


## Concise Communication

# Impact of coronavirus disease 2019 (COVID-19) pandemic on antimicrobial consumption and antimicrobial resistance at a small, local hospital in Japan

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### Abstract

The coronavirus disease 2019 (COVID-19) pandemic negatively affected antimicrobial stewardship programs at hospitals throughout Japan by diverting resources toward managing the pandemic. However, antimicrobial stewardship needs to continue regardless of hospital size or supervening crises. Herein, we discuss the impact of COVID-19 on antimicrobial stewardship at a small, local hospital in Japan.

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Antimicrobial stewardship programs (ASPs) are central to preventing inappropriate antimicrobial use which contributes to increased antimicrobial resistance (AMR). However, the sidelining of ASPs during the coronavirus disease 2019 (COVID-19) pandemic has demonstrated that the importance of antimicrobial stewardship is not fully appreciated by the healthcare system.<sup>1</sup>

Because COVID-19 is a viral infection, antimicrobials are obviously ineffective against it. Moreover, only 8% of patients with COVID-19 have a bacterial coinfection at admission.<sup>2</sup> However, antimicrobials continue to be prescribed to many patients with COVID-19.<sup>2</sup> The reasons for antimicrobial use in these cases include the putative need to prevent viral pneumonia and an increased rate of healthcare-associated infections.<sup>3</sup> A previous survey also noted that ASPs were not always implemented fully because of pandemic-related pressures on medical resources.<sup>4</sup> As a result, the use of antimicrobial agents increased, and it is now thought that the COVID-19 pandemic may accelerate AMR and the arrival of the post-antimicrobial era.<sup>5</sup>

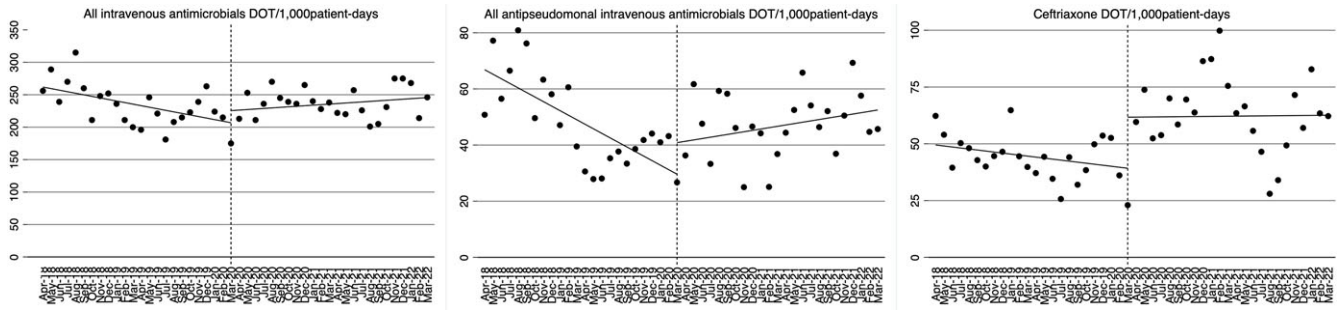
Previous studies have reported antimicrobial consumption and AMR at large academic hospitals or tertiary-care centers during the current pandemic.<sup>6,7</sup> However, the impact of the pandemic on antimicrobial consumption and AMR at small hospitals has remained unclear. Thus, we conducted a retrospective study of antimicrobial use and the incidence of drug-resistant organisms at a small, local hospital in Japan.

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### Materials and Methods

The present, quasi-experimental, observational study was conducted at Tama-Nambu Chiiki Hospital, a 287-bed community hospital in Tokyo, Japan with 26 subspecialties but no infectious disease physician. The hospital has admitted patients with mainly mild to moderate COVID-19 since March 2020 at the request of the Tokyo Metropolitan Government. Specifically, we assessed the impact of the current pandemic on antimicrobial consumption and AMR in a period before the pandemic, defined as March 2018 to March 2020, and a period during the pandemic, defined as April 2020 to March 2022. Trends and levels in overall intravenous antimicrobial consumption and antipseudomonal antimicrobials, ceftriaxone, and vancomycin, expressed as days of therapy (DOT) per 1,000 patient days (PD), and the incidence of multidrug-resistant organisms (MDROs), including methicillin-resistant *Staphylococcus aureus* (MRSA) and extended-spectrum  $\beta$ -lactamase-producing *Enterobacteriaceae* (ESBL-E), were assessed as the primary outcome. The incidence of catheter-associated urinary tract infection (CAUTI) per 1,000 PD was also tracked as the secondary outcome. Before the pandemic, an ASP pharmacist (0.7 full-time equivalent (FTE)) implemented a preauthorization protocol for broad-spectrum antimicrobials used as a syndrome-specific intervention for bloodstream infections (BSIs) from March 2018 and a postprescription review and feedback (PPRF) from April 2019. During the pandemic, the ASP pharmacist was recruited for work in infection prevention and had less time for ASP (~0.2 FTE). Segmented regression analysis of an interrupted time series for autocorrelation was used to assess the changes in antimicrobial use and the incidence of MRSA, ESBL-E, and CAUTI.  $P < .05$  was considered statistically significant. The institutional review board at Tama-Nambu Chiiki Hospital approved this study.



**Fig. 1.** Changes in intravenous antimicrobial use before and during the pandemic. Intravenous antimicrobials (total, antipseudomonal, and third-generation cephalosporins). Note. DOT, days of therapy.

## Results

Between April 1, 2020, and March 31, 2022, the study center admitted 1,444 patients with COVID-19. Supplementary Table 1 shows the basic demographic data and the severity of COVID-19 in the total cohort for each of the six pandemic waves.

Figure 1 shows the changes in intravenous antimicrobial consumption before the pandemic and during the pandemic. Interrupted time-series analysis (ITSA) revealed a change in the slope of overall antimicrobial consumption from  $-2.39$  to  $3.23$  DOT per 1,000 PD ( $P = .01$  for change in trend). Antipseudomonal antimicrobial consumption showed a significant increase from  $-1.62$  to  $2.10$  DOT per 1,000 PD ( $P < .001$  for change in trend), but neither showed a rapid increase ( $+18.6$  DOT per 1,000 PD;  $P = .30$ ;  $+11.2$  DOT per 1,000 PD;  $P = .16$  for change in intercept). The change in DOT per 1,000 PD for ceftriaxone also revealed a rapid increase ( $+22.5$  DOT per 1,000 PD;  $P = .02$  for change in intercept). Except for fluoroquinolones, the DOT per 1,000 PD for carbapenems, piperacillin-tazobactam, and cefepime showed a trend toward a significant increase (Supplementary Fig. 1).

Moreover, ITSA revealed a significant increase in the incidence of ESBL-E from  $-0.01$  to  $0.02$  per 1,000 PD ( $P < .01$  for change in trend) and CAUTI from  $-0.09$  to  $0.21$  per 1,000 PD ( $P < .001$  for change in trend) in Supplementary Fig. 2.

## Discussion

We assessed antimicrobial consumption, MDRO incidence, and the CAUTI rate in a small Japanese hospital actively receiving patients with COVID-19 during the pandemic. The consumption of intravenous antimicrobials, especially antipseudomonal antimicrobial agents, increased significantly. Moreover, the incidence of ESBL-E and CAUTI also showed an increasing trend, reaffirming the importance of appropriate antimicrobial use and infection prevention programs during the pandemic.

At the study center, a designated ASP pharmacist assisted with the treatment of BSI and the implementation of PPRF before the pandemic. As a result, the use of all intravenous antimicrobials as measured by DOT showed a significantly decreasing trend. However, during the pandemic, the discontinuation of ASP activities may have resulted in increased antimicrobial consumption. It has been reported that discontinuation of ASP increased intravenous antimicrobial consumption.<sup>8</sup> In contrast, hospitals that continued to conduct ASP during the pandemic reported no change in intravenous antimicrobial consumption.<sup>9</sup> Thus, even in small hospitals like the one where this study was conducted,

having a consistent and reliable ASP is critical to controlling the use of antimicrobial agents and preventing AMR.

Although we found no change in the incidence of MRSA, we detected an increase in the ESBL-E incidence during the pandemic, suggesting that the use of antipseudomonal agents and third-generation cephalosporin had increased. Similarly, although the trend in the use of urinary catheters did not change between the periods before the pandemic and during the pandemic, CAUTI incidence increased significantly. During the fifth pandemic wave (July–September 2021), the number of severe COVID-19 cases increased, coupled with an increase in urinary catheter dwell time. During the sixth pandemic wave (January–March 2022), the number of elderly patients with COVID-19 increased because of delays in administering the third vaccination, possibly accounting for the higher proportion of high-risk patients with asymptomatic bacteriuria during this period.

Increased use of antipseudomonal agents and third-generation cephalosporins was associated with ESBL-E and CA-UTI incidences. Thus, adherence to appropriate antimicrobial use and appropriate device management is important even during a crisis like the current pandemic.

This study had several limitations. Because the study was conducted at a single, small hospital in Japan, the findings may not be generalizable to other settings. Surveillance of oral antimicrobial prescriptions, other MDROs, and healthcare-associated infections other than CAUTI was not done because of limitations in time and personnel. The number of COVID-19–related admissions during the pandemic varied widely; thus, it may not be appropriate to evaluate the monthly data. Few, severely ill patients were admitted, possibly resulting in differences in trends from other hospitals with a higher proportion of severely ill patients. Possibly, secondary bacterial infections following the hospitalization of COVID-19 patients contributed to the increased antimicrobial consumption.

The COVID-19 pandemic disrupted ASP and infection prevention and control programs at the study center. The present study demonstrated a correlation between antimicrobial use and the incidences of CAUTI and ESBL-E, suggesting that ongoing implementation of antimicrobial stewardship and infection prevention and control programs are vital to health care at all times, regardless of any supervening crisis.

**Supplementary material.** To view supplementary material for this article, please visit <https://doi.org/10.1017/ash.2022.324>

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**Conflicts of interest.** The authors declare no conflicts of interest related to this work.

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