ORIGINAL ARTICLE

# The Use of the WHO AWaRe Tool to Optimize Antibiotic Selection after Surgery


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## ABSTRACT


***Key words:***
***Antibiotic stewardship; Escherichia coli; Klebsiella pneumoniae***



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***Background:*** *Antibiotic resistance is a global health problem that needs urgent attention. WHO introduced AWaRe (Access, Watch, Reserve) classification of antibiotics to help in optimizing antibiotic use.* ***Objective:*** *This study aimed to evaluate the efficacy of the WHO AWaRe classification in guiding antibiotic selection and optimizing treatment outcomes for pathogens isolated from post-surgical patients at Mansoura University Hospitals.* ***Methodology:*** *A retrospective analysis was conducted on microbiological cultures obtained from post-surgical patients between January 2022 and December 2023. Samples included blood, urine, sputum, wound swabs, surgical drains, and aspirates. Automated identification of isolates was performed using the Vitek 2 system, while antibiotic susceptibility was assessed using the Kirby-Bauer disk diffusion method and Vitek 2. Antibiotics were categorized according to the WHO AWaRe classification.* ***Results****: Out of 1159 cultures, 401 (34.6%) were positive, with Gram-negative bacteria accounting for 73.6% of isolated organisms and Gram-positive bacteria for 26.4%. Escherichia coli (34%) and Klebsiella spp. (20%) were the predominant Gram-negative organisms, while Staphylococcus aureus and coagulase-negative staphylococci represented 19% of total isolates. Antibiotic susceptibility testing revealed variable resistance patterns, with carbapenems showing high efficacy against Enterobacter cloacae and E. coli but reduced activity against Acinetobacter baumannii. Aminoglycosides and Piperacillin/Tazobactam were effective against most isolates, while resistance to β-lactams and fluoroquinolones was prominent.* ***Conclusions****: The WHO AWaRe classification is a valuable framework for optimizing antibiotic selection in post-surgical infections. The study highlights the predominance of Gram-negative bacteria and their resistance patterns, emphasizing the need for targeted antibiotic stewardship to preserve the efficacy of critical antibiotics.*


## INTRODUCTION

Antimicrobial resistance is considered a major health threat for patients and healthcare providers. It challenges the control of infectious diseases, jeopardizes any medical progress and imposes huge treatment costs. Antibiotics, which are one of the greatest discoveries that have revolutionized medicine and saved millions of lives, are losing their effectiveness due to the global rapid spread of resistant bacteria. Resistance has emerged even to newer, more potent antimicrobial agents which can be attributed to the misuse or overuse of antibiotics [1].

Improving use of antibiotics through antibiotic stewardship is one of the key interventions necessary to curb the further emergence and spread of antimicrobial resistance (AMR). It is also important for ensuring appropriate treatment. For that reason, WHO in 2017 introduced the Access, Watch, Reserve ("AWaRe") classification of antibiotics in its Essential Medicines List. The classification is a tool for antibiotic stewardship at local, national and global levels with the aim of reducing antimicrobial resistance. This tool categorizes antibiotics into three groups—Access, Watch, and Reserve—based on their spectrum of activity, the potential for resistance development, and the need for their judicious use [2].

Despite the availability of this classification, its application in clinical settings, particularly in post-surgical environments, remains underexplored especially in resource-limited settings [3]. Moreover, most studies have focused on community-acquired infections, with limited research addressing the specific challenges associated with post-surgical infections, which often involve multidrug-resistant organisms [4].

Therefore, this study aimed to apply the WHO AWaRe classification to guide antibiotics selection and assess their efficacy against pathogens isolated from post-surgical patients at Mansoura University Hospitals.

## METHODOLOGY

**Subjects and Methods:**

This study is a retrospective analysis of routinely available microbiological cultures from post-surgical patients admitted to Mansoura University Hospitals in the period between Jan-2022 to December–2023, with different signs and symptoms of infections.

Different sample types such as blood, urine, sputum, wound swab, drain aspirate, peritoneal fluid aspirate, and throat swab were included in the study. The samples were cultured on the suitable media in the microbiology laboratory. Culture media were selected according to the type of sample including blood agar, MacConkey agar, CLED agar and Chocolate agar. Automated identification of isolates was performed by Vitek 2 system to identify gram-positive and gram-negative bacteria using (GP and GN identification cards, respectively) (*Biomérieux, Marcy l'Etoile, France*).

Although anaerobic cultures were available, the results were excluded because it is not a routine work in our laboratory and performed only by request. Antibiotic susceptibility testing was done by Kirby-bauer disk diffusion method according to Clinical and Laboratory Standards Institute (CLSI) performance standards [5]. Isolates with multidrug resistance were also assessed for susceptibility by Vitek 2 system.

In this study, we applied the WHO AWaRe classification of antibiotics to categorize our antibiotics into 3 main groups: Access antibiotics which can be prescribed by all hospital physicians empirically with activity against wide range of commonly encountered susceptible pathogens, Watch antibiotics including most of the high priority antibiotics and are prescribed by consultant physicians only and Reserve antibiotics which should be treated as last resort option when all alternatives have failed or not suitable in order to preserve their clinical effectiveness.

## RESULTS

Out of 1159 microbiologic cultures obtained from post-surgical patients at Mansoura University Hospitals, 401 (34.6 %) cultures were positive. 295 (73.6%) were gram negative and 106 (26.4%) were gram-positive. The majority of the species were obtained from female patients (54.0%; 46% from males) with an average age of 33 ± 19.16 y and 30 ± 17.6 y, respectively. Most samples were obtained from surgical drains (49.5%) **(Table 1).**

As regards the distribution of different microorganisms identified by Vitek 2 system, *E. coli* was the commonest organism (34%), followed by *Klebsiella* (20%), *Staph. aureus* and *Coagulase negative staphylococci* (CONS) (19%), *Pseudomonas* (9%), *Enterococcus* (7%), *Enterobacter cloacae* (6%), *Proteus* (2%) and other gram-negative bacteria including *Serratia*, *Salmonella* and *Citrobacter spp.* (3.1%) **(Figure 1).**

Based on the WHO AWaRe classification of antibiotics, a detailed antibiogram and heatmap including all isolated gram-positive and gram-negative bacteria are illustrated in **Table 2 and Figure 2**.

**Table 1: Distribution of microorganisms in each sample type**

| Sample Type | Gram Negative (No) | Gram Positive (No) | Total (No) | Total (%) |
|---|---|---|---|---|
| Blood | 42 | 15 | 57 | 14.2% |
| Urine | 60 | 33 | 93 | 23.2% |
| Sputum | 44 | 22 | 66 | 16.5% |
| Wound | 18 | 10 | 28 | 7.0% |
| Surgical Drains | 124 | 23 | 147 | 36.7% |
| Ascitic Fluid | 7 | 3 | 10 | 2.5% |
| Total | **295 (73.6%)** | **106 (26.4%)** | **401** | **100%** |

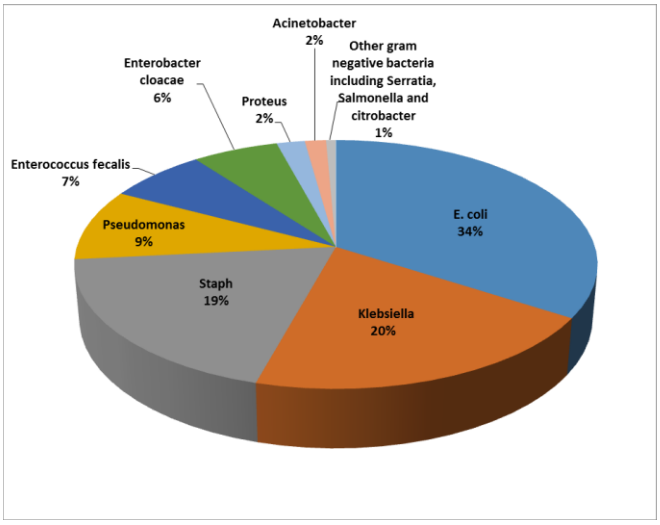


**Fig. 1:** Automated identification by Vitek 2 system

**Table 2:** Antibiogram for isolated bacteria at Mansoura University Hospitals

| AWaRe group | Selected antibiotic | The percentage of susceptible bacteria % | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Gram negative bacteria | | | | | | | Gram positive bacteria | | |
| | | E-coli | Klebsiella | Pseudomonas | Enterobacter cloacae | Proteus | Acinetobacter baumanii | Other gram negative bacteria | Staph: S.aureus | Staph: CONS | Enterococcus fecalis |
| **Access** | Ampicillin | 47 | 21.3% | - | 69 | 48 | - | 21.5 | 33.3 | 30 | 70 |
| | Oxacillin/Cloxacillin | - | - | - | - | - | - | - | 72 | 67 | - |
| | Clindamycin | - | - | - | - | - | - | - | 75 | 62.2 | 10 |
| | Gentamicin | 61 | 50 | 79 | 90 | 91.3 | 61 | 55 | 92 | 88 | 45 |
| | Doxycycline | 22.5 | 14.3 | 33.3 | 35.2 | 16 | 47 | 58.9 | 68 | 71 | 33.3 |
| | Amikacin | 66.6 | 50.9 | 91 | 100 | 90.9 | 45.2 | 90 | 88 | 75 | 40 |
| **Watch** | Ampicillin/Sulbactam | 61 | 77.1 | - | 82 | 79 | 60 | 63.3 | 83.4 | 87 | 92 |
| | Piperacillin/tazobactam | 65 | 57.1 | 54.5 | 80.5 | 63 | 46 | 56.7 | 77.8 | 71.4 | 82.5 |
| | Ciprofloxacin | 59.1 | 37.5 | 48.5 | 98 | 48.3 | 11.5 | 75 | 50 | 53 | 53 |
| | Levofloxacin | 54.6 | 32.2 | 54 | 95 | 67.5 | 12.1 | 70.8 | 61.1 | 56 | 54 |
| | 3rd generation Cephalosporins | 47.9 | 47.1 | 21.2 | 75 | 64 | 8.5 | 52.8 | 55.8 | 39.9 | - |
| | 4th generation Cephalosporins: Cefipime | 51.7 | 53.6 | 33.3 | 82 | 62.5 | 24 | 62.5 | 80 | 77 | - |
| | Erythromycin | 18 | 22 | 11 | 26 | 40 | 8 | 50% | 70.8 | 61 | 19.6 |
| | Vancomycin | - | - | - | - | - | - | - | 92 | 100 | 79 |
| | Imipenem | 90 | 77.2 | 81 | 100 | 83.9 | 66 | 80 | - | - | - |
| | Meropenem | 88 | 79.5 | 84 | 100 | 94 | 58.7 | 80.2 | - | - | - |
| **Reserve** | Colistin | 100 | 88 | 95 | - | - | 82 | 100 | - | - | - |
| | Linezolid | - | - | - | - | - | - | - | 96 | - | 100 |
| | Tigecycline | - | - | - | - | - | - | - | 100 | - | 100 |

Not all isolates tested against every antibiotic listed
CONS: coagulase negative staphylococci

**Figure 2:** A heatmap illustrating the antibiotic susceptibility of different bacteria to various antibiotics.

**Table 3** provides evidence-based recommendations for optimizing empirical antibiotic therapy in post-surgical settings at Mansoura University Hospitals to improve patient outcomes and address antibiotic resistance effectively.

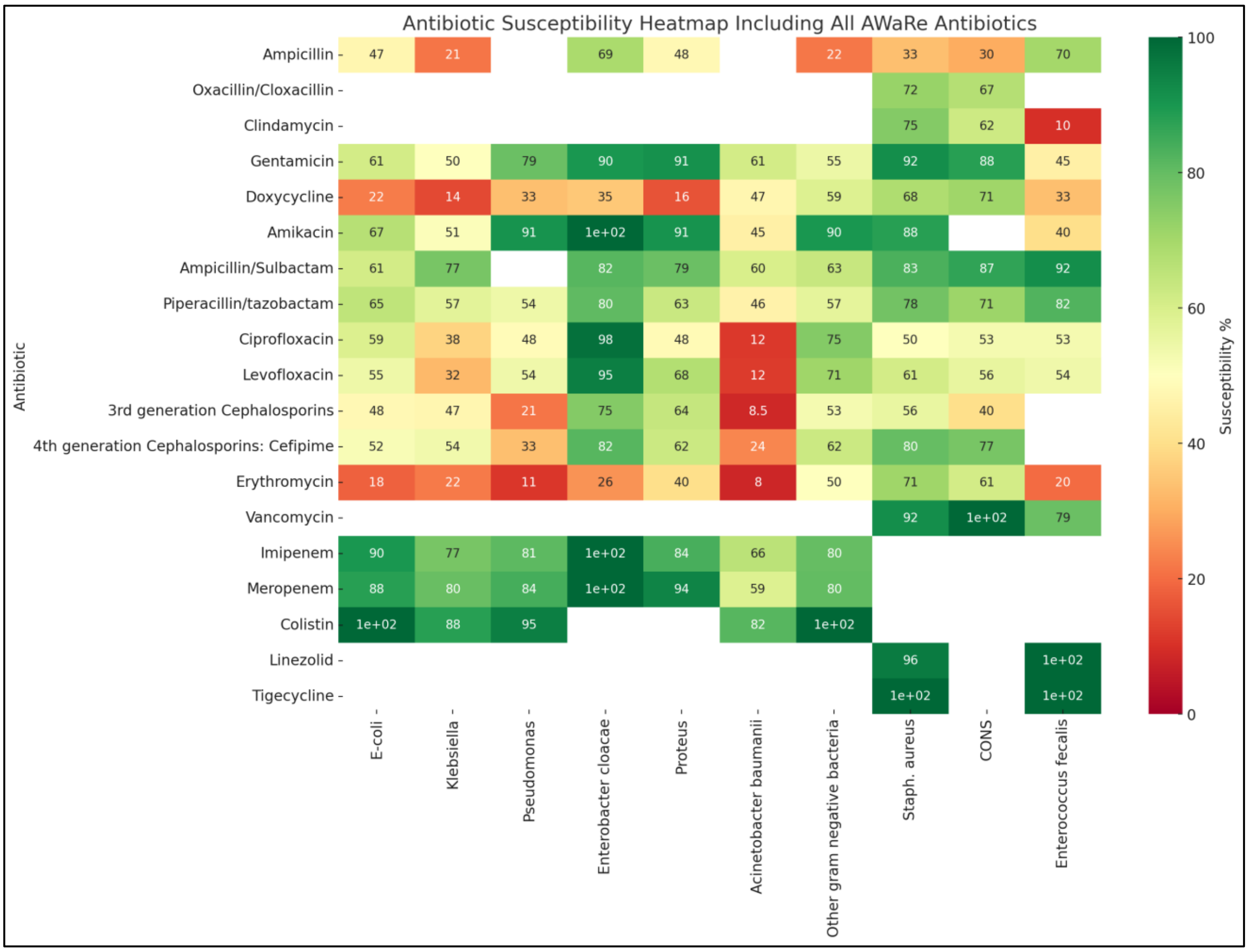


**Table 3:** Evidence-Based Recommendations for Optimizing Empirical Antibiotic Therapy in Post-Surgical Settings

| **Pathogen** | **Recommended Empirical Therapy** |
|---|---|
| Escherichia coli (E. coli) | Piperacillin/Tazobactam, Gentamicin |
| Klebsiella spp. | Piperacillin/Tazobactam, Gentamicin |
| Staphylococcus aureus | Oxacillin, Clindamycin |
| Coagulase-negative Staphylococci (CONS) | Oxacillin, Clindamycin |
| Pseudomonas spp. | Piperacillin/Tazobactam, Ciprofloxacin |
| Enterococcus faecalis | Ampicillin, Vancomycin (if MRSA suspected) |
| Enterobacter cloacae | Piperacillin/Tazobactam, Gentamicin |
| Proteus spp. | Gentamicin, Piperacillin/Tazobactam |
| Acinetobacter baumannii | Consult local guidelines (often multidrug-resistant) require targeted therapy based on susceptibility testing. |
| Other Gram-Negative Bacteria (e.g., Serratia, Salmonella, Citrobacter) | Piperacillin/Tazobactam, Ciprofloxacin |

*Reserve antibiotics like Meropenem, Colistin, and Linezolid should be reserved for cases where multi-drug resistance is confirmed, and first-line antibiotics are ineffective.

## DISCUSSION

Antibiograms are useful tools to collect data about antibiotic susceptibility rates within the facility, thus, tracking the bacterial resistance and establishing guidelines for the selection of the appropriate empirical antibiotics[6 7]. Most of the positive cultures were isolated from surgical drains followed by UTI. This is in accordance with many studies where UTIs and SSIs were the most common sites for infection with change of their order depending on many factors as locality, patient population and hospital settings. Also, this is understandable considering post-surgical patients were our study population [8, 9].

Out of the total pathogenic isolates, Gram Negative bacteria constituted 73.6% of the isolated organisms. A similar percentage of 74.41% of Gram-Negative bacteria was reported by a recent study in Egypt [10]. This agrees with the US National Healthcare Safety Network recent data indicating that Gram-negative bacteria are the cause of about 30% of hospital-acquired infection [11].

In our study, *E. coli* (34%), *Klebsiella spp.* (20%) and *Staphylococci* (19%) were the most isolated organisms. This agrees with a study in Ghana where the most common isolates were *E. coli, Klebsiella* and *Pseudomonas spp* [12]. In contrast, another study that was conducted only on various ICUs, revealed that *Klebsiella spp* was the commonest organism followed by *E. coli* [10]. *Staphylococcus aureus* was the most common organism in ***Hegazy et al.*** study [13]. This difference can be attributed to different study populations as their work focused only on ICU while our study included samples from post-surgical patients.

Aminoglycoside antibiotics, such as amikacin and gentamicin, categorized under the Access group, were used in this study. When comparing sensitivity rates against *E. coli* between this study and the findings of Negm et al. [10] , amikacin demonstrated a similar sensitivity of 66%, while gentamicin showed a higher sensitivity of 61% compared to 46.8% in their study. In the case of *Acinetobacter spp*., it exhibited the lowest sensitivity to amikacin at 45.2%, which is significantly higher than the previously reported 5%.

Ampicillin, 3rd and 4th generation cephalosporin showed the least activity against the pathogens. These mostly belong to class β-lactam antibiotics, as in agreement with ***Dodoo et al.*** [12] indicating the need to apply antibiotic stewardship programs effectively to help combat the worldwide increase in β-lactams resistant bacteria. Resistance of Gram-negative rods to these β-lactam antibiotics is repeatedly reported in Africa [14, 15].

In this study, high resistance of the *Pseudomonas* and *Acinetobacter spp*. to the third & fourth generation cephalosporins was detected suggesting possible circulating ESBL-producing organisms. *Pseudomonas aeruginosa* showed sensitivity of 21.2%, 33.3% to third & fourth generation cephalosporins respectively which agrees with previous studies[16,17]. Meanwhile *Acinetobacter spp.* showed a sensitivity pattern to the same antibiotic classes of 8.5%, 24% respectively. This is in concordance with Negm et al. [10] study where the sensitivity was 3%.

Carbapenems used in this study were imipenem and meropenem with variable sensitivity patterns. The highest sensitivity of 100% for both antibiotics was detected in *Enterobacter cloacae*. Meanwhile, *E. coli* showed 90% and 88% imipenem and meropenem sensitivity. *Klebsiella spp*. showed 77.2%, 79.5% imipenem and meropenem sensitivity. As for *Acinetobacter baumannii*, it showed the least sensitivity pattern achieving 66%, 58.7% sensitivity to imipenem and meropenem respectively. Higher resistance patterns were reported by other studies where carbapenem resistance ranged from 52%-79% respectively [18, 19]. Interestingly, another study reported 100% carbapenem resistance among *Acinetobacter baumannii* thus raising concerns about the increase in carbapenem resistance, a Watch list antibiotic [20]. In our locality, carbapenem resistance has grown widely, which can be attributed to the unrestricted access to antibiotics and the lack of a national antibiotic stewardship program [21].

The quinolones often tested in this study were ciprofloxacin and levofloxacin. Increasing resistance to fluoroquinolones was found in our study especially in klebsiella and Acinetobacter spp. with moderate sensitivity in Gram positive bacteria. Similar resistance patterns were also reported, especially in *E. coli* and *K. pneumoniae* in Rwanda and Zambia respectively [14, 17]. This increasing resistance may be attributed to increased prejudicious use of fluoroquinolones.

Colistin is the most tested polymyxin and a WHO reserve list antibiotic[22]. Although it showed high sensitivity reaching 100% in *E. coli* and other Gram-Negative bacteria, less sensitivity to colistin was detected specially in *Pseudomonas* (95%), *Klebsiella* (88%), and *Acinetobacter spp*. (82%) which may indicate the development of a resistance pattern. This comes in accordance with a study in Egypt where a susceptibility of colistin was at 96.2, 94.7, and 89.9% sensitivity for *K. pneumoniae, E. coli, and Acinetobacter baumannii*, respectively and a 79.4% susceptibility for *Pseudomonas aeruginosa*[10] Additionally, in another study from a teaching hospital in Egypt, colistin-resistant strains were isolated from 51 patients with an incidence of 1.1% [23]. This indicates its effectiveness but raises an alarming sign that stewardship efforts regarding its use should be continued to avoid the spread of colistin resistant bacteria.

As for Gram positive bacteria, Staphylococci spp. represented 19% of the total isolated organisms while Enterococci was 7%. Regarding the antibiotic sensitivity of *Staph aureus*, sensitivity to vancomycin was 92% which is comparable to other studies who reported 100% sensitivity [24, 25]. Meanwhile, another study reported lower rate of 76.8% and they owed that to frequent empirical use of vancomycin[10]. As for Enterococci, they showed 79 % vancomycin sensitivity which was reported by another study in Saudi Arabia reaching 67% sensitivity which is alarming indicating increase in Vancomycin Resistant Enterococci (VRE) [26].

As for linezolid, it achieved almost complete sensitivity in *Staph aureus* and Enterococci which is confirmed by other studies[13, 24]. Hence, it remains an effective antibiotic against gram positive bacteria but Reserve antibiotic that should be used cautiously to avoid emergence of resistant strains.

The strength of this study is large number of samples and focusing on the samples from post-surgical patients' allowing the opportunity to monitor the strains of bacteria and their antimicrobial susceptibility pattern in this specific patient population, helping to put evidence-based recommendations for the selection of appropriate empirical antibiotics. However, being a single-center study may limit the generalizability of the findings to other settings or populations.

## CONCLUSION

This study demonstrates the effectiveness of the WHO AWaRe classification in guiding antibiotic selection for post-surgical infections, particularly in resource-limited settings. The predominance of Gram-negative bacteria, notably *E. coli* and *Klebsiella spp.*, and their varying resistance patterns highlight the urgent need for targeted antibiotic stewardship. By applying the AWaRe framework, this study provides evidence-based recommendations for empirical therapy, emphasizing judicious use of Reserve antibiotics to prevent resistance escalation and preserve the efficacy of critical antibiotics in clinical settings.

**Supplementary information**

**Authors' contributions:** M. Elshaer, M. Eldegwi and D.K. wrote the main manuscript text. M. Eldegwi carried out study analysis and prepared figures and tables. D.K. contributed to samples ordering and data collection. M.S revised the final draft. All authors have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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All research activities adhered to the Declaration of Helsinki and approved by the Institutional Review board, Faculty of Medicine, Mansoura University (approval no. R.24.12.2975).

**Consent to participate:** Informed consent was obtained from all individual participants and/or their legal guardians included in the study.

**Competing interests:** The authors have no competing financial or personal interests to declare.

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