

COVID-19 vaccine breakthrough infection among fully vaccinated healthcare workers in Duhok governorate, Iraqi Kurdistan: A retrospective cohort study

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Abstract

The aims of this study were: to determine the incidence of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) infection among vaccinated healthcare workers (HCWs), assess risk factors associated with the vaccine breakthrough (BT), and compare the effectiveness of vaccine manufacturers against SARS-CoV-2 variant of concern among HCWs in Duhok governorate. It is a multicenter retrospective cohort study, which enrolled 944 HCWs through March 2022. COVID-19 vaccinated HCWs aging 18 and above were included. A random sampling process was performed by asking the participants to fill out a standardized questionnaire by means of interviews or participant-completed surveys. Fully vaccinated HCWs with positive polymerase chain reaction tests were considered to have vaccine BT infection. Two hundred and eighty-four (30.1%) out of 944 vaccinated HCWs had SARS-CoV-2 infection postvaccination, of whom 241 (84.9%) were fully vaccinated, concluding that the incidence of BT infection is 25.5%. There were 422 (44.7%) males and 522 (55.3%) females. Most vaccine BT infections had developed in SARS-CoV-2 Omicron variant (53.5%). The majority of BT infections were mild to moderate (95.5%). Occupation, namely dentist was a significant risk factor, with a *p* value of 0.001. HCWs with a history of SARS-CoV-2 infection prevaccination were more prone to a vaccine BT infection (*p* value =0.002). Pfizer vaccine manufacturers revealed the highest effectiveness against BT infection (*p* value =0.0001). Paramedics showed a significant association with the disease severity (*p* value =0.02). The three available vaccine manufacturers in the Duhok governorate are effective against COVID-19 BT infections. Dentists and paramedics were significantly associated with poor COVID-19 outcomes.

KEYWORDS

break through infections, COVID-19, Duhok, fully vaccination, healthcare workers, Iraqi Kurdistan, vaccine effectiveness

1 | INTRODUCTION

The severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) pandemic has devastated the world in terms of health, economy, business, science, tourism, and many other life branches.^{1,2} As the COVID-19 vaccine manufacturer companies started to be administered globally, the despondency consequences of COVID-19 were mitigated.^{3,4}

COVID-19 vaccines commenced to be administered in Iraq in February 2021, in particular, the first vaccine was given in the Duhok governorate on March 26, 2021.⁵ Sinopharm was the first vaccine manufacturer company that had been administered in Iraq, followed by AstraZeneca and Pfizer⁶; scientific trials showed that the three vaccines manufacturer companies were successful to achieve herd immunity and they provide high efficacy against COVID-19 infection.^{7,8}

However, there are several factors affecting vaccines' effectiveness; the difference in the heterogeneity of the population receiving the vaccines, the emergence of virus mutation, and the dominance of a new variant of concern (VOC) had been shown to negatively impact vaccine effectiveness.^{9,10} The increased duration postvaccination had waned vaccine efficacy as well.¹¹⁻¹³ Other risk factors such as age, gender, occupation, prior COVID-19 infections, COVID-19 variants, vaccine types, and coexisting diseases may decrease vaccine effectiveness.^{4,10,14-16} These risk factors, separately or together, could result in vaccine breakthrough (BT) infections. Vaccine BT infection happens when a fully vaccinated individual gets COVID-19 infection.¹¹

As the Delta variant, SARS-CoV-2 B.1.617 lineage was first reported in October 2020 in India and thereafter became predominant globally.¹⁷ Research showed that Pfizer and AstraZeneca vaccines had a barely distinguishable inhibitory effect on the Delta variant.¹⁸ On the other hand, the Omicron variant was discovered to be the highest in resistance for neutralization by COVID-19 vaccines from different manufacturing companies.^{19,20} Hence, CDC recommended additional booster doses among persons aged ≥ 18 years.^{21,22} The clinical trials proved that three messenger RNA (mRNA) vaccine doses would elicit potent variant cross-neutralization, including Omicron.²³

From the start of the pandemic, health care workers (HCWs) have been the most vulnerable group to exposure to the SARS-CoV-2 virus due to the nature of their job.²⁴ Hence, HCWs were the priority of receiving COVID-19 vaccines, as recommended by the Advisory Committee on Immunization Practices and World Health Organization (WHO).^{25,26}

The first insight regarding vaccine safety and adverse effects among the Iraqi population has been addressed in our previous study in 2021.⁶ However, deprivation of real-world data settings regarding vaccine efficacy and incidence of SARS-CoV-2 vaccine BT infection had raised the impetus to perform this study. Therefore, the aims of this study were: to determine the incidence of SARS-CoV-2 infection among fully vaccinated HCWs, assess risk factors associated with the vaccine BT, and compare the effectiveness of vaccine manufacturers against SARS-CoV-2 VOC among HCWs in the Duhok governorate.

2 | METHODOLOGY

2.1 | Study design

This multicenter retrospective cohort study enrolled 944 HCWs from Duhok province and its districts: Zakho, Semel, and Aqre. Data had been collected through March 2022. The HCWs included were from tertiary and secondary referral hospitals, primary healthcare centers (PHCs), and COVID-19 centers.

2.2 | Participants

Vaccinated HCWs aging 18 and above were included, ranging from physicians, nurses, pharmacists, dentists, paramedics, laboratory technicians, health sector administrators, and others. Any HCW who received their vaccine outside the country from a company unavailable in Iraq was excluded from the current study.

2.3 | Sampling and data collecting

The random sampling process was performed by asking the participants to fill a standardized questionnaire form by means of interviews or participant-completed surveys. The questionnaire form firstly consisted of questions regarding demographic information, for instance, age, gender, occupation, workplace, and comorbid diseases. COVID infection and vaccine information were the second part; which included a history of COVID infection pre-vaccination, vaccine type, and number of doses. The last part represented if the participant was partially or fully vaccinated, had COVID-19 infection postvaccination in fully vaccinated that is, BT infection, when they got the infection, and severity of infection. The questionnaire included information regarding potential confounders related to workplace and community attitudes, for example, whether the participant had any close contact with a COVID-19 infected person in the postvaccination period and restrictions to the COVID-19 prevention recommendations such as social distancing, hand washing, wearing masks, and so forth.

Participants with a positive polymerase chain reaction (PCR) test with at least one symptom were considered to have vaccine BT infection. Participants with negative PCR tests were excluded from having a vaccine for BT infection regardless of the existence of symptoms. Participants who were vaccinated with the first dose of COVID-19 vaccine and exceeded 14 days post-vaccine, or those who received the second dose and have not exceeded 14 days post-vaccine, were defined as partially vaccinated. However, participants who were vaccinated with two doses and 14 days and more post-second doses were considered as fully vaccinated.²⁷

As Duhok governorate had passed through three waves since the start of vaccine availability, vaccine BT infection time had been separated into three groups; infections that had developed from March until June 2021, were considered to be during the

B.1.351 (Beta) wave. Infections from July to December 2021, were considered to be during the B.1.617.2 (Delta) wave. Lastly, infections from January until the time of sampling, which was March 2022, were considered to be during the 2 B.1.1.529 (Omicron) wave.²⁸

2.4 | Ethical consideration

The study was reviewed and approved by the scientific and the Ethics Committee of the College of Pharmacy at the University of Duhok on February 13, 2022 (Reference No. 116). Healthcare workers had submitted their informed consent before participation.

2.5 | Statistical analysis

All data were analyzed by Statistical Package for the Social Sciences software version 22. Descriptive statistics were carried out for the demographic variables and medical anamnesis. Fisher's exact and χ^2 tests were used to find the associated risk factors for developing SARS-CoV-2 infection postvaccination. Odds ratio of 1 and *p* value of ≤ 0.05 was considered statistically significant.

3 | RESULTS

3.1 | Study population

Two hundred and eighty-four (30.1%) out of 944 of vaccinated HCWs had SARS-CoV-2 infection postvaccination, of whom 241 (84.9%) were fully vaccinated, concluding that the incidence of SARS-CoV-2 infection is 25.5%. The other 43 (15.1%) had infection after being partially vaccinated (Figure 1).

3.2 | Demographic and clinical characteristics

There were 422 (44.7%) males and 522 (55.3%) females. The age of the majority (86.1%) was less than 50 years. A 10.1% of HCWs had at least one comorbid disease; hypertension (51.6%) and diabetes mellitus (19.8%) were the most frequent diseases, followed by hypothyroidism (9.5%) and osteoarthritis (7.4%), asthma and chronic bronchitis (2.1%), GIT diseases (3.2%), other details are shown in Table 1.

Most of the participants were nurses (24.4%) and physicians (24%), followed by pharmacists (17.7%), dentists (4.6%), paramedics (3.8%), and others included laboratory technicians, security, and administrator workers, which constituted 25.5%. Only 7.6% of HCWs were working in COVID-19 specialized centers, other 92.4% were workers from tertiary and secondary referral centers and PHCs. A 52.4% had a history of SARS-CoV-2 infection before getting the vaccine.

Pfizer vaccine receivers were 61.3%, whereas 20.7% and 10.4% were AstraZeneca and Sinopharm receivers respectively.

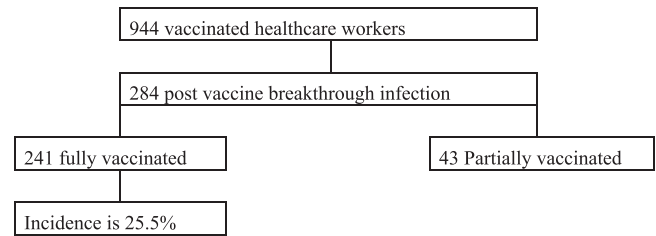


FIGURE 1 Flowchart of the studied population

Seventy-two (7.6%) of HCWs received mixed vaccines meaning at first administered two doses of Sinopharm vaccine but the booster was Pfizer dose or two doses of AstraZeneca and one Pfizer booster.

Most vaccine BT infections had developed in SARS-CoV-2 B.1.1.529 (Omicron) variant period 53.5%, and 41.1% were during B.1.617.2 (Delta) variant. Regarding the severity of infection, only 10 (4.1%) cases out of 241 were severe to critical and required ventilation, the other 231 (95.5%) were mild to moderate. A 68.5% of infected HCWs had close contact with SARS-CoV-2 infected people, The majority (75.5%) were following the COVID-19 prevention rules. All data are shown in Table 1.

3.3 | Associated risk factors of vaccine breakthrough infection

We found that gender, age, comorbidity, and workplace have no relation to developing vaccine BT infection (*p* value: 0.817, 0.119, 0.603, and 0.551, respectively). Occupation appeared to be a significant risk factor for infection. Dentists were the most vulnerable group for vaccine BT infection with 41.5%, followed by pharmacists and physicians 35.2%, and 33.6%, respectively, with a *p* value of 0.001.

HCWs with a history of SARS-CoV-2 infection before vaccination appeared to be more prone to a vaccine BT infection with a *p* value of 0.002. Regarding vaccine manufacturers, 42% of AstraZeneca receipts had vaccine BT infection, followed by Sinopharm recipients 27.4%. Pfizer vaccine effectiveness appeared to be the highest, a *p* value of 0.0001. The booster dose showed no significant association with BT infection, a *p* value of 0.334. Details are shown in Table 2.

3.4 | Associated risk factors for having severe SARS-CoV-2 vaccine breakthrough infection

All variables were not associated with COVID-19 severity; the only occupation being paramedics (*p* value =0.02) as shown in Table 3.

4 | DISCUSSION

The incidence of COVID-19 BT infections depends on the laboratory testing time. The magnitude of BT infections is mitigated by vaccine effectiveness.²⁹ In our study, the incidence of COVID-19 BT

TABLE 1 Demographic characteristics of study population *N* = 944

Variables	Numbers	Percentage (%)
Gender		
Male	422	44.7
Female	522	55.3
Age		
Less than 50	813	86.1
50 and above	131	13.9
Comorbidity		
Yes	95	10.1
No	849	89.9
Diseases <i>N</i> = 95		
Hypertension	49	51.6
Diabetes mellitus	19	19.8
Hypothyroidism	9	9.5
Osteoarthritis	7	7.4
Asthma	2	2.1
Cancer	1	1.1
UC or IBD	3	3.2
Allergic rhinitis	2	2.1
Chronic bronchitis	2	2.1
Fatty liver disease	1	1.1
Occupation		
Physician	227	24
Pharmacist	167	17.7
Nurse	230	24.4
Dentist	43	4.6
Paramedic	36	3.8
Others	241	25.5
Place of work		
COVID-19 center	72	7.6
Other healthcare services	872	92.4
History of COVID-19 infection prevaccination		
Yes	495	52.4
No	449	47.6
Vaccine manufacturer		
Pfizer	579	61.3
AstraZeneca	195	20.7
Sinopharm	98	10.4
Mixed vaccines	72	7.6
Doses		
One dose	70	7.4

(Continues)

TABLE 1 (Continued)

Variables	Numbers	Percentage (%)
Two doses	746	79
Three doses	128	13.6
COVID-19 infection postvaccination		
Yes	284	30.1
No	669	69.9
Time of infection postvaccination <i>N</i> = 284		
After being partially vaccinated	43	15.1
After being fully vaccinated	241	84.9
Characteristics of vaccine breakthrough infection <i>N</i> = 241		
Period of infection		
Beta period	13	5.4
Delta period	99	41.1
Omicron period	129	53.5
Severity of infection		
Mild to moderate	231	95.9
Severe to critical	10	4.1
COVID-19 patients contact		
Yes	165	68.5
No	76	31.5
Restriction to prevention recommendations		
Yes	182	75.5
No	59	24.5

Abbreviations: IBD, irritable bowel disease; UC, ulcerative colitis.

infection among fully vaccinated HCWs was found to be 25.5%. This finding confirms that the three available vaccine manufacturers are effective against COVID-19 BT infections. However, a lower incidence of BT infection with higher vaccine effectiveness (more than 90%) was reported from studies in the United States¹⁶ and United Kingdom.³⁰ The higher incidence rate could be explained by the domination of Omicron wave (53.5%) during our study period, whereas at the time of other studies, there was no omicron as VOC. The existence of multiple mutations in the spike protein of the mentioned variants has been associated with increased immune evasion after natural infection and vaccination.^{19,31} The potential lower vaccine effectiveness in the current study is also justified by the waning of vaccine immune response after a few months of the second dose. Similarly, studies from Israel,¹¹ Qatar,¹² and the United States,¹³ documented a reduction in vaccine effectiveness after a few months following the second vaccine dose. Hence, to prevent the aforementioned events, booster doses seem to be highly effective in reducing BT infections. In the Duhok governorate, the vaccine coverage of HCWs is fairly satisfactory (60%); however, the administered booster doses are inadequate.⁵

TABLE 2 Associated risk factor of vaccine breakthrough infection among fully vaccinated HCWs in Duhok

Variables	No. of fully vaccinated, breakthrough infection (%) N= 241	No. of fully vaccinated, no breakthrough infection (%) N= 660	Total	p Value
Gender				
Male	106 (26.4)	296 (73.6)	402	0.817
Female	135 (27.1)	364 (72.9)	499	
Age				
Less than 50	214 (27.7)	559 (72.3)	773	0.119
50 and more	27 (21.1)	101 (78.9)	128	
Comorbidity				
Yes	22 (24.4)	68 (75.6)	90	0.603
No	219 (27)	592 (73)	811	
Occupation				
Physician	73 (33.6)	144 (66.4)	217	0.001
Pharmacist	57 (35.2)	105 (64.8)	162	
Nurse	52 (24.5)	160 (75.5)	212	
Dentist	17 (41.5)	24 (58.5)	41	
Paramedic	3 (8.3)	33 (91.7)	36	
Other	39 (16.7)	194 (83.3)	233	
Place of work				
COVID center	20 (29.9)	47 (70.1)	67	0.551
Other HC services	221 (26.5)	613 (73.5)	834	
History of COVID infection prevaccination				
Yes	145 (31.1)	321 (68.9)	466	0.002
No	96 (22.1)	339 (77.9)	435	
Vaccine manufacturer				
Pfizer	121 (22)	428 (78)	549	0.0001
AstraZeneca	79 (42)	109 (58)	188	
Sinopharm	26 (27.4)	69 (72.6)	95	
Mixed vaccines	15 (21.7)	54 (78.3)	69	
Booster shots				
Yes	29 (23.2)	96 (76.8)	125	0.334
No	212 (27.3)	564 (72.7)	776	

Abbreviation: HCW, healthcare workers.

In the present study, considering risk factors associated with vaccine BT among fully vaccinated HCWs; we did not find a significant association of BT infection with gender, age, comorbid diseases, place of work, and booster vaccine. However, dentists were

TABLE 3 Associated risk factors for severe vaccine breakthrough infection

Variable	Mild to moderate (%) N = 231	Severe to critical (%) N = 10	Total	p Value
Gender				
Male	102 (96.2)	4 (3.8)	106	0.795
Female	129 (95.6)	6 (4.4)	135	
Age				
Less than 50	206 (96.3)	8 (3.7)	214	0.368
50 and more	25 (92.6)	2 (7.4)	27	
Comorbidity				
Yes	21 (95.5)	1 (4.5)	22	0.922
No	210 (95.9)	9 (4.1)	219	
Occupation				
Physician	72 (98.6)	1 (1.4)	73	0.02
Pharmacist	56 (98.2)	1 (1.8)	57	
Nurse	49 (94.2)	3 (5.8)	52	
Dentist	17 (100)	0 (0)	17	
Paramedic	2 (66.7)	1 (33.3)	3	
Other	35 (89.7)	4 (10.3)	39	
Place of work				
COVID center	19 (95)	1 (5)	20	0.842
Other HC sectors	212 (95.9)	9 (4.1)	221	
History of COVID infection prevaccination				
Yes	137 (94.5)	8 (5.5)	145	0.191
No	94 (97.9)	2 (2.1)	96	
Vaccine manufacturer				
Pfizer	117 (96.7)	4 (3.3)	121	0.89
AstraZeneca	75 (94.9)	4 (5.1)	79	
Sinopharm	25 (96.2)	1 (3.8)	26	
Mixed vaccines	14 (93.3)	1 (6.7)	15	
Booster shots				
Yes	27 (93.1)	2 (6.9)	29	0.429
No	204 (96.2)	8 (3.8)	212	
Period of Infection				
Beta	12 (92.3)	1 (7.7)	13	0.804
Delta	95 (96)	4 (4)	99	
Omicron	124 (96.1)	5 (3.9)	129	
COVID-19 patients contact				
Yes	159 (96.4)	6 (3.6)	165	0.556
No	72 (94.7)	4 (5.3)	76	

TABLE 3 (Continued)

Variable	Mild to moderate (%) N = 231	Severe to critical (%) N = 10	Total	p Value
Restriction to prevention recommendations				
Yes	173 (95.1)	9 (4.9)	182	0.277
No	58 (98.3)	1 (1.7)	59	

associated with increased BT infection. In parallel, practicing dentistry is linked with a higher rate of acquiring COVID-19 infection and hence an increased risk of BT infections.¹⁴ Therefore, improving preventive measures with aerosol-generating procedures in high-risk exposure setting as Duhok dental centers is highly indicated.³² Furthermore, the history of prior COVID-19 infection was significantly associated with increased BT infection. Contrary to other research the menace of BT infection was lower amongst previously infected people.^{4,33} Stamatatos et al. reported that previously infected COVID-19 patients will benefit from immunization as it will significantly increase neutralizing antibody responses against vaccine-matched and emerging variants. However, little research showed that prior infection in vaccinated people did not significantly reduce the risk of BT infection.³⁴ Overall, the contradicting finding in our study is a paradox. Hence, further prospective studies with larger sample sizes are a necessity for a better understanding. Additionally, we found that mixed vaccines (78.3%) and Pfizer manufacturers (78%) were potentially more effective than others in preventing BT infections ($p = 0.0001$). Whereas, the AstraZeneca vaccine (58%) was the least effective against the BT infection. This finding was consistent with the findings of Stouten et al.⁴ in a prospective cohort study in Belgium who reported a higher BT infection with AstraZeneca vaccine than mRNA vaccines. In Duhok governorate the most widely used vaccine is the Pfizer manufacturer,⁵ which may, in part, explain the reasonable rate of BT infections.

In this study, we found that only occupation, namely the paramedic profession was associated with severe disease outcomes, whereas other variables did not show significant association (Table 3). In Iraq, paramedics are the frontline workers in facing COVID-19 infection in the intensive care units, hence they are more prone to severe outcomes.³⁵ However, the low sample number of paramedics with BT infection in the current study “only 3” when compared with other occupations’ sample sizes, had limited the veracity of this outcome. Overall, infection control practices to prevent transmissions of infectious diseases is under the WHO target.³⁶ Although we did not find other parameters to be associated with a severe outcome; other studies reported that increasing age,⁸ COVID-19 naïve people,⁴ comorbid diseases,³⁷ vaccine unboosted people²² were poor outcomes in patients with BT infections.

The main limitation in the present study was: several patients had prevaccination COVID-19 infection, providing them with natural immunity. This might bias the effect of the vaccine with COVID-19 BT. Another limitation was that the retrospective nature of the study

included self-reported HCWs with BT infection, thus it missed asymptomatic cases and consequently underestimates the true incidence of the infection.

In conclusion, the incidence of COVID-19 BT infection among fully vaccinated HCWs was 25.5%. Hence the three available vaccine manufacturers in the Duhok governorate are effective against COVID-19 BT infections. Dentists were associated with increased BT infection. Therefore, improving preventive measures with aerosol-generating procedures in high-risk exposure settings is paramount. The frontline HCWs, in particular, paramedics were significantly associated with poor COVID-19 outcomes.

AUTHOR CONTRIBUTIONS

Conceptualization: Hind B. Almufty and Masoud M. Ameen Mamani. *Methodology:* Hind B. Almufty, Masoud M. Ameen Mamani, Ali H. Ali. *Formal analysis:* Hind B. Almufty. *Writing:* Hind B. Almufty and Muayad A. Merza. *Reviewing, editing, and supervising:* Muayad A. Merza.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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