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Clinical characteristics of patients infected with SARS-Cov-2 omicron in Shanghai: focusing on mild type

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Abstract: *Omicron emerged in late February in Shanghai and rapidly reached an epidemic expansion. However, clinical features of patients infected with omicron and potential risk factors of extending viral clearance was not further described in China. We conducted an observational study among patients in hospital from March 19th to April 10th2022 in Shanghai. Clinical data including demography, vaccination and symptoms were all collected through electronic questionnaire. Viral loading was evaluated by real-time PCR for nasopharyngeal swabs every other day after admission. 267 patients were included in this study and all of them were classified as mild type. The rate of vaccination against SARS-Cov-2 was 86.52% (231/267), and 133 individuals received three doses. Compared to patients vaccinated, unvaccinated participants were older ($p < 0.0001$) and had a longer period of viral clearance [14.5 days (11-17.5) vs 11 days (9-13), $p < 0.0001$] as well as length of hospital stay [17 days (13-19) vs 13 days (9-17), $p = 0.0021$]. Among the 134 symptomatic patients, female (50.75% vs 35.34%, $p = 0.0110$) and cluster cases (49.25% vs 33.83%, $p = 0.0106$) took a greater proportion. Cough [106 (79.10%)], sputum production [66(49.25%)] and sore throat [40(29.85%)] ranked top three among symptoms. The time for viral clearance was significantly longer among symptomatic individuals than asymptomatic patients [11.5 days (10-14) vs 10.5 days (8-13), $p = 0.0339$], as well as the length of hospital stay [15 days (12-17) vs 9 days (9-17), $p < 0.0001$]. In multivariate logistics regression, it showed patients vaccinated against SARS-Cov-2 was lower risk of clearing viral over 11 days (OR, 0.41; 95%CI, 0.17-0.96), but individuals with comorbidity was at increased risk of clearing viral over 11 days (OR, 2.11; 95% CI, 0.17-0.96). Individuals infected with omicron present symptoms such as cough, sputum production or sore throat. Patients with comorbidity may have a longer period of viral clearance when infected with Omicron. Receiving vaccination against SARS-Cov-2 may be helpful.*

Keywords: *omicron, symptom, vaccination, complication, viral clearance*

1. Introduction

Since December 2019, Coronaviral disease has affected our health all over the world[1] and more than 6 million people have lost their lives because of infection with severe acute respiratory syndrome coronaviral 2 (SARS-CoV-2) by far. Survivors from COVID-19 still suffer from complications associated with COVID-19 including physical and mental problem in the next two years as described in a follow-up study[2].

SARS-Cov-2 had evolved in the past two years and now the world is suffering from the fifth wave of SARS-Cov-2[3],[4], which was named as omicron by World Health Organization (WHO) and followed the variants such as alpha, beta and delta. Omicron was firstly discovered on Nov 11th 2021 in South Africa[5]

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and reported on Nov 24th [6]. This variant caused increasing cases and reached a rapid epidemic in South Africa[4]. Meanwhile it spread in more than 90 countries, demonstrating high transmission potentiality and becoming the dominant variant of SARS-Cov-2 all over the world. Different from the original sequence, omicron embraces over 30 mutations from the previous lineages[7], which results in immunity escape built by vaccine against SARS-Cov-2 [8] or preceding infection[9] and thus leads to the pandemic worldwide.

Several studies reported clinical features of patients during the omicron expansion[10-15]. In Korea, half of the 40 patients infected with omicron demonstrated mild symptoms including sore throat and fever while others were asymptomatic[10]. Symptoms of patients during the omicron epidemic varied from those during the delta prevalence [13, 16]. A prospective study in South Africa indicated the three classic COVID-19 symptoms (fever, loss of smell and persistent cough) were less commonly detected among patients infected with omicron[16]. Infection with omicron presented less severe disease among vaccinated participants in comparison with that during delta wave, as indicated by the lower rate of hospitalization, ICU admission and case fatality in previous studies[12-16].

In Shanghai, China, people faced the wave of omicron from late February 2022 and then experienced a rapid expansion[17]. Our government is making a great effort in fighting against SARS-Cov-2 omicron and holds on to the dynamic zero policy, including the health sector effort, reducing mass gather, social distance, and lockdown of district. All the effort is trying to minimize the number of infected cases and reduce the incidence of severe cases or death associated with omicron. However, clinical data of people during omicron wave was not further described in China, though there were some studies aiming to explore the potential effect of antiviral drugs among Chinse including VV116[18]. Given the outbreak of SARS-Cov-2 omicron variant in Shanghai, herein we conducted an observational study to obtain the general description among patients and tried to explore the potential factors for SARS-cov-2 omicron.

2. Methods

This was an observational study from March 19th to April 10th in 2022 in Ruijin Hospital, Shanghai China. Patients with laboratory-confirmed SARS-Cov-2 infection were recruited, and informed consents were obtained from all the patients before enrollment.

Demographic data including sex, age, disease history, symptoms, vaccination status including vaccination dose were all collected through electronic questionnaire mainly by self-report under the help of medical workers. The patient was considered as cluster-case if at least two individuals were confirmed infection with SARS-Cov-2 at the same time in the same region. Changes of symptoms during the medical inspection and isolation period were also collected.

Nasopharyngeal swabs were collected for viral loading test by real-time PCR every other day after admission. Viral were cleared if the cycle threshold (Ct) value for both ORF1ab and N gene was more than 35 for two consecutive tests with an interval of at least 24h as adopted in a previous study[18]. The duration of viral clearance was determined by the interval from the date of the first positive testing to the date of viral clearance.

Severity of SARS-Cov-2 was defined according to the Chinese Guideline for the Diagnosis and Treatment of COVID-19 Infection (the ninth version) as following:(1) Mild type. Mild clinical symptoms, without abnormal radiological findings; (2) Common type. Fever, cough, and other symptoms, manifested as pneumonia on chest computed tomography (CT); (3) Severe type. If one of the following conditions is met: respiratory distress, respiratory rate $\geq$ 30 per minute, or in resting state, finger oxygen saturation (SaO2) $\leq$ 93% at room air, or partial pressure of arterial oxygen (PaO2)/concentration of oxygen inhaled (FiO2) $\leq$300 mmHg; (4) Critical type. If one of the following conditions is met: respiratory failure occurs and mechanical ventilation is needed or shock occurs or patients with other organs dysfunction requiring ICU treatment.

3. Statistical analysis

Continuous variables were presented as median (interquartile range, IQR), and categorical variables were described as number (percentage). For comparative analysis, ANOVA or non-parametric testing was for continuous variables while chi-qua testing or Fisher's exact testing was used for categorical variables when appropriate. Odds ratio (OR) was calculated by univariate and multivariate logistics regression, which was presented with 95% confidence intervals (95% CI). A two-side p value <0.05 was

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considered as statistically significant. All the process was used by SAS software, version 9.4 (SAS Institute Inc).

4. Results

4.1. Baseline of patients recruited

Among the 269 patients were included at admission. 2 of the 269 were transferred to ICU and the remaining 267 with SpO2 > 93% were classified as mild type during the period. As shown in Table1, 152 of the patients were male with the ratio about 56.93% and most of them were younger than 65 years old. 84 patients had at least one complication, while hypertension [51(19.10%)], diabetes [18(6.74%)] and cardiovascular disease [14(5.24%)] were the most common comorbidity. None of them had cancer or received glucocorticoids. 231 of them received vaccination against SARS-Cov-2, of whom 73(27.34%) completed two doses and 133(49.81%) received the third booster dose, though the exact dose of vaccine was not available for 18 vaccinated patients. More than half of them [134(50.19%)] had symptoms onset and none of the patients received antiviral drugs. *Baseline of patients recruited See Table 1*

Table 1. Baseline of patients recruited

Data was presented as median (IQR) for continuous variables, and number (percentage) for categorical variables.

[+]18 vaccinated patients did not provide their exact dose of vaccine.

	Total
Age, years	49(33-59)
Male	152(56.93%)
BMI, kg/m^2	23.32(21.23-25.81)
Current smoker	32(11.99%)
Comorbidity	
None	183(68.54%)
Any	84(31.46%)
Hypertension	51(19.1%)
Diabetes	18(6.74%)
Cardiovascular disease	14(5.24%)
Vaccination	
No	36(13.48%)
Yes	231(86.52%)
Vaccination dose[+]	
1	7(2.62%)
2	73(27.34%)
3	133(49.81%)
Cluster case	111(41.57%)
Symptom	
None	133(49.81%)
Any	134(50.19%)
Duration of viral clearance, days	11(9-13)
Length of stay, days	14(9-17)

4.2. Comparison between patients vaccinated and unvaccinated

Vaccination played an important role in fighting against SARS-Cov-2. As described in Table 2, patients in the unvaccinated group were older compared to those vaccinated individuals [48(32-56) vs 59(45-73), $p < 0.0001$], and patients elder than 65-year took a greater ratio in the unvaccinated group ($p < 0.0001$). Compared to those vaccinated, the ratio of patients with comorbidity was higher among people unvaccinated (66.67% vs 25.97%, $p < 0.0001$). Duration of both viral clearance and hospital stay was longer among those not receiving vaccination than participants vaccinated [14.5 days (11-17.5) vs 11 days (9-13), $p < 0.0001$; 17 days (13-19) vs 13 days (9-17), $p = 0.0021$; respectively].

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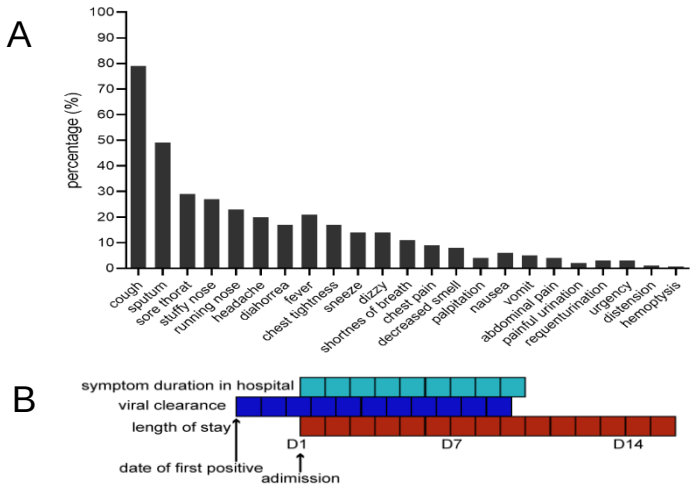
Table 2. Comparison between patients unvaccinated or vaccinated

	Unvaccinated N = 36	Vaccinated N = 231	*p*
Age, years	59(45-73)	48(32-56)	<**0.0001**
Male	16(44.44%)	135(58.44%)	0.115
BMI, kg/m^2	22.43(20.95-24.82)	23.44(21.39-25.91)	ns
Current smoker	4(11.11%)	28(12.12%)	0.8622
Comorbidity			<**0.0001**
None	12(33.33%)	171(74.03%)	
Any	24(66.67%)	60(25.97%)	
Hypertension	16(44.44%)	35(15.15%)	<**0.0001**
Diabetes	7(19.44%)	11(4.76%)	**0.0048**
Cardiovascular disease	9(25%)	5(2.16%)	<**0.0001**
Cluster case	17(47.22%)	94(40.69%)	0.4597
Duration of viral clearance, days	14.5(11-17.5)	11(9-13)	<**0.0001**
Length of stay, days	17(13-19)	13(9-17)	**0.0021**

4.3. Comparison between patients asymptomatic and symptomatic

As mentioned above, 134 patients had symptoms when infected with omicron. Distribution of symptoms was described in Figure 1A, cough [106 (79.10%)], sputum production [66(49.25%)] and sore throat [40(29.85%)] ranked the top three among the 23 symptoms in total. Among these symptomatic patients, disease course was presented as Figure 1B including the duration of symptoms after admission and the period to clear viral since the first positive day of SARS-Cov-2, as well as the length of hospital stay during medical inspection.



A. Distribution of symptoms among patients with symptoms; B. Disease course of patients with symptom onset.

Figure 1. Distribution of symptoms and disease course among symptomatic patients

Potential difference was also investigated between individuals with symptoms and those asymptomatic as shown in Table 3. No difference was detected for age, BMI, smoking status, comorbidity, or vaccination. Compared to those asymptomatic, female took a greater proportion among those with symptoms (50.75% vs 35.34%, p = 0.0110). Among those symptomatic patients, there were more cluster cases than those without symptoms (49.25% vs 33.83%, p = 0.0106). It took longer time to clear viral for symptomatic patients than those asymptomatic [11.50 days (10-14) vs 10.50 days (8-13), p = 0.0339]. What's more, the length of stay in hospital was also significantly longer for symptomatic patients compared to asymptomatic individuals [15 days (12-17) vs 9 days (9-17), p < 0.0001].

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Table 3. Comparison between patients with and without symptoms

	Asymptomatic N = 133	Symptomatic N = 134	*p*
Age, years	51(37-62)	48(32-55)	ns
Male	86(64.66%)	66(49.25%)	**0.011**
BMI, kg/m^2	23.44(21.39-25.71)	23.13(21.13-25.81)	ns
Current smoker	20(15.04%)	12(8.96%)	0.126
Comorbidity			0.2018
None	96(72.18%)	87(64.93%)	
Any	37(27.82%)	47(35.07%)	
Hypertension	26(19.55%)	25(18.66%)	0.8529
Diabetes	11(8.27%)	7(5.22%)	0.3208
Cardiovascular disease	7(5.26%)	7(5.23%)	0.9885
Vaccination			0.1587
No	14(10.53%)	22(16.42%)	
Yes	119(89.47%)	112(83.58%)	
Cluster case	45(33.83%)	66(49.25%)	**0.0106**
Duration of viral clearance, days	11(8-13)	11(10-14)	**0.0339**
Length of stay, days	9(9-17)	15(12-17)	**<0.0001**

4.4. Comparison between patients clearing viral within or over 11 days

It took about 11 days (IQR, 9-13) to clear viral for all the patients. We further divided them into two groups: one group clearing viral within 11 days and the other group clearing virus over 11 days. No difference was detected for sex, ratio of cluster cases or BMI between the two groups as presented in Table 4. Compared to individuals clearing viral within 11 days, age was older among those with the virus clearance duration over 11 days (p = 0.0047). The percentage of participants with complication was significantly higher among those clearing viral over 11days than those clearing viral within 11 days (p = 0.001), and the same trend was also detected for hypertension (p = 0.0155), but not for diabetes (p = 0.1378). A lower rate of vaccination was detected in the group with viral clearance duration over 11 days than that of patients clearing virus within 11 days (p = 0.0037) while the length of hospital stay was also longer for patients clearing viral over 11 days (p <0.0001).

Table 4. Comparison between patients clearing viral within or over 11 days

	Within 11 days N = 119	Over 11 days N = 148	*p*
Age, years	44(30-55)	51(36.5-61)	0.0047
Male	64(53.78%)	87(58.78%)	0.4124
BMI, kg/m^2	23.03(21.48-25.64)	23.44(21.16-25.89)	ns
Current smoker	16(13.45%)	16(10.81%)	0.51
Comorbidity			0.001
None	94(78.99%)	89(60.14%)	
Any	25(21.01%)	59(39.86%)	
Hypertension	15(12.61%)	36(24.32%)	0.0155
Diabetes	5(4.2%)	13(8.78%)	0.1378
Cardiovascular disease	3(2.52%)	11(7.43%)	0.1095
Vaccination			0.0037
None	8(6.72%)	28(18.92%)	
Any	111(93.28%)	120(81.08%)	
Cluster case	42(35.29%)	60(40.54%)	0.0619
Length of stay, days	10(9-15)	16(12.5-19)	<.0001

4.5. Risk factors contributing to viral clearance

The time window of viral clearance is an important indicator during outbreak of infectious disease. We further explored the potential factor may have an impact on the course of viral clearance as showing in Figure 2. In univariate logistic regression, age (OR, 1.43; 95%CI, 1.04-1.96), complication (OR, 2.49; 95%CI, 1.44-4.32) and hypertension (OR, 2.23; 95%CI, 1.15-4.31) increased the risk of clearing virus over 11 days, while receiving vaccination favored a shorter duration of virus clearance (OR, 0.31; 95%CI,

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0.14-0.71). In multivariate logistic regression, complication (OR, 2.11; 95%CI, 1.19-3.74) and vaccination (OR, 0.41; 95%CI, 0.17-0.96) still had an impact on the duration of viral clearance.

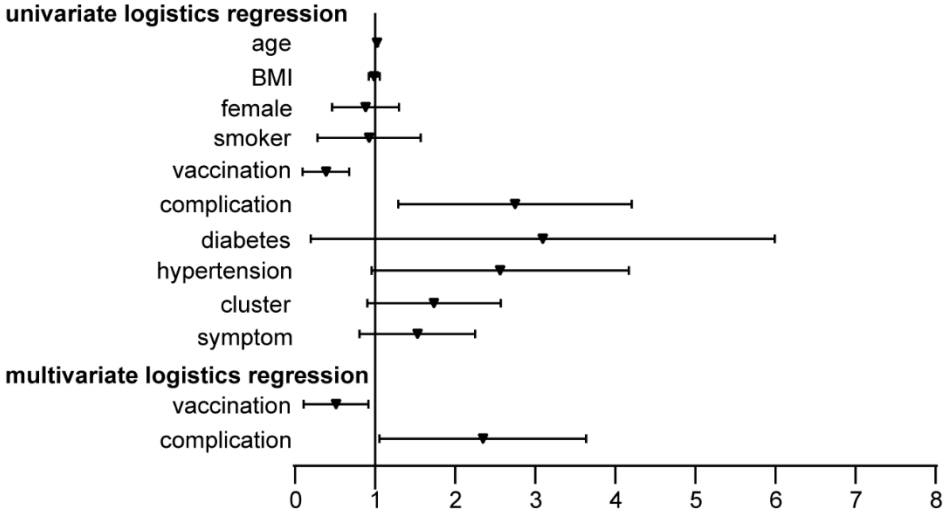

Figure 2. Risk factor for viral clearance

Risk factor for viral clearance was calculated by univariate and multivariate logistics regression. Data was presented as OR with 95% CI in forest plot.

5. Discussion

In late February 2022, Shanghai faced sharply increased cases during the omicron prevalence, which reached an epidemic in March, and the newly infected cases were peaking at 27719 on April 13rd [17]. Clinical feature of patients infected with omicron in China has not been described. We here described the clinical features of 267 patients infected during omicron wave in China. Half of the patients had symptoms onset and all of them were classified as mild type. It took about 11 days (IQR, 9-13) to clear viral for them. Complication and vaccination status played a role in the duration of viral clearance.

As presented in our study, cough, sputum production and sore throat were the most common symptoms, which aligned with a previous study in our country aiming to explore the effectiveness of VV116 against SARS-Cov-2[18]. Symptoms in Chinese people differed from patients in other countries including South Africa[16] and Korea[10]. In South Africa where SARS-Cov-2 omicron variant was first reported, headache, runny nose and sore throat were the most common symptoms among the patients with at least two doses of vaccine[16]. In Korea, sore throat, fever and headache ranked the top three, but there were only 40 participants in the study[10]. There were also patients compliant of digestive discomfort, painful urination or decreased smell in our research, suggesting multiple organs besides respiratory system were also involved when infected during omicron epidemic, which was consistent with other studies [16, 19, 20]. And this impact of SARS-Cov-2 on health may be long-term as indicated by an observation study on COVID-19 with two-year follow up[2]. But, loss of smell was less prevalent in our study, which was similar to the previous report during omicron wave[16] and this was different from patients infected with other SARS-Cov-2 variants in 2020 [21]. A community based comparative study showed that compared to infection during SARS-Cov-2 delta variant prevalence, sore throat and hoarse voice were much more commonly detected in patients during omicron wave, however the classic symptoms in COVID-19 like fever, loss of smell and persistent cough were less common [16].

We found that it took more than one week for patients to relive their discomfort. In ZOE COVID study[16], the duration of symptoms was 5(3-9) days among patients with at least two doses of anti SARS-Cov-2 vaccine; additionally, people who received three vaccine doses tend to recover within one week during omicron prevalence, which was distinct from our study[16]. The potential reason for the different duration may be that patients in the two studies were at different vaccination status. In addition, symptomatic patients were more likely to be cluster-cases in our study. Our country has hold on to the dynamic-zero policy in fighting against COVID-19 since 2019 with the aim to reduce infection. The government of Shanghai has implemented a lot of control and prevent measures in the war of SARS-Cov-2 omicron variant since late February 2022, for example keeping social distance and wearing mask.

SARS-Cov-2 has evolved into different phylogenetically lineages. COVID-19 epidemic burdens the

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number of cases needing hospitalization or even requiring ICU intervention. The current predominant variant omicron is less serious and lethal, as it is proved by many comparative studies focusing on infection during omicron versus delta[15, 16, 22] . Clinical severity, ratio of hospitalization, and ICU admission as well as worse outcomes were lower when omicron was prevalent than that of the delta expansion period. Despite the two (2/269, 0.74%) who were transferred to ICU, the patients in the current study were classified as mild type according to the guideline. According to the new published research, the ratio of severe or critical type during omicron prevalence in our country was as low as 0.065%, which was conducted in multi center[23]. The which was similar to the study reported in France in which none of the patients belonged to severe or even critical type[11].

Humans have done lots of work and obtained great progress in the fight against SRAS-Cov-2, including the production of vaccine or antiviral drugs[9, 24-26]. The current variant omicron with mutations in its spike glycoprotein and some deletions[7, 27], obtained enhanced transmissibility and lead to more infected cases. In vitro study, omicron showed increased replication[28]. The mutations in omicron rase the question about potential protectiveness of vaccine. Antibody evasion was detected in SARS-Cov-2 omicron[29]. Current available antiviral therapy or vaccine was less effective against omicron[26], and reinfection of omicron was about 0.31% for all the patients and it was higher among female and unvaccinated patients[30], indicating mutations of omicron resulted in immunity escape built by vaccination or preceding infection[9, 31, 32]. However, the potential role of vaccine in viral clearance during omicron epidemic was not studied. There were four kinds of vaccine available before omicron outbreak and our country has experienced a mass vaccination campaign since December 2020. About 62% of people over 60 years received vaccination and only 38% received a booster dose in shanghai as reported[17]. In the current study, 86.52% (231/267) individuals received at least one dose of vaccine. The ratio of vaccination was similar to that of another study conducted in our country, and duration of viral clearance was longer than that of patients treated with VV116[18]. We further found that vaccinated patients were with a shorter duration of viral clearance compared to people unvaccinated. What's more, vaccination played a protective role in clearing viral as indicated by multivariate regression model, but complication was a risk factor for viral clearance. Together with the previous finding that vaccine had a protectiveness against symptom infection and moderate effective against hospitalization[27], we call for vaccination against SARS-Cov-2 as soon as possible.

There are several limitations. Firstly, the study was conducted in a single center and the vaccination dose was collected through self-report. All the patients were classified as mild type and none of them had chest imaging during the period for that all of them were with SpO2>93%. Secondly, we did not explore the duration from the last vaccination date to infection onset, and 18 vaccinated patients did not provide their exact dose of vaccine. Thirdly, we found that hypertension effected the duration of viral clearance in univariate logistic regression, and angiotensin-converting enzyme-2 (ACE-2) receptors was the entry for SARS-Cov-2 into cells[33]. However, whether their daily drugs including ACE inhibitors and angiotensin II receptor blockers were not further studied. Only complication and vaccination played a role in the duration of viral clearance in multivariate logistic regression, thus we did not think hypertension drugs may have an impact on viral clearance duration. Lastly but not the least, possible past infection with SARS-Cov-2 was not analyzed for that our government is always trying to restrict the spread of SARS-Cov-2 and no epidemic was detected in shanghai in the past two years. What's more, preceding infection did not provide additional protectiveness against SARS-Cov-2 beyond vaccination[15].

With a high vaccination coverage, here we described the clinical characteristics of people infected during omicron wave in China and found that vaccination may be partially helpful in clearing viral while complication extends the duration, providing additional knowledge about omicron infection. Further research with a larger population in China is needed to provide a full descript of omicron infection including severe cases. Besides the nationwide network such as building shelter hospital and hotels, wearing mask and keeping social distance, we are still on the way of fighting against SARS-Cov-2. Given high transmission capacity of omicron, target effective vaccine and antiviral drugs are still in great need.

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