



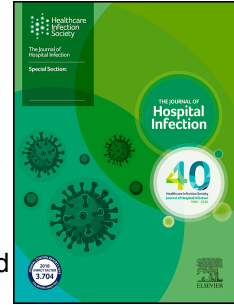
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Antimicrobial Overuse in COVID-19 – Reasons to remain vigilant as we approach the winter “twindemic”.

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Sir,

Antimicrobial overuse and an increased incidence of hospital-acquired infection (HAI) in Coronavirus Disease 2019 (COVID-19) patients have likely aggravated antimicrobial resistance (AMR) incidence. 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 remains at the core of quality improvement efforts. Early in the pandemic, antimicrobial prescribing in 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 COVID-19 [3] and guidelines recommended intensified AMS efforts targeting empiric antibiotic prescribing [4].

We retrospectively reviewed empiric antimicrobial prescribing and HAI from 56 COVID-19 patients admitted to the intensive care unit (ICU) in our 800-bed tertiary referral hospital, during the fourth COVID-19 wave (27th June to 18th December 2021) in Ireland. [Table 1]. Infections that occurred on day three onwards of hospital admission were deemed HAIs. Data was 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 occurred in only 5% of patients admitted directly to ICU from the community. Despite this low prevalence, the majority of patients (81%, 26 of 32) with no evidence of bacterial co-infection were prescribed empiric antimicrobials. Twenty-four (43%) patients, 23 mechanically ventilated, developed HAI. The most common HAI was ventilator-associated pneumonia (n=21). Two patients developed urinary tract infection, one *C. difficile* infection and one an intravascular catheter-associated HAI. In our COVID-19 patient cohort, when HAI patients were compared to patients with no co-infection, HAI patients had a longer mean length-of-stay, received more antimicrobials (mean five +/- 2 courses) and were more likely to be colonised with an AMR organism [Table 1].

Preliminary Australian data suggests 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 ICU where our more vulnerable patients are placed. This is supported by recent US data where ventilator-associated infection events had the largest increase across all HAI in 2021, 51% higher than the same period in 2019. [5]

The prevalence of empiric antimicrobial prescribing in COVID-19 patients remains incongruently high despite relatively low rates of co-infection. Provision, utilisation and expert interpretation of appropriate rapid diagnostic investigations to confirm or out rule co-infection in these critically ill patients could provide clinicians with the confidence to not prescribe and to rationalise or discontinue antimicrobials [6]. A recent meta-analysis demonstrated 25% of community-acquired 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 infection [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 ICU patients irrespective of COVID-19 diagnosis. The high prevalence of empiric antimicrobial prescribing in COVID-19 patients highlights the need for continued focus on antimicrobial and diagnostic stewardship efforts to prevent accelerating the silent threat of antimicrobial resistance.

References

1. Rubin R. The Dreaded “Twindemic” of Influenza and COVID-19 Has Not Yet Materialized— Might This Be the Year?. *JAMA*. 2022 Sep 21.
2. Klein EY, Monteforte B, Gupta A, Jiang W, May L, Hsieh YH, Dugas A. The frequency of influenza and bacterial coinfection: a systematic review and meta-analysis. *Influenza and other respiratory viruses*. 2016 Sep;10(5):394-403.
3. Vaughn VM, Gandhi TN, Petty LA, Patel PK, Prescott HC, Malani AN, Ratz D, McLaughlin E, Chopra V, Flanders SA. Empiric antibacterial therapy and community-onset bacterial coinfection in patients hospitalized with coronavirus disease 2019 (COVID-19): a multi-hospital cohort study. *Clinical Infectious Diseases*. 2021 May 15;72(10):e533-41.
4. Sieswerda E, de Boer MG, Bonten MM, Boersma WG, Jonkers RE, Aleva RM, Kullberg BJ, Schouten JA, van de Garde EM, Verheij TJ, van der Eerden MM. Recommendations for antibacterial therapy in adults with COVID-19—an evidence based guideline. *Clinical Microbiology and Infection*. 2021 Jan 1;27(1):61-6.
5. Lastinger LM, Alvarez CR, Kofman A, Konnor RY, Kuhar DT, Nkwata A, Patel PR, Pattabiraman V, Xu SY, Dudeck MA. Continued Increases in HAI Incidence During the Second Year of the COVID-19 Pandemic. *Infection Control & Hospital Epidemiology*. 2022 May 20:1-9.
6. Pandolfo AM, Horne R, Jani Y, Reader TW, Bidad N, Brealey D, Enne VI, Livermore DM, Gant V, Brett SJ. Intensivists’ beliefs about rapid multiplex molecular diagnostic testing and its potential role in improving prescribing decisions and antimicrobial stewardship: a qualitative study. *Antimicrobial Resistance & Infection Control*. 2021 Dec;10(1):1-8.
7. Burk M, El-Kersh K, Saad M, Wiemken T, Ramirez J, Cavallazzi R. Viral infection in community-acquired pneumonia: a systematic review and meta-analysis. *European Respiratory Review*. 2016 Jun 1;25(140):178-88.
8. Shengchen D, Gu X, Fan G, Sun R, Wang Y, Yu D, Li H, Zhou F, Xiong Z, Lu B, Zhu G. Evaluation of a molecular point-of-care testing for viral and atypical pathogens on intravenous antibiotic duration in hospitalized adults with lower respiratory tract infection: a randomized clinical trial. *Clinical Microbiology and Infection*. 2019 Nov 1;25(11):1415-21.

Table 1: Table: Patient characteristics of 56 COVID-19 patients admitted to a single centre intensive care unit (ICU) during the fourth wave in Ireland.

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

	No Infection N=32 (%)	Hospital (ICU)- Acquired Infection N=24 (%)	Co-Infection on ICU admission N=4
Age (years)	54 \pm 16	52 \pm 16	50 \pm 6
Male	23(72)	13(54)	3
Body Mass Index (kg/m ²)	29.8 \pm 4.9	30.6 \pm 6.8	28.9 \pm 2.6
Length of ICU Stay (days)	7.8 \pm 6.1	29.2 \pm 24.9	23.8 \pm 25.8
Ventilation Status			
- Mechanically ventilated	18 (56)	23 (96)	3
- Mean ventilated days	8 \pm 5	24 \pm 22	20 \pm 18
Mortality (At ICU discharge)	10 (31)	8 (33)	1
Prescribed empiric antimicrobials			
- Number of antimicrobial courses	1 \pm 1	5 \pm 2	4 \pm 2
Antimicrobial resistant organisms			
- VRE colonisation	4 (7)	7 (13)	0
- CPE colonisation	1 (2)	1 (2)	1 (2)
- ESBL infection (UTI)	0	3 (5)	0
- MRSA infection (VAP)	0	1 (2)	0
- MRSA colonisation	0	1(2)	0

VRE: Vancomycin Resistant Enterococci.

CPE: Carbapenemase-Producing Enterobacterales

ESBL: extended spectrum beta-lactamase producing Enterobacterales.

MRSA: Meticillin-resistant *Staphylococcus aureus*

UTI: Urinary tract infection

VAP: ventilator associated pneumonia