



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Letter to the editor

Impact of the COVID-19 pandemic on multidrug-resistant hospital-acquired bacterial infections



Sir,

We read with attention the paper by de Carvalho *et al.* that was recently published in this Journal [1]. The authors evaluated the incidence of carbapenem-resistant Gram-negative bacteria in device-associated infections between 2019 and 2020 and correlated their findings with the incidence and the spread of the COVID-19 pandemic. They found a significant increase in *Acinetobacter baumannii* infections in 2020 compared to 2019, and a consequent increase in the empiric prescription of polymyxins. To date, the impact of the COVID-19 pandemic on the occurrence of multidrug-resistant (MDR)

bacteria has been evaluated in several reports [2–5]; notably, the longer duration of antimicrobial therapy for the management of respiratory complications of COVID-19 infection may have a devastating impact on infection control, leading to possible outbreaks of MDR bacteria in hospitals. Further, data on the increased incidence of specific MDR Enterobacterales (e.g. *Klebsiella pneumoniae*) or methicillin-resistant *Staphylococcus aureus* (MRSA) are still conflicting [6–8]. In this study, we compared the incidence of different hospital-acquired infections (HAIs) due to MDR bacteria in the period 2017–2019 (pre-COVID-19 period) and 2020 (COVID-19 period) in hospitalized patients at Garbagnate Milanese Hospital, Milan, Italy, a tertiary referral hospital that was fully converted to a COVID-19 hospital from March 2020.

Micro-organisms were included in the analysis only if they were found in blood, sputum, or urine of patients with systemic or local symptoms of infection at least seven days after hospital admission. Systemic or local features of infection at the time of diagnosis of HAI were fever or septic shock, pneumonia

Table I

Incidence of hospital-acquired infection in 2020 (COVID-19 period) vs 2017–2019 (no COVID-19 period)

	OR (CI)	RR (CI)	IRR (CI)	P
CRAB	6.75 (1.96–23.28)	1.9 (1.91–2.18)	6.91 (1.98–37.04)	<0.001
<i>Staphylococcus aureus</i>				
MSSA	0.40 (0.12–1.31)	0.45 (0.12–1.28)	0.4 (0.08–1.29)	0.12
MRSA	1.03 (0.79–1.33)	1.02 (0.82–1.26)	1.02 (0.79–1.31)	0.85
<i>Escherichia coli</i>				
Not resistant	0.17 (0.07–0.40)	0.21 (0.09–0.40)	0.18 (0.07–0.40)	<0.001
ESBL ⁺	0.83 (0.64–1.07)	0.89 (0.76–1.05)	0.84 (0.68–1.06)	0.16
CR	12.23 (3.30–45.32)	3.81 (2.16–4.75)	36.15 (5.00–1584.33)	<0.001
<i>Klebsiella pneumoniae</i>				
Not resistant	0.26 (0.06–1.08)	0.3 (0.05–1.08)	0.26 (0.03–1.00)	0.05
ESBL ⁺	1.33 (1.01–1.73)	1.25 (1.01–1.53)	1.29 (1.02–1.66)	0.037
CR	2.39 (1.70–3.34)	1.88 (1.49–2.34)	2.24 (1.59–3.13)	<0.001
<i>Pseudomonas aeruginosa</i>				
Not resistant	0.44 (0.16–1.25)	0.50 (0.16–1.23)	0.45 (0.12–1.25)	0.11
ESBL ⁺	0.48 (0.67–1.05)	0.52 (0.68–1.12)	0.49 (0.66–1.05)	0.09
CR	1.84 (1.27–2.66)	1.58 (1.19–2.04)	1.78 (1.21–2.57)	0.001
<i>Proteus mirabilis</i>				
Not resistant	1.82 (0.83–4.02)	1.57 (0.8–2.59)	1.81 (0.72–4.15)	0.13
ESBL ⁺	0.182 (0.07–0.45)	0.22 (0.08–0.52)	0.19 (0.06–0.45)	<0.001
<i>Enterococcus faecium</i>				
VSE	0.78 (0.37–1.68)	0.82 (0.39–1.52)	0.78 (0.32–1.69)	0.53
VRE	3.5 (2.08–5.88)	2.36 (1.68–3.07)	3.39 (1.95–5.84)	<0.001

CI, confidence interval; OR, odds ratio; IRR, incidence rate ratio; CRAB, carbapenem-resistant *Acinetobacter baumannii*; MSSA, methicillin-susceptible *Staphylococcus aureus*; MRSA, methicillin-resistant *S. aureus*; ESBL⁺, extended spectrum β-lactamase-producing; CR, carbapenem-resistant; VSE, vancomycin-susceptible *Enterococcus faecium*; VRE, vancomycin-resistant *E. faecium*.

<https://doi.org/10.1016/j.jhin.2022.02.015>

0195-6701/© 2022 The Healthcare Infection Society. Published by Elsevier Ltd. All rights reserved.

demonstrated by X-ray or computed tomography of the thorax, or pyuria; any of these had to be accompanied by a raised serum C-reactive protein level. The following bacteria were considered causes of HAI: carbapenem-resistant *A. baumannii* (CRAB), methicillin-susceptible *S. aureus* (MSSA), MRSA, extended-spectrum β -lactamase (ESBL)-producing or carbapenem-resistant (CR) *Escherichia coli*, *K. pneumoniae*, *Proteus mirabilis*, and *Pseudomonas aeruginosa*, and vancomycin-susceptible or -resistant (VRE) *Enterococcus faecium*. Finally, we compared the incidence rate ratio (IRR) of all these HAIs in 2020 with the incidence in the period 2017–2019.

Table 1 summarizes the differences in the IRR of the HAI in the two periods considered. CRAB was isolated from 16 subjects in 2020 compared to 45 in 2017–2019 ($P < 0.001$); MRSA was diagnosed in 79 versus 311 subjects, respectively ($P = 0.85$). CR-*E. coli* was found in nine subjects in 2020 vs 0 in 2017–2019 ($P < 0.001$); CR-*K. pneumoniae* was found in 57 patients in 2020 vs 101 in 2017–2019 ($P < 0.001$) and CR-*P. aeruginosa* in 43 vs 97 patients in 2020 and 2017–2019, respectively ($P = 0.001$). Finally VRE was found in 27 subjects in 2020 vs 32 in 2017–2019 ($P < 0.001$). The IRR of ESBL-producing bacteria was not statistically significant for *E. coli* and *P. aeruginosa*; a significant, though modest, increase in ESBL-producing *K. pneumoniae* was observed in 2020 compared with 2017–2019 ($P = 0.037$), whereas a significant reduction was found for *P. mirabilis* ($P < 0.001$). The incidence of non-MDR bacteria in 2020 vs 2017–2019 was not statistically different for the majority of bacteria, except for reductions in *E. coli* ($P < 0.001$) and *K. pneumoniae* ($P = 0.05$) (Table 1). These data demonstrate that the COVID-19 pandemic led to a significant increase in MDR hospital-acquired bacterial infections, specifically CRAB, carbapenem-resistant Enterobacteriales, and VRE.

Our data were from a single hospital based in Lombardy, an area where the prevalence of MDR bacteria was very high even before the COVID-19 pandemic. Either of these factors may partially explain the differences between our results and those from other geographical areas, where the incidence of MDR HAI declined during the COVID-19 period [4,6,8]. Nevertheless, our data show the potential for MDR bacteria to cause infections in COVID-19 patients. The infective complications due to prolonged hospitalization and immune suppression in these patients may cause a further worsening of their prognosis.

Conflict of interest statement

None declared.

Funding sources

None.

References

- [1] de Carvalho Hessel Dias VM, Tuon F, de Jesus Capelo P, Telles JP, Fortaleza CMCB, Pellegrino Baena C. Trend analysis of carbapenem-resistant Gram-negative bacteria and antimicrobial consumption in the post-COVID-19 era: an extra challenge for healthcare institutions. *J Hosp Infect* 2022;120:43–7.
- [2] Donà D, Di Chiara C, Sharland M. Multi-drug-resistant infections in the COVID-19 era: a framework for considering the potential impact. *J Hosp Infect* 2020;106:198–9.
- [3] Monnet DL, Harbarth S. Will coronavirus disease (COVID-19) have an impact on antimicrobial resistance? *Euro Surveill* 2020;25:2001886.
- [4] Hirabayashi A, Kajihara T, Yahara K, Shibayama K, Sugai M. Impact of the COVID-19 pandemic on the surveillance of antimicrobial resistance. *J Hosp Infect* 2021;117:147–56.
- [5] Canton R, Gijon D, Ruiz-Garbayosa P. Antimicrobial resistance in ICUs: an update in the light of the COVID-19 pandemic. *Curr Opin Crit Care* 2020;26:433–41.
- [6] Bentivegna E, Luciani M, Arcari L, Santino I, Simmaco M, Martelletti P. Reduction of multidrug-resistant (MDR) bacterial infections during the COVID-19 pandemic: a retrospective study. *Int J Environ Res Public Health* 2021;18:1003.
- [7] Tiri B, Sensi E, Marsiliani V, Cantarini M, Priante G, Vernelli C, et al. Antimicrobial stewardship program, COVID-19, and infection control: spread of carbapenem-resistant *Klebsiella pneumoniae* colonization in ICU COVID-19 patients. What did not work? *J Clin Med* 2020;9:2744.
- [8] Wee LEI, Conceicao EP, Tan JY, Magesparan KD, Amin IBM, Ismail BBS, et al. Unintended consequences of infection prevention and control measures during COVID-19 pandemic. *Am J Infect Control* 2021;49:469–77.

M. Bongiovanni^{a,*}

G. Barilaro^b

U. Zanini^c

G. Giuliani^d

^aDepartment of Infectious Diseases, Ente Ospedaliero Cantonale, Lugano, Switzerland

^bDepartment of Autoimmune Diseases, Hospital Clinic, Universitat de Barcelona, Catalonia, Spain

^cPneumology Unit, Garbagnate Hospital, ASST Rhodense, Italy

^dDepartment of Laboratory Medicine, Garbagnate Milanese, ASST Rhodense, Italy

* Corresponding author. Address: EOC: Repubblica e Cantone Ticino Ente Ospedaliero Cantonale, Department of Infectious Diseases, Lugano 69030, Switzerland. Tel.: +41 782224324. E-mail address: Marco.Bongiovanni@eoc.ch (M. Bongiovanni)

Available online 1 March 2022