

Antimicrobial stewardship: a Tunisian experience

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Antibiotic resistance (AMR) is a major public health problem. Indeed, experts estimate that in 2050, 10 million deaths will be attributable to AMR. It is now proven that the emergence of bacterial resistance is directly correlated with excessive use of antibiotics.¹ A study analysing the trends and drivers of antibiotic consumption from 2000 to 2015 in 76 countries demonstrates that the latter increased by 65%.² In order to fight AMR, in 2016 the World Health Organization (WHO) launched a global plan of action that covers several areas including the implementation and promotion of Antimicrobial Stewardship Programmes (ASP) and the monitoring of antibiotic consumption.³

Until 2018, there was no national ASP in Tunisia. According to Klein *et al.*, Tunisia is the second highest consumer of antibiotics in the world² and national data on AMR are alarming. Tunisian multicentre data show that the resistance of *E. coli* strains to third-generation cephalosporins increased from 3.9% to 19.3% and resistance to

ciprofloxacin increased from 13.5% to 25.6% between 2004 and 2017. During the same period, resistance of *K. pneumoniae* strains isolated from bloodstream infections to imipenem increased from 0 to 12.1%.⁴ In our institution, a multidisciplinary university hospital with 850 beds, more than 30% of the pharmacy budget is spent on antibiotics. Regarding antibiotic mis-usage, we observed that 35.7% of inpatients are on antibacterials of which 45.8% patients received an inappropriate prescription.

Building on these findings, we started an ASP in July 2014. We took three major steps. The first step was the implementation of an antibiotic management team (AMT) with a part-time Infectious Diseases (ID)

specialist. The role of the “Antibiotherapy Referent (AR)” was to provide antibiotic therapy advice to prescribers. The second step was to centralise all antibiotic advice requests. The third step was that all requests and responses were documented. Antibiotic therapy advice forms were created and AR responses were computer recorded.

This paper describes AR activity from 1 July 2014 to 31 December 2018. During the study period, 3,872 requests were registered. The requests came from surgical departments (1,742 / 45% cases), medical departments (1,587 / 41% cases) and emergency and intensive care wards (543 / 14% cases). ID requests were made by senior doctors (1,641 / 42.4% cases), specialist trainees (948 / 24.5% cases) and generalist trainees (1,283 / 33.1% cases). To respond to requests, AR consulted patients’ medical records (3,016 / 77.9% cases) and moved to the patients’ beds (759 / 19.6% cases). In 97 cases (2.5%), antibiotic advice was given by phone call. Among all requests, 78.1% (n=3,024) were on antibiotic therapy

management, 10.3% (n=399) were on the patient transfer and 8.2% (n=318) were on diagnostic advice (Figure). It is worth noting that the main reason for antibiotic management requests is antibiotic therapy adjustment which represents 66.1% (1,999 requests) of all the requests (3,024). The AR was asked to initiate antibiotics in 798 cases (26.4%) while discontinuation of antibiotic therapy was requested in 227 (7.5%) (Table). The AR’s intervention resulted in cessation / avoidance of antibiotic therapy in 419 cases (13.8%). When an antibiotic adjustment was recommended (1,363 cases), de-escalation was proposed in 409 cases (30%). Finally, concordance between prescriber requests and AR’s advices was 65.5%.

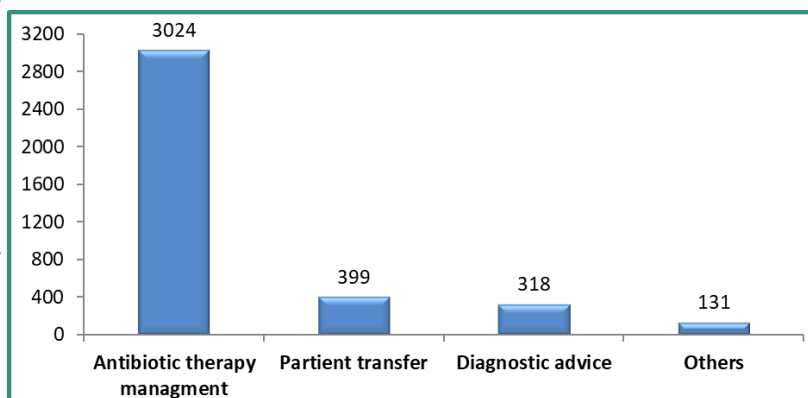


Figure: Reasons for infectious diseases requests.

Our findings manifested by worrying antibiotic consumption data, AMR and the demand from antibiotic prescribers for ID advice show a real need for the implementation of an ASP in our hospital. This need affects all medical and surgical wards and all categories of physicians from trainees to senior doctors. We have noticed that trainees made the highest number of requests reaching 57.6% while senior doctor requests represent 42.4% of all the cases. We have shown that ASP can reduce antibiotic consumption and hospitalisation length-of-stay. Reduced antimicrobial use contributes to a reduction in mortality. Moreover, ASP leads to reduced AMR.^{5,6}

Molina *et al.*, proved that an education-based ASP was effective in decreasing the mortality rate of multidrug bloodstream infection through sustained reduction in antibiotic use.⁷ The goal of an ASP is to improve antimicrobial use. This involves choosing the right drug for the appropriate diagnosis, the correct dose and the adequate duration of treatment. Creation of an AMT is crucial to a successful ASP. Its mission is to devise a strategy for rational use of antibiotics.^{8,9} In our local context, an ID specialist acted as the AR. His decisions are more likely to be accepted and

applied by prescriber physicians due to his in-depth knowledge and expertise in the field of antibiotic therapy but the fact that he is part-time is an obstacle to better ASP implementation. In fact, face-to-face interaction was largely impossible due to AR time constraints and advice was mostly provided in patients' records. Our referent chose a post-prescription approach which gives prescribers the option to request advice or not to. A pre-prescription approach is a better means of controlling antibiotic consumption but is less accepted by prescribers. Indeed, it allows the physician to benefit from the expert knowledge of the AR before antibiotic prescription. However, it requires the recruitment of full-time and well-trained AMT.^{7,9,10}

Regardless of the chosen approach, experience in different countries shows that the presence of an antibiotic therapy referent results in better patient treatment and is cost-effective.^{5,9} We found 65.5% concordance between requests and referent opinion. However, we were unable to check that the AR advice has been followed in cases of discordant opinions.

In conclusion, our experience shows that there is a need for the implementation of a full-time multidisciplinary ASP team. We also believe that a pre-prescription approach and the implementation of patients' electronic medical records will allow the proper use of antimicrobials in a cost-effective way. Therefore, institutional support is needed for a successful ASP.

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Prescriber requests*	Antibiotic referent advices
Start antibiotics 798 requests (26.4%)	Start 527 cases (66%)
	No 271 cases (34%)
Stop antibiotics 227 requests (7.5%)	Stop 91 cases (40%)
	Continue antibiotics 136 cases (60%)
Antibiotherapy adjustment 1999 requests (66.1%)	Modification 1363 cases (68.2%)
	No modification 579 cases (29%)
	Withdrawal 57 cases (2.8%)

*In total 3024 requests
Table: Breakdown of antibiotic therapy management requests and ID referent decisions