

WHO'S AWARE CLASSIFICATION AS A TOOL OF ANTI-MICROBIAL STEWARDSHIP PROGRAM: A TEACHING HOSPITAL-BASED STUDY

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ABSTRACT

Objectives: The aim of the study was to evaluate the antimicrobial utilization pattern and compare it with the World Health Organization's (WHO's) access, watch, and reserve (AWaRe) framework for the effective implementation of anti-microbial stewardship program (ASP) for tackling antimicrobial resistance (AMR).

Methods: This was a prospective, observational study conducted by the Department of Pharmacology in association with the Department of Orthopedics, Sher-I-Kashmir Institute of Medical Sciences. Data pertaining to all 208 patients was obtained from the wards of Medical College and Hospital, Bemina, Srinagar, India, for 6 months.

Results: The total number of patients in our study was 208, among them 74 patients received anti-microbial agents (AMAs) from the WHO's access category whereas 134 were prescribed AMAs from the watch category. The percentage of AWaRe AMAs usage in comparison to the WHO criteria was 35.5% for the access list (WHO optimal value $\geq 60\%$), whereas it was 64.4% for the watch list (WHO optimal value $\leq 40\%$).

Conclusion: The government of India has no doubt taken a few steps to address this issue but a proactive approach is the need of the hour to minimize AMR saving precious lives and reduce global economic burden, further prescribing doctors should undergo periodic training to update their knowledge. Standard guidelines as developed by AIIMS and WHO should be followed across all the health facilities in India.

Keywords: Access, watch, and reserve, Antimicrobial resistance, Antimicrobial stewardship program, Antimicrobial agents.

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INTRODUCTION

Antimicrobial treatment has improved patient healthcare immensely in terms of decreased morbidity as well as mortality; however, inappropriate use of these drugs has resulted in the emergence of resistant organisms which render these drugs ineffective which in turn complicates patient treatment.

Antimicrobial resistance (AMR) poses a threat to global health care as it makes the drugs ineffective thus increasing morbidity as well as mortality [1]. Around 70 lakh people may die annually because of AMR with experts predicting this number to go up to 10 million by 2050 if no action is taken [2]. Studies have shown that the maximum broad spectrum is used in India [3,4].

The anti-microbial stewardship program (ASP) aims to promote the judicious use of antibiotics by restricting their use only in patients with evidence or with high suspicion of any infections as decided by the clinical examination, thus reducing misuse/overuse of them but at the same time ensuring timely effective treatment for patients with bacterial infections [5].

The WHO in 2017 came with a unique classification of anti-microbial agents (AMA) called access, watch, and reserve (AWaRe) drug list in which drugs are divided into three categories (AWaRe) as a tool for the implementation of ASP. Access drugs are narrow-spectrum antibiotics, effective against a vast number of infections, least resistance potential, and are recommended as the first and second choice for most common clinical syndromes whereas watch list have broader spectrum

antibiotics with a higher risk of developing resistance thus their use has to be restricted. The reserve list of drugs is to be used only as a last resort treatment when the drug-resistant organism is confirmed [6].

METHODS

Our research was prospective and observational in nature and conducted by the pharmacology department in collaboration with the orthopedics department, Sher-I-Kashmir Institute of Medical Sciences, Medical College and Hospital (SKIMS-MCH), Srinagar, India, for 5 months. Our research was successfully approved by the Institutional Research Ethics Committee and assigned the protocol ID (IEC/80/2022). Around 208 patients of different age groups and both genders who were admitted in the indoor patients' department wards of the orthopedic department were enrolled in the research.

Methodology

This research was conducted on the patients admitted to the orthopedic wards. Collection of the data of all the 208 patients was obtained from the case files. Every patient included in the research was monitored twice, first on the day of admission and second on day 4 of the admission/day discharge whichever came earlier.

RESULTS

The total number of patients in our study was 208, among them 74 patients received anti-microbial drugs from the WHO's access category while 134 were prescribed antimicrobials from the Watch category. In our study, no patient was prescribed any antimicrobial

from the reserve list while 32 patients were prescribed multiple antimicrobials belonging to access as well as the watch list (Table 1, Fig. 1). Among the access group, only amikacin was prescribed while as six different types of anti-microbial were prescribed from the watch list which included cefuroxime in 112, ceftriaxone in six, ofloxacin in four, levofloxacin in two, cefepime in six, and piperacillin with tazobactam in four patients (Table 2).

A total of 240 antimicrobials were prescribed in 208 patients (Fig. 2). Amikacin was prescribed in 31% of patients, cefuroxime (47%), ceftriaxone and cefepime (2% each), ofloxacin (<2%), piperacillin with tazobactam (<2%), and levofloxacin (1%).

Table 3 and Fig. 3 shows the overall percentage of AWaRe antibiotics usage in comparison to the WHO criteria, 35.5% of patients were given antimicrobials from the access list (WHO optimal value ≥60%) whereas 64.4% of the patients were prescribed the drugs belonging to the watch list (WHO optimal value ≤40%).

DISCUSSION

The discovery of anti-microbial drugs has completely changed the human health landscape by increasing life expectancy by around two decades and saving millions of lives since then [7]. However, the emergence of deadly resistant organisms can have a devastating effect on human civilization in the future as no treatment will be effective against these organisms. The use of antimicrobials was aimed to ensure that rightful patients receive these drugs in the proper dose and duration, as per the guidelines, and according to his/her clinical needs besides at the lowest price [8].

If the drug prescribed is not as per these criteria, it will be labeled as irrational and inappropriate [9]. Studies done in South Asia have found overuse of antimicrobials is rampant besides being poor in prescribing patterns [10]. Polypharmacy is a rule rather than an exception [11] thus leading to AMR in which bacteria, viruses, and fungi do not respond to these drugs. As per the WHO data, the AMR results in 50 million deaths yearly and further annual global costs will be 3.4 trillion US dollars pushing 28 million population into poverty by 2050 [12].

In developing countries such as India, misuse/irrational use of antimicrobials is rampant due to inappropriate dispensing, easy availability of antibiotics as over-the-counter (OTC) drugs besides the tendency of the patient to self-medicate and the lack of knowledge among the prescribing physicians, all this speeds up AMR [12]. To address this problem, ASP was launched which aimed to decrease the unnecessary use of antimicrobials but at the same time ensuring effective treatment of patients with infections [13]. At the patient level, stewardship has been defined as the optimal selection, dosage, and duration of antimicrobial treatment that results in the best clinical outcome for the treatment or prevention of infection, with minimal toxicity to the patient and minimal impact on subsequent resistance [14].

To tackle AMR and facilitate the implementation of ASP, in 2017 WHO came up with the AWaRe list in which AMAs are divided into three (AWaRe) groups, the list was later updated in 2021 with 78 more AMAs added to the list, taking the total number to 258. It is a useful tool for monitoring antibiotic usage, defining targets, and monitoring the effects of stewardship policies that aim to optimize AMA use and curb AMR [15].

In our study, the prescription consisted of antibiotics from access and watch lists to a tune of 35.5% and 64.4%, respectively, which is a significant deviation from the WHO guidelines which recommend that a minimum of 60% AMAs prescribed should belong to the access list whereas remaining 40% from the watch list [16]. The AMAs belonging to the access group are narrow spectrum, and have the least chance of developing resistance besides having a good safety profile while those belonging to watch group have a higher chance of developing resistance,

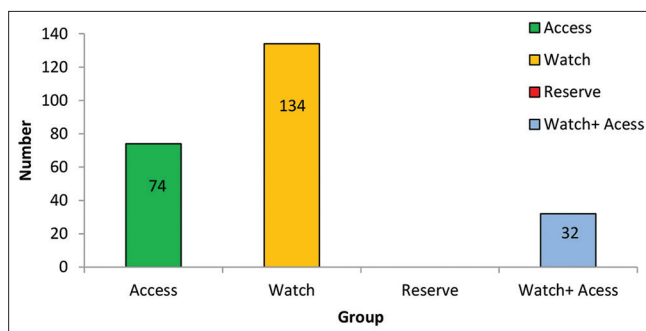


Fig. 1: Total number of antibiotics as prescribed as per access, watch, and reserve classification

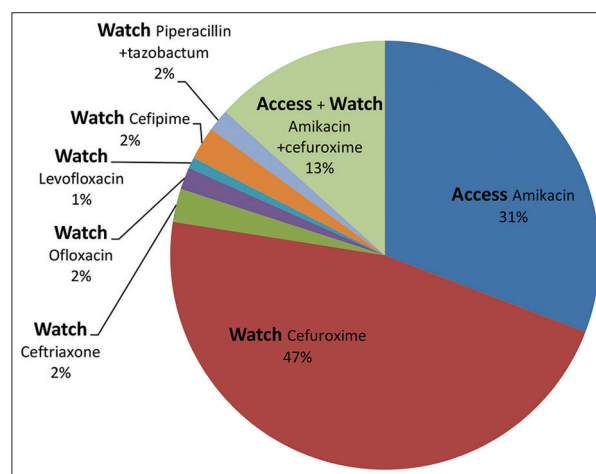


Fig. 2: Individual drugs from each group of access, watch, and reserve classification

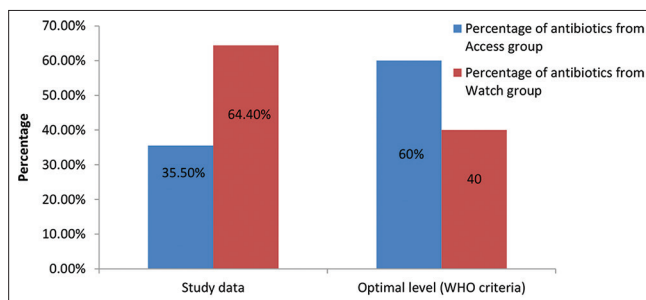


Fig. 3: Comparison of the study data with the World Health Organization access, watch, and reserve classification in 208 patients

Table 1: Total number of antibiotics as prescribed as per AWaRe classification

| WHO aware category | Number of antibiotics prescribed (n=208) |
|--------------------|--|
| Access | 74 |
| Watch | 134 |
| Reserve | 0 |
| Access+watch | 32 |

AWaRe: Access, watch and reserve, WHO: World Health Organization

indicated in patients presenting with severe infections or when an invading organism is likely to be resistant. Reserve group is indicated only in multi-resistant infections [16,17]. In our study, only one drug (amikacin) was prescribed from the access list whereas six groups of

Table 2: Individual drugs from each group of AWaRe classification

| Group | Drug | Number (n=240) |
|-----------------|-------------------------|----------------|
| Access Watch | Amikacin | 74 |
| | Cefuroxime | 112 |
| | Ceftriaxone | 6 |
| | Ofloxacin | 4 |
| | Levofloxacin | 2 |
| | Cefepime | 6 |
| Reserve | Piperacillin+tazobactam | 4 |
| | None | 0 |
| Access+watch | Amikacin+cefuroxime | 32 |

AWaRe: Access, watch, and reserve

Table 3: Comparison of the study data with WHO AWaRe classification

| Category | Study data (%) | Optimal level (WHO criteria) (%) |
|---|----------------|----------------------------------|
| Percentage of antibiotics from access group | 35.5 | ≤60 |
| Percentage of antibiotics from watch group | 64.40 | ≥40 |

AWaRe: Access, watch, and reserve, WHO: World Health Organization

AMAs were prescribed from the watch list which included cefuroxime, ceftriaxone, ofloxacin, levofloxacin, cefepime, and piperacillin with tazobactam. Cefuroxime was prescribed in the maximum number of patients whereas levofloxacin was the least prescribed. No drug was prescribed from the reserve group; however, a small number (13%) of the patients were prescribed AMAs from both assess and watch list. In India, the rate at which AMAs from access groups are used has been declining relative to the broad-spectrum ones in the watch and reserve groups, which are often prescribed inappropriately. In 2019, only 27% of prescribed AMAs came from the access list, compared to more than 50% from the watch list. India is now the epicenter of AMR. About 47% of *Staphylococcus aureus* are not only resistant to methicillin but also to penicillin and carbapenems. Infections due to resistant organisms have directly killed nearly 300,000 people in India including newborn babies in 2019 alone and have been a factor in one million deaths that year [18].

The Indian government in 2017 under the national health policy identified AMR as a concerning issue and as such highlighted the need for pharmacovigilance and prescription audits which is the need of the hour [19]. The Indian government also launched its national action plan on AMR, which identified six priorities to combat AMR, including education, training, surveillance, and improved infection control [20]. However, very little has changed on the ground level as AMA use goes unchecked. Increased use of AMAs is directly linked to AMR [21]. Self-medication, availability of AMA as OTC drug, less number of laboratories for doing culture sensitivity, unethical prescribing of AMAs by taking gifts from the pharmaceutical companies, decentralized drug regulation in which a state drug authority can approve a drug bypassing the central drug authority (CDSCO), lack of awareness among prescribing physicians, availability of irrational fixed dose combinations of AMAs besides pressure from the patients side to prescribe AMAs are the hurdles in the way of smooth implementation of ASP in India.

CONCLUSION

The government of India has no doubt taken few steps to address this issue but a proactive approach is the need of hour to minimize AMR saving precious lives and reducing global economic burden, further prescribing doctors should undergo periodic training to update their knowledge. Standard guidelines as developed by AIIMS and WHO should be followed across all the health facilities in India, further the hospital

formulary should be made available with reference to the national list of essential medicines, antimicrobial policy, and community awareness program should be conducted periodically in the public platforms.

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CONFLICT OF INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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