Chasing resistance: analyzing the fight against hospital infections

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The antibiotics we rely on to treat bacterial infections are becoming increasingly ineffective as antibiotic resistance spreads around the globe.[1] Certain bacterial pathogens, such as *Pseudomonas aeruginosa*, have been identified as major contributors to this escalating burden of resistance.[2] *P. aeruginosa*, an opportunistic pathogen, is responsible for a significant number of healthcare-associated infections, and is estimated to be associated with over 300,000 annual deaths.[3]

In the current issue of The Lancet Regional Health—Europe, Sastre-Femenia et al.[4] conduct a large-scale analysis of *P. aeruginosa* isolates obtained from hospitalized patients across Spain in 2022, comparing these findings with data collected five years earlier in 2017. Their study encompasses a comprehensive analysis of antibiotic resistance in *P. aeruginosa*, evaluating resistance to 13 different antibiotics in over 3000 clinical isolates of *P. aeruginosa,* and genome sequencing the isolates with the most concerning resistance profiles to elucidate the basis of this resistance.

In 2017, the situation painted a grim picture: antibiotic resistance on a nation-wide scale was high in *P. aeruginosa,* exceeding 20% for most available anti-pseudomonal antibiotics, with the exception of polymyxins and newer β-lactam/β-lactamase inhibitor combinations. Alarmingly, there was a high prevalence of extensively drug-resistant (XDR) *P. aeruginosa* isolates (15.2%), which are resistant to at least one agent in all but one or two antibiotic classes.[5] The key revelation from this study is a substantial improvement to this scenario. Sastre-Femenia et al.[4] report a widespread reduction in antibiotic resistance in *P. aeruginosa* between 2017 and 2022. This reduction is shown for the older as well as newer antibiotics used to treat *P. aeruginosa* infections and can be observed all across Spain. Promisingly, there is also a significant decrease in the prevalence of XDR isolates, from 15.2% in 2017 to 5.9% in 2022. These strains present substantial treatment challenges due to the limited availability of effective antibiotics.

The significance of such a reduction in antibiotic resistance over a five-year period offers hope for efforts to combat antibiotic resistance, and clearly raises the question of—how? What are the underlying mechanisms responsible for this observed decline in resistance? The authors suggest that the efforts of the Spanish national plan of antibiotic resistance (PRAN), the adoption of newer β-lactam/β-lactamase inhibitor combinations, and effects of the COVID-19 pandemic may all be contributing factors. The PRAN will include infection control measures, aiming to reduce hospital transmission, infections, and the subsequent demand for antibiotics, along with antibiotic stewardship initiatives, aiming to curtail unnecessary antibiotic use, potentially playing a role in this reduction.[6] The effects of the COVID-19 pandemic on antimicrobial resistance are intriguing, and likely complex. The pandemic saw the implementation of enhanced measures to try and limit virus transmission, but, on the other hand, COVID-19 hospitalisations have been linked to secondary hospital-acquired bacterial infections, as well as misuse of antibiotics, particularly early in the pandemic.[7,8]

Another pertinent question arising from this study, is how do these trends in Spain compare with those in the rest of Europe and the world? Many countries, including Spain, have implemented national action plans to combat antimicrobial resistance. This study provides a robust methodology for conducting similar analyses globally, which could be applied to offer valuable insights into the effectiveness of these initiatives. Furthermore, the study points to the importance of investigating the mechanisms of antibiotic resistance. Characterizing mutational and acquired resistance mechanisms, particularly in isolates like XDR ST235 that are shown to increase in prevalence and be associated with multiple acquired resistance genes,[9] can illuminate how these genes are disseminated. Future research could explore the movement of acquired resistance genes, potentially through mobile genetic elements,[10] to better understand the spread of resistance.

In conclusion, the findings of this study offer hope in the battle against antibiotic resistance, showcasing a remarkable reduction in resistance levels over just five years. This work serves as a valuable benchmark for future large-scale efforts to monitor resistance over time, and the wealth of data provided here is likely a

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highly useful resource for the scientific community and policymakers alike. However, understanding the driving forces behind this decline and assessing its global relevance are essential next steps. Moreover, investigating the mechanisms underpinning antibiotic resistance remains a crucial endeavour as we continue to combat this pressing public health threat.

Contributors

RMW and JB conceived, wrote, commented, and revised the final document.

Declaration of interests

The authors have no conflict of interest to declare.

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