Preplanned Studies

A Comparison of Clinical Characteristics of Infections with SARS-CoV-2 Omicron Subvariants BF.7.14 and BA.5.2.48 — China, October–December 2022

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Summary

What is already known about this topic?

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continues to evolve, the clinical manifestations resulting from different SARS-CoV-2 variants may demonstrate significant variation.

What is added by this report?

We conducted a comparative analysis of the clinical features associated with SARS-CoV-2 Omicron subvariants BF.7.14 and BA.5.2.48 infections. The results of our study indicate that there are no substantial differences in clinical manifestations, duration of illness, healthcare-seeking behaviors, or treatment between these two subvariants.

What are the implications for public health practice?

Timely identification of alterations in the clinical spectrum is crucial for researchers and healthcare practitioners in order to enhance their comprehension of clinical manifestations, as well as the progression of SARS-CoV-2. Furthermore, this information is beneficial for policymakers in the process of revising and implementing appropriate countermeasures.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has demonstrated ongoing adaptations in humans and its infections display a wide array of clinical manifestations (*1*). Although the symptoms caused by various SARS-CoV-2 variants may be similar (*2*), certain variants have been associated with increased severity or heightened transmissibility (*3*–*4*).

According to surveillance data from the China CDC (*5*), the proportions of the Omicron subvariants BF.7.14 and BA.5.2.48 have increased since late September 2022 in China. The BF.7.14 variant has become widespread in Beijing Municipality, Tianjin Municipality, and Inner Mongolia Autonomous Region, whereas the BA.5.2.48 variant has been predominant in other provincial-level administrative divisions (PLADs). Public controversy arose if infected individuals in Beijing exhibited more severe symptoms than their counterparts in Shanghai Municipality, Guangdong Province, and other PLADs in southern China. To address these concerns, we conducted a retrospective study employing a telephone survey to examine the differences in clinical characteristics of infections with BF.7.14 and BA.5.2.48 subvariants.

In Beijing, respiratory samples from both imported and local cases have been routinely collected. These samples include nasopharyngeal swabs, oropharyngeal swabs, and sputum. The sample collection process is detailed in a previous study conducted by our team (*6*).

For this study, we randomly selected samples with sufficient viral load (*Ct* <32) collected from October to December 2022. Utilizing next-generation sequencing, we found all 527 patients were infected with the Omicron variant, with 371 and 156 individuals being infected with the BF.7.14 and BA.5.2.48 subvariants, respectively. Ethics approval for this study was granted by the Ethics Committee of the Beijing Center for Disease Prevention and Control (2021-1G-3012).

The structured questionnaire was created by public health professionals from the Beijing Center for Disease Prevention and Control, as well as clinical experts from Beijing Shijitan Hospital. This 67-question survey addressed participant demographics, coronavirus disease 2019 (COVID-19) vaccination status, comorbidities, duration of illness, clinical manifestations, healthcare-seeking behaviors, and treatment.

A third-party survey company executed the telephone survey which took place between March 2 and 6, 2023. The survey commenced with a brief introduction to the study, and questionnaires were completed by individuals who provided verbal consent to participate. Comorbidities and symptoms were discussed in-depth, with explanations given as

necessary. The estimated time for completion ranged from 7 to 15 minutes.

Responses were gathered and entered into a Word Processing System (WPS, version13.33.0; Kingsoft, Beijing, China) spreadsheet. Data analysis was conducted using SPSS software (version 19.0; IBM, Armonk, NY, USA). Descriptive statistics, including frequencies and proportions, were computed for each item in the questionnaire. Median values with interquartile range (*IQR*) and means with standard deviation were reported. Student's *t*-tests were utilized to compare continuous measures. For dichotomous measures, chi-square (χ^2) tests were carried out, and contingency corrections or Fisher's exact tests were employed when data did not fulfill the standard χ^2 test criteria. Mann-Whitney *U* tests were applied to compare median values. A probability value of $P \leq 0.05$ was considered statistically significant, and all statistical tests were two-sided.

Among the 527 patients who were contacted via telephone, a total of 339 (64.3%) responded and completed the questionnaire. The response rate for the BF.7.14 infection group was 65.2% (242/371), and for the BA.5.2.48 group, it was 62.2% (97/156, χ^2=0.445, P=0.505). In the case of 31 patients under 18 years of age, their parents were surveyed through phone calls as proxies for the patients themselves.

Table 1 displays the participants' background characteristics. No statistically significant differences were observed in terms of age or sex. Additionally,

TABLE 1. Background characteristics of the patients.

Characteristic	BF.7.14 infection	BA.5.2.48 infection	Statistic	*P* value
Age [years old, (M, *IQR*)]	41 (30.8–55.3)	41 (29.5–52.0)	11454.500*	0.729
Male (*n*, %)	150 (62.0)	60 (61.9)	<0.001*	0.983
BMI [kg/m², ($\bar{X}$, SD)]	24.7 (3.9)	24.5 (4.4)	−0.353†	0.724
COVID-19 vaccination (*n*, %)			0.402§	0.526
None	21 (8.9)	8 (8.3)		
1 dose	4 (1.7)	1 (1.0)		
2 doses	47 (20.0)	18 (18.8)		
≥3 doses	163 (69.4)	69 (71.9)		
Comorbidities (*n*, %)				
Hypertension	44 (18.2)	11 (11.3)	2.385*	0.123
Metabolic disorders	23 (9.5)	9 (9.3)	0.004*	0.949
Cardiovascular diseases	14 (5.8)	5 (5.2)	0.052*	0.820
Cerebrovascular diseases	7 (2.9)	1 (1.0)	0.390*	0.532
Lung diseases	8 (3.3)	3 (3.1)	<0.001§	>0.999
Tumors	3 (1.2)	2 (2.1)	0.005§	0.945
Rheumatic diseases	1 (0.4)	3 (3.1)	2.276§	0.131
Health-related behaviors				
Smoking	61 (25.2)	15 (15.5)	3.779*	0.052
Alcohol consumption	65 (26.9)	19 (19.6)	1.965*	0.161
Routine exercise	136 (56.2)	48 (49.5)	1.258*	0.262
Education level (*n*, %)			4.661*	0.198
Junior high school or below	97 (40.1)	31 (32.0)		
Senior high school (or equivalent)	63 (26.0)	21 (21.6)		
Undergraduate	70 (28.9)	38 (39.2)		
Postgraduate	12 (5.0)	7 (7.2)		

Abbreviation: M=median; *IQR*=interquartile range; BMI=body mass index (only applied to ≥18 years old); $\bar{X}$=average; SD=standard deviation; COVID-19=coronavirus disease 2019.
* χ^2 test.
† Student's *t*-test.
§ χ^2 test with contingency correction.

there was no significant difference in body mass index (BMI, weight/height^2) calculated for adults (i.e., age ≥ 18 years). Approximately 70% of the patients reported having received three or more doses of the COVID-19 vaccine, though vaccination completion rates did not significantly impact infection rates.

The three most common comorbidities in both the BF.7.14 and BA.5.2.48 infection groups were hypertension (18.2%, 44/242 *vs.* 11.3%, 11/97), metabolic disorders (9.5%, 23/242 *vs.* 9.3%, 9/97), and cardiovascular diseases (5.8%, 14/242 *vs.* 5.2%, 5/97), with no significant differences observed between the groups. Health-related behaviors such as smoking, alcohol consumption, and regular exercise showed no statistically significant differences between the two groups. Furthermore, the difference in education levels between the groups was not statistically significant.

Table 2 presents the patients' clinical characteristics. All manifestations were thoroughly examined, and no significant differences in symptoms between the groups were found, with the exception of fever. More than

TABLE 2. Clinical characteristics of the patients.

Characteristic	BF.7.14 infection	BA.5.2.48 infection	Statistic	*P* value
Symptoms (*n*, %)				
Fever			12.273*	0.007
No fever (<37.3 °C)	111 (35.0)	25 (27.8)		
Low-grade fever (37.3 °C–38.0 °C)	68 (21.5)	14 (15.6)		
Middle-grade fever (38.1 °C–39.0 °C)	96 (30.3)	31 (34.4)		
High fever (≥39.1 °C)	42 (13.2)	20 (22.2)		
Cough	128 (52.9)	46 (47.4)	0.829*	0.362
Swallowing difficulty	95 (39.6)	28 (28.9)	3.423*	0.064
Fatigue or muscle weakness	70 (29.2)	23 (23.7)	1.029*	0.310
Muscle pain	58 (24.2)	18 (18.6)	1.245*	0.265
Difficulty in movement	40 (19.8)	16 (19.0)	0.021*	0.884
Headache	39 (16.3)	13 (13.4)	0.448*	0.503
Taste or smell disorder	38 (15.9)	11 (11.3)	1.151*	0.283
Sleep disorder	39 (16.3)	10 (10.3)	1.962*	0.161
Joint pain	30 (12.6)	11 (11.3)	0.095*	0.758
Vomiting or diarrhea	23 (9.6)	10 (10.3)	0.041*	0.839
Breathing difficulties	31 (12.9)	6 (6.2)	3.202*	0.074
Cognitive impairment	20 (8.3)	9 (9.3)	0.078*	0.779
Dizziness	17 (7.1)	6 (6.2)	0.093*	0.760
Personality change	22 (9.2)	3 (3.1)	3.711*	0.054
Chest pain	14 (5.8)	4 (4.1)	0.399*	0.527
Hair loss	7 (2.9)	1 (1.0)	0.402†	0.526
Conjunctivitis	4 (1.7)	0 (0.0)	0.524†	0.469
Skin rash	3 (1.3)	0 (0.0)	–§	0.560
Number of symptoms			2.839*	0.242
None	40 (16.5)	13 (13.4)		
1–3 symptoms	98 (40.5)	49 (50.5)		
≥4 symptoms	104 (43.0)	35 (36.1)		
Length of illness [day, (M, *IQR*)]	10.0 (5.0–18.5)	7.5 (3.0–26.8)	8656.000¶	0.619

Abbreviation: M=median; *IQR*=interquartile range.
* χ^2 test.
† χ^2 test with contingency correction.
§ Fisher exact test.
¶ Mann-Whitney *U* test.

60% of participants reported fever measured by a body temperature of ≥37.3 °C. The research classified fever into four categories: no fever (<37.3 °C), low-grade fever (37.3 °C–38.0 °C), middle-grade fever (38.1 °C–39.0 °C), and high fever (≥39.1 °C). A significant difference was discovered among the fever categories (χ^2=12.273, *P*=0.007). Patients infected with BA.5.2.48 had a higher prevalence of high fever compared to those infected with BF.7.14 (22.2%, 20 cases *vs*. 9.7%, 22 cases).

Cough was exhibited by approximately half of the participants in both the BF.7.14 (52.9%, 128/242) and BA.5.2.48 (47.4%, 46/97) groups. Additionally, 39.6% (95/240) and 28.9% (28/97) of patients in the BF.7.14 and BA.5.2.48 infection groups, respectively, reported a sore throat or difficulty swallowing. These symptoms ranked among the top three, while 16.5% (40/242) of individuals infected with BF.7.14 and 13.4% (13/97) of those infected with BA.5.2.48 remained asymptomatic. No significant difference in symptoms was noted between the groups. Participants infected with BF.7.14 experienced symptoms for a median duration of 10.0 days (*IQR*: 5.0–18.5), while those infected with BA.5.2.48 reported symptom relief after a median duration of 7.5 days (*IQR*: 3.0–26.8).

The healthcare-seeking behaviors of participants are depicted in Table 3. The majority of the BF.7.14 (76.9%, 186/242) and BA.5.2.48 (77.3%, 75/97) infected participants were admitted to hospitals or Fangcang alternative care sites. The median hospital stay for both groups was 12.0 days. A small percentage of patients infected with BF.7.14 (4.5%, 11/242) and BA.5.2.48 (1.0%, 1/97) required admission to intensive care units for further treatment.

DISCUSSION

To the best of our knowledge, this study is the first to compare the clinical characteristics of infections with SARS-CoV-2 Omicron subvariants BF.7.14 and BA.5.2.48, addressing public concerns about disparities in clinical severity. The results indicate that the baseline characteristics of the two infection groups were comparable, with no significant differences found in age, sex, BMI, vaccination status, comorbidities, health-related behaviors, or education levels. Furthermore, our findings suggest no significant differences in clinical manifestations, duration of illness, healthcare-seeking behaviors, or treatment.

In this study, the researchers investigated a broad spectrum of clinical manifestations, encompassing both physical and mental symptoms, as documented in previous studies (*1*,*7*). However, no noteworthy differences were observed across the groups, with the exception of fever severity. The duration of hospitalization for patients in this study was considerably shorter than that reported in an Italian study, where the median hospital stay was 30 days (*IQR*: 12–80) (*8*). This outcome may be attributed to the dynamic zero-COVID-19 policy implemented in Beijing, which mandated medical isolation for infected individuals in order to mitigate community transmission. Consequently, several patients with mild disease severity were admitted to hospitals.

The BA.5.2.48 and BF.7.14 subvariants exhibited 59 and 57 high-frequency non-synonymous mutations, respectively, both originating from the BA.5 lineage of the Omicron variant (*9*). The spike protein, situated on the surface of the SARS-CoV-2 virus, plays a crucial role in virus attachment and entry into host cells (*10*). Numerous mutations within the spike protein have been directly linked to infectivity, transmissibility, and immune evasion capabilities (*11*). Notably, the BF.7.14 and BA.5.2.48 subvariants shared identical mutation sites in the spike protein, with the exception of R346T and C1243F. Prior research has suggested that the symptoms of BF.7 infection are analogous to those connected to infections with other Omicron subvariants (*12*).

Our study presents several limitations. First,

TABLE 3. Healthcare-seeking behaviors and treatment of the patients.

Behaviors or treatment	BF.7.14 infection	BA.5.2.48 infection	Statistic	*P* value
Outpatient treatment (*n*, %)	5 (2.1)	4 (4.1)	0.478*	0.489
Admission to hospitals or Fangcang ACS (*n*, %)	186 (76.9)	75 (77.3)	0.008†	0.928
Length of hospital stay [day, (M, *IQR*)]	12 (8.0–15.0)	12 (10.0–15.0)	8277.500§	0.745
Admission to ICU (*n*, %)	11 (4.5)	1 (1.0)	1.581†	0.209

Abbreviation: ACS=alternative care site; M=median; *IQR*=interquartile range; ICU=intensive care unit.
* χ^2 test with contingency correction;
† χ^2 test;
§ Mann-Whitney *U* test.

participants received the survey via telephone approximately four months after their infection, which may introduce recall bias. Consequently, they might not accurately remember pertinent details of their illness, resulting in potential under-reporting of manifestations. Longitudinal studies could provide valuable information for researchers and healthcare practitioners to better comprehend the clinical manifestations and evolution of SARS-CoV-2, as well as to identify changes in the clinical spectrum in a timely manner. Second, our study represents a small subset of the infected population in Beijing. Although the limited sample size might not precisely reflect the broader population, it still offers insights into the clinical manifestations caused by subvariants of SARS-CoV-2, especially considering the scarcity of evidence from previous studies.

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