

Commentary

Antibiotic prescriptions for COVID-19 patients increased during the BA.5 period

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Abstract: The initial omicron (B.1.1.529) severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) subvariants, BA.1 and BA.2 (BA.1/2), were progressively displaced by BA.5 in Japan, which showed not only higher transmissibility and less pathogenicity, but also differences in antibiotic use according to the difference in the clinical course of BA.5 compared with BA.1/2 infections. BA.5 patients received more antibiotics, especially ampicillin/sulbactam, although ceftriaxone and meropenem were used significantly in the BA.1/2 period. These data suggest an increased incidence of aspiration pneumonia in elderly patients in the BA.5 period, and we should consider changing the management tactics for COVID-19.

Keywords: Antimicrobial stewardship, Aspiration pneumonia, Ampicillin/sulbactam, Ceftriaxone, SARS-CoV-2

How to cite this paper:

Ebina, S., Seki, M., Karaushi, H., Shimizu, A., & Mitsutake, K. (2023). Antibiotic prescriptions for COVID-19 patients increased during the BA.5 period. *World Journal of Medical Microbiology*, 2(1), 11–13. Retrieved from <https://www.scipublications.com/journal/index.php/wjmm/article/view/579>

Received: November 24, 2022

Accepted: January 1, 2023

Published: January 3, 2023



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1. Commentary

Omicron (B.1.1.529) became the dominant variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in 2022, and the initial omicron subvariants,

BA.1 and BA.2 (BA.1/2), were being progressively displaced by BA.5 in many countries, including Japan [1, 2].

BA.5 showed greater transmissibility and a higher level of immunological evasion than BA.1/2, but it appeared to have less pathogenicity [2]. In addition, when we focused on and investigated antibiotic use, the clinical course and management of COVID-19 patients also appeared to differ between the BA.1/2 period and the BA.5 period.

In Japan, COVID-19 BA.1/2 patients were predominant from January to March 2022, followed by BA.5 patients from July to September 2022. There were a total of 135 BA.1/2 patients and 160 BA.5 patients in each period, but the rate of antibiotic use was significantly different between the two periods, though the numbers of patients and their ages appeared similar (Table 1). Mortality was significantly lower in BA.5 period than in the BA.1/2 period, as in previous reports from other countries [3, 4]. Though similar between the groups, there was a tendency for increased bacterial infections affecting the respiratory system (pneumonia), abdomen (abscess, colitis, and cholangitis), and brain (abscess and meningitis). These data suggest an increase in secondary and/or simultaneous bacterial infections rather than pure viral infections in BA.5 cases.

Table 1. Comparison with patients' characteristics between BA.1/2 period and BA.5 period in 2022.

		Jan-Mar (n=135, BA.1)	Jul-Sep (n=160, BA.4/5)	p value	
Age		66.5+-16.0	68.7+-19.0	0.14	
Antibiotics (+)		14.8%(20/135)	26.3% (42/160)	0.016*	
	Respiratory		10.4%(14/135)	16.9% (27/160)	0.14
	Urinary		1.5%(2/135)	0.6%(1/160)	0.47
	Abdomen		1.5%(2/135)	5.0%(8/160)	0.09
	Skin		0.7%(1/135)	1.9%(3/160)	0.4
	Brain		0	1.3%(2/160)	0.19
	Bacteremia		0.7%(1/135)	0	0.28
	Unknown		0	0.6%(1/160)	0.36
Total Mortality		7.9%(10/135)	1.7% (2/160)	0.008**	

The antibiotics used in each case were then analyzed, and it was found that ampicillin/sulbactam (ABPC/SBT) was prescribed significantly more often to hospitalized COVID-19 patients in the BA.5 period than in the BA.1/2 period (Table 2). In contrast, ceftriaxone (CTRX) and meropenem (MEPM) were prescribed significantly more often for hospitalized COVID-19 patients in the BA.1/2 period than in the BA.5 period. These data suggest that mild aspiration pneumonia might be more common in COVID-19 patients in the BA.5 period, because ABPC/SBT was used for this type of pneumonia to cover anaerobes, though CTRX was used for community-acquired pneumonia in young persons, and MEPM was used for very severe pneumonia in Japan. Indeed, the patients who received ABPC/SBT in the BA.5 period were significantly older than the patients who received CTRX in the BA.1/2 period (77.95±11.96 vs 74.3±13.6 years, $P<0.01$).

Table 2. Comparison with antibiotics prescription between BA.1/2 period and BA.5 period in 2022.

	Jan-Mar (n=135)					Jul-Sep (n=160)								p value
	Respiratory	Urinary	Abdomen	Skin	Bacteremia	Total	Respiratory	Urinary	Abdomen	Brain	Skin	Unknown	Total	
AZM	1					1							0	0.139
ABPC/SBT	6	1				7	22		2		1	2	27	0.039*
TAZ/PIPC	2				1	3	4		3				8	0.726
CEZ	1	1		1		3				2	2		4	0.502
CTRX	3					3							0	0.009**
CAZ						0	1						1	0.492
CMZ			1			1			2				2	0.952
MEP	1		1			2							0	0.035*
DRP						0		1					1	0.492
Total	14	2	2	1	1	20	27	1	8	2	3	2	43	

Therefore, the difference in the COVID-19 patients between the BA.1/2 period and the BA.5 period needs to be considered. The importance of antimicrobial stewardship was recommended in the early stage of the COVID-19 pandemic around 2020 because the rate of secondary pneumonia was suggested to be from 3% to 15% [5, 6], and it was considered that pure viral pneumonia was predominant in COVID-19, although, in influenza infection, secondary bacterial pneumonia was common, and more than 30% of influenza pneumonia patients co-infected with bacteria were found [7]. The excessive use of antibiotics and the appearance of resistant bacteria have been concerns previously, but we might have to use antibiotics in the BA.5 era in the same manner as for influenza.

Ethics and statistical analysis: The analysis was approved by the Committee for Clinical Scientific Research of Saitama Medical University International Medical Center on July 6, 2022 (#2022-032), and the patients provided written, informed consent for use of their specimens, although the samples were collected as part of routine laboratory analyses.

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