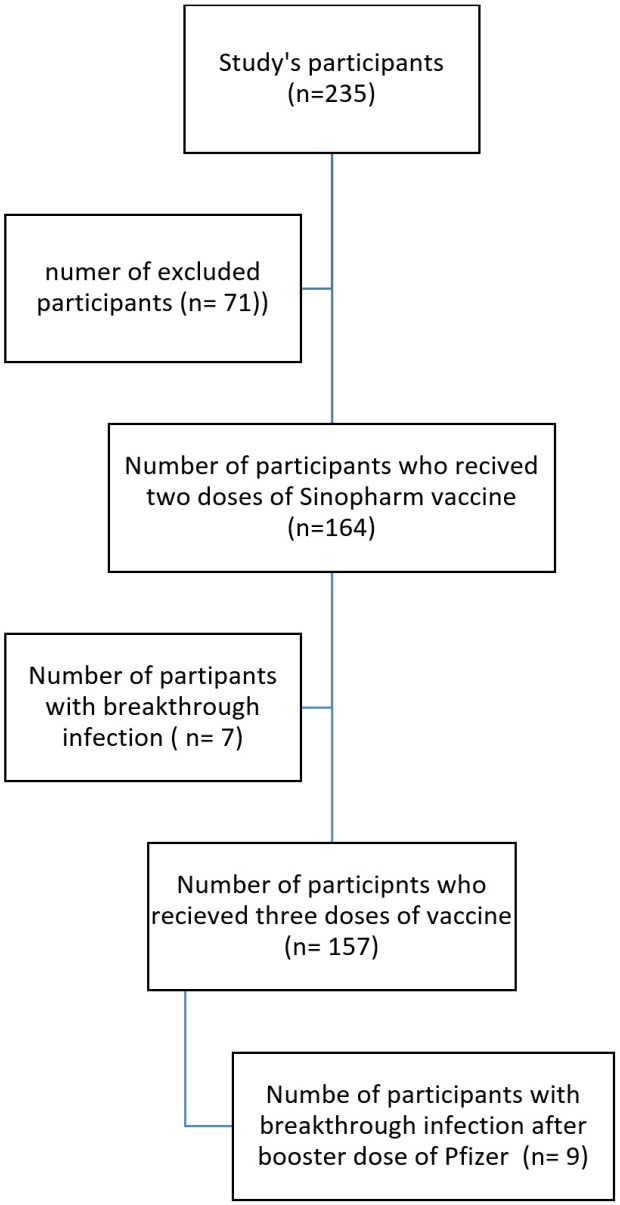

Figure. A diagram shows the participants selection in the study

Table 1. Demographic characteristics of study subjects

Variables	Mean (±SD)	N	(%)
Age	42(±9)		
Age group	21 – 30	21	12.8
	31 – 40	57	34.8
	41 – 50	55	33.5
	51 – 60	22	13.4
	61 – 70	8	4.9
	71+	1	.6
Sex	Male	119	72.6
	Female	45	27.4
Chronic diseases	Yes	34	20.7
	No	130	79.3

Table 2. Participants number with side effects after the two doses of Sinopharm vaccine

	Adverse reaction (no.%)	No adverse reaction (no.%)	Overall
First dose of vaccine	82(50)	82(50)	164
Second dose of vaccine	94(57.3)	70(42.3)	164

period for the vaccine to take effect, as well as an additional 90 days, following the completion of vaccination regimen, and the same period for the booster dose of Pfizer. Figure illustrates the distribution of study samples.

Outcome

The co-primary outcomes of the study were determining the rate of COVID-19 breakthrough infection and safety. The breakthrough infection of COVID-19 was defined as a positive PCR test for SARS-CoV-2 along with consistent clinical features occurring two weeks after the second dose of the two-dose series or two weeks after a booster-dose vaccine. Additionally, the participants with breakthrough infection were categorized into mild, moderate, and severe based on the severity of the symptoms. Individuals with no clinical and radiological features of the lower respiratory tract were categorized as mild cases. Individuals who displayed clinical and radiographic indications of lower respiratory tract infection and maintained oxygen saturation levels of 94% or higher on ambient air were categorized as having moderate cases. Severe cases were determined

Table 3. Common side effects post two doses of Sinopharm vaccine

Adverse reaction	First dose (No. %)	Second dose (No. %)
Fever	16 (9.8)	18 (11)
Injection site pain	66 (40.2)	51 (31.1)
Myalgia	13 (7.9)	9 (5.5)
Headache	3 (1.8)	4 (2.4)
Others	15 (9.1)	17 (10.4)

Table 4. Side effects onset day after administration of Sinopharm doses

Side effect onset day	After 1st dose (no. %)	After 2nd dose (no. %)
First day	73 (44.1)	64 (39)
Second day	10 (6.1)	6 (3.7)

based on individuals exhibiting oxygen saturation (SpO2) levels below 94% on ambient air, having a ratio of partial pressure of arterial oxygen to the fraction of inspired oxygen (PaO2/FiO2) below 300 mmHg, respiratory distress, or greater than 50% lung infiltrates shown on a chest image. The assessment of safety was based on the presence and documentation of local and systemic events within 14 days after the vaccination.

Molecular detection of SARS-CoV-2

Reverse Transcriptase Polymerase Chain Reaction test (RT-PCR) was used for confirmation of SARS-CoV-2 infection following the local protocol 22.

Statistics

The analysis of data was performed using SPSS (25). The data were presented as Mean, Standard Deviation (M±SD) values, Odds Ratio (OR), Standard Deviation (SD), and Confidence Intervals of 95% (CI 95%). Logistic regression analysis was utilized to evaluate the relationship between different factors and post-vaccination infections. The Chi-squared test was utilized to find the associations, and p-values of ≤0.05 were considered significant. The relationship between various factors and IgG levels was determined by the Mann-Whitney-Wilcoxon test.

Table 5. The relationship between different factors and breakthrough infections

Variables		Post-vaccination infection		Statistical analysis		
		Yes	No	P-value	OR	95%CI
Age	Mean ± SD	40.43±10.907	42.22±9.944	0.642	0.981	0.906-1.063
Sex	Male n(%)	2 (4.65)	43 (95.35)	0.945	0.997	0.927-1.073
	Female n(%)	5 (4.39)	114 (95.61)			
Previous history ofCOVID-19	n(%)	1 (2.86)	35 (97.14)	0.617	0.980	0.917-1.049
Post-vaccination IgG Level	Positive n(%)	7 (4.96)	141 (95.04)	0.374	1.050	1.013-1.088
	Negative n(%)	0 (0)	16 (100)			
First dose side effect	Yes n(%)	2 (2.5)	80 (97.5)	0.246	0.963	0.92-1.027
	No n(%)	5 (6.49)	77 (93.51)			
Second dose side effect	Yes n(%)	4 (4.44)	90 (95.56)	0.992	1.000	0.936-1.067
	No n(%)	3(4.48)	67 (95.52)			

Ethics

The consent for conducting this project was gained from the Scientific Committee of the University of Zakho, College of Medicine (UoZEC 22A11). Additionally, verbal approval was obtained from each participant prior to taking the vaccine, answering the questionnaire, and giving blood samples.

RESULTS

Demographic characteristics of study subjects

After implementing exclusion criteria, a total of 164 out of 235 volunteers were included in the study. Among them, 119 (72.6%) were males. The mean age was 42± 9 (Table 1).

Post-Sinopharm-vaccination side effects

After the Sinopharm vaccination, volunteers had some side effects. Approximately 50% of participants had side effects after the initial dose and 57.3% after the last dose (Table 2). The most predominant post-vaccine side effect was an injection-site effect (40.2%) (Table 3). About 44.1% of participants developed side effects on the first day after administration of the first dose, as well as 39% of participants after taking the second dose of the vaccine (Table 4).

Post-vaccination breakthrough infections

In this study, 7/164 (4.26%) contracted the infection. The relationship between different factors and breakthrough infections was studied. No significant association was found (Table 5).

Table 6. Post-booster dose of Pfizer vaccination side effects

Side Effect	After first dose (No. %)
Fever	49 (31.2)
Injection site pain	109 (69.4)
Myalgia	30 (19.1)
Headache	13 (8.3)
Others	30 (19.1)

Table 7. Side effect onset day after booster dose of vaccination

Side effect onset day	After booster dose (No. %)
First day	115 (73.2)
Second day	13 (8.3)

Side effects after booster dose of Pfizer vaccine

Seven (4.3%) volunteers who were infected with SARS-CoV-19 after taking the second dose of the vaccine were excluded for assessing the efficacy of Pfizer as a booster dose and further analysis. Consequently, the total number of volunteers who took the booster dose was 157. Among them, 81.5% of participants developed side effects. Among other side effects, injection site pain was identified as the most frequently reported (69.4%) (Table 6). Furthermore, 73.2% of volunteers developed side effects on the first day of taking the vaccine (Table 7).

Table 8. The correlation between different variables factors and breakthrough infection

Variable		Post-booster vaccination Infection		Statistical analysis		
		Infected (n=9)	Not infected (n=148)	P-value	OR	95%CI
Age	Mean ± SD	38.67± 10.03	42.44±9.93	0.270	0.985	0.888-1.034
Sex	Male n(%)	7 (5.7)	107(93.3)	0.720	1.341	0.267-6.724
	Female n(%)	2(4.7)	41(95.3)			
Booster dose side effects	Yes n(%)	7(5.5)	121(94.5)	0.756	1.280	0.252-6.508
	No n(%)	2(6.9)	27(93.1)			

Association between different factors and infection after receiving vaccine

After receiving boosters, 9/157 (5.73%) contracted the infection. Age, sex, previous history of COVID-19 infection, and booster dose side effects were used as associated factors for studying the association with post-booster vaccination infections. Worth mention, no association was recorded (Table 8).

DISCUSSION

Firstly, this project aimed at investigating the occurrence of breakthrough infections of COVID-19 in subjects who completed the BBIBP-CorV vaccine in an area that experienced multiple severe outbreaks. The results revealed that a small proportion of individuals, 4.26%, developed the infection following the completion of their primary vaccination schedule. This was higher than that stated in a previous study carried out in the region after being administered two doses of the Oxford-AstraZeneca vaccine (6.71%).[22] Notably, all of these cases were mild and were able to recover with proper treatment at home. Subsequently, we conducted an investigation to identify any potential factors that may be linked to the occurrence of breakthrough infections. Our analysis revealed that there were no statistically significant associations between breakthrough COVID-19 and demographic characteristics such as sex, and age. The findings of our study state that a relatively small number of patients contracted COVID-19 after the completion of the BBIBP-CorV vaccine, which implies that the vaccine is efficient in avoiding infections, particularly severe cases. It should be noted that the sample size of the study is small. Therefore, it is crucial to consider the results of this study in conjunction with additional research and data on vaccine effectiveness before drawing any conclusions.

Additionally, current study found that the most prevalent side effects experienced by participants after receiving dual doses of the vaccine were localized pain and discomfort at the site of injection, as well as a fever that persisted for a brief period of time. These symptoms were reported by a significant number of participants, and were generally considered to be mild in nature and did not require any medical intervention. This aligns with the findings of other studies, where similar side effects have been reported as the most common among vaccine recipients.[22,23] A previous study conducted in Iraq showed that the occurrence of post-vaccination adverse reactions was higher after the first dose than the second dose.[22] However, it is important to note that the finding of previous study contrasts with the results of the current study and a study conducted in the United Kingdom,[24] which reported a higher incidence of adverse reactions after the second dose of the vaccine. This concordance between the two studies suggests that the higher occurrence of adverse reaction following the second dose may be a consistent finding across different populations and settings.

Subsequently, we evaluated the incidence of breakthrough infections among subjects who have received a booster dose of the Pfizer vaccine. It was revealed that 5.7% of the individuals who received the booster subsequently contracted the infection. We then conducted further investigations to identify any potential factors that may be associated with the breakthrough infections. Our analysis did not reveal any significant associations between demographic characteristics such as age,

sex, and the development of side effects, and the contraction of the infection. This suggests that these factors may not play a significant role in the occurrence of breakthrough infections following the booster dose of the Pfizer vaccine. In this study, no significant adverse effects were reported after the administration of an additional dose of the Pfizer vaccine. This suggests that administering a heterologous booster vaccine may not be associated with severe side effects. The limitations of the study are the small sample size and short-time for following up the cases after the administration of booster dose. Further studies are needed to study the risk of developing long COVID-19 after booster dose administration breakthrough infection.

To conclude, our findings indicate that administering a heterologous booster dose to subjects who received a vaccination schedule with BBIBP-CorV offers significant degree of protection against COVID-19, encompassing severe illness and mortality. Furthermore, the results suggest that heterologous boosters may be more effective than homologous boosters for all outcomes, providing additional evidence for a "mix and match" approach.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

NRH designed the study and supervised the work. WLA conducted sample collection and interviewed participants. MRA performed data curation and analysis. WLA, NAR and NRH wrote the manuscript. NAR and NRH reviewed and edited the manuscript. All authors read and approved the final manuscript for publication.

FUNDING

None.

DATA AVAILABILITY

All datasets generated or analyzed during this study are included in the manuscript.

ETHICS STATEMENT

This study was approved by the Scientific Committee of the University of Zakho, College of Medicine, Iraq, with reference number UoZEC 22A11.

INFORMED CONSENT

Written informed consent was obtained from the participants before enrolling in the study.

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