

VACCINATION COVERAGE AGAINST COVID-19 AMONG PEOPLE LIVING WITH HIV INFECTION IN THE CZECH REPUBLIC

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SUMMARY

Objectives: The pandemic of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has affected hundreds of millions of individuals globally. Vaccination has become a promptly effective preventive procedure. People living with HIV (PLHIV) are in increased risk of many infections including COVID-19. We aimed to analyse the first phase of vaccination (January 2021–June 2022) in the Czech Republic in PLHIV focusing on vaccination coverage, vaccine hesitancy and breakthrough infections.

Methods: In this single-centre, open-label, prospective study we have enrolled 1,758 PLHIV with median age of 42.5 years and median CD4+ T cells count (cluster of differentiation) 800/μL.

Results: Vaccination coverage was 84.7% and first booster dose was received by 71.7% of those who completed vaccination. Only 78 individuals (4.4%) have actively rejected vaccination. The most frequent vaccination scheme (60.3%) was Comirnaty vaccine plus booster of the same vaccine. There was a significant difference between vaccinated and unvaccinated individuals in age, CD4+ count, CD4/CD8 ratio, virological suppression on antiretroviral therapy (ART) duration of HIV and level of education ($p < 0.001$). Prevalence of breakthrough infection was seen in 21.4%. There was no significant difference among individual vaccines ($p = 0.715$). Individuals with breakthrough infections were statistically younger ($p = 0.001$) with some risk factors in 25.1%.

Conclusion: In this prospective study we have seen higher vaccination coverage against COVID-19 in PLHIV in the Czech Republic in comparison with the general Czech population. Hesitancy, resulting in rejection of vaccination, was lower in our cohort as regards affinity to the HIV clinic, and breakthrough infections were noticed and occurred particularly in younger age groups.

Key words: HIV, COVID-19, vaccination, hesitancy, breakthrough infections

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INTRODUCTION

The outbreak of the COVID-19 pandemic caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in late 2019 has posed a severe threat to global public health. By 4 May 2025, there was more than 777 million confirmed cases of COVID-19 with more than 7 million deaths, as reported by the World Health Organization (WHO) (1). In the Czech Republic, more than 4.8 million cases were detected resulting in over 43 thousand deaths over the same period (2). The overall mortality of COVID-19 is 1.0%, but individuals with various comorbidities or impaired immunity including people living with HIV (PLHIV) are at higher risk of both severe course and mortality from this infection (3–11).

One of the most effective tools for control of infectious diseases and for protection of public health is vaccination. Since the beginning of the pandemic, intensive efforts have been made to develop an effective vaccine against COVID-19, and the first

vaccines against the disease were approved for practical use in late 2020 (12–17).

In the Czech Republic, the vaccination campaign officially started on 1 January 2021, and the vaccination was carried out in specialised vaccination centres. Specific population groups (healthcare workers, hospitalised people > 65 years of age or persons with defined risk factors such as chronic obstructive pulmonary disease, arterial hypertension, obesity with BMI > 35 kg/m², cardiovascular disease, and haemato-oncological disease) were vaccinated initially. From 1 March 2021 the campaign was extended for all individuals aged > 65 and patients with risk factors including all HIV patients regardless of their CD4+ count. From 4 June 2021, this was extended to the whole population > 16 years of age. All information on the type of the vaccine and date of administration, as well as all results of tests for SARS-CoV-2 infection (PCR, detection of antigen or antibody), are collected centrally by the Institute of Health Information and Statistics of the Czech Republic (IHIS).

Because vaccination against COVID-19 plays a crucial role in the protection of PLHIV against this infection and there is still a lack of data regarding this high-risk population group, we conducted a study that would analyse the approach to vaccination against COVID-19 and the vaccination coverage and efficacy among PLHIV in the Czech Republic (18–22).

MATERIALS AND METHODS

The study was conducted at the HIV centre of the University Hospital Bulovka, Prague, as an open-label, observational, prospective study between 1 January 2021 and 30 June 2022. The basic enrolment criteria were known HIV infection and age > 18 years.

The following data were collected from all participants: age, sex, degree of education, date of HIV diagnosis, and initiation of antiretroviral therapy (ART). Also, the following laboratory markers were collected: immune system markers – absolute number of CD4⁺ T cells per μ L (T-lymphocytes responsible for the proper function of the human immune system due to stimulation of other immune cells) and CD8⁺ T cells per μ L (responsible for recognising and destroying infected cells) at the initiation of vaccination, nadir CD4⁺ count (person's lowest-ever CD4⁺ count), CD4/CD8 ratio (indicator of the immunological status and disease progression), and viral load of HIV RNA copies/mL (number of viral particles in blood). We collected the date of the first dose of COVID-19 vaccine.

From persons with breakthrough infection (PCR or antigen positivity for SARS-CoV-2 infection following ≥ 14 days after all administered doses of COVID-19 vaccine) we collected information about factors associated with higher risk of severe course of COVID-19: smoking status, obesity, diabetes mellitus, chronic pulmonary and cardiovascular diseases.

Subsequent COVID-19 vaccines were available in the Czech Republic within the study period: Comirnaty (Pfizer/BioNTech), Spikevax (Moderna/NIAID), Vaxzevria (Oxford/Astra-Zeneca) with a recommended scheme of two doses plus booster dose and Janssen COVID-19 (J&J, Janssen) vaccine with single recommended dose plus booster; in some cases a different vaccine as a booster was used than in the basic scheme, as later remarked in our study. Clinical data were obtained from our medical documentation.

All the COVID-19 data including the time of vaccination, type of vaccine used and the results of all tests for the detection of SARS-CoV-2 infection were taken from the central national electronic system, the IHIS database. This enabled collection of data from all the patients registered in our HIV centre who were vaccinated at other facilities.

All the participants who rejected the vaccination were asked in person or over the phone if they would consider vaccination in the future or refuse it, and the reasons of their decision.

The research project was approved by the Ethics Committee of University Hospital Bulovka (01/2021/10580/EK-Z) and all enrolled individuals signed informed consent.

Statistical Analyses

Continuous data are presented as medians with 25th and 75th percentiles and ranges characterising their variability. Two-sample

Mann-Whitney test was used to evaluate the differences between groups. Categorical data are displayed as absolute frequencies and percentages. Differences in proportions between groups were analysed using Fisher's exact test.

The cumulative probability of completing the basic vaccination scheme was estimated using Kaplan-Meier curves. Unvaccinated participants were censored at the end of the study. Vaccination coverage in the Czech general population was obtained from age-specific data processed by IHIS (23). The group of PLHIV was compared with an eligible general population aged 16 years and over. Overall data on the Czech population were obtained from sources published by the Czech Statistical Office (24). Differences in Kaplan-Meier curves between subgroups were tested with the two-sample log-rank test. Comparison with the population curve was based on the one-sample log-rank test.

All statistical tests were carried out at the significance level of 0.05. Statistical software Stata, release 17 (StataCorp LLC, College Station, TX, USA) was used for data manipulation.

RESULTS

The study included 1,758 participants, who constituted 80.3% of all HIV-infected individuals registered at our centre at the start of the study period. The study cohort consisted of 1,564 (89.0%) male patients and of 194 (11%) female patients (Table 1). As shown in Table 2, median age at the time of the initiation of the vaccination was 42.5 years (range 18–82), median CD4⁺ count was 800/ μ L (range 0–2,880), median CD8⁺ count was 944/ μ L (range 707–1,291). Median nadir of CD4⁺ count was 359/ μ L (range 0–1,622). At baseline, 1,455 (82.8%) individuals were virologically suppressed on ART (HIV RNA < 20 copies/mL); 303 enrollees (17.2%) were not on ART or were on therapy with HIV RNA ≥ 20 copies/mL (Table 1).

Of the study participants, 1,489 completed the primary vaccination scheme (consisting of one or two doses as recommended by the manufacturer) and overall vaccination prevalence in the cohort was 84.7%. The most prevalent scenario of vaccination consisted of two doses of Comirnaty plus booster dose of the same vaccine (907 patients, 60.3%). The most frequent primary

Table 1. Cohort characteristics, categorical variables (N = 1,758)

Characteristics	n	%
Sex		
Females	194	11.0
Males	1,564	89.0
Viral load		
HIV RNA < 20 copies/mL	1,455	82.8
HIV RNA ≥ 20 copies/mL	303	17.2
Vaccination scheme		
Completed basic scheme	1,489	84.7
Incomplete scheme	14	0.8
Completed scheme + booster	1,078	61.3
Rejecting vaccination	78	4.4
Unvaccinated	255	14.5

vaccination scheme was two doses of Comirnaty (1,337 patients), then two doses of Spikevax (58 patients), one dose of Jansen (57 patients), and two doses of Vaxzevria (26 patients). Use of different vaccines within our study group is consistent with general population in the Czech Republic, based mostly on its availability. Comirnaty vaccines were used in 85% as the first two doses in the general population (24). Even the appreciably higher proportion (93%) of Comirnaty vaccine in our cohort can reflect preferences of mRNA vaccines in PLHIV based on vaccination guidelines in 2021. As a booster dose, there were only three vaccines recommended: Comirnaty, Spikevax, and Vaxzevria. The booster dose was received by 1,078 enrollees, i.e., 72.4% of all patients who completed primary vaccination scheme (Table 1, Fig. 1).

Only 255 (14.5%) individuals remained completely unvaccinated. A total of 78 (4.4%) individuals were identified as actively rejecting vaccination, the reasons for not being vaccinated of the rest of the patients remain unknown.

Between subgroups of vaccinated and unvaccinated persons there is a statistically significant difference in all analysed parameters: median age was 42.9 and 40.0 ($p < 0.001$), median CD4+ count was 813/ μ L and 681/ μ L ($p < 0.001$), median CD4/CD8 ratio was 0.86 and 0.75 ($p = 0.069$), and HIV RNA < 20 copies/mL was seen in 84.9% and 70.2% ($p < 0.001$), respectively. Vaccinated individuals, compared to unvaccinated individuals, have been diagnosed as HIV infected for a longer period of time: 8.4 and 6.4 years ($p < 0.001$), and are more likely to have a university education: 30.4% and 16.7% ($p < 0.001$), respectively (Table 3). Details of evolution of vaccination coverage are described in Figure 2.

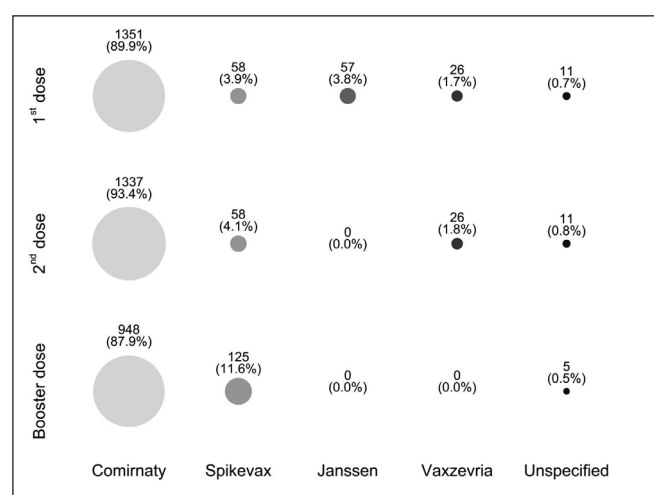


Fig. 1. Share of vaccines in individual vaccination phases.

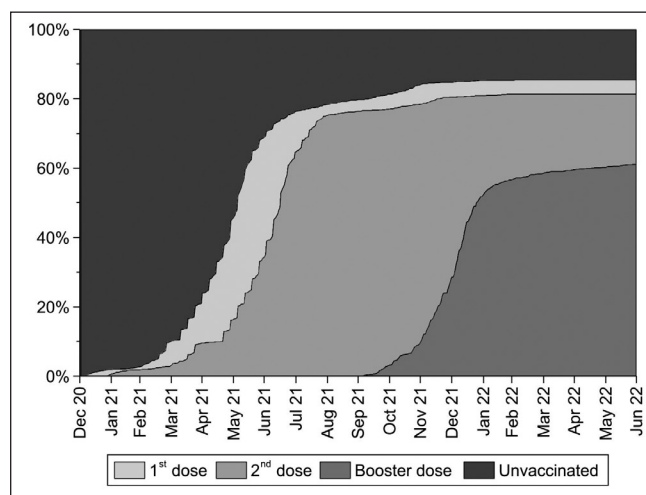


Fig. 2. Trends in vaccination coverage of people living with HIV over time.

From the fourth month of the vaccination campaign a faster increase in vaccination coverage was observed in people with HIV aged over 40 years, than in younger individuals. A sharp increase in vaccination coverage among younger individuals occurred approximately 1.5 months later than in older individuals, and 50% vaccination coverage among individuals under 40 years of age was recorded 29 days after the same criterion was reached in individuals aged 40 years and older. Vaccination coverage achieved at the end of the study was about 6 percentage points

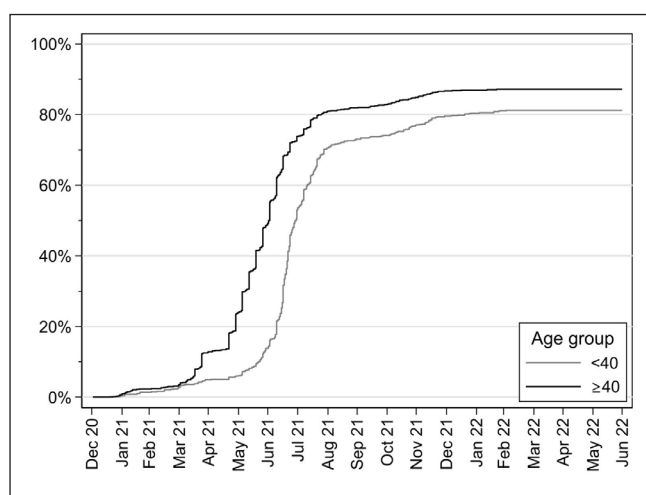


Fig. 3. Time course of vaccination coverage among people living with HIV by age groups.

Table 2. Cohort characteristics, numerical variables (N=1,758)

Characteristics	Median	25th–75th percentile	Range
Age	42.5	35.4–49.2	7.0–82.3
CD4+ count (cells/ μ L)	800	590–1,042	0–2,880
CD4+ nadir (cells/ μ L)	359	200–525	0–1,622
CD8+ count (cells/ μ L)	944	707–1,291	88–6,112
CD4/CD8 ratio	0.85	0.58–1.19	0.00–4.24

Table 3. Analysed parameters in cohort of vaccinated and unvaccinated people living with HIV

Characteristics	Vaccinated (n = 1,503)	Unvaccinated (n = 255)	p-value
Females, n (%)	132 (8.8)	62 (24.3)	< 0.001
Age, median (25th–75th percentile)	42.9 (35.9–49.6)	40.0 (33.7–47.5)	< 0.001
CD4+ count, median (25th–75th percentile)	813 (612–1,056)	681 (457–916)	< 0.001
CD4+ nadir, median (25th–75th percentile)	362 (209–526)	310 (163–520)	0.069
CD8+ count, median (25th–75th percentile)	955 (713–1,292)	866 (665–1,278)	0.057
CD4/CD8 ratio, median (25th–75th percentile)	0.86 (0.59–1.20)	0.75 (0.45–1.19)	0.004
HIV RNA, n (%)			
< 20 copies/mL	1,276 (84.9)	179 (70.2)	< 0.001
≥ 20 copies/mL	227 (15.1)	76 (29.8)	
Time since HIV diagnosis (years), median (25th–75th percentile)	9.1 (5.7–13.7)	7.8 (4.0–12.4)	< 0.001
Time since ARV initiation (years), median (25th–75th percentile)	6.5 (4.4–11.3)	5.7 (3.3–9.5)	0.002
Education*			
Basic	148 (11.0)	45 (22.1)	< 0.001
Secondary/vocational	786 (58.6)	125 (61.3)	
University	408 (30.4)	34 (16.7)	

*Education status was available for 1,342 vaccinated and 204 unvaccinated individuals.

lower among younger individuals (Fig. 3). In line with these findings, the log-rank test shows highly significant difference of the curves between age groups ($p < 0.001$).

The study cohort of people living with HIV achieved vaccination coverage of 84.7% which significantly exceeds the reference data for the general adult population in the Czech Republic (63.5%). The trend in vaccination coverage in the first 7 months of the campaign was very similar for people living with HIV/AIDS (PLWHA) and the general population (Fig. 4), but thereafter the further growth in vaccination coverage was slower in the general population. This results in a significant difference between curves (log-rank test $p < 0.001$).

In total, 328 vaccinated patients have experienced confirmed infection of COVID-19 after the vaccination. Three hundred and nineteen individuals (21.4%) were fully vaccinated at the time of

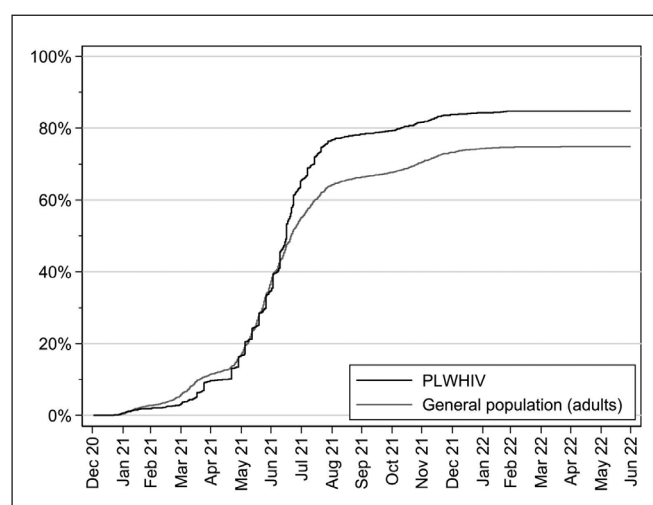
being diagnosed positive for COVID-19 and such infections were classified as breakthrough. The number of breakthrough cases in our subgroup with completed scheme of Comirnaty vaccine was 219 (21.7%). Among vaccines with two shots of Spikevax were 9 (15.5%) cases of breakthrough, in the Vaxzevria subgroup were 6 (23.1%) cases of breakthrough, and in the group of persons vaccinated with single dose of Johnson & Johnson were 11 (19.3%) cases of breakthrough. The difference between these subgroups does not reach the level of statistical significance ($p = 0.715$).

The difference in median age between persons without or with breakthrough infections was statistically significant: 44.1 and 41.5 years ($p = 0.001$), respectively.

Prevalence of pre-defined risk factors among individuals with breakthrough infection was 25.1% (80 cases), namely obesity – 11.6% (37 cases), arterial hypertension – 11.0% (35 cases), diabetes mellitus or impaired fasting glycaemia – 7.5% (24 cases), and pulmonary disease (bronchial asthma, chronic obstructive pulmonary disease, sleep apnoea) – 5.3% (17 cases). Difference in prevalence of individual risk factors were ranging from 5.3%–11.6%. Prevalence of smoking in the subgroup of persons with breakthrough infections was 44.0%.

DISCUSSION

Our study cohort is highly representative with its proportion of 80.3% within the whole group of patients registered at the HIV centre of University Hospital Bulovka and more than half (55.0%) of all PLHIV in the Czech Republic at the time of the initiation of COVID-19 vaccination (25). The cohort reflects the structure of PLHIV in the Czech Republic in terms of age, proportion between sexes and percentage of persons being virologically suppressed on ART. Those individuals without ART or those with HIV RNA ≥ 20 copies/mL were mostly recently diagnosed prior to initiation of ART or those having just started ART.

**Fig. 4.** Comparison of vaccination coverage over time among people living with HIV and adult general population.

In our study cohort, we have found significantly higher vaccination coverage among PLHIV (84.7%) than from reported data for the general Czech population (63.5%), probably because of targeted counselling and promotion of vaccination during continuous dispensation (23). This finding correlates with reports from other countries, where vaccination coverage against COVID-19 in the general population and among PLHIV ranges from 57.2 to 81.2% and from 55.0 to 72.0%, respectively (26–28). Our vaccination coverage shows good results in comparison with the US population of PLHIV (large cohort of patients in New York State) and the 68% vaccination rate of completed vaccinations at the comparable period of time (28).

Comparison of vaccinated vs. unvaccinated persons shows that those unvaccinated are younger, more likely with no ART, with a lower level of education, and with lower CD4+ count. Unsurprisingly, more educated and aged patients displayed greater interest in being vaccinated (29, 30). Similarly, Tesoriero et al. has found lower vaccination coverage among PLHIV who were not virally suppressed (≥ 200 HIV RNA copies/mL) and among those with low drug adherence (27).

Availability of vaccination against COVID-19 was limited in the same period of time in Europe (31). Since June 2021, in parallel with improved vaccine availability, a larger difference becomes apparent in vaccination coverage between our study cohort and the general population. A difference of approximately 10% has appeared and remained without major change until the end of study period. This feature can be explained by the following factors: HIV infection is self-identified as a risk factor by PLHIV and COVID-19 disease awareness in PLHIV is high. Easy access to vaccination is definitely a key factor which has a positive impact on vaccination coverage in our study cohort. In contrast to our HIV centre, many European countries prefer to perform vaccination against COVID-19 in specialised vaccination centres. In such an eventuality, vaccination is provided to PLHIV at the same place as to the general population.

We have seen vaccination hesitancy as a driving factor of insufficient vaccination coverage in the general population as in PLHIV (32–35). In case of the Czech Republic, we assume an even larger impact on the general population than in our study cohort. Also, there is a wide spectrum of important factors starting with disease awareness, socioeconomic status, level of education, and public health settings, which is well documented in different studies (36–39).

Despite effective vaccination, there is still an occurrence of breakthrough cases of COVID-19 after a completed vaccination regimen. The overall risk of breakthrough infections is low, but in the large cohort study Coburn et al. revealed that PLHIV are at a higher risk than general population, although the rate of breakthrough infections is on the rise (40). The severity of breakthrough infection is in general associated with the pre-existing comorbidities, e.g., cardiovascular disease, chronic kidney disease or obesity with essential hypertension (41). The frequency of breakthrough infections is not affected by viral suppression, apart from high CD4+ (≥ 500 cells/mm³), which was associated with fewer infections; on the other hand, PLHIV with CD4+ < 350 cells/mm³ had a 59% increased risk of severe breakthrough infections than the general population (40, 42). Some studies showed a higher risk of breakthrough infections in PLHIV who did not receive a booster dose (43). In our study cohort, breakthrough infections

only had a mild course, maybe because of the high CD4+ count of the infected patients.

Limitations in our study are partially caused by the structure of our study cohort, which is the PLHIV population in the Czech Republic. There is a low number of female patients, which reflects the situation in the country with dominant cases of MSM (men having sex with men) patients. There is also a low number of individuals without ART, with low CD4+ count and persons with unstable housing. Comorbidities were analysed only in the group of patients with breakthrough infections, as there was a lack of the data for the rest of the patients. Another limitation is the relatively short duration of study period with potential impact on incidence of breakthrough infections. In our study cohort we did not analyse the safety aspects of vaccination with its risk factors, which makes it unfeasible for comparison of persons with and without breakthrough infection.

CONCLUSIONS

Vaccination is an essential preventive measure in the fight against the COVID-19 pandemic. According to the data from our study, the first wave of vaccination conducted in our HIV centre during the first 18 months of the vaccination campaign in the Czech Republic succeeded in a high vaccination rate in the cohort of our patients. As seen in our study, targeted and accessible care in combination with motivated patients can result in very high vaccination coverage, possibly because of awareness and proper guidance during the vaccination process. This seems to be one of the main tools in the prevention of COVID-19 in the whole population.

Conflicts of Interest

None declared

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