

VACCINE BREAKTHROUGH CASES AMONG HOSPITALISED PATIENTS IN THE INTENSIVE CARE UNIT FOR COVID-19 IN NORTH-EASTERN BULGARIA

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ABSTRACT

Background: COVID-19, caused by SARS-CoV-2, continues to spread globally, with vaccines being the most effective way to control the pandemic. Studies show a significant reduction in infection, hospitalisations, severe disease, and death after vaccination.

The aim of the study was to determine the share of breakthrough infections among critically ill patients with severe COVID-19 who had been admitted to the intensive care unit (ICU) of a hospital at the beginning of the delta-variant pick.

Material and methods: For a period of 10 months a total of 740 patients diagnosed with COVID-19, were treated in the intensive care unit of the University Hospital "St. Marina-Varna", with persons. Information on the vaccination status of all 740 hospitalised patients was extracted from the National information system "Register of immunized persons against COVID-19", including the type and date of COVID-19 vaccine administration, where available. After that, descriptive statistics were performed with the collected data.

Results: Out of 740 patients, 19 (2.6%) had received at least 1 dose of vaccine, and 721 (97.4%) - none. Only ten (1.35%) of the studied severely and critically ill patients had completed the vaccination cycle (without a booster dose).

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Conclusion: Our findings show that when fully administered, vaccines are highly effective against laboratory-confirmed SARS-CoV-2 infection leading to ICU admission. Our findings reinforce the value of widespread COVID-19 vaccination, underscore the importance of completing the vaccination cycle for either of the mRNA-based vaccines, and may help motivate persons who remain hesitant about being vaccinated.

Keywords:

vaccination, hospitalisation, COVID-19, Bulgaria, intensive care unit

INTRODUCTION

The coronavirus disease 2019 (COVID-19), caused by *Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)*, has spread around the world in successive waves, continuing to nowadays.. The rapid and successful development of COVID-19 vaccines was a significant hallmark of this pandemic (1, 2). Vaccination is the most effective way to control a pathogen with pandemic potential; however, vaccination rates are still below the target level in most countries (3). The anti-vaxxer movement and vaccine hesitancy are serious public health issues.

Due to the new technology and the quick development of the vaccine, the COVID-19 vaccination has given rise to some widespread myths, associated with concerns and doubts about the safety and efficacy of the new products.

These tendencies also applied to Bulgaria. Concerns regarding the efficacy and safety of COVID-19 vaccines have been stoked by rumours, false information, and conspiracy theories, which have put into question the necessity of immunisation. As a result, Bulgaria ranks at the bottom line among all EU nations regarding the proportion of individuals immunised against COVID-19, (4).

The Bulgarian Ministry of Health initiated a COVID-19 vaccination campaign on December 27, 2020, among the group of medical staff, and later nationwide. By October 2021, 2.86 million Bulgarians had received either BNT162b2 (Comirnaty; Pfizer-BioNTech), ChAdOx1 nCoV-19 (Vaxzevria; Oxford-AstraZeneca), mRNA-1273 (Spikevax, previously COVID-19 Vaccine Moderna), or Ad26.COV2 (Janssen [Johnson & Johnson]) (5).

A UK community-based study including users of the COVID Symptom Study app showed a significant reduction in post-vaccination infections, starting from day 12 after the first dose (6). These findings were recapitulated in a UK-based, real-world, case-control study (7). National surveillance data from the first four months of Israel’s vaccination campaign showed that two doses of BNT162b2 reduced both symptomatic and asymptomatic infections, COVID-19-related hospitalisations, severe disease, and death (8).

A vaccine breakthrough case was defined as a cluster-associated case in a person who completed all recommended doses of a US Food and Drug Administration-authorized COVID-19 vaccine (2 doses of Pfizer/BioNTech [<https://www.pfizer.com>] or Moderna [<https://www.modernatx.com>], or one dose of Johnson & Johnson [<https://www.jandj.com>]) >14 days before collection of a SARS-CoV-2–positive specimen (9). During ten months, with the domination of the delta variant of the virus, this study aimed to identify all vaccine breakthrough cases among hospitalised patients in the intensive care unit (ICU) for COVID-19 in north-eastern Bulgaria.

MATERIAL AND METHODS

For ten months (from January 1 to October 31, 2021) the number of patients with COVID-19 diagnoses treated in the ICU of the University Hospital (UH) St. Marina-Varna, was 740. This University Hospital serves the entire region of North-Eastern Bulgaria and, was among the first hospitals at the national level treating COVID-19 cases.

The Informatics Department of Bulgarian Ministry of Health provided datasets for the COVID-19 vaccination campaign. Information on the vaccination status of all 740 hospitalised patients was checked and extracted from the National Information System Register of Immunised Persons against COVID-19, including the type and date of COVID-19 vaccine administration. Descriptive statistical analysis was performed with IBM SPSS v.25.

According to the Interactive Manual for COVID-19 Treatment issued by the Ministry of Health, admission to the ICU is recommended for severely and critically ill patients subjected to clinical procedures III and IV (including non-invasive or invasive ventilation). From the patients with proven COVID-19 infection hospitalised at University Hospital “St. Marina – Varna”, we chose those who underwent treatment according to the clinical procedures III and IV (10).

RESULTS

For a period of 10 months (from January 1, 2021, to October 30, 2021) a total of 740 patients with COVID-19 diagnoses were treated in the intensive care unit of the University Hospital St. Marina-Varna, who are (with a severe and critical course, non-invasive or invasive ventilation, in need of intensive care, clinical procedure 3 or 4). Of these, 19 (2.6%) were already vaccinated, and 721 (97.4%) were not. Thus, only ten (or 1.35%) of the severely and critically ill patients, during this period had a completed vaccination cycle (without a booster dose (Table 1).

There were no statistically significant differences between the mean age of unvaccinated (64.92 ± 13.8 years) and fully vaccinated (64.4 ± 12.4 years) critically

Table 1. Vaccination status, sex and age group

Variables	Unvaccinated (N=721)	Fully vaccinated (N=10)
Age	64.92 +/- 13.8 (2-94)	64.4 +/- 12.4 (41-76)
Age category – no. (%)		
<18 years	8 (1.1%)	-
18-49 years	95 (13.2%)	2 (20%)
50-65 years	207 (28.7%)	2 (20%)
>65 years	411 (57%)	6 (60%)
Sex		
Male sex – no./ (%)	428 (59.4%)	6 (60%)
Female sex – no./ (%)	293 (40.6%)	4 (40%)

Table 2. Vaccination status and type of vaccines

Immunized SARS-CoV-2 vaccination status – no. (%)¶	
Unvaccinated	721 (97.4%)
First vaccine dose within 0–13 days (Before the immune response.)	6 (0.8%)
Partially vaccinated - one dose (excl.Jansen)	9 (1.2%)
Fully vaccinated	10 (1.4%)
Among fully vaccinated patients, vaccine product received – no. (%)	
Moderna two doses	1 (10%)
Pfizer-BioNTech two doses	3 (30%)
Astra Zeneca two doses	1 (10%)
Jansen [Johnson & Johnson]	5 (50%)
Among fully vaccinated patients, days between second vaccine dose and hospital admission – median (IQR)	77.5 (14-218)
Among non fully vaccinated patients, days between first vaccine dose and hospital admission – median (IQR)	14 (14-150)

ill patients (T-test 0.372, $p > 0.05$). In addition, there were no differences between the distribution by age groups of those vaccinated and unvaccinated (Pearson $\chi^2 = 3,979$, $p > 0.05$).

The sex distribution in the vaccinated and unvaccinated groups was not significantly different, either (Pearson $\chi^2 = 0.198$, $p > 0.05$).

Among the severely ill vaccinated patients, 9 or 47.4% had an incomplete vaccination status, i.e., with only the first vaccine dose: seven individuals with Comirnaty (BioNTech/Pfizer), and two - with ChAdOx1 nCoV-19 (Oxford-AstraZeneca), (Table 2).

In 6 cases (31.6%) of severely ill vaccinated patients, clinical procedure III or IV was required within 14 days of their first dose (10 severe cases of COVID-19 infection within one month of the first dose).

Of the ten persons who had breakthrough infections, 3 (30%) received the Pfizer/BioNTech vaccine, 1 (10%) received the Moderna vaccine, 1 (10%) received the ChAdOx1-S vaccine, and 5 (50%) received the Johnson & Johnson vaccine.

Ten COVID-19 case patients met our definition of fully vaccinated before symptom onset. Among these, the median age was 66.5 years (41–76 years), and the median time between the final vaccine dose and symptom onset was 77.5 days (14–218 days). These breakthrough cases included five patients vaccinated with the Johnson & Johnson product,

three patients vaccinated with the Pfizer-BioNTech product, one patient vaccinated with the Moderna product, and one patient vaccinated with the Astra Zeneca product.

DISCUSSION:

Our analysis, similar to those already published, found that frailty was associated with post-vaccination infection in older adults (≥ 65 years) after their first vaccine dose before Vaccination completion (11-14). The median time from vaccination completion to intensive care treatment with SARS-CoV-2-positive specimen collection was similar to other publications (9, 11, 15).

Our results are relevant for post-vaccination health policies and highlight the need to balance personal protective measures for those at risk of post-vaccination infection with the adverse effects of ongoing social restrictions. Strategies, such as prioritising booster vaccinations and optimised infection control measures, could be considered for at-risk groups.

Following two vaccination doses, only slight variations in vaccine efficacy were seen between the delta and alpha variants. After the initial dosage, there were more noticeable absolute variations in the efficiency of the vaccination. This discovery might bolster initiatives to optimise vaccination uptake in susceptible groups by administering two doses (7).

This study demonstrates that the SARS-CoV-2 may spread promptly in a population with several vaccinations and can infect individuals irrespective of their vaccination status during the peak of an epidemic wave. Vaccination is still a vital method to reduce COVID-19-related disease and mortality (16, 17). Data shows that Delta version of SARS-CoV-2 is highly contagious (18). Some investigations have demonstrated that vaccine effectiveness was lower during delta variant predominance than against earlier variants due to a longer time after immunisation and a waning immunity (14, 19, 20). The vaccination status was assigned through matching with an immunisation information system; persons who did not have vaccination data were assigned to the unvaccinated group, which could lead to misclassification bias.

This observational study was the first to examine the breakthrough cases among hospitalized patients with severe SARS-CoV-2 infection after the first and second doses of COVID-19 vaccination in Bulgaria. Vaccination was definitely associated with reduced odds of ICU hospitalization after the first or second dose as compared with no immunization.

Overall, regarding real-life observational data, full immunization with mRNA vaccines or viral vector vaccine (AZD1222) effectively prevents SARS-CoV-2 infection against the original strain and Alpha and Beta variants but has reduced effectiveness against the Delta strain (21-23).

CONCLUSIONS

In conclusion, major epidemiologic questions about breakthrough infections, such as the comparative infectiousness of fully vaccinated and non-fully vaccinated persons, viral shedding duration, and vaccine-derived immunity, remain. However, our findings underscore the need for fully vaccinated persons to take precautions to prevent transmission of SARS-CoV-2 to themselves and others, such as wearing a mask in public indoor settings or crowded outdoor environments, particularly during substantial or high transmission. Although critical to reducing illness and death from COVID-19, vaccination should be complemented by layered mitigation strategies to address the COVID-19 pandemic (24).

These findings reaffirm the high protective effect

of COVID-19 vaccines against severe COVID-19, associated with emergency department and urgent care visits, and underscore the importance of full COVID-19 vaccination (15, 25).

The classical epidemiology of communicable diseases has long shown that immunisation is only part of a set of control measures to interrupt the epidemic process, and every infectious disease requires an integrated approach.

Our analysis of ten month medical visits showed that completed vaccinations are highly effective against laboratory-confirmed SARS-CoV-2 infection leading to ICU admission. These findings reinforce the value of widespread COVID-19 vaccination, underscore the importance of completing vaccination for both vector vaccines and mRNA-based vaccines, and may help motivate people who remain hesitant about being vaccinated.

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