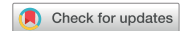


BRIEF REPORT



Transmission of SARS-CoV-2 variant B.1.1.7 among vaccinated health care workers

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ABSTRACT

Background: Vaccination against COVID-19 is among the most effective measures to stop the spread of the disease. However, acceptance of vaccination against COVID-19 among HCWs has not been universal and emergence of new variants with increased transmissibility, reduced neutralization by BNT162b2 vaccine-elicited sera and ability to cause breakthrough infections in vaccinated individuals is concerning. The aim of this study was to compare viral load, clinical presentation at diagnosis and type of exposure among vaccinated (with BNT162b2) and non-vaccinated healthcare workers (HCWs).

Methods: Prospective cohort of HWCs diagnosed with COVID-19 by nasopharyngeal PCR from 4 January to 14 April. Viral loads were expressed by the cycle threshold (Ct) in PCR.

Results: During the study period 55 HCWs were found positive for SARS-CoV-2, most of whom (44/55) were identified from March 28 to April 14 during an in-hospital COVID-19 outbreak. Of the 55 HCWs, 21 were fully vaccinated and another three had received one dose. Most cases (54/55) were due to variant B.1.1.7. Vaccinated and unvaccinated HCWs did not differ significantly in regards to age, gender, site of acquisition, presence of symptoms at diagnosis and viral load.

Conclusions: This study found a similar viral load in vaccinated and non-vaccinated HCWs infected by SARS-CoV-2 variant B.1.1.7, suggesting potentially reduced efficacy of BNT162b2 in preventing transmission of B.1.1.7.



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Introduction

Since the beginning of the COVID-19 pandemic, exposure of healthcare workers (HCWs) to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has been an important concern [1]. In particular, asymptomatic carriage of SARS-CoV-2 may lead to the horizontal spread of the virus among HCWs, with a risk for hospital outbreaks [2]. Vaccination against COVID-19 has been regarded as the most effective measure to stop the spread of the virus, along with the protective measures applied by each individual [3]. However, acceptance of vaccination against COVID-19 among HCWs has not been universal [4,5] and the emergence of new variants with increased transmissibility, reduced neutralization by BNT162b2 vaccine-elicited sera and ability to cause breakthrough infections in vaccinated individuals are of particular concern [6].

On the other hand, the emergence of newer variants of SARS-CoV-2, such as the variant B.1.1.7, have raised concerns as there is evidence for higher viral RNA loads in nasopharyngeal swabs and longer persistence among infected individuals, even though the evidence so far suggests that vaccination with BNT162b2 may effectively prevent the rise of variant B.1.1.7 in high-risk populations [7–9].

The aim of this study was to compare viral load, clinical presentation at diagnosis and type of exposure among vaccinated (with BNT162b2) and non-vaccinated healthcare workers (HCWs).

Methods

Study design

In our hospital, more than 80% of HCWs (1800/2,250) have been vaccinated against COVID-19 with the BNT162b2 mRNA vaccine from January 4 to April 14. Within the same time period, all confirmed (by nasopharyngeal PCR) COVID-19 cases were recorded. Recorded PCR tests were taken in the context of outbreak surveillance screening or due to the development of associated symptoms. RNA was extracted from the nasopharyngeal swabs using the KingFisher™ Flex Purification System, KingFisher (ThermoFisher, Waltham, MA, USA) according to the manufacturer's instructions. Detection of SARS-CoV-2 in nasopharyngeal samples was carried out using the TaqPath COVID-19 assay (ThermoFisher, Waltham, MA, USA). This diagnostic Real-Time PCR assay specifically targets N, ORF1ab and S genes and in the case of the SARS-CoV-2 B.1.1.7 variant,

a failure in amplification of the S gene is observed, resulting in the so-called 'S gene drop out' effect. The QuantStudio5 Real-Time PCR System was used for the detection of SARS-CoV-2 genomes in the specimens.

For each case, the following data were recorded; age, gender, the probable site of exposure (acquisition by in-hospital exposure versus by household contact), the viral load as expressed by the PCR cycle threshold (Ct), the infecting strain, the presence and type of symptoms at diagnosis, and need for hospitalization until May 12. Conduction of this study was approved by the Ethics Committee of the University Hospital of Heraklion.

Statistical analysis

Data are presented as numbers (%) for categorical variables and median (interquartile range, IQR) or mean (\pm standard deviation, SD) for continuous variables. The above-mentioned statistics were calculated with GraphPad Prism 6.0 (GraphPad Software, Inc., San Diego, CA).

Results

During the study period, 55 HCWs were found positive for SARS-CoV-2 with a nasopharyngeal RT-PCR test. Most cases (44/55) were identified from 28 March to 14 April during an in-hospital COVID-19 outbreak. Notably, strict epidemiological protocols have been implemented, including universal masking, indicating the possible transmissibility of new SARS-CoV-2 variants. Demographics, site of acquisition, viral load (expressed by PCR Ct values), SARS-CoV-2 strain, symptoms and need for hospitalization among affected HCWs are summarised in [Table 1](#).

Among all 55 PCR-positive HCWs, 24 (44%) had received at least one dose of the BNT162b2 vaccine, and 21 were fully vaccinated (diagnosed with COVID-19 > 2 weeks after the second dose). The three individuals that had one dose, had received that 11, 20 and 22 days before the positive PCR result. In 23 of 24 positive HCW, PCR showed the SARS-CoV-2 B.1.1.7 variant, in one single subject the B.1.177 variant. Up till May 12, only 2 HCWs required hospitalization, both of which were not vaccinated. Vaccinated (with at least one dose) HCWs did not differ significantly compared to non-vaccinated HCWs in regard to age, gender and epidemiological exposures.

Interestingly, the viral load expressed by the Ct values did not differ significantly between vaccinated and

Table 1. Comparison of characteristics between vaccinated and unvaccinated healthcare workers with COVID-19.

	All HCWs (n = 55)	Non-vaccinated (n = 31)	Vaccinated (n = 24) ^a	p
Age (years), mean (SD)	42.3 (9.9)	43.1 (9.8)	41.3 (10.1)	.5269
Male gender, n (%)	14 (25.5)	6 (19.4)	8 (33.3)	.3502
Likely hospital acquisition, n (%) ^b	31 (79.5)	17 (77.3)	14 (82.4)	1
Acquisition by household contact, n (%)	8 (20.5)	5 (22.7)	3 (17.6)	1
Day of diagnosis post exposure, median (IQR)	5 (4.8–7)	5.5 (5–7)	4.5 (4–5)	.2796
Day of positive PCR from symptom start, median (IQR)	1 (0–2)	2 (1–2.8)	1 (0–1.3)	.0926
Ct values, median (IQR)	18.5 (15–25.3)	18.5 (13.5–24)	18.5 (16–26) ^c	.6957
Strain B.1.1.7	54 (98.2) ^d	30 (96.8)	24 (100)	1
Hospital admission ^e	2 (3.6%)	2 (6.5%)	0 (0%)	.4990
Any symptom	42 (76%)	23 (75%)	19 (79%)	.7561
Cough, n (%)	16 (29.1)	12 (38.7)	4 (16.7)	.1332
Nasal congestion, n (%)	15 (27.3)	2 (6.5)	13 (54.2)	.0001
Rhinorrhea, n (%)	7 (12.7)	1 (3.2)	6 (25)	.0352
Sore throat, n (%)	16 (29.1)	9 (29)	7 (29.2)	1
Fever or low-grade fever, n (%)	9 (16.4)	7 (22.6)	2 (8.3)	.2713
Anosmia/ ageusia, n (%)	1 (1.8)	0 (0)	1 (4.2)	.4364

Ct: cycle threshold; HCWs: healthcare workers; IQR: interquartile range; SD: standard deviation.

^an = 3 partially vaccinated (1 dose, 10, 20 and 22 days before the positive PCR), n = 14 completely vaccinated (2 doses and at least 2 weeks from last vaccination).

^bMost (44/45) identified from 28 March to 14 April 2021 during an in-hospital outbreak. ^cExcluding the 3 partially vaccinated cases, the median Ct value was 18 (IQR = 15.5–25.5). No difference in the statistical significance of these results occurred when these 3 partially vaccinated cases were excluded, with the exception of cough. ^dThere was one non-vaccinated patient infected with the strain B.1.177. ^eUntil May 12.

non-vaccinated HCWs, even though the time from symptom onset to positive PCR in vaccinated (with at least one dose) and unvaccinated symptomatic HCWs did not differ significantly. Furthermore, symptomatic infection was equally common in both vaccinated and non-vaccinated patients. However, the type of symptoms differed significantly. Specifically, rhinorrhea and nasal congestion were significantly more frequent in vaccinated HCWs, while cough and fever were more common albeit not significantly in non-vaccinated subjects. Of note, when the three partially vaccinated cases were excluded from the analysis, no significant difference in these results occurred, with the exception of cough, which was less frequent in the vaccinated HCWs than in the non-vaccinated ones, in a statistically significant way.

Discussion

An important question about the efficacy of SARS-CoV-2 vaccines is their ability to reduce viral transmission. In particular, all available vaccines bypass the natural route of infection, which might compromise optimal induction of mucosal immunity in the upper respiratory tract. Data from Israel show a high efficacy (90%) of BNT162b2 for preventing asymptomatic infection [10], suggesting the vaccine's potential for halting the spread of SARS-CoV-2. Furthermore, two studies (one from Tel Aviv and one from Pittsburgh) reported substantially lower viral load in BNT162b2-vaccinated compared to non-vaccinated patients [11,12]. These findings have important implications on epidemiological measures, given that viral load is a major determinant of transmissibility [13]. Accordingly, recent interim CDC recommendations

obviate the need for quarantine of fully vaccinated people following exposure to SARS-CoV-2 [14].

In contrast to the above studies, our study showed comparable viral loads among vaccinated vs. non-vaccinated HCWs infected by variant B.1.1.7, suggesting sub-optimal protection of SARS-CoV-2 vaccines against new variants as compared to wild-type SARS-CoV-2. Furthermore, a recent report from Tel Aviv raises concern about breakthrough SARS-CoV-2 infection by variants of concern (including B.1.1.7 and B.1.351) among BNT162b2-vaccinated individuals. A statistically significant higher risk of breakthrough infections by B.1.1.7 was found only in partially vaccinated but not fully vaccinated individuals. Of note, a direct comparison of viral loads in vaccinated vs non-vaccinated individuals was not reported. Interestingly, a very recent review concluded that after vaccination with the mRNA-1273 and BNT162b2 vaccines, their neutralization activity decreased slightly against SARS-CoV-2 variants carrying the E484K (like variant B.1.1.7) or N501Y or the K417N-E484K-N501Y combination of mutations (like variant B.1.1351) [15].

One limitation of the present study is the small number of HCWs included and another is a failure to identify sources of transmission. Furthermore, other conditions, such as diabetes or other underlying conditions were not taken into account. Finally, HCWs vaccinated with BNT162b2 were not stratified based on the duration of vaccination.

To conclude, our findings add to the accumulating evidence regarding a potentially lower efficacy of BNT162b2 against variant B.1.1.7 and raises concerns about limited protection offered by available vaccines

on COVID-19 transmission. This highlights the need for continuing protective measures to prevent the spread of SARS-CoV-2 infection and the need for more clinical data regarding vaccines' efficacy against new variants. Furthermore, our study highlights the high frequency of mild symptoms in vaccinated patients, specifically nasal congestion and rhinorrhea in the absence of fever or cough, suggesting that a high index of suspicion is required not to miss the diagnosis in vaccinated HCWs. Finally, recommendations on epidemiological exposures of vaccinated HCWs should take into consideration the results of our studies.

Author contributions

DPK contributed to the conceptualization, investigation, methodology, project administration, supervision and writing of the original draft. PI, SK, EA, MS and EV, contributed to data curation, formal analysis, investigation, methodology, software, validation and writing of the original draft. GC contributed to validation and writing, review and editing of the manuscript. GS contributed to the investigation, software, validation and writing, review and editing of the manuscript.

Disclosure statement

DPK reports lecture honoraria from Pfizer, MSD, ViiV and Angelini. The rest of the authors have no conflict of interest.

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