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Short Communication

Effectiveness of COVID-19 vaccination among people living with HIV during a COVID-19 outbreak[☆]



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Received 12 November 2021; received in revised form 24 March 2022; accepted 16 April 2022

Available online 5 May 2022

KEYWORDS

SARS-CoV-2;
Pandemic;
Vaccine
effectiveness;
Immunogenicity

Abstract COVID-19 vaccination is recommended for at-risk populations, but the vaccine effectiveness in people living with HIV (PLWH) remains incompletely understood. Here we demonstrate that COVID-19 vaccination was clinically effective among PLWH during the outbreak setting with a low endemicity of COVID-19 where non-pharmaceutical interventions were strictly implemented.

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[☆] The preliminary analyses of these data were presented as Abstract 866 at the 29th Conference on Retroviruses and Opportunistic Infections, Virtual, February 12–16, 2022.

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Introduction

People living with HIV (PLWH), particularly those with severe immunodeficiency, are at higher risk for poorer COVID-19 outcomes.¹ Although COVID-19 vaccination is recommended for at-risk populations, the vaccine immunogenicity and efficacy in PLWH remain incompletely understood. Delayed and suboptimal serologic responses to some vaccines (eg, against hepatitis A) have been shown among PLWH; however, vaccination was still highly effective during an outbreak setting in the era of combination antiretroviral therapy (cART).² Previous studies on COVID-19 vaccine responses in PLWH only included medically stable individuals, which demonstrated that antibody and cellular immune responses seemed to be similar between PLWH and those without HIV.^{3,4} However, individuals with profound immune deficiency may fail to mount adequate antibody responses after completion of vaccine series.⁵ Therefore, the US Centers for Disease Control and Prevention recommends a supplemental dose for PLWH with CD4 count <200 cells/mm³.⁶ Since the booster vaccination was not widely rolled out due to shortages of vaccine supply and overloaded public health infrastructure during the outbreak worldwide, we aimed to evaluate the effectiveness of COVID-19 vaccination among PLWH during the second wave of COVID-19 outbreak in Taiwan.

Methods

This prospective cohort study was conducted at a university hospital during a large-scale community COVID-19 outbreak in northern Taiwan. Beginning on 22 March, 2021, the Taiwan Centers for Disease Control implemented a vaccination program that provided 2 doses of COVID-19 vaccine to at-risk populations, though the vaccine shortages had precluded most vaccinees from completing the second scheduled doses of vaccination during the early phase of the outbreak. In this study, all adult PLWH seeking HIV care at the university hospital from 1 March to 30 September, 2021 were included and advised to receive 2 doses of COVID-19 vaccine. Individuals were excluded from the study if they had been diagnosed with SARS-CoV-2 infection before 1 March, 2021. Different types of COVID-19 vaccines were distributed in the vaccination program, including ChAdOx1 nCoV-19 (AZD1222), BNT162b2 (Pfizer-BioNTech), mRNA-1273 (Moderna), and MVC-COV1901 (Medigen) vaccines. All the vaccines have been authorized for emergency use by the Taiwan Food and Drug Administration with an estimated vaccine efficacy of >50%.⁷

In Taiwan, several non-pharmaceutical interventions (NPIs) have been strictly implemented since January 2020, such as border control and quarantine, case detection and isolation, contact tracing of confirmed cases, face mask use, and social distancing. The combination of NPIs and high degree of public adherence had contributed to successful COVID-19 control, with no new indigenous cases between May and December, 2020.⁸ However, a community COVID-19 outbreak began right after the implementation of vaccination program and reached a peak in May 2021 in northern Taiwan. During the period of the second wave of COVID-19 outbreak, a total of 14,504 indigenous cases were

reported as of 30 September, 2021 (Fig. 1A). In response to the outbreak, health authorities imposed soft lockdown measures from May to July 2021.

To estimate the effectiveness of COVID-19 vaccination among PLWH, we compared the incidence of confirmed SARS-CoV-2 infections between participants not receiving vaccination (unvaccinated group), those only receiving the first dose of vaccine (partially-vaccinated group), and those completing 2 doses of vaccine (fully-vaccinated group). We considered an induction period of 14 days after the administration of COVID-19 vaccination for developing immunity.⁴ The cohort was dynamic; therefore, participants who were initially included in the unvaccinated and partially-vaccinated groups could subsequently be included in the partially- and fully-vaccinated groups, respectively, after receiving vaccines. Participants were followed until undergoing vaccination, occurrence of incident SARS-CoV-2 infection, death, loss to follow-up, or the end of this study on September 30, 2021, whichever occurred first. Polymerase-chain-reaction (PCR) tests, the diagnostic tests to detect SARS-CoV-2 infection, were performed for individuals with symptoms suggestive of COVID-19 or potential exposure risks. The incidence rate ratios (IRRs) were estimated by Poisson regression with the use of STATA software version 17.0 (Stata Corporation, College Station, TX). This substudy was nested in a main study of investigating the evolution of seroresponses to COVID-19 vaccines among PLWH. The main study was approved by the Research Ethics Committee (registration number, 202106149RIND) and each participant gave his or her written informed consent. This substudy aimed to track the vaccination status of all PLWH when the national COVID-19 vaccination program was implemented. Because provision of COVID-19 vaccination was part of the public health response to the ongoing COVID-19 outbreak, the substudy was not considered as research requiring approval by the Research Ethics Committee and the informed consent was waived.

Results

Between 1 March to 30 September, 2021, 3131 adult PLWH without previous SARS-CoV-2 infection were included. Of these, 492 (15.7%) did not undergo vaccination, 2303 (73.6%) only received the first dose of COVID-19 vaccine, and 336 (10.7%) had completed 2 doses of vaccination. The most frequently used vaccines were ChAdOx1 nCoV-19 (1750/2639, 66.3%), followed by mRNA-1273 (595/2639, 22.5%) and BNT162b2 (162/2639, 6.1%). Since the cohort was dynamic, 3128 participants contributed 516,892 person-days of follow-up (PDFU) to the unvaccinated group, 2476 contributed 139,163 PDFU to the partially-vaccinated group, and 236 contributed 12,011 PDFU to the fully-vaccinated group (Table 1). The baseline characteristics were generally comparable between the 3 groups. Because various vaccines were available in different study periods, participants in the fully-vaccinated group tended to have received BNT162b2, Sinovac, and Sinopharm vaccines and have not received mRNA-1273 and MVC-COV1901 vaccines compared with participants in the partially-vaccinated group.

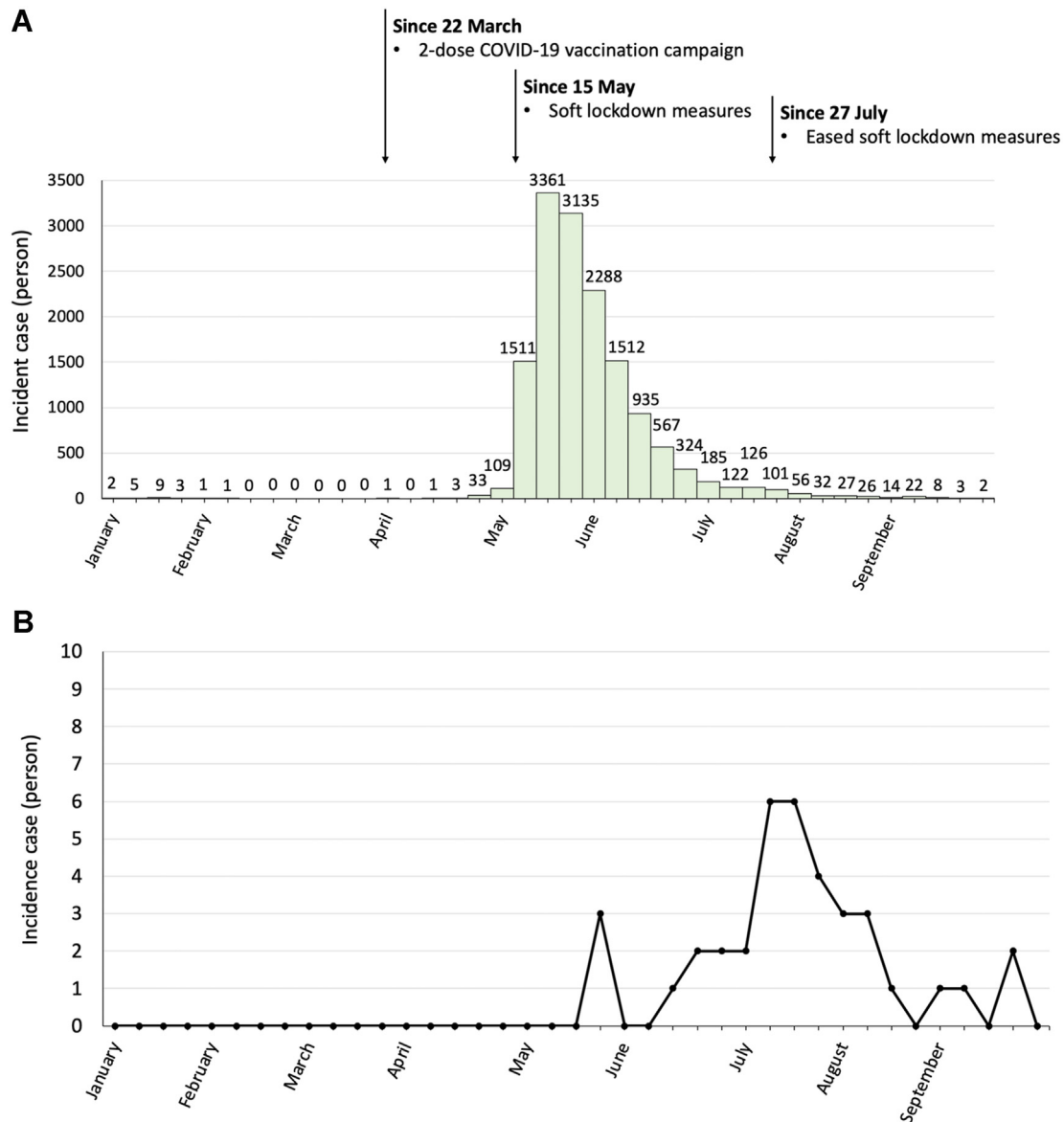


Figure 1. Weekly number of confirmed cases of SARS-CoV-2 infection by onset date in 2021. A, Indigenous cases in Taiwan and corresponding non-pharmaceutical interventions (NPIs). B, PLWH with SARS-CoV-2 infection at the hospital.

The number of confirmed cases of SARS-CoV-2 infection among PLWH seeking HIV care at the hospital is shown in Fig. 1B. During the follow-up, 37 PLWH (1.2%) acquired SARS-CoV-2 infections, 33 (89.2%) in the unvaccinated group and 4 (10.8%) in the partially-vaccinated group (Table 1). The incidence rate of SARS-CoV-2 infection was 6.4 per 100,000 PDFU in the unvaccinated group, which decreased to 2.9 and 0 per 100,000 PDFU in the partially- and fully-vaccinated groups, respectively (Table 1). After adjusting for age, sex, as well as baseline CD4 count and plasma HIV RNA load (PVL), the incidence rate ratio was 0.47 (95% CI, 0.17–1.32) in the partially-vaccinated group and <0.01 in the fully-vaccinated group compared with that in the unvaccinated group. The estimated vaccine effectiveness was 53.4% and 99.9% for single- and 2-dose COVID-19 vaccination, respectively. No vaccinees with a CD4 count <200 cells/mm³ acquired SARS-CoV-2.

Discussion

In this study of COVID-19 vaccination during the outbreak setting where NPIs have been strictly implemented, we found that COVID-19 vaccination was clinically effective in preventing SARS-CoV-2 infection among PLWH. While single-dose COVID-19 vaccination provided >50% protection, the addition of a second dose further increased the vaccine effectiveness to approximately 100%. Our study conducted among PLWH on stable antiretroviral therapy suggests that two doses of COVID-19 vaccine effectiveness was high during the circulation of B.1.1.7 variant.

Previous clinical trials of COVID-19 vaccine enrolled a small number of PLWH without advanced immune suppression. In an immunogenicity study of ChAdOx1 nCoV-19 vaccine, only 104 PLWH who were virally suppressed with CD4 counts >500 cells/mm³ were included. Compared with

Table 1 Baseline characteristics and outcomes of the PLWH who contributed follow-up periods in unvaccinated and vaccinated groups.

Variable	Unvaccinated group (n = 3128) ^a	Partially-vaccinated group (n = 2476)	Fully-vaccinated group (n = 236)	P value
Age, median (IQR), years	41 (35–50)	41 (35–50)	41 (34–50)	0.470
Male sex, n (%)	3121 (99.8)	2472 (99.8)	236 (100)	0.688
Receiving cART, n (%)	3126 (99.9)	2474 (99.9)	236 (100)	0.893
INSTI and NRTIs	2906 (92.9)	2300 (92.9)	217 (91.9)	0.857
Boosted PI and NRTIs	13 (0.4)	11 (0.4)	0 (0)	0.594
NNRTI and NRTIs	197 (6.3)	155 (6.3)	19 (8.1)	0.550
Boosted PI and INSTI	10 (0.3)	8 (0.3)	0 (0)	0.684
Baseline CD4 count, median (IQR), cells/mm ³	625 (467–809)	635 (478–825)	587 (463–779)	0.163
Baseline PVL, median (range), log ₁₀ copies/mL	UD (UD-6.23)	UD (UD-6.23)	UD (UD-5.77)	0.841
PVL <20 copies/mL, n (%)	2592 (82.9)	2080 (84.0)	205 (86.9)	0.195
Types of vaccine, n (%)				
ChAdOx1 nCoV-19	NA	1744 (70.4)	169 (71.6)	0.712
mRNA-1273	NA	592 (23.9)	36 (15.3)	0.003
MVC-COV1901	NA	110 (4.4)	4 (1.7)	0.044
BNT162b2	NA	11 (0.4)	10 (4.2)	<0.001
Others ^b	NA	18 (0.7)	17 (7.2)	<0.001
Vaccination period, n (%) ^c				<0.001
March–April, 2021	NA	37 (1.5)	8 (3.4)	
May–July, 2021	NA	2029 (81.9)	119 (50.4)	
August–September, 2021	NA	410 (16.6)	109 (46.2)	
Confirmed cases of SARS-CoV-2 infection, n (%)	33 (1.1)	4 (0.2)	0 (0)	<0.001
Follow-up duration, PDFU	516,892	139,163	12,011	–
Incidence rates of SARS-CoV-2 infection, cases per 100,000 PDFU	6.4	2.9	0	–

^a Three participants had received COVID-19 vaccination at least 14 days before 1 March, 2021, for which they did not contribute follow-up periods in the unvaccinated group.

^b Participants received Sinovac and Sinopharm COVID-19 vaccines in China.

^c The date on which participants received the first dose of vaccination for the partially-vaccinated group, or the second dose of vaccination for the fully-vaccinated group.

Abbreviations: CART, combination antiretroviral therapy; INSTI, integrase strand transfer inhibitor; IQR, interquartile range; NA, not available; NRTI, nucleoside reverse-transcriptase inhibitor; NNRTI, non-nucleoside reverse-transcriptase inhibitor; PDFU, person-days of follow-up; PI, protease inhibitor; PLWH, people living with HIV; PVL, plasma HIV RNA load; UD, undetectable.

HIV-negative individuals, ChAdOx1 nCoV-19 induced similar full-length spike-binding IgG, receptor-binding domain-binding IgG, and SARS-CoV-2 neutralizing responses in PLWH.⁴ The comparable humoral and cellular immune responses were also shown in 12 PLWH receiving BNT162b2 vaccine and 14 receiving mRNA-1273 vaccine.^{3,9} Although vaccine immunogenicity is highly predictive of protection from SARS-CoV-2 infection, the data on vaccine effectiveness among PLWH remain limited. In phase 2 study of NVX-CoV2373 (Novavax) vaccine during B.1.351 variant predominantly circulating in South Africa, 2684 participants were enrolled, with 6% being medically stable PLWH. The overall efficacy of 2-dose vaccination was 49.1% in the combined HIV-negative and HIV-positive populations, which was lower than that in HIV-negative individuals (60.1%).¹⁰ Due to the small population of PLWH, the study was not powered to conclude a lower vaccine efficacy in this population. Our study was conducted in a large cohort of PLWH

receiving effective antiretroviral therapy and our results of high vaccine effectiveness might provide supportive clinical data to previous immunogenicity studies conducted among PLWH.

Our study has several limitations. First, NPIs are critical components of pandemic control and have been highly adhered to in Taiwan. Since lifting NPIs was not possible during an outbreak in the real-world setting, this study evaluated the combined effect of vaccination campaign and NPIs. Second, the vaccinated groups included less PLWH and had shorter follow-up duration than the unvaccinated group. However, most PLWH received COVID-19 vaccination during the second wave of COVID-19 outbreak, which might underestimate the impact of vaccination rollout. Finally, different types of COVID-19 vaccines were administered during the vaccination campaign. Nevertheless, the majority of vaccines have an acceptable vaccine efficacy demonstrated in clinical trials.

In conclusion, we found that COVID-19 vaccination was effective in preventing SARS-CoV-2 infection during the outbreak setting where NPIs were strictly implemented. Our results of high vaccine effectiveness support the completion of the primary COVID-19 vaccine series for PLWH in the cART era.

Declaration of competing interest

All authors declare no conflict of interest.

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