EDITORIAL

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Antimicrobial Stewardship Opportunities: An Example from Oman

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Antimicrobial resistance (AMR) is a growing public health concern that poses a major threat to human health on a global scale. It jeopardizes the effectiveness of several life-saving treatments. The excessive use, misuse, and abuse of antimicrobials in both humans and animals are key factors contributing to AMR.[1]

Antimicrobial stewardship (AMS) is a strategy to ensure the responsible use of antimicrobial medicines. However, decreased consumption of antibiotics may be an appropriate objective in cases of overconsumption, where people continue to die from infectious diseases due to inadequate access antibiotics.[2] AMR and antimicrobial consumption are two essential pillars of AMS.

AMR and AMS have recently gained significant political attention. During the 2015 World Health Assembly, all member states committed to develop national action plans against AMR by 2017, and the World Health Organization reported on their progress in 2017.[3] Antibiotic resistance was also identified as a global priority during the G20 Summit in July 2017 and the United Nations General Assembly in September 2016.[4]

The implementation of AMS programs in Oman and other Gulf Cooperation Council (GCC) states was largely driven by the increased burden of AMR. Several studies have reported the presence of extended-spectrum β-lactamase-producing bacteria, pan drug-resistant gram-negative bacilli, and the identification of novel and rare resistance mechanisms such as OXA-48-type and NDM-1 carbapenemases, which have been associated with hospital outbreaks and increased mortality.[5–11]

To address the growing burden of AMR in Royal Hospital, a tertiary care hospital in Oman with 1200 beds, an AMS team was established in 2014. The team consists of an infectious diseases consultant and a clinical pharmacist working as part time. The objectives were to rationalize antibiotic prescriptions, preserve remaining antibiotics, enhance patient safety, and reduce costs. An analysis of 969 meropenem antibiotics prescriptions was conducted to identify specialties with the highest rates of overuse/misuse. The findings revealed that general surgeons and general internists had ordered 200 and 231 meropenem prescriptions, respectively. Other specialties that exhibited high rates of prescriptions were intensive care unit, nephrology, and hematology (data unpublished). Furthermore, a retrospective audit of clinicians antimicrobial prescribing patterns among adult patients that were admitted to the acute medicine wards over a four-week period showed that approximately 37% of antimicrobial usage was unnecessary or inappropriate. On average, each patient received 2.5±1.1 antimicrobials. The most frequently prescribed antimicrobials were piperacillin/tazobactam, followed by amoxicillin/clavulanic acid and clarithromycin. Antimicrobial agents were predominantly prescribed for community-acquired pneumonia followed by urinary tract infection. Microbiological cultures were obtained from only 25% of patients prior to initiating antimicrobial therapy. The most common isolated organisms were gram-negative bacteria; 66% of the obtained cultures were negative. Antimicrobial agents were used empirically in 79% of cases. The dosage, route, and frequency of prescribed antimicrobials

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were deemed appropriate in 66%, 70%, and 68% of cases, respectively.[12]

In 2015, an interdisciplinary AMS committee was established, reporting directly to the Royal Hospital Director General. The committee comprised the AMS team, pharmacists, infectious diseases physicians, infection control specialists, physicians, microbiologists, nursing staff, hospital administrators, and information system specialists, as available and appropriate.

The infectious disease physicians coordinated the AMS program, overseeing its implementation, and leading educational activities. Clinical pharmacists played a role in coordinating AMS activities, organizing regular meetings with key stakeholders, and monitoring implementation progress. Infection control professionals provided guidance on infection control practices, assisted in the implementing recommendations, and guided surveillance activities. Microbiologists contributed by providing antibiograms every two years.

The team engages in daily AMS activities that require tremendous efforts but have effective long-term gains. These activities include conducting daily multi-disciplinary rounds with departments that handle the highest volume of patients and/or the highest use of antibiotics, conducting surveillance activities on healthcare-associated infections and reporting resistant organisms, developing guidelines for the appropriate use of antimicrobial therapy for common infections, and implementing policies on appropriate methods for obtaining microbiological cultures.

The AMS program had a significant impact on the annual rates of multi-drug resistant organisms in hospitals, with a reduction from 2.8 per 1000 patient days in 2014 to 0.6 per 1000 patient days in 2017. Similar reductions were observed in rates of methicillin-resistant *Staphylococcus aureus* from 4.2 per 1000 patient days in 2014 to 2.3 per 1000 patients days in 2017, and carbapenem resistance Enterobacteriaceae from 2 per 1000 patient days to 0.61 per 1000 patients days (unpublished hospital surveillance data). Furthermore, the AMS program has resulted in estimated cost savings of 70 000–80 000 USD annually from 2017 onwards. However, the process of monitoring compliance, appropriateness of use, and measurement of antimicrobial consumption was time-consuming. Therefore, the integration of information technology was imperative. In 2016, a customized pre-authorization approval electronic order form for restricted antimicrobials was developed for the Al Shifa System (National Electronic Medical Record). This allowed prescribers to electronically order restricted antimicrobials for 72 hours, after which approval from the AMS team was required. The selection of restricted antimicrobials was based on risk of *Clostridium difficile* infection, broad spectrum activity, and cost. The restricted antimicrobials included meropenem, tigecycline, clindamycin, colistin, linezolid, moxifloxacin, voriconazole, caspofungin, and liposomal amphotericin. Additionally, an innovative electronic AMS tracking system was locally developed with the Ministry of Health's information technology team. The system consists of a dashboard to document, monitor, and track antimicrobial use per agent, specialty, and ward. The system also electronically measures antimicrobial utilization by calculating aggregated ratios using the defined daily dose or the days of therapy and helps in time optimization, and provides medical information that is easily retrievable for the improvement of patient care and research. It allows prompt feedback to the prescribers by providing individual, ward or specialty consumption data, and enhances the opportunity to educate both the prescribers and the public. The system enables a deeper understanding of local trends of antimicrobial prescribing practices among clinicians in the context of benchmarking national data.

Establishing an effective AMS program is complex and involves a various factors related to efficiency, human factors, and systems. AMS faces challenges such as limited human resources, the availability of champions, willingness of healthcare workers to participate, time constraints, and lack of compensation for stewardship activities. Furthermore, barriers like insufficient funding and information technology support, resistance from colleagues, misconceptions about the importance of AMS, and lack of awareness can hinder the smooth functioning of AMS.[13] Our program gained acceptance by primary stakeholders based on three main pillars: restriction, prospective audit and feedback, and continuous education. However, we faced challenges related to the need for human resources and lack of collaboration from clinical pharmacists.

At the national level, Oman reported 'sustained capacity', which is the highest positive response to

the question regarding the level of "Optimizing antimicrobial use in human health" in 2021, as per the "Tracking AMR Country Self-Assessment Survey" coordinated by Quadripartite Organizations on AMR. However, in 2022 response, Oman regressed two levels and reported "developed capacity".[14]

Although the strategic plan for combating AMR in the GCC countries identified six measurable elements to encourage prescribers to preserve the efficacy of antimicrobials, several studies concluded that the situation of AMS in the GCC countries has not significantly improved over time and require substantial improvement.[15] A cross-sectional survey conducted in 2014 assessed the situation and barriers to the implementation of AMS in acute care hospitals in the GCC states. The study concluded that although AMS existed in 62% of the participating hospitals, 75% of them reported a lack of human and financial resources as the major barriers to improvement.[16] Published articles noted some progress but also flagged many challenges.[17–19]

Furthermore, a recently published paper indicated that the prevalence of AMR in Eastern Mediterranean countries, including Oman, remains high and is likely increasing over time.[11] The study reported on the AMS core capacities for 20 of the 22 Eastern Mediterranean countries. Only one (5%) country had dedicated national funding for AMS, four (20%) countries had established national AMS technical working groups, and one (5%) had developed an AMS implementation plan. Thirteen (65%) countries reported having an Essential Medicines List, with two of them adopting World Health Organization access, watch, and reserve classification. Five (25%) countries had treatment guidelines, and 10 (50%) countries had a prescription-only sale policy for antibiotics, but only five enforced this policy.[11]

Another study reviewed the potential negative impact that COVID-19 pandemic had on AMS. The authors highlighted increased consumption across all classes of antimicrobials during the pandemic in Arabic countries. Challenges to implementing AMS during COVID-19 included a shortage of AMS experts, lack of education and training, poor communication, and a lack of specialized health information technology.[20] In our hospital, during the initial six months of the COVID-19 pandemic, 92.98% of 584 patients admitted with COVID-19 pneumonia received empiric antibiotics, while initial bacterial coinfection was rare and was confirmed in only 0.86% of patients.[21]

Another study identified five key areas to promote cross-regional collaboration: training and education, building capacity, infrastructure strengthening and support, enhancing regional research, and improving regional surveillance recommendations for future initiatives.[22]

Most studies have concluded that implementation of AMS programs has positive clinical outcomes, and have highlighted the importance of leadership and accountability to improve AMS programs at national and hospital levels. The main barriers identified include a lack of dedicated staff, workload, and funding.[11,20,22,23]

AMS program interventions have proven to have a significant impact on the practice of antimicrobial utilization, reduction of AMR, and cost savings. Integrating technology in AMS progam is crucial to support, monitor and collect real-time data. There are few published data on national and hospital levels of AMS program or AMS activities from Oman, the Gulf region, and other Arab countries.

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