Antibiotic Consumption and Bacterial Resistance Rates in Hospitalized COVID-19 Patients: A Retrospective Study During the 3 First Surges

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To the Editor—During the coronavirus disease 2019 (COVID-19) pandemic, experts warned about the risk of increased antibiotic prescription and its impact on antimicrobial resistance (AMR) emergence at a population level [1–3]. But several studies report conflicting results, and the impact of COVID-19 on antibiotic prescription and emergence of AMR remains unclear [4, 5].

Our objective was to collect, analyze, and compare antibiotic consumptions and bacterial resistances in our hospital during the 3 first surges of COVID-19 cases.

We performed a monocentric retrospective study in our French university hospital, including a 26-bed infectious disease department (IDD) and a 15-bed intensive care unit (ICU), which managed patients with COVID-19.

For the three first surges (March–April 2020, October–November 2020, and March–April 2021), we assessed antibiotic consumption, expressed as defined daily dose (DDD) per 1000 patient-days (PD), as well as bacterial resistance rates from sample collections for diagnosis purpose, using the year 2019 as our reference point. Data collection was carried out using the local computerized patient record system (ORBIS, Dedalus HealthCare, Germany).

Patients were informed of institutional indicator monitoring (resistance and antimicrobial consumption data) at admission, and that their clinical data could be used, after anonymization, for research purposes. No formal statistical testing was performed on our data. The research was conducted in accordance with the Declaration of Helsinki, and national and institutional standards.

Antibiotic consumption was, respectively: for the whole hospital, 696, 652, and 620 DDD/1000 PD for the first, second, and third surges compared to 505 in 2019; for the IDD, 1083, 894, and 789 DDD/1000 PD versus 1070 in 2019; and for the ICU, 1382, 819, and 1108 DDD/1000 PD versus 1052 in 2019 (Figure 1).

Total consumption of third-generation cephalosporins (3GC) increased 4-fold during the first surge (174 vs 43 in 2019), and returned to baseline levels during the second and third surges (72 and 49, respectively). In the ICU, consumptions of carbapenems increased during COVID-19 surges: respectively 115, 148, and 194 versus 79 in 2019, contrary to IDD (11, 5, and 18 vs 29 in 2019).

Resistance rates of *Pseudomonas aeruginosa* resistant to carbapenems increased as well (33%, 28%, and 37% vs 19% in 2019), whereas we observed stable rates of extended-spectrum β-lactamase–producing Enterobacterales (ESBL-EB) (Figure 2).

Overall, consumption of antibiotics globally increased during the 3 first COVID-19 surges compared to our baseline period, with a significant increase in the ICU during the first surge. This increase was due to initial delays in COVID-19 diagnosis, immunosuppressive treatments (corticosteroids and tocilizumab), and increase in carbapenems use during the second and third surges.

On the contrary, antibiotic consumption decreased in the IDD, due to updated knowledge about the low incidence of superinfections among non–critically ill patients during COVID-19 hospitalization [6, 7].

Increased rates of resistance to carbapenems with stability of ESBL-EB suggest a selection pressure rather than an increase in cross-transmission of multidrug-resistant organisms (MDROs).

Indeed, a systematic review and meta-analysis performed in North America, Europe, and other geographical settings during the first 18 months of the COVID-19 pandemic showed that AMR was relatively high among patients with bacterial coinfections, especially in ICU [8]. The most common MDROs documented were carbapenem-resistant *Acinetobacter baumannii*, methicillin-resistant *Staphylococcus aureus*, *Klebsiella pneumoniae*, and *P aeruginosa*.

Moreover, a major increase in the rate of bloodstream infections caused by Amp-C–producing Enterobacterales and 3GC-resistant *P aeruginosa* was also observed in the January–April 2020 period in 25 hospitals of the Paris area, concomitant with an increase in 3GC consumption, mainly in ICU, reinforcing the hypothesis of a selection pressure mechanism [9].

Finally, various determinants may result in an increase or a decrease in AMR [10].

In our study, we found several known factors present in ICU, including overprescription of broad-spectrum antibiotics and an increase in the number of patients. An increase in prescriptions of azithromycin, and understaffed antimicrobial stewardship teams, could also favor AMR emergence. However, some factors could decrease antibiotic prescription, and therefore AMR emergence, which were present in IDD and ICU wards: lower rates of bacterial coinfections and healthcare-associated infections, and postponed surgical interventions involving antibiotic prophylaxis, possibly resulting in surgical complications requiring antibiotic prescriptions.

Finally, MDRO importations were probably limited by the worldwide lockdowns, with fewer hospitalizations from other countries with high prevalence of MDRO, or of chronically ill patients, and fewer transfers from long-term care facilities.

The impact of the COVID-19 pandemic on AMR emergence might vary

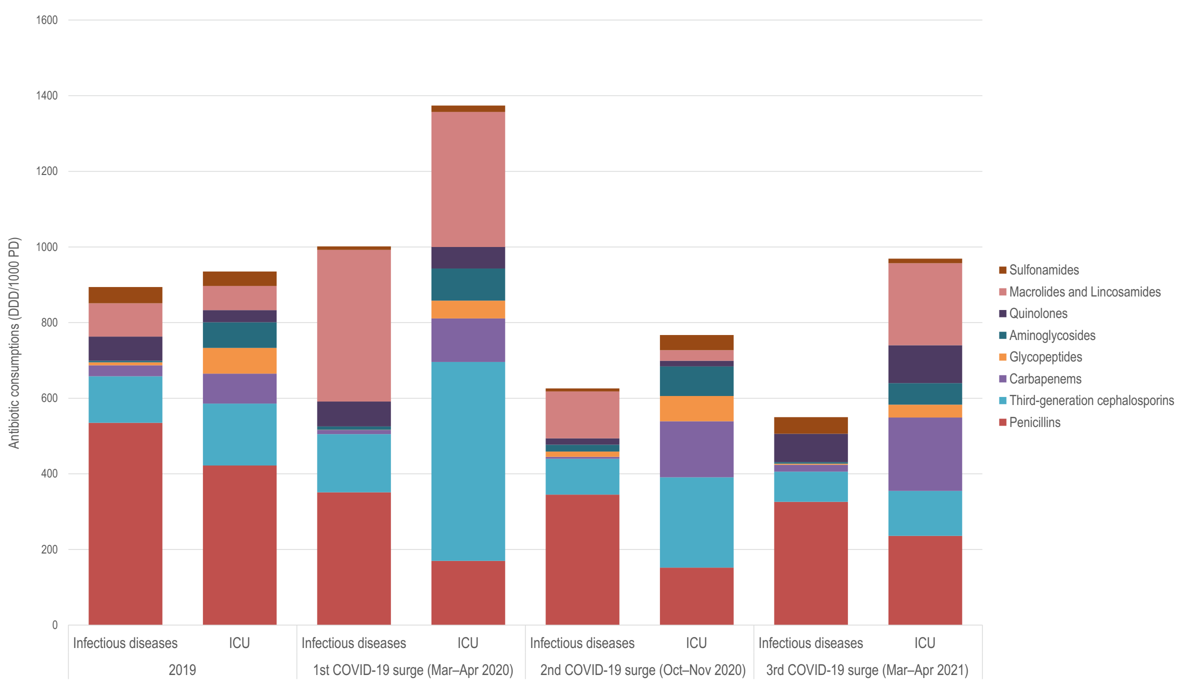

Figure 1. Antibiotic consumptions in the infectious diseases department and intensive care unit (defined daily dose per 1000 patient-days). Abbreviations: COVID-19, coronavirus disease 2019; DDD, defined daily dose; ICU, intensive care unit; PD, patient-days.

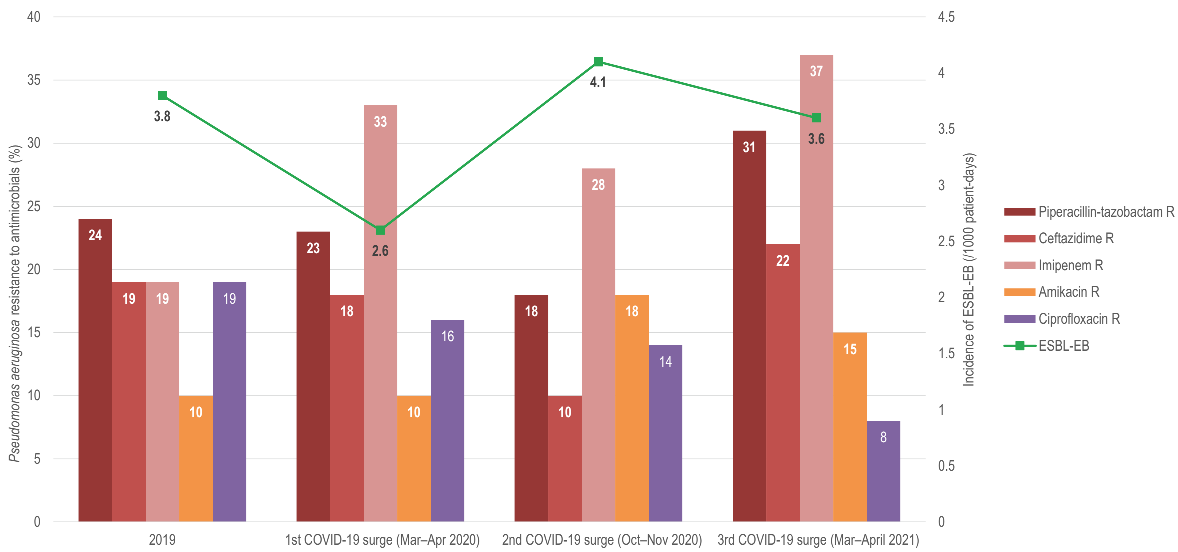

Figure 2. Rates of extended-spectrum β-lactamase–producing Enterobacterales and *Pseudomonas aeruginosa* resistance. Abbreviations: COVID-19, coronavirus disease 2019; ESBL-EB, extended-spectrum β-lactamase–producing Enterobacterales; R, resistant.

depending on the setting (hospital or community) and the country.

Furthermore, the impact of changes in antibiotic prescriptions and infection prevention and control practices, such as well-fitting medical masks, gloves and gowns, and mandatory hand hygiene and appropriate use of personal protective equipment, on AMR emergence would unlikely be instantaneous, which should be taken into account in analyzing those data.

Notes

Patient consent. Considering the retrospective study design, data collection from preexisting medical records, and respect for the anonymity of the patients included (referred to as studies "Hors Loi Jardé" in France), no ethical approval or administrative approval was necessary for this study. The research was conducted in accordance with the Declaration of Helsinki. Patients were informed that their clinical data could be used, after anonymization, for research purposes.

Potential conflicts of interest. The authors: No reported conflicts of interest.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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