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Journal of Hospital Infection

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## Letter to the Editor

### Antimicrobial overuse in COVID-19 – reasons to remain vigilant as we approach the winter ‘twindemic’

Sir,

Antimicrobial overuse and increased incidence of hospital-acquired infection (HAI) in patients with coronavirus disease 2019 (COVID-19) have likely aggravated the incidence of antimicrobial resistance (AMR). As the winter season looms and discussion regarding the predicted ‘twindemic’ of influenza and COVID-19 intensifies [1], it is imperative that antimicrobial stewardship (AMS) and HAI prevention remain at the core of quality improvement efforts. Early in the pandemic, antimicrobial prescribing for COVID-19 was based on clinical experience of influenza, in which bacterial co-infection occurs in 23% of patients [2]. However, as the pandemic progressed, data indicated a low rate of bacterial infection in patients with COVID-19 [3], and guidelines recommended intensified AMS efforts targeting empiric antibiotic prescribing [4].

We retrospectively reviewed empiric antimicrobial prescribing and HAI in 56 patients with COVID-19 admitted to the intensive care unit (ICU) in our 800-bed tertiary referral hospital during the fourth pandemic wave (27<sup>th</sup> June–18<sup>th</sup> December 2021) in Ireland (Table I). Infections that occurred on day 3 of hospital admission onwards were deemed to be HAIs. Data were obtained from critical care and laboratory information systems. At this time in Ireland, influenza preparedness efforts intensified as public health experts expressed concern regarding the potential re-emergence of influenza virus infection in 2021/22 after the winter lockdowns of 2020/21.

In our study, microbiological evidence of co-infection was found in only 5% of patients admitted directly to the ICU from the community. Despite this low prevalence, the majority of patients (81%, 26/32) with no evidence of bacterial co-infection

were prescribed empiric antimicrobials. Twenty-four (43%) patients, 23 of whom were mechanically ventilated, developed HAI. The most common HAI was ventilator-associated pneumonia ( $N=21$ ). Two patients developed urinary tract infection, one developed *Clostridioides difficile* infection, and one developed an intravascular-catheter-associated HAI. In our COVID-19 patient cohort, when patients with HAI were compared with patients without co-infection, patients with HAI had a longer mean hospital stay, received more antimicrobials (mean  $5 \pm 2$  courses), and were more likely to be colonized with an AMR organism (Table I).

Preliminary Australian data suggest that a surge in influenza cases may be sooner than expected, providing an opportunity to demonstrate vigilance. HAI remains a significant patient safety issue, and requires ongoing infection prevention focus, specifically in ICUs where the more vulnerable patients are placed. This is supported by recent US data where ventilator-associated infection events had the largest increase across all HAIs in 2021, 51% higher than the same period in 2019 [5].

The prevalence of empiric antimicrobial prescribing in patients with COVID-19 remains incongruently high despite relatively low rates of co-infection. Provision, utilization and expert interpretation of appropriate rapid diagnostic investigations to confirm or rule out co-infection in these critically ill patients could provide clinicians with the confidence not to prescribe, and to rationalize or discontinue antimicrobials [6]. A recent meta-analysis demonstrated that 25% of community-acquired cases of pneumonia are of viral aetiology [7], and the use of molecular testing for viral/atypical pathogens has been shown to reduce antimicrobial use in patients hospitalized for lower respiratory tract infections [8].

As we approach this winter season and with the relaxation of pandemic public health measures, it is essential that HAI prevention and AMS have equal focus in the ‘twindemic’ preparedness discussions. HAI prevention needs to remain at the core of quality improvement for all patients, specifically those patients in ICUs, irrespective of COVID-19 diagnosis. The high prevalence of empiric antimicrobial prescribing in patients with COVID-19 highlights the need for continued focus on antimicrobial and diagnostic stewardship efforts to prevent acceleration of the silent threat of AMR.

<https://doi.org/10.1016/j.jhin.2022.10.006>

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Table 1

Patient characteristics of 56 patients with coronavirus disease 2019 admitted to a single centre intensive care unit (ICU) during the fourth wave in Ireland

	No infection N=32 (%)	Hospital (ICU)-acquired infection N=24 (%)	Co-infection on ICU admission N=4
Age (years)	54 ± 16	52 ± 16	50 ± 6
Male	23 (72)	13 (54)	3
Body mass index (kg/m <sup>2</sup> )	29.8 ± 4.9	30.6 ± 6.8	28.9 ± 2.6
Length of ICU stay (days)	7.8 ± 6.1	29.2 ± 24.9	23.8 ± 25.8
Ventilation status			
Mechanically ventilated	18 (56)	23 (96)	3
Mean ventilator-days	8 ± 5	24 ± 22	20 ± 18
Mortality (at ICU discharge)	10 (31)	8 (33)	1
Prescribed empiric antimicrobials	26 (81)	24 (100)	4
Number of antimicrobial courses	1 ± 1	5 ± 2	4 ± 2
Antimicrobial-resistant organisms			
VRE colonization	4 (7)	7 (13)	0
CPE colonization	1 (2)	1 (2)	1 (2)
ESBL infection (UTI)	0	3 (5)	0
MRSA infection (VAP)	0	1 (2)	0
MRSA colonization	0	1 (2)	0

VRE, vancomycin-resistant enterococci; CPE, carbapenemase-producing Enterobacterales; ESBL, extended-spectrum beta-lactamase-producing Enterobacterales; MRSA, methicillin-resistant *Staphylococcus aureus*; UTI, urinary tract infection; VAP, ventilator-associated pneumonia.

Data presented as number of patients (%) or mean ± standard deviation.

#### Conflict of interest statement

None declared.

#### Funding sources

None.

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