Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Immunogenicity of a third dose of inactivated COVID-19 vaccine in people living with HIV-1, HBV, and tuberculosis during the Omicron variant epidemic: A cross-sectional study

To the editor

Recent Syed's study reported that the effectiveness of one dose of the COVID-19 mRNA vaccine peaked at month 1 after immunization (77% for BNT162b2 and 88.2% for mRNA-1273), following this, a decline was observed at month 2 (67.6% for BNT162b2 and 84.5% for mRNA-1273).[1] However, the effectiveness of two doses of BNT162b2 could be 94%.[2]

Recent real-world studies performed the investigation of the sustainability of immune memory stimulated by the COVID-19 vaccines in healthcare individuals.[2-4] It has been known that the immunogenicity of the COVID-19 mRNA vaccine was higher than the inactivated vaccine in normal and immunocompromised patients.[2,5,6] One previous study revealed that the antibodies (Abs) of two doses of inactivated vaccine immunization peaked at ~1 month in cirrhosis people and significantly declined between months 3 and 6.[7] Even though some individuals' serum IgG and neutralizing antibodies (NAbs) declined substantially or were negative after receiving a second dose of inactivated vaccine injection, SARS-CoV-2 specific memory B and T cells can persist in blood until month 5, and a third vaccination could induce robust humoral and cellular immune recall responses.[3]

Vaccinated individuals received the third dose of inactivated COVID-19 vaccine, NAbs are important indicators used in evaluating the protective immunity after vaccine injection. NAbs that block the interaction between spike proteins and their receptor angiotensin-converting enzyme 2 (ACE2) are particularly important for preventing the onset of COVID-19 during the SARS-CoV-2 wild-type (wt) or variant strain prevalence.[2] Nevertheless, the effectiveness of the third dose of inactivated COVID-19 vaccine-induced NAbs in people living with HIV-1, HBV, and tuberculosis has not been evaluated like the normal population.

In this study, we sought to investigate the humoral immune responses and viral neutralization capacity stimulated by a third dose of inactivated COVID-19 vaccine in people living with specific underlying infectious diseases during Omicron prevalence. It will help to know the protective efficacies of the third dose of vaccine on these individuals. We perform a cross-sectional study during the Omicron variant epidemic in Wuxi of China from February 10th, 2022 to May 30th, 2022 (Ethics No. 2021–004–1). During the local Omicron epidemics, the frequency of nucleic acid testing for citizens was once a day. This study also included the IgG status of newly diagnosed SARS-CoV-2 individuals during the epidemic of the Omicron variant strain. We obtained the date and adverse reactions of all individuals for COVID-19 vaccination before the analysis and determined that the participants did not experience serious adverse reactions. This study excluded the individuals who had not received a third dose of the vaccine. The SARS-CoV-2 IgG positive rates, NAb inhibition rates, and statistical differences between people living with HIV-1, HBV, tuberculosis, and healthy control (HC) were calculated.

In China, the older, less educated, and lower incomes population show higher willingness and probability of vaccination.[8] From September 2021, the high-risk and normal populations, such as healthcare workers, police officers, community workers, and people with underlying diseases, have voluntarily participated in the third dose of inactivated COVID-19 vaccination. From November 2021, the local epidemic strain was diagnosed with the Omicron variant, followed by intermittent outbreaks. During the local Omicron variant epidemic from February to May 2022, 56.4% of SARS-CoV-2 infected people were IgG-positive at admission, with a positive rate similar to that of HC individuals (Table 1). After vaccination, people living with HIV-1 (all age group), HBV (18–39 years), and tuberculosis (≥ 40 years) who were not infected with SARS-CoV-2 produced significantly lower IgG-positive rates than those in the corresponding age group of HC. The IgG overall positivity rankings: HC (59.7%) > SARS-CoV-2 (56.4%) > HBV (44.3%) > HIV-1 (37.1%) > tuberculosis (24.4%). Notably, there were significant differences in SARS-CoV-2 IgG positivity and NAb inhibition rates (neutralizing activities) in the tuberculosis group between 18 and 39 years (52.6%) and ≥ 40 years (24.9%) ($p = 0.0001$), and between tuberculosis and HC groups over 40 years of age ($p < 0.01$) (Table 1, Fig. 1). During the Omicron epidemic, only two SARS-CoV-2 infected people showed severe respiratory symptoms, both of whom had hypertension and did not complete the third vaccination, while the rest showed mild symptoms or were asymptomatic.

Previous studies have not found the effects of age, gender, or ABO blood type on the immunogenicity of the COVID-19 vaccine,[1,4] and this study showed a significant reduction in IgG positivity and neutralizing activity in the tuberculosis group over 40 years of age. Patients aged 18–39 years with HIV-1, HBV, and tuberculosis produced more effective NAbs. This suggests that age differences may affect Ab positivity, effectiveness, and retention time.

Overall, COVID-19 mRNA vaccination is safe for people living with HIV-1,[9] but the safety and immunogenicity of a third dose of inactivated vaccine in people living with HIV-1, HBV, and tuberculosis have not been evaluated in detail. In our cross-sectional study, the results showed that these people received the third vaccine with no obvious adverse reactions. In our previous study during the SARS-CoV-2 wt strain epidemic, we found that people living with HBV or tuberculosis comorbidities, as well as people over the age of 40 years, suffered more severe symptoms,[10] so we have divided participants into these two age groups. The limitation of this study is that there was a statistical difference between the HBV

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Table 1
Immunogenicity comparisons of the third dose of inactivated COVID-19 vaccine for people living with HIV-1, HBV, and tuberculosis.

Groups (years)	Age (all, years)	[a]p	Age (positive, years)	[a]p	Positive Rates (%)	[b]p	[a]p	Inhibitory Rates (%)	[b]p	[a]p
HIV-1 (n = 94)	42.5 ± 11.1	0.5848	42.1 ± 11.4	0.7048	37.1		0.0014	66.3 ± 17.9		0.2330
18–39 (n = 44)	32.5 ± 4.7	0.0535	32.7 ± 3.8	0.1500	38.6	0.3259	0.0066	68.7 ± 14.4	0.4655	0.5119
≥40 (n = 50)	51.3 ± 6.7	0.9916	52.0 ± 7.6	0.3059	32.0		0.0001	63.8 ± 21.2		0.0877
HBV (n = 96)	44.0 ± 10.0	0.1525	43.9 ± 8.5	0.1964	44.3		0.0293	71.7 ± 9.6		0.7110
18–39 (n = 46)	33.6 ± 4.1	0.0057	34.6 ± 3.1	0.0132	43.3	0.8198	0.0397	74.7 ± 8.0	0.4532	0.7755
≥40 (n = 50)	50.3 ± 6.6	0.4745	48.9 ± 5.9	0.5271	44.9		0.3930	69.9 ± 10.2		0.4282
TB (n = 95)	43.2 ± 14.0	0.4130	40.7 ± 11.9	0.9040	24.4		0.0000	63.3 ± 17.0		0.1022
18–39 (n = 41)	29.4 ± 5.7	0.5714	30.3 ± 5.5	0.9885	52.6	0.0001	0.4588	66.8 ± 17.2	0.1088	0.3490
≥40 (n = 54)	53.8 ± 7.8	0.1346	50.4 ± 6.8	0.8053	24.9		0.0000	55.8 ± 14.4		0.0044
SARS-CoV-2 (n = 709)	36.3 ± 15.0	0.7565	40.8 ± 14.1	0.9843	56.4#		0.6363	–	–	–
1–39 (n = 285)	25.1 ± 8.4	0.0024	26.5 ± 8.2	0.0732	54.0#	0.5688	0.9724	–	–	–
≥40 (n = 424)	51.0 ± 6.7	0.7944	50.9 ± 6.8	0.4869	58.0#		0.5844	–	–	–
Healthy Control (n = 69)	41.5 ± 12.5	NA	41.1 ± 11.2	NA	59.7		NA	74.0 ± 16.5		NA
18–39 (n = 32)	30.2 ± 5.7	NA	30.3 ± 5.7	NA	57.8	0.5092	NA	72.9 ± 20.1	0.7424	NA
≥40 (n = 37)	51.3 ± 7.2	NA	49.9 ± 5.1	NA	59.5		NA	75.0 ± 13.2		NA

Notes: The quantification of the SARS-CoV-2 IgG against the virus spike protein was carried out using INNOVITA® 2019-nCoV IgM/IgG kit by following the manufacturer's instructions. Statistical significant differences were analyzed using the unpaired t-test and Chi-square test; The statistical differences of inhibition rates were analysis only among NAb positive people. Data are presented as the mean ± standard deviation (SD) of the mean. #, the positivity of IgG was the first result at the time of admission. a, means a statistical comparison of the corresponding data between the people with underlying disease and healthy control in each age group; b, means a statistical comparison of the two age groups in each classification; -, means not participating in statistical analysis; A p-value < 0.05 is considered statistically significant. HIV-1, human immunodeficiency virus; HBV, hepatitis B virus; TB, tuberculosis; NA, not available.

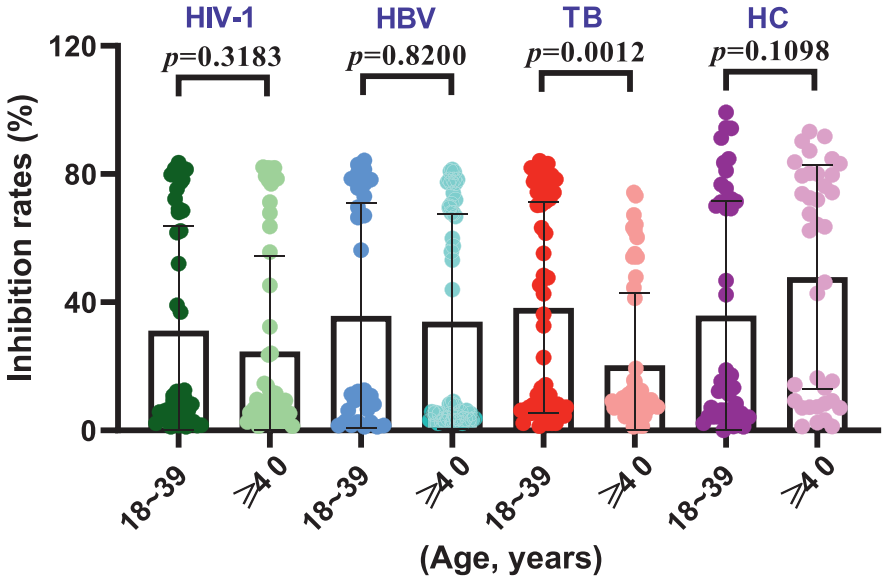

Fig. 1. Comparison of SARS-CoV-2 neutralizing antibody (NAb) inhibition rates in various groups. Peripheral blood from the third dose of inactivated COVID-19 vaccine vaccinated comprehensively was collected during the Omicron variant epidemics. NAbs were detected using the competitive ELISA. The microplate was coated with a recombinant human ACE2 receptor protein (hACE2), and horseradish peroxidase-labeled receptor-binding domain (HRP-RBD) protein was prepared as an enzyme-binding complex. The mixed serum sample and HRP-RBD protein were incubated, then transferred to the hACE2-coated plate. HRP-RBD without binding NAbs binds to hACE2, and the colored substrate values were read at a wavelength of 450 nm after the enzyme reaction and terminating reaction. Inhibition rate = [1-OD_{450} (sample) / OD450 (mean of negative control)] × 100%; Inhibition rate ≥ 20% is considered positive; Inhibition rate < 20% is considered negative. HIV-1, human immunodeficiency virus; HBV, hepatitis B virus; TB, tuberculosis; HC, healthy control. Statistical significant differences in NAb inhibition rates were analyzed in all people using the unpaired t-test. A p-value < 0.05 was considered statistically significant.

and HC groups at the age of 18–39 years, and the age difference may affect the IgG positive rate and NAbs inhibition rate in the HBV group.

In summary, despite the use of the third dose of inactivated COVID-19 vaccine, and the low effectiveness of an inactivated vaccine against Omicron (2), the vaccine showed weaker immunogenicity in people living with HIV-1, HBV, and tuberculosis compared with HC, and also had a weaker ability to inhibit viral infections. Age as a core factor is critical to influencing the immunogenicity of the vaccine in tuberculosis patients. Therefore, most populations should also find more means to prevent and control exposure to SARS-CoV-2, such as wearing well-fitted masks, avoiding crowded places, keeping a safe distance, etc.

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Declaration of Competing Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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