Hiroshima J. Med. Sci.
Vol. 72, No. 1·2, 1~4, June, 2023
HIMJ 72–1

Effect of vaccine booster dose on coronavirus disease 2019 prevention by age group: Analysis of data collected at polymerase chain reaction centers in Hiroshima Prefecture, Japan

Yuki MIYOSHI[1)], Odgerel CHIMED-OCHIR[1)], Yui YUMIYA[1)], Eisaku KISHITA[2)], Junko TANAKA[3)], and Tatsuhiko KUBO[1,*)]

1) Department of Public Health and Health Policy, Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan
2) Hiroshima Prefectural Health and Welfare Bureau, Hiroshima, Japan
3) Department of Epidemiology, Infectious Disease Control and Prevention, Graduate School of Biomedical & Health Sciences, Hiroshima University, Hiroshima, Japan

ABSTRACT

For three years, the world has faced the coronavirus disease (COVID-19) pandemic, and vaccination against severe acute respiratory syndrome coronavirus 2 remains the best defense. In Japan, vaccination with a booster dose started in early December, with healthcare workers receiving priority, followed by elderlies aged > 65 years. We aimed to assess the effectiveness of vaccine boosters in preventing infection in various age groups of Japanese people in Hiroshima. A pre-administered questionnaire, the J-SPEED-style COVID-19 polymerase chain reaction (PCR) center version, was used to collect data from PCR centers in Hiroshima Prefecture between February 1, 2022 and March 17, 2022. The highest infection rate was observed in those aged between 10 and 19 years (6.0%), whereas the lowest infection rate was observed in those aged 45–64 years and > 65 years (3.3%). For all age groups, three doses of the vaccine provided lower infection rates than two doses. Elderlies aged > 65 years with booster doses (odds ratio [OR] = 0.499, 95% confidence interval [CI] = 0.400–0.622) were less infected compared to the same groups who received two doses, followed by those aged 45–64 years (OR = 0.663, 95% CI = 0.558–0.788) and 20–44 years (OR = 0.758, 95% CI = 0.655–0.877). In general, those aged > 65 years who received three doses (OR = 0.499, 95%CI = 0.400–0.622) were less likely to be infected with COVID-19 than those aged < 65 years (OR = 0.674, 95%CI = 0.604–0752). We analyzed the association between vaccination status and infection status; therefore, we recommend future research using data on the exact vaccination date and infection status.

Key words: *COVID-19*, *Vaccine Effect*, *Hiroshima*, *J-SPEED*

INTRODUCTION

For three years, the world has faced the coronavirus disease 2019 (COVID-19) pandemic, and vaccination against severe acute respiratory syndrome coronavirus 2 remains the best defense[2,5)]. As of March 1, 2022, of the world's population, 55.44% has been vaccinated with full dose and 17.93% has received vaccine booster doses[7)]. This robust response to boosters is associated with several concerns, including possible side effects, their efficacy, and whether the elderly and younger people can equally benefit in terms of infection prevention, severity, and fatality. Several studies have suggested that vaccine boosters have an age-associated effect on the prevention of serious conditions, indicating that vaccinations significantly reduce severity and death rate among the elderly[1,6)]. However, age-associated effects of vaccine breakthrough infections are largely unexplored. Therefore, we assessed the effectiveness of vaccine boosters in preventing infections in various age groups in Hiroshima, Japan.

MATERIALS AND METHODS

Data collection

In Hiroshima Prefecture, Japan, polymerase chain reaction (PCR) centers, where all the residents had access to free testing, were established. When people come to the centers, they are requested to fill out a pre-administered questionnaire known as the Japanese Surveillance in Post-Extreme Emergencies and Disasters (J-SPEED)-style COVID-19 form. This data collection form was developed to obtain health data in various fields such as public health centers, recuperation hotels, online treatment centers, oxygen centers, PCR centers,

* Corresponding author: Prof. Tatsuhiko Kubo MD, PhD, Professor, Department of Public Health and Health Policy, Graduate School of Biomedical and Health Sciences, Hiroshima University, 1-2-3 Kasumi, Minami-ku, Hiroshima 734-0037, Japan
Tel (mobile): +81-80-7014-1029, E-mail: tkubo@hiroshima-u.ac.jp

and hospitals in May 2020. The form was developed based on the lessons learned from the Great East Japan Earthquake in 2011 with the concept of simplifying and standardizing health data collection to gather almost real-time data.

The J-SPEED-style COVID-19 PCR Center version comprises 58 items, including demographic information, work types, symptoms, existing diseases, vaccination status, prevention practice from COVID-19, and PCR test results. Those receiving a positive PCR test were considered “infected.”

Data analysis

Data collection at the PCR centers began on April 1, 2021; however, information on vaccination status has only been available since December 20, 2021. In Japan, vaccination with a third booster dose started in early December, with healthcare workers receiving priority, followed by elderly people aged > 65 years. Other individuals were received the vaccine booster in mid-January. Therefore, we used the data from February 1, 2022 to March 17, 2022. Overall, 124,160 individuals underwent PCR testing in Hiroshima Prefecture during this period.

We extracted information on the demographics, vaccination status, and PCR test results. We categorized age into five groups as follows: 0–9 years old (children), 10–19 years old (teenagers), 20–44 years old (adults), 45–64 years old (adults), and > 65 years (elderly). The data of those who were vaccinated with two doses and passed 14 days later and those who were vaccinated with three doses were selected to compare the vaccine effect between these two groups.

First, we analyzed the number of participants tested and the infection rate for each vaccination status according to age group and sex. Second, logistic regression was used to determine the association between vaccination status and infection rates in each age group separately, and the respective odds ratios were compared. Additionally, owing to the small sample size, participants aged < 10 years were not included in the logistic regression analysis. Vaccination effects were compared between those who were vaccinated with two doses and those who were vaccinated with three doses for each group. SAS Version 9.4 (SAS Institute, Inc., Cary, NC, USA) was used for data analysis.

Ethical approval was obtained from the Hiroshima University (approval number: E-2508). This study was funded by the Japan Agency for Medical Research and Development (AMED (grant no.21fk0108550h0001).

RESULTS

Table 1 presents the age distribution of the infection rates of individuals tested between February 1, 2022 and March 17, 2022 according to vaccination status. After removing data with missing age information, data of 91,130 people were analyzed. Men accounted for 52.8% (48,097), non-pregnant women for 46.3% (42,218), and pregnant women for 0.9% (728). The highest infection rate was observed in those aged 10–19 years (6.0%), whereas the lowest infection rate was observed in those aged 45–64 years and > 65 years (3.3%). For all age groups, three doses of the vaccine provided lower infection rates than those vaccinated with two doses.

Table 2 summarizes the association between vaccination status and infection rate by age group. Both the crude and adjusted models demonstrate that older people are less likely to be infected than younger individuals. In the adjusted model, the lowest odds of being infected in those with three doses compared to those with two doses of vaccine were observed in those aged > 65 years (odds ratio [OR] = 0.499, 95% confidence interval [CI] = 0.400–0.622) followed by those aged 45–64 years (OR = 0.663, 95% CI = 0.558–0.788), and those aged 20–44 years (OR = 0.758, 95% CI = 0.655–0.877). People aged > 65 years had lower odds of being infected (OR = 0.499, 95% CI = 0.400–0.622) than those aged < 65 years (OR = 0.674, 95%CI = 0.604–0752).

DISCUSSION

We analyzed the infection rate among 91,130 persons aged 0 to 108 years tested at Hiroshima Prefecture’s PCR centers between February 1, 2022 and March 17, 2022, who were vaccinated with two doses and three doses in different age groups. Individuals who were vaccinated with the three doses were considerably more protected than those who received two doses. In general, those aged > 65 years who had received three doses of the vaccine were less likely to be infected with COVID-19 than those aged < 65 years.

To date, several attempts have been made to examine the effectiveness of vaccination according to age. Numerous studies have reported that those aged ≥ 60 years should be prioritized to reduce deaths and severity[2]. However, vaccine efficacy by age may have inconsistencies in terms of infection prevention. For example, Bubar et al.[2] have revealed that prioritizing the vaccine for adults aged 20–49 years reduced the cumulative incidence. Other studies have reported a greater reduction in the incidence in younger generations[6–8]. The viral geometric mean titer (GMT) values of the younger groups were greater than those of the older groups, suggesting that the younger groups were more immunogenic[10–12]. Fuentes et al.[3] suggested immunosenescence, which is a novel concept that describes age-associated structural alterations of innate and adaptive immune functions, as the cause of lower GMT. Other studies have also indicated that in the elderly, changes in immune organs are most noticeable in the thymus, where the activity of thymocytes and thymic epithelial cells is reduced; hence, the immune response substances are reduced, and immune function is diminished[9,13]. However, older participants demonstrated a greater reduction in the infection rate in the current study. Context-specific factors, such as transmission rates, vaccination rollout speeds, and estimates of naturally acquired immunity[2], and other factors, such as the completeness and validity of the data sources, study design, and potential methodological biases[8], may

Table 1 Infection status of people tested at Hiroshima Prefecture polymerase chain reaction centers by age group.

Age	Vaccinated with two doses			Vaccinated with booster dose			Total		
	Number of people tested	Number of infected people	Infection rate	Number of people tested	Number of infected people	Infection rate	Number of people tested	Number of infected people	Infection rate
All people tested									
0–9	71	0	0.0%	7	0	0.0%	78	0	0.0%
10–19	6,776	409	6.0%	151	5	3.3%	6,927	414	6.0%
20–44	34,101	1,734	5.1%	5,616	216	3.8%	39,717	1,950	4.9%
45–64	26,914	942	3.5%	6,564	159	2.4%	33,478	1,101	3.3%
65+	5,425	238	4.4%	5,505	123	2.2%	10,930	361	3.3%
Total	**73,287**	**3,323**	**4.5%**	**17,843**	**503**	**2.8%**	**91,130**	3,826	4.2%
Male									
0–9	34	0	0.0%	5	0	0.0%	39	0	0.0%
10–19	3,492	263	7.5%	66	3	4.5%	3,558	266	7.5%
20–44	19,050	999	5.2%	1,965	78	4.0%	21,015	1,077	5.1%
45–64	15,754	514	3.3%	2,330	57	2.4%	18,084	571	3.2%
65+	2,649	105	4.0%	2,752	56	2.0%	5,401	161	3.0%
Total	**40,979**	**1,881**	**4.6%**	**7,118**	**194**	**2.7%**	**48,097**	2,075	4.3%
Female, Non-pregnant									
0–9	33	0	0.0%	2	0	0.0%	35	0	0.0%
10–19	3,260	144	4.4%	85	2	2.4%	3,345	146	4.4%
20–44	14,492	710	4.9%	3,535	137	3.9%	18,027	847	4.7%
45–64	11,098	426	3.8%	4,214	102	2.4%	15,312	528	3.4%
65+	2,759	132	4.8%	2,740	67	2.4%	5,499	199	3.6%
Total	**31,642**	**1,412**	**4.5%**	**10,576**	**308**	**2.9%**	**42,218**	1,720	4.1%
Female, Pregnant									
0–9	1	0	0.0%	0	0	NA	1	0	0.0%
10–19	21	2	9.5%	0	0	NA	21	2	9.5%
20–44	536	25	4.7%	109	1	0.9%	645	26	4.0%
45–64	42	1	2.4%	19	0	0.0%	61	1	1.6%
Total	**600**	**28**	**4.7%**	**128**	**1**	**0.8%**	**728**	29	4.0%

Table 2 Association between vaccination and infection status in different age groups

Age	Model 1				Model 2			
	Odds Ratio	95% LI	95% UI	*P* value	Odds Ratio	95% LI	95% UI	*P* value
10–19	0.533	0.217	1.307	0.169	0.557	0.227	1.369	0.202
20–44	0.747	0.647	0.863	< .0001	0.758	0.655	0.877	0.0002
45–64	0.684	0.577	0.811	< .0001	0.663	0.558	0.788	< .0001
65+	0.498	0.399	0.621	< .0001	0.499	0.4	0.622	< .0001
Under 65	0.667	0.599	0.744	< .0001	0.674	0.604	0.752	< .0001
Over 65	0.498	0.399	0.621	< .0001	0.499	0.4	0.622	< .0001

LI - Lower Interval; UI - Upper Interval
Model 1 is unadjusted. Model 2 is adjusted by gender.
Probability of being infected with COVID-19 was modeled by comparing individuals receiving booster dose with those receiving two doses of vaccine (reference).

all contribute to the heterogeneity of age-associated vaccine effects across studies in different countries.

However, in our context, the following are possible explanations for the greater reduction in infection among the older participants. First, in Japan, the third dose of vaccination started on December 1, 2021, with healthcare workers receiving priority, followed by those aged > 65 years. Consequently, sufficient time has passed for the third dose to take effect in those aged > 65 years, and they are more likely to demonstrate a greater impact of the third dose during the study period (February 1, 2022 to March 17, 2022) than the younger population. By contrast, for persons aged < 65 years, the elapsed time was insufficient for the third dose to take effect, as it is more likely to have been tested shortly after vaccination. According to an Israeli research group, the rate of confirmed infection was lower in the booster group than in the non-booster group by a factor of 11.3 at least 12 days after the booster dose, and the rate of confirmed infection at least 12 days after vaccination was lower than the rate after 4 to 6 days by a factor of 5.4[1]. Second, we hypothesized that the majority of elderly people who underwent testing at PCR centers were more health-conscious because the majority of those aged > 65 years (28%) underwent PCR testing to check their health status, whereas the majority of those aged < 65 years (47%) underwent PCR testing to confirm being "infection-free". Therefore, those who visited the PCR center may be more likely to take daily precautions, such as wearing masks, washing hands frequently, and refraining from mass gathering and travel, which might have resulted in the significant reduction of COVID-19 incidence among them. Third, because younger people are more socially active than those aged > 65 years, they are more vulnerable to COVID-19. Considering that no vaccination can completely protect against COVID-19, having more social contacts likely results in a greater infection risk among young individuals. Lastly, all the studies we examined virtually were published during a period when the Delta variants were the most prevalent mutations, while the Omicron variants dominated during the study period. Therefore, the characteristics of only Omicron variants were mirrored in the current study.

The present study has several limitations that warrant mention. First, the population used in the current study may not accurately reflect the general situation in Hiroshima Prefecture, as it includes only 25% of people aged > 70 years and 12% of people aged < 70 years among the total number of infections reported in Hiroshima Prefecture during the study period[4]. Thus, more than one-third of individuals infected with COVID-19 had their infection verified in clinics or hospitals, public health centers, and private PCR test points, and these data were not analyzed in the current study. Second, in the PCR Center form, we only recorded the number of doses of the vaccine they received, and no information on when they were vaccinated was included. Hence, we were unable to determine the number of days that passed the previous dose of vaccine, and the effect of the vaccine may likely differ between those who were tested shortly after the third dose and those who were tested many weeks later. Therefore, the study results might have been biased because vaccination effects are expected to appear at least 12 days after inoculation, thus causing an underestimation of the preventive effects in the younger age groups. Considering the above limitations, incorporating individual vaccination data into an individual's infection status will help capture the true picture of vaccine effectiveness. Therefore, we recommend future research using vaccination data along with infection status.

(Received August 29, 2022)
(Accepted September 8, 2022)

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