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Vaccination against COVID-19 among healthcare workers as a cocoon strategy for people living with HIV

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ABSTRACT

Introduction: Healthcare professionals working in infectious disease units are often engaged in the care of patients with HIV infection. A cocoon vaccination strategy may protect those who are immunocompromised from a severe course of COVID-19.

Methods: The research was conducted between January 2021 and June 2022. The study participants were 450 healthcare workers (HCWs) from the Hospital for Infectious Diseases in Warsaw who were vaccinated against COVID-19 with the BNT162b2 mRNA vaccine (Pfizer-BioNTech) –, thefirst available type of vaccine in Poland. Sera were collected according to the schedule of the study. Statistical analyses were performed with non-parametric tests: Wilcoxon's test was used to compare dependent numerical variables, and Fisher's exact test and the Chi-squared test to compare categorical variables. A p value of <0.05 was considered statistically significant.

Results: Among the 450 HCWs working in the Hospital for Infectious Diseases in Warsaw 412 (91,5 %) were vaccinated against COVID-19. In total 170 (41,3 %) vaccinated HCWs were included in the final analysis. Their median age was 51 years [interquartile range (IQR): 41–60 years] and median body mass index (BMI) was 25.10 [IQR: 22.68–29.03]. Most of the cohort consisted of women (n = 137, 80.59 %), with the majority working directly with patients (n = 137, 73.21 %). It was found that as early as 14 days after the second dose of the vaccine, 100 % of the study participants achieved a positive result for SARS CoV-2 S-RBD antibodies. There were 168 subjects who had had a COVID-19 diagnosis before entering study and after vaccination 65 HCWs was diagnosed with COVID-19.

Conclusions: Due to the fact that people living with HIV with severe immunodeficiency may have an incomplete immune response to COVID vaccination and be at risk of a severe course of the disease, the cocoon strategy of vaccinating medical personnel may be beneficial for these patients.

1. What's new?

The study evaluated serological markers of immunological response of COVID-19 vaccination among healthcare workers working in an infectious disease centre. The novelty of this research includes the assessment of the number of COVID-19 cases among vaccinated employees in the centre where a significant number of people living with HIV (PLWH) are under medical care. Such observation provides a valuable insight for future recommendations on COVID-19 vaccination and the introduction to the cocoon strategy for PLWH who may develop only a partial, immunological memory response after COVID-19

infection or vaccination.

2. Introduction

Vaccination has become the best healthcare intervention – saving millions of lives. As one of the best strategies for the primary prevention of infectious diseases, vaccines have significantly reduced morbidity and mortality in the general population.[1] Despite these benefits, there is still a problem with low levels of vaccination coverage; for example, influenza vaccination coverage in Poland is one of the lowest in the European Union, with only 3.7 % of Poles immunized.[2,3]

Vaccinations are an essential strategy in preventing the spread of the COVID-19 pandemic and reducing the risk of both a severe course of the disease and death.[4] However, we are still uncertain as to whether immunocompromised individuals respond to vaccination to the same extent as immunocompetent ones in the long-term, which is compounded by the fact that COVID-19 vaccination coverage among the general public is quite low in Poland (59.3 %).[5] Healthcare professionals working in infectious disease units are often engaged in the care of HIV positive individuals. These individuals seem to have a similar risk of COVID-19 infection as HIV negative ones, but if exposed to SARS-CoV-2, they are more likely to have a worse outcome.[6] Some of these individuals may also develop only partial, immunological memory after COVID-19 infection or vaccination.[7,8]

Such people should be given special care in order to protect them from life-threatening infections. One possible way to prevent those who are immunocompromised from experiencing a severe course of COVID-19 is to use the cocoon vaccination strategy. This is generally recommended as a part of a comprehensive strategy for preventing communicable diseases to protect the most vulnerable people from acquiring a particular infectious disease by vaccinating those in their immediate environment.[9–11] Once vaccinated, a person may no longer be a source of infection for non-vaccinated people. This method may reduce transmission among people who are in close contact with each other, but also help in achieving a herd immunity effect.[12]

However, to the best of our knowledge, there is a lack of up-to-date data concerning the use of the cocoon vaccination strategy against SARS-CoV-2 among PLWH. In this study, we have assessed how healthcare workers (HCWs) responded to vaccination against COVID-19 in an infectious disease center.

3. Methods

The study was conducted between January 2021 and June 2022. The study participants were HCWs from the Hospital for Infectious Diseases in Warsaw. Approximately 400 HIV positive patients are treated monthly in this center, and employees treat both HIV positive and COVID-19 patients. In this infectious disease center, 450 people were employed and 412 (91,5 %) of them vaccinated against COVID-19 with the BNT162b2 mRNA vaccine (Pfizer-BioNTech) – the first available type of vaccine in Poland. Sera were collected on the day of the first dose of the BNT162b2 mRNA vaccine, on the day of the second dose of vaccine (three weeks after the first dose), and on the day of the third vaccine dose (nine months after the first vaccine dose). Sera were additionally collected at fourteen days and at six months after both the second dose and the third dose of the vaccine (Fig. 1). The levels of S-RBD antibodies (indicating a response to the vaccination) were measured using a MAGLUMI SARS CoV-2 S-RBD IgG kit. MAGLUMI® SARS-CoV-2 S-RBD IgG kits are characterized by 99.6 % specificity and 100 % sensitivity, according to the manufacturer's information. These kits have been approved in the European Union for sale and have received a CE certificate.

The antibody level ≥4.33 BAU/mL for S-RBD antibodies was interpreted as positive, according to laboratory standards. Samples that had values above 433 BAU/mL were diluted and measured at a ratio of 1:10 or 1:20 (if necessary). It allowed the analysis range to be extended to 8660 BAU/mL – during the last stage of the study, almost all serum samples were diluted twice.

The criteria that confirmed a diagnosis of COVID-19 were a positive result from a nasopharyngeal swab using PCR for SARS CoV-2, and symptoms such as fever, cough, runny nose, general weakness, sore throat, muscle pain, and loss of smell and/or taste.

Participants were asked to complete a standardized questionnaire after each vaccine dose to include data concerning comorbidities, age, weight, sex, and any adverse events (self-reported) that occurred after each vaccine dose.

Statistical analyses were used to compare patients with S-RBD antibodies at ≥433 BAU/mL and those with S-RDB antibodies at <433 BAU/mL, at six months after the third dose of the vaccine. Non-parametric tests were used accordingly: Wilcoxon's test was used to compare dependent numerical variables, and Fisher's exact test and the Chi-squared test were used to compare categorical variables.

A p value of <0.05 was considered significant. All analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

The study was approved by the Bioethics Committee of the Medical University of Warsaw (No. KB/2/2021).

4. Results

Among 450 HCWs working in the Hospital for Infectious Diseases in Warsaw 412 (91,5 %) were vaccinated against COVID-19. Overall, 228 participants were recruited into the study. Thirty-two study participants were excluded from the analysis, as at least one blood sample was missing from the study schedule. A further 26 people were excluded in the next step due to issues in the required standardized questionnaire. In total, 170 persons working at the Hospital for Infectious Diseases in Warsaw were included in the final analysis. In the cohort, 137 (80.59 %) study participants were female and 33 (19.41 %) were male. Their median age was 51 years [interquartile range (IQR): 41–60 years]. Their median body mass index (BMI) was 25.10 [IQR: 22.68–29.03]. More than two thirds of the cohort worked directly with patients (n = 122, 73.21 %) (Table 1).

It was found that as early as 14 days after the second dose of the vaccine, 100 % of the study participants achieved a positive result for SARS CoV-2 S-RBD antibodies (Fig. 2). The number of subjects out of the total with positive SARS CoV-2 S-RBD antibodies according to the testing schedule and levels at particular time points are shown in
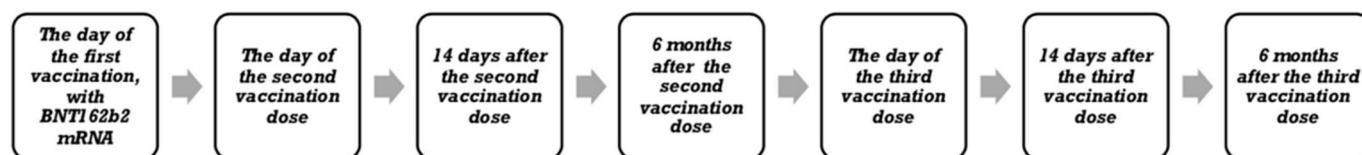
Table 1
Baseline characteristics for the study participants from the Hospital for Infectious Diseases in Warsaw.

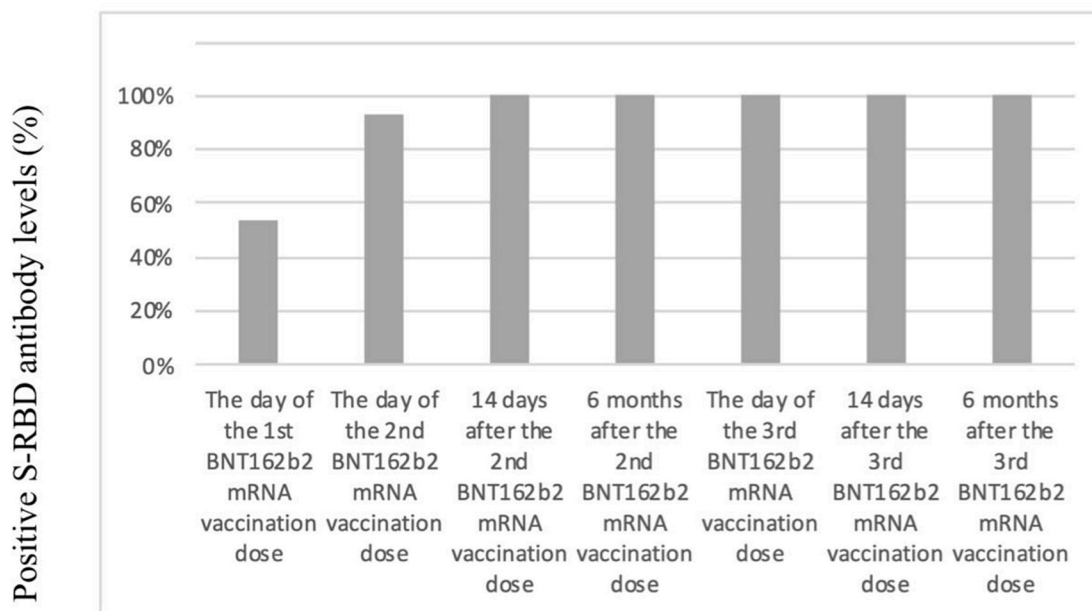| Characteristic	Number of patients with available data	ALL
Age in years, median [IQR]	170	51 [41–60]
BMI in kg/m², median [IQR]	159	25.10 [22.68–29.03]
Female sex, n (%)	170	137 (80.6)
Hospital employees working directly with patients, n (%)	168	122 (73.2)
• Doctors, n (%)		51 (30.3)
• Nurses, n (%)		63 (37.5)
• Medical assistants, n (%)		8 (4.7)

Abbreviations:
BMI – body mass index.
IQR – interquartile range.

Fig. 1. Scheme showing the steps of the study for vaccination and samples.

Fig. 2. The percentage of subjects with positive levels of SARS CoV-2 S-RBD antibodies at particular time points.

Table 2

The number of persons out of the group of 170 employees who were found to be positive for SARS CoV-2 S-RBD antibodies on consecutive days of testing, and data for the median and interquartile ranges for anti-S-RBD antibody titers (BAU/mL) measured during the observation period.

Time point	The day of the 1st BNT162b2 mRNA vaccination dose	The day of the 2nd BNT162b2 mRNA vaccination dose	14 days after the 2nd BNT162b2 mRNA vaccination dose	6 months after the 2nd BNT162b2 mRNA vaccination dose	The day of the 3rd BNT162b2 mRNA vaccination dose	14 days after the 3rd BNT162b2 mRNA vaccination dose	6 months after the 3rd BNT162b2 mRNA vaccination dose
Total nr of tested S-RBD	228	187	193	209	184	178	170
Positive S-RBD antibodies, n (%)	54 (23.7)	175 (93.5)	193 (100)	209 (100)	184 (100)	178 (100)	170 (100)
Level of S-RBD antibodies (BAU/mL), median [IQR]	1.818 [1.171–27.750]	226.600 [99.455]	3338.2 [757.4–5791.0]	224.9 [103.6–353.7]	170.2 [68.7–396.6]	4525.8 [2804.9–7712.6]	817.9 [402.2–3124.9]

Table 2.

Despite the time elapsed between subsequent vaccine doses, S-RBD antibody levels remained high; with higher antibody titers observed six months after the third dose of the vaccine (817.9 [402.2–3124.9], median [IQR], BAU/mL) than six months after the second dose of the vaccine (224.9 [103.6–353.7], median [IQR], BAU/mL)

Study participants were compared in terms of their S-RBD antibody levels six months after the third dose. In total, 123 (72.3 %) subjects had S-RBD antibodies ($\geq$433 BAU/ml) six months after the third dose of BNT162b2 mRNA vaccination and 47 (27.7 %) participants had S-RBD antibodies (<433 BAU/ml) six months after the third dose. No significant differences were found between the groups regarding age (51 vs 54 years, $p = 0.072$), BMI (25.64 vs 24.61, $p = 0.299$), working directly with patients (86 vs 36, $p = 0.565$), or concomitant diseases (37 vs 9, $p = 0.305$) (Table 3).

After the first dose of BNT162b2 mRNA vaccine, we noted only one COVID-19 infection, and after the second dose of BNT162b2 mRNA vaccine there were 15 infections. We observed the largest number of COVID-19 infections after the third dose of the vaccine – n=49. All these infections were observed in HCWs working directly with patients. The course of the infection was mild and none of these study participants required hospitalization or medical care (Table 4).

5. Discussion

In our study, we found that as early as 14 days after the second dose of the vaccine, 100 % of the HCWs in an infectious diseases center in Warsaw had achieved a positive result for S-RBD antibodies, which indicates a favorable humoral response to vaccination. Polack et al. in their trial, reported that the vaccine efficacy of the Covid-19 mRNA vaccine BNT162b2 was 95 % across different subgroups.[13] HCWs is a specific group, and being on the front line, are recognized as one of the groups with the highest risk of exposure to COVID-19 infection.[14] Prior to the availability of COVID-19 vaccines, 14 % of COVID-19 cases reported to the WHO were among HCWs.[15] In other reports, these accounted for 3.8–19 % of all COVID-19 cases, which would make them the most vulnerable occupational group.[16,17] This is why HCWs were a priority group for COVID-19 vaccination. In a study which Pilishvili et al. conducted among 1482 HCWs in the USA, it was found that the BNT162b2 vaccine was highly effective against symptomatic Covid-19

Table 3

The study participants' baseline characteristics, including a comparison between persons with S-RBD antibodies at ≥433 BAU/ml and persons with S-RBD antibodies at <433 BAU/ml, 6 months after the third vaccine dose.

Characteristic	Number of patients with available data	ALL	S-RBD antibodies ≥433 BAU/ml six months after the third dose × n = 123	S-RBD antibodies<433 BAU/ml six months after the third dose × n = 47	*p* value
Age in years, median [IQR]	170	51 [41–60]	51 [39–59]	54 [45–62]	0.0726
BMI in kg/m^2, median [IQR]	170	25.10 [22.68–29.03]	25.64 [22.50–29.36]	24.61 [22.86–27.09]	0.2997
Female sex, n (%)	170	137 (80.6)	103 (84.4)	34 (72.3)	0.0824
Hospital employees working directly with patients, n (%)	168	122 (73.2)	86 (70.5)	36 (76.6)	0.5657
Concomitant diseases	170	46 (27.0)	37 (35.6)	9 (25.0)	0.3052
● myocardial infarction in the past, n (%)	–	2 (1.2)	2 (1.6)	0 (0.0)	1.0000
● hypertension, n (%)	–	32 (18.8)	24 (19.5)	8 (17.0)	0.8279
● asthma, n (%)	–	6 (3.5)	6 (4.9)	0 (0.0)	0.1887
● interstitial lung disease, n (%)	–	1 (0.6)	1 (0.8)	0 (0.0)	1.0000
● immunosuppressive treatment, n (%)	–	3 (1.7)	2 (1.6)	1 (2.1)	1.0000
● obesity, n (%)	–	2 (1.2)	2 (1.6)	0 (0.0)	1.0000
● type 2 diabetes mellitus, n (%)	–	2 (1.2)	1 (0.8)	1 (2.1)	0.4777
● chronic hepatitis, n (%)	–	3 (1.7)	2 (1.6)	1 (2.1)	1.0000
COVID-19 diagnosis before entering study	168	38 (22.6)	28 (22.8)	10 (21.3)	1.0000

Abbreviations:

BMI - body mass index.

COPD - chronic obstructive pulmonary disease.

Table 4

The number and type of healthcare workers who were infected with COVID-19 during vaccination schedule.

Healthcare workers	COVID-19 after the first dose of BNT162b2 mRNA vaccine n = 1	COVID-19 after the second dose of BNT162b2 mRNA vaccine n = 15	COVID-19 after the third dose of BNT162b2 mRNA vaccine n = 49
Nurse (number, %)	1 (100)	8 (53)	22 (45)
Doctor (number, %)	–	2[14]	12 (24.5)
Laboratory diagnostician (number, %)	–	–	3[6]
Administrative employee (number, %)	–	4[26]	11 (22.5)
Medical assistant (number, %)	–	1[7]	–
Pharmacist (number, %)	–	–	1[2]

among health care personnel. The effectiveness of a two-dose regimen using the BNT162b2 vaccine was 89 %, and this was found to be similar across racial and ethnic groups, and also among persons with underlying conditions and risk factors associated with an increased risk of severe Covid-19.[18] As in our findings, vaccine effectiveness with two doses (full immunization) of mRNA vaccines was 90 % (95 %, CI = 68%–97 %) against RT-PCR-confirmed SARS-CoV-2 infection in a study by Thompson et al. conducted among HCWs. The data complements reports by demonstrating that the vaccines can also reduce the risk of infection, regardless of the symptom status of the COVID-19-associated illness. We have achieved similar results in our study – after being vaccinated with two doses of the BNT162b2 mRNA vaccine, none of the HCWs who contracted COVID-19 required either hospitalization or medical care.

In an Israeli study of HCWs, vaccination with two doses of the BNT162b2 mRNA vaccine was associated with significantly lower incidence rates for both symptomatic and asymptomatic SARS-CoV-2 infections, and the vaccine effectiveness was estimated to be 97 %.[19] PLWH may have an incomplete immune response to vaccinations; however, suppression of HIV viremia and recovery of the immune system are protective factors against future infections and serious clinical forms of the disease.[20–23] On the other hand, advanced HIV disease, which results in a depletion in the number of CD4$^+$ T-cells and ongoing inflammatory processes connected with HIV viremia, is a risk factor for SARS-CoV-2 infection and a severe course of the disease, despite vaccination.[24,25] Moreover, due to effective combination antiretroviral therapy (cART), we are observing aging of this population, which is a very positive aspect, but older people are at higher risk of chronic diseases. What is more, older individuals with co-morbidities, such as chronic kidney disease, hematological malignancies, or solid tumors, are at higher risk of severe COVID-19 disease and mortality compared to the general population. These patients are less likely to develop a full immune response after vaccination because of their immunocompromised status, which is due to the nature of the particular diseases and immunosuppressive treatment, among others.[26–29] Originally, cocooning was used to protect infants against the serious complications that may have arisen from infection with *Bordetella pertussis*.[30–33] Beneficial results of cocooning have also been observed with rotavirus, pneumococcal, and influenza vaccinations.[34–36]

There are some limitations that should be mentioned regarding our study. First of all, compared to other studies, the cohort of HCWs in the infectious disease center in Warsaw was not very large. However, it was a selected group of HCWs who were taking care of both COVID-19 and PLWH patients. Second, our study was conducted among a generally healthy and relatively young group of people, which may have contributed to optimal immune responses. We also did not analyze PLWH data, and only indirect methods were able to show how important vaccination was among HCWs who were in close contact with them. Further studies are needed to evaluate the beneficial effects of the cocoon strategy as applied to PLWH in regard to COVID-19 vaccination over the long-term.

Despite these limitations and when considering the above information and reports from the literature, it should be assumed that if PLWH have incomplete immune responses to COVID-19 vaccination and at risk of a severe course of the disease, the cocoon strategy for vaccinating medical personnel may be beneficial for these patients.

6. Conclusions

The results of our study indicate a favorable humoral response to vaccination among HCWs working with both PLWH and COVID-19 patients in an infectious disease center. Further studies are needed to evaluate this effect over the long-term.

CRediT authorship contribution statement

Agata Skrzat-Klapaczyńska: Writing – original draft, Methodology, Formal analysis, Conceptualization. **Justyna Kowalska:** Writing – review & editing, Supervision, Formal analysis, Conceptualization. **Filip Fijołek:** Writing – original draft, Data curation. **Marcin Paciorek:** Methodology, Investigation. **Carlo Bieńkowski:** Investigation, Formal analysis. **Dominika Krogulec:** Visualization, Investigation. **Andrzej Horban:** Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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