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RESEARCH ARTICLE

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Comparison of self-reported symptoms in COVID-19 patients who had or had not previously received COVID-19 mRNA vaccination

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ABSTRACT

Although mRNA coronavirus disease 2019 (COVID-19) vaccines have been reported for high effectiveness against symptoms, it remains unclear whether post-vaccination infections are less symptomatic than infections in vaccine-naive individuals. We included patients with COVID-19 diagnosed by polymerase chain reaction tests during Japan's alpha and delta variant epidemics. COVID-19 symptoms at approximately 4 weeks were compared based on COVID-19 vaccination status. In total, 398 cases (372 symptomatic and 26 asymptomatic; 286 unvaccinated, 66 vaccinated with one dose, and 46 with two doses) were analyzed. The most common symptoms were fever (78.4%), fatigue (78.4%), cough (74.4%), loss of taste or smell (62.8%), and headache (59.8%). Post-vaccination infections were significantly less likely to be symptomatic. Possible confounder-adjusted odds ratios of two vaccine doses against fatigue, dry eyes and mouth, insomnia, fever, shortness of breath, unusual muscle pains, and loss of taste or smell were 0.18 (95% confidence interval [CI]: 0.09–0.38), 0.22 (95% CI: 0.08–0.59), 0.33 (95% CI: 0.14–0.80), 0.31 (95% CI: 0.15–0.63), 0.36 (95% CI: 0.16–0.76), 0.40 (95% CI: 0.19–0.82), and 0.44 (95% CI: 0.22–0.87), respectively. Post-vaccination infections after two mRNA COVID-19 vaccine doses show milder and fewer symptoms than infections in unvaccinated patients, highlighting the effectiveness of vaccination.

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Introduction

During the coronavirus disease 2019 (COVID-19) pandemic, several highly efficacious vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) were developed and made available globally.[1–4] In Japan, Pfizer's novel vaccine against SARS-CoV-2 was approved for production and marketing on February 14, 2021. Temporary vaccination based on the Immunization Law began for healthcare workers on February 17, 2021, while vaccination for the elderly began on April 12, 2021. The target age for vaccination was changed from "≥16 years" to "≥12 years and older" on June 1, 2021. The vaccine manufactured by Takeda/Moderna was approved for production and marketing on May 21, 2021. Vaccination using the Takeda/Moderna vaccine began on May 24, 2021, for the elderly. Beginning on June 17, 2021, the 18–64-year-old age group was added to the target-group population, while vaccination at work sites began on June 21, 2021. The age range for vaccination was changed from "≥18 years" to "≥12 years" on August 2, 2021. The vaccine manufactured by AstraZeneca was approved for production and marketing on May 21, 2021, and has been available as a temporary vaccination for people aged ≥ 40 and over since August 2, 2021. However, infections after receiving COVID-19 vaccines are not uncommon.[5] Several factors may cause these infections, including individual factors, such as those related to a lower immune response to the vaccine,[6] reduced protection against infection due to waning immunity after vaccination,[7–10] and viral factors, such as the emergence of new variants of strains.[11]

The viral load in polymerase chain reaction (PCR) specimens from SARS-CoV-2 infected individuals is higher in symptomatic than in asymptomatic individuals.[12,13] Receiving two mRNA vaccine doses 14–149 days before either delta or omicron infection is significantly associated with a lower viral RNA load.[13] Infections have been reported to have lower viral loads or more rapid viral declines among vaccinated individuals than among unvaccinated individuals.[14,15] Thus, there is a lower possibility for transmission in vaccinated than in unvaccinated cases of infected patients. Regarding clinical outcomes, vaccinated patients with COVID-19 have a lower risk of hospitalization or death from serious illness than infected unvaccinated individuals.[16,17] However, there are limited reports on the epidemiology of symptoms among patients with mild to moderate SARS-CoV-2 infections. Several European studies have reported a lower occurrence rate of various symptoms,[18,19] and

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a decreased number of symptoms[20] in individuals who were infected with SARS-CoV-2 after vaccination. However, the extent of this phenomenon has not been well documented in Asian countries, including Japan.

In this study, we compared the symptoms between adult COVID-19 patients who had or had not received COVID-19 vaccination.

Materials and methods

Study design and participants

This cross-sectional study among adults infected with SARS-CoV-2 used data from a case-control study. The objective of the latter was to evaluate vaccine effectiveness against SARS-CoV-2 infection and COVID-19-related hospitalization in Japan between June 4 and September 26, 2021, when the alpha and delta variants were dominant.[21] We recruited the participants at 2 weeks after introducing the COVID-19 vaccine to each age group. Cases included symptomatic or asymptomatic patients infected with SARS-CoV-2 (≥16 years of age) who were diagnosed using a PCR test undertaken at hospitals or diagnosed by PCR at public health centers as part of active surveillance for all close-contact subjects. Hospital or public health center staff informed patients of the study purpose and the conditions of cooperation in the study. If patients agreed to participate in this study, the research administration office telephoned to explain the details of the cooperation and sent them the study documents and questionnaire. The study protocol was approved by the Ethics Committee of Saga University (approval nos: R2–39 and R3–28). Due to the utilization of data from a previously published case-control study, we did not conduct a sample size calculation for this study.

Data collection

Participants were asked to answer a self-administered questionnaire when their symptoms improved or when the period of isolation was over, and to return it to the administrative office by post-mail. In Japan, patients infected with SARS-CoV-2 had to be admitted to a hospital or isolated in a home or hotel for 14 days during this study period.[22] If participants did not return the questionnaire, the administration office would send a reminder letter. Participation in the survey was decided by the patient of their own free will, and consent was considered to have been given when the patient completed and returned the questionnaire. The details of the questionnaire have been reported elsewhere;[21] it included demographic characteristics, comorbidities, lifestyle, family members, personal protective health behaviors and measures, and vaccination status. Vaccinated individuals responded to a questionnaire regarding the vaccine used (Pfizer-BioNTech: BNT162b2 or Moderna: mRNA-1273), lot number, number of doses, and date of vaccination, based on their vaccination certificate. We collected information on symptoms they had experienced, including fever (temperature of 37.5 degrees Celsius or higher), fatigue, cough, loss of taste or smell, headache, unusual muscle pains, runny nose, diarrhea, shortness of breath, insomnia, dry eyes and mouth, chest pain, hair loss, and difficulties with memory. Patients infected with SARS-CoV-2 chose an answer for each symptom from the following: "never: never appeared," "past: previously present but currently absent," or "current: currently present."

Definitions and outcomes

Patients infected with SARS-CoV-2 who selected "past" or "current" for at least one symptom were defined as symptomatic, while those who selected "never" for all symptoms were defined as asymptomatic. The outcomes assessed in this study included the presence of any COVID-19 symptom (symptomatic), as well as specific symptoms and the number of symptoms experienced (0–14 symptoms).

Statistical analysis

Characteristics of participants according to vaccination status and symptomatic status were compared using the chi-squared test or Fisher's exact test. Multivariable logistic regression models were used to calculate odds ratios (ORs) with 95% confidence intervals (CIs) of vaccine doses against each symptom and number of symptoms. The selection of covariates was based on their univariate associations with vaccination dose and symptomatic status. Covariates that were associated with both vaccination dose and symptomatic status were considered as potential confounders and were adjusted for in the analysis. We employed age (in 10-year intervals) as an adjusted covariate. Two-sided 95% CIs for ORs that did not include 1.0 were statistically significant. The level of significance was set at $P < .05$. All analyses were conducted using SAS software (ver. 9.4 for Windows; SAS Institute, Cary, NC, USA).

Results

Among 612 potential cases who were PCR-diagnosed as SARS-CoV-2, 398 (65%) were enrolled (male: 208, female: 190; mean age: 41.7 ± 14.7 years) for this analysis. Among the cases, 372 patients (93.5%) were symptomatic, while 26 (6.5%) were asymptomatic. The mean duration between the PCR test date and when patients answered the questionnaire was 26.9 days (standard deviation [SD] was 8.4 days).

Tables 1 and 2 present the characteristics of the study participants categorized by vaccine status and symptomatic status, respectively. Vaccination status was significantly associated with study area, age group, diagnosed period, comorbidity, as well as certain protective health behaviors, including maintaining a distance of over 1.5 meters during contact and indoor gatherings involving five or more people (Table 1). While symptomatic patients were significantly less likely than asymptomatic patients to have vaccine doses and report a current drinking habit. At the same time, they were significantly more likely than asymptomatic patients to be 20–49-year-old and live with a family member who commuted to and from work or school (Table 2). Based on these findings, it was observed that age could potentially act as a confounding factor in the relationship between vaccination status and symptomatic status.

Figure 1 shows self-reported symptoms according to the duration of days between the PCR test date and when patients answered the questionnaire within 7 days, 8–28 days, and >28

Table 1. Characteristics of the study participants according to vaccination doses ($n = 398$).

		Vaccination dose						
		0 ($n = 286$)		1 ($n = 66$)		2 ($n = 46$)		
		n	%	n	%	n	%	*P*-values
Sex	Women	138	48.3	28	42.4	25	54.3	.75
Area	Fukuoka city	282	98.6	57	86.4	42	91.3	<.001
Age group	16–19	21	7.3	1	1.5	0	0.0	<.001
	20–29	54	18.9	9	13.6	5	10.9	
	30–39	74	25.9	7	10.6	7	15.2	
	40–49	74	25.9	10	15.2	9	19.6	
	50–59	44	15.4	25	37.9	10	21.7	
	60–69	14	4.9	8	12.1	8	17.4	
	70-	5	1.7	6	9.1	7	15.2	
PCR test	June	1	0.3	2	3.0	0	0.0	<.01
	July	35	12.2	19	28.8	7	15.2	
	August	241	84.3	41	62.1	36	78.3	
	September	9	3.1	4	6.1	3	6.5	
Any comorbidity		53	18.5	21	31.8	22	47.8	<.001
Protective health behaviour								
	Wear a mask during contact with anyone	271	94.8	64	97.0	45	97.8	.53
	Wash hands for over 20 s each time	166	58.0	45	68.2	31	67.4	.19
	Use a hand sanitizer	256	89.5	59	89.4	43	93.5	.70
	Keep over 1.5 m during contact with anyone	225	78.7	60	90.9	40	87.0	<.01
	Regular ventilation and disinfection	233	81.5	56	84.8	37	80.4	.78
	Dinner for 5 or more people	14	4.9	8	12.1	0	0.0	.02
	Obtain information on COVID-19 regularly	229	80.1	56	84.8	42	91.3	.15
Lifestyle	Current smoking	77	26.9	14	21.2	11	23.9	.76
	Current alcohol drinking	152	53.1	34	51.5	33	71.7	.18
Live in a single-family home		199	69.6	36	54.5	25	54.3	.07
I commute to work or school		225	78.7	53	80.3	37	80.4	.93
Family members commute to work or school		210	73.4	45	68.2	30	65.2	.36

Data were analyzed using a Chi-square test.

Table 2. Characteristics of the study participants according to symptomatic or asymptomatic SARS-COV2 infections ($n = 398$).

		Symptomatic case ($n = 372$)		Asymptomatic case ($n = 26$)		
		n	%	n	%	*P*-value
Vaccinated dose	0	273	73.4	13	50.0	<.01
	1	63	16.9	3	11.5	
	2	36	9.7	10	38.5	
Sex	Female	179	48.1	12	46.2	.85
Area	Fukuoka city	355	95.4	26	100.0	.31
Age group	16–19	21	5.6	1	3.8	.04
	20–29	65	17.5	3	11.5	
	30–39	83	22.3	5	19.2	
	40–49	89	23.9	4	15.4	
	50–59	72	19.4	7	26.9	
	60–69	28	7.5	2	7.7	
	70–	14	3.8	4	15.4	
PCR test	June	3	0.8	0	0.0	.55
	July	56	15.1	5	19.2	
	August	300	80.6	18	69.2	
	September	13	3.5	3	11.5	
Any comorbidity		88	23.7	8	30.8	.41
Protective health behavior						
Wear a mask during contact with anyone		356	95.7	24	92.3	.42
Wash hands for over 20 s each time		225	60.5	17	65.4	.68
Use a hand sanitizer		335	90.1	23	88.5	.24
Keep over 1.5 m during contact with anyone		304	81.7	21	80.8	.20
Regular ventilation and disinfection		305	82.0	21	80.8	.20
Dinner for five or more people		22	5.9	0	0.0	.22
Obtain information on COVID-19 regularly		307	82.5	20	76.9	.15
Lifestyle	Current smoking	96	25.8	6	23.1	.16
	Current alcohol drinking	200	53.8	19	73.1	<.001
Live in a single-family home		246	66.1	14	53.8	.13
I commute to work or school		294	79.0	21	80.8	.20
Family members commute to work or school		273	73.4	12	46.2	.02

Data were analyzed using a Chi-square test or Fisher's exact test.

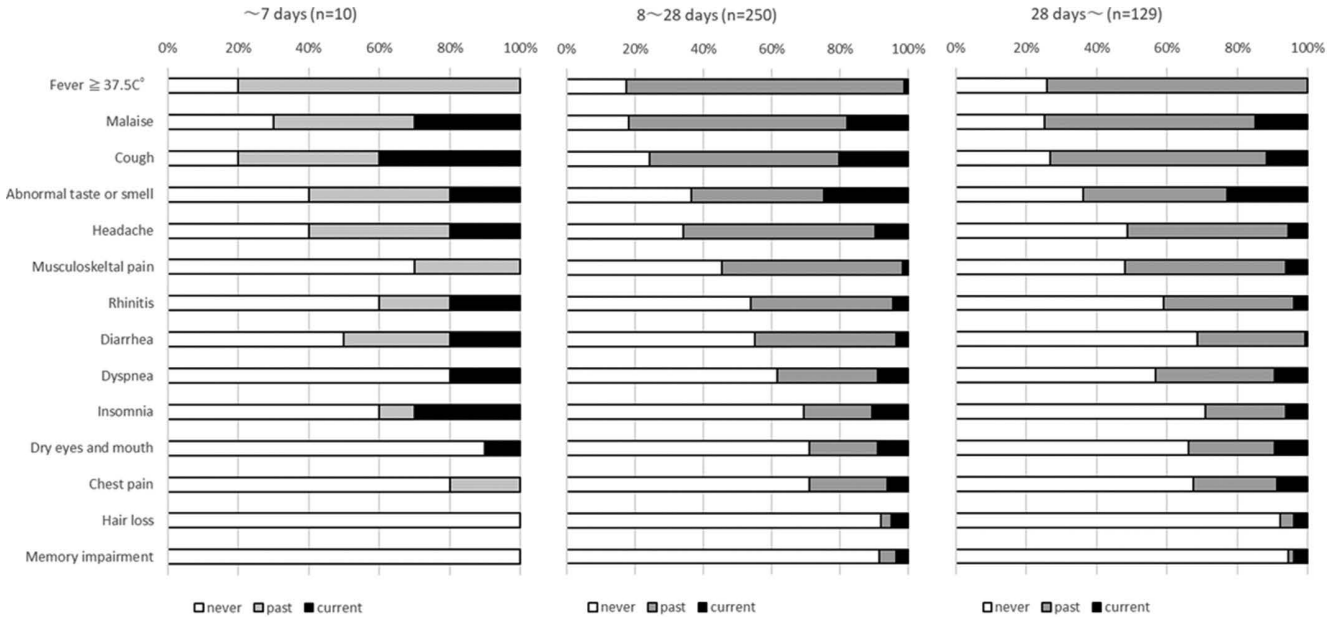

Figure 1. Self-reported symptoms according to days between diagnosis and reported date among SARS-CoV-2-infected cases ($n = 398$).

days. Fever was the most common symptom but disappeared faster than the other symptoms. Fatigue, cough, and headache were common symptoms that decreased with time, but some continued for >1 month. Although most symptoms decreased, the proportion of patients with loss of taste or smell was not diminished. Hair loss and brain fog appeared at 8–28 days after diagnosis, although their proportions were small.

Table 3 shows the association between vaccination doses and self-reported symptoms of SARS-CoV-2 infection. Patients with COVID-19 who had a fever, fatigue, loss of taste or smell, headache, unusual muscle pains, diarrhea, shortness of breath, insomnia, and dry eyes and mouth were significantly less likely to have two doses of the COVID-19 vaccine. The adjusted odds ratios (aORs) of two vaccination doses were detected for almost all symptoms, but not a runny nose. Compared to those in unvaccinated patients, the adjusted aORs of post-vaccination infections were approximately 0.2 against fatigue and dry eyes and mouth; approximately 0.3 against fever and insomnia; and approximately 0.4 against shortness of breath, unusual muscle pain and loss of taste or smell. Compared with the unvaccinated patients, patients vaccinated with two doses showed lower aORs against any symptoms. This association was robust for patients with more than four symptoms.

Figure 2a shows the distribution of the number of self-reported symptoms among patients infected with SARS-CoV-2. Approximately half of patients experienced six to nine symptoms, and approximately 10% of patients infected with SARS-CoV-2 experienced > 10 symptoms. The proportion of vaccinated patients decreased as the number of symptoms increased (Figure 2b).

Discussion

The major findings of this study indicate that post-vaccination infections after two doses of the mRNA COVID-19 vaccine showed milder and fewer symptoms compared to infections in unvaccinated individuals during Japan's alpha and delta variant epidemics. These findings highlight the benefits of COVID-19 vaccination in reducing the severity of symptoms. Specifically, post-vaccination infections were less likely to show symptoms, such as fatigue, dry eyes and mouth, insomnia, fever, shortness of breath, unusual muscle pains, and loss of taste or smell, than infections in unvaccinated individuals. Furthermore, post-vaccination infections were associated with a lesser total number of symptoms than in unvaccinated patients.

These findings align with previous studies that have reported a significantly lower risk of symptomatic infection with two doses of mRNA vaccine compared to being unvaccinated.[18–20] Antonelli et al. found, in a study based in the UK, that post-vaccination SARS-CoV-2 infection was associated with reduced odds of hospitalization or having more than five symptoms in the first week of illness compared with unvaccinated infection.[20] They also reported a lower frequency of almost all symptoms in post-vaccination infection compared to unvaccinated infection. Our study's findings align with Antonelli et al.'s results, showing similar odds ratios for symptoms such as fever, loss of smell, fatigue, and more than five symptoms.

The time between when the vaccine was received and the diagnosis of COVID-19 may have influenced the presence of symptoms. We performed a sensitivity analysis, considering a buffer period between vaccination and diagnosis (Supplemental Table S1). While we acknowledge that the power in our study may have been insufficient to detect statistical significance, we consistently observed higher aORs for any symptom in individuals who received two vaccine doses compared to those who received only one dose. These findings suggest a potential trend toward a stronger protective effect with the completion of the two-dose vaccination regimen. Further investigations with larger sample sizes are necessary to delve deeper into this observation.

Table 3. Age adjusted odds ratio (aOR) of vaccine doses against COVID-19 symptoms among SARS-CoV-2 infected cases ($n = 398$).

	All cases ($n = 398$)		Vaccination dose														
			0 ($n = 286$)			1 ($n = 66$)				2 ($n = 46$)							
	n	%	n	aOR	(95%CI)	n	crude OR	(95%CI)	aOR*	(95%CI)	n	crude OR	(95%CI)	aOR*	(95%CI)	$P_{\text{for trend}}$ for crudeOR	$P_{\text{for trend}}$ for aOR
Fever ≧37.5C°	312	78	236	1	ref.	52	0.79	(0.41–1.53)	1.13	(0.54–2.37)	24	0.23	(0.12–0.45)	0.31	(0.15–0.63)	<.01	<.01
Fatigue	312	78	244	1	ref.	46	0.4	(0.21–0.74)	0.45	(0.23–0.89)	22	0.16	(0.08–0.31)	0.18	(0.09–0.38)	<.01	<.01
Cough	296	74	218	1	ref.	47	0.77	(0.42–1.40)	0.78	(0.41–1.48)	31	0.65	(0.33–1.27)	0.67	(0.32–1.38)	.20	.23
Loss of taste or smell	250	63	198	1	ref.	33	0.44	(0.26–0.77)	0.59	(0.33–1.05)	19	0.31	(0.17–0.59)	0.44	(0.22–0.87)	<.01	.01
Headache	238	60	183	1	ref.	35	0.64	(0.37–1.09)	0.78	(0.44–1.40)	20	0.43	(0.23–0.81)	0.57	(0.29–1.11)	<.01	.09
Unusual muscle pains	211	53	168	1	ref.	29	0.55	(0.32–0.95)	0.71	(0.39–1.28)	14	0.31	(0.16–0.60)	0.40	(0.19–0.82)	<.01	.01
Runny nose	173	43	125	1	ref.	29	1.01	(0.59–1.73)	1.29	(0.72–2.31)	19	0.91	(0.48–1.71)	1.13	(0.58–2.22)	.81	.54
Diarrhea	159	40	123	1	ref.	24	0.76	(0.44–1.32)	0.72	(0.40–1.30)	12	0.47	(0.23–0.94)	0.48	(0.23–1.00)	.03	.04
Shortness of breath	156	39	124	1	ref.	22	0.65	(0.37–1.15)	0.63	(0.34–1.14)	10	0.36	(0.17–0.76)	0.36	(0.16–0.76)	<.01	<.01
Insomnia	118	30	93	1	ref.	18	0.78	(0.43–1.41)	0.68	(0.36–1.28)	7	0.37	(0.16–0.86)	0.33	(0.14–0.80)	.02	.01
Dry eyes and mouth	118	30	94	1	ref.	19	0.83	(0.46–4.49)	0.71	(0.38–1.32)	5	0.25	(0.10–0.65)	0.22	(0.08–0.59)	<.01	<.01
Chest pain	116	29	94	1	ref.	14	0.55	(0.29–1.04)	0.53	(0.27–1.05)	8	0.43	(0.19–0.96)	0.47	(0.21–1.09)	.01	.03
Hair loss	30	7.5	25	1	ref.	3	0.5	(0.15–1.70)	0.78	(0.22–2.83)	2	0.48	(0.11–2.08)	0.70	(0.15–3.26)	.18	.58
Difficulties with memory	28	7	20	1	ref.	7	1.58	(0.64–3.90)	2.07	(0.78–5.49)	1	0.30	(0.04–2.26)	0.36	(0.05–2.88)	.55	.85
Any symptoms	372	93	273	1	ref.	63	1	(0.28–3.61)	1.28	(0.33–4.92)	36	0.17	(0.07–0.42)	0.21	(0.08–0.56)	<.01	<.01
Number of symptom																	
1〜3	58	15	28	1	ref.	17	2.63	(0.65–10.6)	3.57	(0.78–16.3)	13	0.6	(0.21–1.73)	0.79	(0.23–2.72)	.47	.750
4〜6	110	28	85	1	ref.	16	0.82	(0.21–3.19)	1.01	(0.23–4.56)	9	0.14	(0.05–0.40)	0.14	(0.05–0.45)	<.01	<.01
7〜9	142	36	108	1	ref.	23	0.92	(0.24–3.50)	1.56	(0.30–8.13)	11	0.13	(0.05–0.37)	0.14	(0.04–0.44)	<.01	<.01
10〜	62	16	52	1	ref.	7	0.49	(0.11–2.21)	0.80	(0.13–5.00)	3	0.06	(0.02–0.27)	0.08	(0.02–0.37)	<.01	<.01

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019; aOR, age adjusted odds ratio; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
*Adjusted for age (in 10-year intervals).

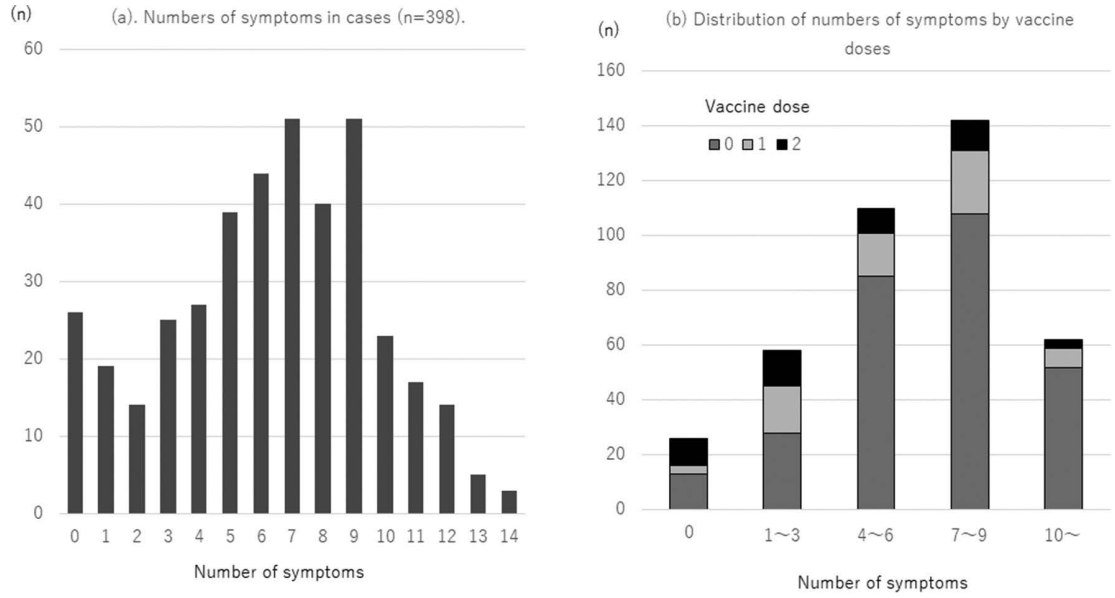

Figure 2. Distributions of numbers of self-reported symptoms (a) according to vaccination dose among SARS-CoV-2-infected cases ($n = 398$).

Interestingly, our study showed smaller ORs (approximately 0.1) for more than five symptoms compared to the UK study, which reported an odds ratio of 0.51.[20] The difference may be partly explained by the shorter duration between vaccination and diagnosis in our study, as the vaccine-induced antibody levels peak around 3–4 weeks after the second dose and gradually decrease.[23] Additionally, vaccine effectiveness against symptomatic COVID-19 infection peaks 1 month after the final dose and then decreases over time.[8] Thus, a shorter duration since the last vaccination in our study may have influenced the odds ratios for patients with more than five symptoms. However, due to the shorter period after introducing COVID-19 vaccine to Japanese population and limited sample size, we were unable to assess the long-term effects (Supplemental Table S1). Notably, patients with COVID-19 who experience more than five symptoms during the first week of illness have a higher risk of developing long COVID-19.[24] Although the mechanism behind long COVID remains poorly understood, the possible roles of persistent viral reservoirs and circulating virus fragments are suspected.[25]

Although a systematic review and meta-analysis reported that individuals with advanced age are more likely to develop severe COVID-19 symptoms,[26] few studies have evaluated whether age is associated with being symptomatic or not.[27,28] Regarding age, we initially observed a decreasing proportion of symptomatic cases with increasing age (Table 2, Supplemental Table S2). However, after adjusting for vaccination status, this association was no longer significant (Supplemental Table S2). This discrepancy may be related to the higher vaccination coverage in the older population during our study period in Japan, potentially contributing to a higher frequency of symptomatic patients in the middle age group.

Vaccine-induced immunity protects against infection, as well as blocks disease progression.[29] However, the mechanism through which various symptoms present a higher dependency on previous vaccination has not been fully identified. The symptoms may be influenced by several factors other than vaccine status, such as virus variants and host status. The strengths of our study include active surveillance of all close contacts, capturing information on both symptomatic and asymptomatic patients, and collecting clinical symptoms from various intervals between diagnosis and reported days. However, our study had several limitations. First, self-reporting of symptoms may introduce information bias and recall bias. Patients were given a questionnaire upon diagnosis and asked to complete and return the questionnaire by mail, either at the time of recovery or after the 2-week recuperation period. The questionnaire aimed to capture patients' self-reported main symptoms associated with COVID-19, allowing them to indicate whether the symptoms were currently present, previously present but currently absent, or never appeared. This approach aimed to mitigate bias in knowledge of COVID-19 symptoms between vaccinated and unvaccinated individuals. However, it is important to acknowledge that self-reporting may be influenced by patients' awareness of their vaccination status, potentially introducing bias. Additionally, collecting responses on symptom presence at the end of the recuperation period may lead to recall bias for symptoms that have already resolved, which could result in underestimation or overestimation. Second, participation bias may have existed. Although we invited all PCR-diagnosed patients to participate, only 65% of potential participants responded.[21] If the participation rate among severe cases was lower than that among mild-to-moderate cases, and if severe cases were less likely to be vaccinated, the effect of the COVID-19 vaccine against post-vaccination infection might have been underestimated. Third, the limited sample size made it challenging to analyze the data by study period, which would reflect virus lineage and duration after vaccination. The power to detect a statistically significant level was insufficient as mentioned earlier. Fourth, despite adjusting several relevant confounders in the statistical model, there may have been residual confounding. Fifth, we lacked information on virus lineage or viral load, which

could have influenced symptoms. Furthermore, recall bias might have occurred in self-reported symptoms. Finally, due to cross-sectional observational design of our study, it is difficult to completely eliminate the possibility of reverse causation or placebo effect. While a randomized controlled trial (RCT) could address this matter, conducting such an RCT after the approval and introduction of the COVID-19 vaccine in Japan would not have been ethical.

Conclusions

Post-vaccination infections after two doses of the mRNA COVID-19 vaccine were associated with milder symptoms compared to unvaccinated infections during Japan's alpha and delta variant epidemics. In addition, post-vaccination infections had fewer symptoms than unvaccinated infections. These results further demonstrate the benefits of choosing vaccination to prevent symptoms of COVID-19.

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Disclosure statement

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Data availability statement

The datasets generated and/or analyzed during the current study are not publicly available due to preserving participant anonymity but are available from the corresponding author on reasonable request (Megumi Hara, harameg@saga-u.ac.jp).

Institutional review board statement

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of SAGA UNIVERSITY (approval nos. R2–39 and R3–28).

Informed consent statement

Informed consent was considered to have been given when the patient completed and returned the questionnaire.

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