Antimicrobial stewardship challenges and innovative initiatives in the acute hospital setting during the COVID-19 pandemic

Ellen Martin¹, Marie Philbin¹*, Gerry Hughes ², 3, Colm Bergin², 3 and Alida Fe Talento 4, 5, 6

¹Antimicrobial Resistance and Infection Control Division of HPSC, 25-27 Middle Gardiner Street, Dublin 1, Ireland; ²Department of Infectious Diseases, St James's Hospital, James's Street, Dublin 8, Ireland; ³School of Medicine, Trinity College Dublin, College Green, Dublin 2, Ireland; ⁴Department of Clinical Microbiology, Beaumont Hospital, Dublin, Ireland; ⁵Department of Clinical Microbiology, Royal College of Surgeons Ireland, Dublin, Ireland

*Corresponding author. E-mail: marie.philbin1@hse.ie

Sir,

As highlighted by Rawson et al.,¹ the consequences of the global pandemic due to coronavirus disease 2019 (COVID-19) for antimicrobial (AM) consumption, AM resistance (AMR) rates and healthcare-associated infections are as yet unknown. Since the diagnosis of the first case of COVID-19 on 29 February 2020 in Ireland, AM stewardship (AMS) teams across the acute hospital sector have adapted to changing work patterns and workloads. The Irish Antimicrobial Resistance and Infection Control (AMRIC) team co-published guidance documents on the antiviral treatment of COVID-19 based on rapid evidence reviews as well as AMS strategies during the pandemic to assist clinicians nationally.², ³

We invited healthcare professionals involved in AMS programmes in the acute hospital setting to participate in an electronic survey hosted on SurveyMonkey⁴ and open for participation from 20 to 25 May 2020. The survey investigated the challenges, if any, the COVID-19 pandemic posed to the effective delivery of AMS with a view to informing interventions to optimize delivery of AMS in the COVID-19 era. Data were collated and analysed on Microsoft Excel® 2019 and SPSS version 26 and are available in detail in Appendices S1 to S7 (available as Supplementary data at JAC Online).

There were 98 respondents from 45 public and private hospitals in Ireland (45/67, 67%), of which 45% (43/95) were AMS and infectious diseases pharmacists, 26% (25/95) were clinical microbiologists and 11% (10/95) were infectious diseases physicians. Seventy-six percent (65/86) reported that COVID-19 had impacted on the effective implementation of AMS programmes locally with a statistically significant decrease in the median score for the effectiveness of AMS programmes from 7 pre-COVID-19 to 5 during COVID-19 (z = 6.584, P < 0.001). The greatest decline in effectiveness was seen in tertiary and general hospitals, most likely due to increased burden of COVID-19 cases in these healthcare facilities.⁴

Table 1 summarizes the unexpected AMS-related occurrences as a result of the pandemic as well as the interventions introduced to circumvent these challenges. The main themes identified related to AM use, MDR organism (MDRO) surveillance, diagnostics, use of experimental agents, medication supply and communication. AMS interventions specific to their COVID-19 patient cohort were identified and proved particularly effective during the acute phase of the pandemic included regular treatment guideline review and updates, introduction of biomarkers such as procalcitonin, review of indication of AMs and use of electronic resources. The majority found the national guidance documents, which were updated regularly, extremely useful.

The key challenges to AMS brought about by COVID-19 were mainly due to the lack of resources as a result of reallocation to COVID-19 planning and management; the difficulties posed by infection prevention and control (IPC) restrictions and social distancing in delivering ward rounds, performing audits, providing education and holding committee meetings; and increased use of AMs due to the difficulty in diagnosis of secondary infections, particularly in patients with severe COVID-19. These challenges for effective delivery of AMS programmes reflect the concerns expressed by Rawson et al.¹

Our findings suggest that successful delivery of AMS in the COVID-19 era requires further resourcing in three key areas: technology, diagnostics and guideline development. Innovative utilization of information and communication technologies (ICT) facilitated education, AMS meetings, virtual ward rounds and clinics as well as handover meetings. This was most noted in hospitals where electronic prescribing and health records are available. Evidence points to the benefit that ICT can have on AMS programmes in terms of increased productivity, more effective case finding, workflow auditing and optimization of infection management.⁵ Furthermore, early literature suggests that electronic healthcare platforms improve the management and review of COVID-19 patients.⁶

Consistent with published literature to date,⁷ the difficulty in diagnosis of bacterial/fungal coinfections, particularly in patients with severe COVID-19, resulted in reports of increased use of empirical AM treatment and consequently increased risks of Clostridioides difficile infection⁸ and emergence of MDRO. Further research into the use of procalcitonin and other biomarkers in the COVID-19 patient cohort to provide diagnostic stewardship is required as these may be useful tools to decrease inappropriate prescribing and support early de-escalation of AM therapy.⁹, ¹⁰

Sustaining MDRO surveillance and compliance with IPC protocols are key areas to focus on going forward.

© The Author(s) 2020. Published by Oxford University Press on behalf of the British Society for Antimicrobial Chemotherapy. All rights reserved.
For permissions, please email: journals.permissions@oup.com.
Table 1. Main themes identified in free-text reporting of unexpected AMS-related occurrences and AMS interventions introduced as a result of COVID-19

| Challenges – unexpected AMS-related occurrences as a result of COVID-19 | Illustrative free-text responses | AMS interventions |
|---|---|---|
| **AM use** | ‘Duplication of antimicrobials, use of restricted antimicrobials, prolonged course of antimicrobials’ | Introduction of specific AM guidelines for COVID-19 patients. |
| Reduced adherence to AM prescribing policy | ‘Less adherence to guidelines, more empiric, broad spectrum prescribing of antibiotics in COVID-19 positive patients’ | Use of preauthorization or restricted prescribing for experimental agents. |
| Increased use of restricted AMs | ‘Widespread prescription of antimicrobials without a clear indication for same due to concern for super-imposed bacterial infections in COVID-19 pneumonia; slow to stop/review [antibiotic] choice despite lack of evidence of bacterial infections; slow to revert to standard guidelines when patient is COVID –ve’ | Extended use of once-daily dosing regimens. |
| Increased use of broad-spectrum agents | ‘…there has been an increase in once daily antimicrobials for COVID-19 positive patients to treat secondary bacterial infection (ceftriaxone and levofloxacin). In patients in whom were initially managed on the COVID-19 pathway who subsequently tested negative with another alternative diagnosis we initially found it difficult to get these patients onto the appropriate antimicrobials for new diagnosis (e.g. co-amoxiclav for [community acquired] pneumonia, co-amoxiclav for urinary tract infection etc)…’ | Frequent review of antiviral and AM therapy in COVID-19 pathway. |
| Increased use of multiple agents | | Follow-up AMS review of patients with ‘SARS-CoV-2 not detected’. |
| Increased prescription duration | | Promotion of HSE guidance on specific antivirals and audit of use to assess prescribing patterns. |
| Increased use of once-daily AMs, e.g. ceftriaxone (one respondent reported increased C. difficile as a result) | | Promotion of iv-oral switch to reduce contact time. |
| Difficulty de-escalating AM regimens | | Introduction of database for experimental agents and antibiotic prescribing in COVID-19 patients. |
| **MDRO surveillance** | ‘(1) Increase in C. difficile cases, likely related to ceftriaxone administration. |
| Decreased screening for MDRO | (2) Increase in MDRO i.e. ESBL, VRE & MRSA, Likely more relates to hand hygiene & PPE rather than AMS. | Work in conjunction with the IPC teams and the microbiology laboratory. |
| Increased C. difficile cases | (3) Reduced screening for MDRO due to use of laboratory diagnostics & staff for COVID-19 PCR, reduced nurses performing swabs, prioritisation of tasks in favour of COVID-19.’ | Continuous education on hand hygiene and other IPC interventions. |
| MDRO outbreaks | | |
| **Diagnostics** | ‘Now have procalcitonin testing which is a positive…’ | Introduction of biomarkers such as urinary antigens and procalcitonin as a serum marker for bacterial coinfection for COVID-19 patients and as a tool to guide antibiotic cessation/de-escalation. |
| Difficulty in diagnosis of coinfections, which led to increased AM prescriptions. | | Regular updates from the AMRIC team of COVID-19 treatment guidance based on evidence from ongoing trials, which are cascaded for implementation locally. |
| **Experimental agents** | ‘Arrhythmia / prolonged QT related to azithromycin use in COVID patients’ | Promotion and implementation of guidelines. |
| High volume of queries | ‘At the initial stages, difficulty ordering sufficient supply of [hydroxychloroquine, azithromycin], kaletra. No longer in use now for COVID. High volume of queries initially, e.g. whether to use IVIG, tocilizumab, safety of reconstituting tocilizumab at ward level.’ | Introduction of database for experimental agents and antibiotic prescribing in COVID-19 patients. |
| Adverse drug reactions | | |
| Prescription of agents not available in Ireland | | |
| Unlicensed use of some agents | | |

Continued
Lastly, national guidance documents were extremely beneficial, particularly in hospitals with less AMS resources, which underlines the importance of further similar evidence-based guidance on the treatment of other infections.

Our survey contributes to an evolving literature on the impact of COVID-19 on AMS and interventions to sustain and deliver effective AMS programmes during this time. Further research is required to quantify the unintended consequences for AMR and the success of different AMS strategies and interventions in reducing AMR in the pandemic and post-pandemic environment.

Acknowledgements

We thank Professor Martin Cormican, Antimicrobial Resistance and Infection Control Division of HPSC, 25–27 Middle Gardiner Street, Dublin 1, Ireland and Department of Clinical Microbiology, Galway University Hospital, Newcastle Road, Galway, Ireland for his review of the paper prior to submission.

We thank all members of the AMS InSight team for their contribution to the development and review of the survey design: Eilmarie Cottrell, Pharmacy Department, Cork University Maternity Hospital, Wilton, Cork, Ireland; Dr Robert Cunney, Department of Clinical Microbiology, Temple Street Children's Hospital, Temple Street, Dublin, Ireland; and Dr Geraldine Maloney, Department of Infectious Diseases, Cork University Hospital, Wilton, Cork, Ireland.

We thank Mala Shah (Pharmacy Department, Cork University Hospital, Wilton, Cork, Ireland), Rebecca Breslin (Pharmacy Department, Galway University Hospital, Newcastle Road, Galway, Ireland) for their contribution to the development of the survey design.

We thank the Irish Society of Clinical Microbiologists, the Infectious Diseases Society of Ireland and the Irish Antimicrobial Pharmacists’ Group for dissemination of the survey and participation of members in the survey.

We thank all survey respondents.

Funding

This study was carried out as part of our routine work.

Transparency declarations

None to declare.

Supplementary data

Appendices S1 to S7 are available as Supplementary data at JAC Online.

References

1 Rawson T, Moore L, Castro-Sanchez E et al. COVID-19 and the potential long-term impact on antimicrobial resistance. J Antimicrob Chemother 2020; 75: 1681–4.

2 HSE. Interim Guidance for the Use of Antiviral Therapy in the Clinical Management of Acute Respiratory Infection with SARS-CoV-2 (COVID-19). https://www.hse.ie/eng/about/who/cspd/ncps/critical-care/sars-cov-2-covid-19.pdf.

3 HSE, AMRIC. Antimicrobial Stewardship in COVID-19. https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/infectionpreventionandcontrolguidance/antimicrobialstewardship/Antimicrobial20Stewardship%20in%20COVID%2019.pdf.

4 HSE Performance Management and Improvement Unit. COVID-19 Daily Operations Update—Acute Hospitals. 23 July 2020. https://www.hse.ie/eng/
services/news/newsfeatures/covid19-updates/covid19-daily-operations-update-2000-23-july-2020.pdf.

5 Davis M, McManus D, Koff A et al. Repurposing antimicrobial stewardship tools in the electronic medical record for the management of COVID-19 patients. Infect Control Hosp Epidemiol 2020; doi:10.1017/ice.2020.281.

6 Mazdeyasna H, Nori P, Patel P et al. Antimicrobial stewardship at the core of COVID-19 response efforts: implications for sustaining and building programs. Curr Infect Dis Rep 2020; 22: 23.

7 Rawson T, Moore L, Zhu N et al. Bacterial and fungal co-infection in individuals with coronavirus: a rapid review to support COVID-19 antimicrobial prescribing. Clin Infect Dis 2020; doi:10.1093/cid/ciaa530.

8 Sandhu A, Tillotson G, Polistico J et al. Clostridioides difficile in COVID-19 patients, Detroit, Michigan, USA, March–April 2020. Emerg Infect Dis 2020; 26: 2272–4.

9 Lippi G, Plebani M. Procalcitonin in patients with severe coronavirus disease 2019 (COVID-19): a meta-analysis. Clin Chim Acta 2020; 505: 190–1.

10 NICE. COVID-19 Rapid Guideline: Antibiotics for Pneumonia in Adults in Hospital. 2020. https://www.nice.org.uk/guidance/ng173/resources/covid19-rapid-guideline-antibiotics-for-pneumonia-in-adults-in-hospital-pdf-66141959536069.