Original Article

Evaluation of antibiotic consumption using WHO -antimicrobial consumption tool and AWaRe classification

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Abstract

Introduction: Antimicrobial resistance is a public health concern with global ramifications. Antibiotic misuse and overuse, are rampant in our country but more alarming is the data on the use of antibiotics primarily because of lack of access is another threat. A majority of the data on drug sales and consumption in India comes from the private sector and is typically gathered from private commercial organization. Because data on antibiotic usage in India is rarely reported, the study's objectives were to estimate antibiotic consumption in ICU patients and also to assess antibiotic usage trends using the WHO AWaRE classification. **Materials and Methods:** A prospective observational study was carried out in the ICU department for six months after obtaining institutional ethics committee approval (P14/2021/14). In-patient records and details on antibiotic prescriptions were collected from the day of admission until they were discharged from the intensive care unit. Data on antibiotic consumption were retrieved from the hospital pharmacy. Descriptive statistics such as frequency, percentages, and means were used to summarize the data. Microsoft Excel 2016 was used for all statistical analyses. **Results:** The results of the study showed that female patients (54%), made up a significant majority of those receiving antimicrobial treatment. The age group between 40–49 years (21.68%) was the most common for those receiving antimicrobial treatment. Surgical prophylaxis (37.34%) emerged as the most common indication. Among the different antimicrobials studied, ceftriaxone 1 gm (108.5 DDD) emerged as the most prescribed antimicrobial. The access group of antibiotics accounted for 55% of the total usage. **Conclusion:** Appropriate use of antibiotics is important to minimize the risk of adverse events and antimicrobial resistance.

Keywords: Antimicrobial consumption, AWaRe classification, defined daily dose

Introduction

Antimicrobial resistance is a public health concern with global ramifications. Hospitals began to experience antimicrobial resistance in the 1950s, but in the decades that followed, overuse of antibiotics has led to the evolution of multidrug-resistant bacteria, increasing costs and complicating the treatment of a wide range of illnesses.[1] The incorrect use of antibiotics by animal and poultry industries has made the problem even worse. Judicious use of these classes of drugs is therefore essential due to the lack of newer antibiotics that are being introduced into the market.[2]

In 2015, at the 71st UN General Assembly, antimicrobial resistance became the fourth health-related topic of discussion.

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It is estimated that more than two million lives would be at risk with an average expenditure of 3.5 billion US dollars annually if no timely action is undertaken.[3] According to available data, the world's population consumed 36% more antibiotics in 2010 than in 2000.[4] Brazil, Russia, India, China, and South Africa, or BRICS, accounted for 75% of the population growth even though they only made up 40% of the world's total population. Of them, 23% of the retail sales volume came from India, a nation where the regulations controlling the over-the-counter sale of antibiotics are laxly applied.[5]

Antibiotic misuse and overuse are rampant in our country, but more alarming is the data of underuse of antibiotics primarily because of lack of access is another threat. The Indian Ministry of Health and Family Welfare published the National Action Plan for containing AMR in April 2017.[6] National surveillance networks for antibiotic use and resistance were established, but this has not yielded the desired results due to improper implantation and monitoring.[6]

A recent global surveillance study that examined antibiotic consumption data from over 65 countries in 2015 did not include India.[7] The majority of the data on drug sales and consumption in India comes from the private sector and is typically gathered from private commercial organizations. Recent studies conducted in India analyzing antibiotic sales data have highlighted that the use of newer antibiotic classes is disproportionately high.[8] Although the usage of antibiotics in India has not been extensively studied, few studies conducted in India that used the AWaRe paradigm have focused only on a particular antibiotic class groupings or used data from earlier studies.[9] The commonly used defined daily dose (DDD), a standard measure of antibiotic use, is hardly used in research conducted in India. The usage of DDD, which is defined as the average maintenance dose per day of a medication for its principal use in adults, has been shown to benefit patients across demographic groups and time.[10] It also provides a measurement that is unaffected by cost, exchange rates, packaging dimensions, or strength.

Because of data on antibiotic usage in India is rarely reported, assessing antibiotic consumption through the application of DDD metrics and AWaRe categorization will facilitate a thorough comprehension of the appropriateness of antibiotic use in India. Considering the aforementioned details, the study's objectives were to estimate the antibiotic consumption in patients admitted to an intensive care unit (ICU) in a tertiary care teaching hospital and also to assess antibiotic usage trends using the WHO AWaRE classification.

Methods

Study design, population, and data collection

A prospective observational study was carried out in the ICU department (Medicine ICU and Surgical ICU) of a tertiary care teaching hospital for six months after obtaining institutional ethics committee approval (P14/2021/14). Simple random sampling was employed to select in-patients who were admitted to the ICU and prescribed antibiotics after receiving their informed consent. In-patient records, which included demographics and details on antibiotic prescriptions (drug name, dosages, frequency of administration, administration techniques, data from culture sensitivity tests, strength and quantity of medications, and source of drug procurement), were collected from the day of admission until they were discharged from an ICU.

Data on antibiotic consumption were retrieved from the hospital pharmacy. The dataset comprised the sales units (monthly number of pharmaceutical packets sold), the moving average total during the study period, and the unique product code for each product. The product's category (injectables, liquids, solids, inhalants, etc.), strength, pack size, price, and whether it is a single formulation or an FDC were among the other details included in the dataset. The drugs that are classified as systemic antibiotics fall under the J01 category of the WHO Anatomical Therapeutic Chemical (ATC) classification system, 22 which covers antibacterials for systemic use with the exclusion of antimycobacterial. Topical medications, eye/ear drops, gel, pessaries, or suppositories were excluded from the analysis as these are not part of the ATC system's J01 subgroup. Only parenteral metronidazole preparations classified as J01 for the treatment of anaerobic bacterial infections were included in our analysis. Single formulations of metronidazole oral FDCs designated as A02 for the eradication of Helicobacter pylori and P01 for amoebiasis, trichomoniasis, and giardiasis are not listed.

Statistical methods

Descriptive statistics such as frequency, percentages, and means were used to summarize the data. Microsoft Excel 2016 was used for all statistical analyses. Antibiotic consumption was measured using the WHO AMC tool and reported in units of DDD. We calculated the total DDD consumed per pack by utilizing the product and pack size data from the hospital pharmacy data and the DDD data of the corresponding formulation from the WHO ATC/DDD index. The antibiotics were categorized using the updated WHO 2021 list in compliance with the AWaRe system and the CDSCO's data was used to determine the approval status.

Results

There were 83 patients in the study who fulfilled the criteria for inclusion. The gender distribution of ICU patients is shown in Figure 1, with a definite trend towards a female predominance. The results of the study showed that, as compared to male patients (46%), female patients (54%), made up a significant majority of those receiving antimicrobial treatment. The age group between 40–49 years (21.68%) was the most common for those receiving antimicrobial treatment, followed by 50–59 (19.27%) and 60–69 years (16.86%) [Figure 2].

The results of the study have also shed light on the indications for antimicrobial therapy [Figure 3], revealing a clear hierarchy in terms of prevalence. Surgical prophylaxis (37.34%) emerged as the most common indication, indicating the widespread use of antimicrobials to prevent infections in surgical procedures. Following closely behind surgical prophylaxis are community-acquired infections (28.90%), highlighting the significant burden of infectious diseases that individuals in the community face. Furthermore, hospital-acquired infections (14.45%) were identified as another prevalent indication for antimicrobial therapy, underscoring the challenges posed by infections acquired during hospitalization. This was followed by medical prophylaxis which made up 9.63% of all the indications for antimicrobial therapy. Table 1 provides valuable insights into the consumption patterns of various antimicrobials, as measured by Defined Daily Doses (DDD). Among the different antimicrobials studied, ceftriaxone 1 gm (108.5 DDD) emerged as the most commonly prescribed antimicrobial, indicating its widespread use in clinical settings. Following closely behind ceftriaxone in terms of consumption is Levofloxacin 750 mg (94.5 DDD), another commonly prescribed antimicrobial agent known for its efficacy in treating respiratory and urinary tract infections. Additionally, piperacillin + tazobactam 4.5 gm (60.43% DDD) was identified as another frequently prescribed antimicrobial, reflecting its effectiveness in treating severe infections caused by multidrug-resistant organisms.

In addition to employing DDD to measure the consumption of each antimicrobial, the AWaRe classification approach was also employed to represent antimicrobial consumption in Figure 4. The study revealed that the access group of antibiotics accounted for the largest proportion of antimicrobial consumption, representing 55% of the total usage. The high consumption of antibiotics classified in the access group can be attributed to their broad spectrum of activity and affordability, making them widely accessible and commonly prescribed for a variety of bacterial infections. Following the access group, the study highlighted that the watch group of antibiotics constituted 45% of the overall consumption. Antibiotics within the watch group are considered to have a higher resistance potential and are recommended for more restricted use.

In contrast, the study identified that the reserve group of antibiotics accounted for only 5% of the total consumption. Antibiotics in the reserve group are reserved for the treatment of severe infections caused by multidrug-resistant pathogens and considered as last-resort options when other antibiotics have failed. The limited consumption of antibiotics in the reserve group reflects their restricted use and emphasizes the need for conservation to preserve their effectiveness for critical cases.

Patients

The distribution of bacteria found in cultures from ICU patients is displayed in Table 2. It was found that 86% of the

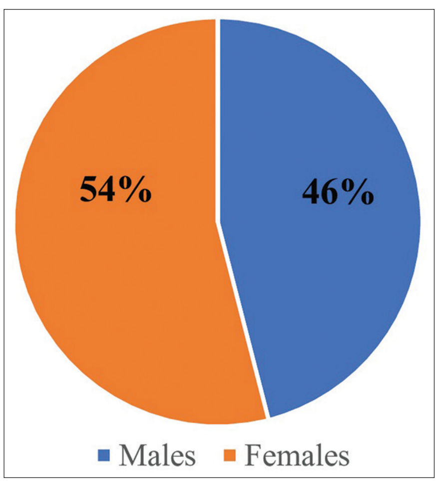

Figure 1: Gender distribution of patients admitted in ICU

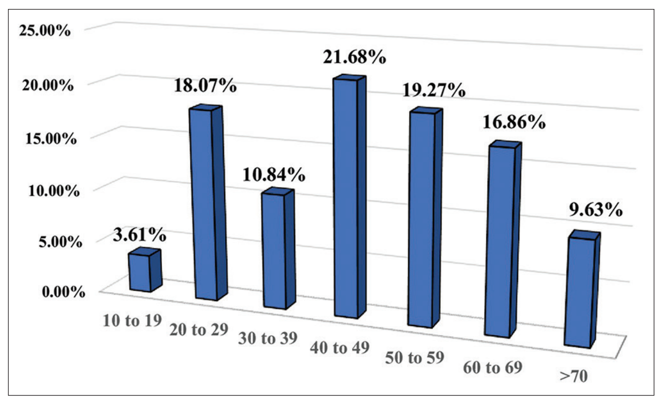

Figure 2: Age distribution of patients (in years) admitted in ICU

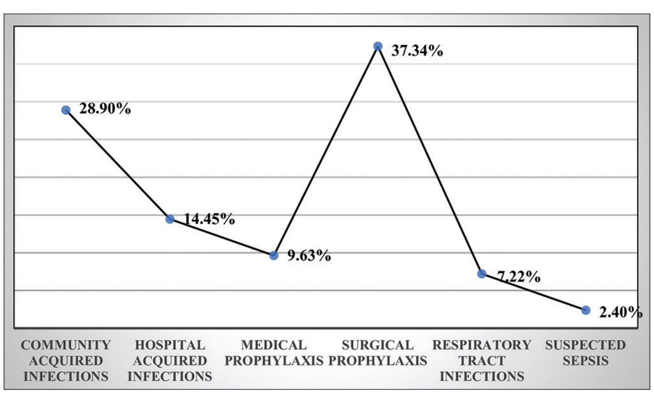

Figure 3: Indications of antimicrobial therapy

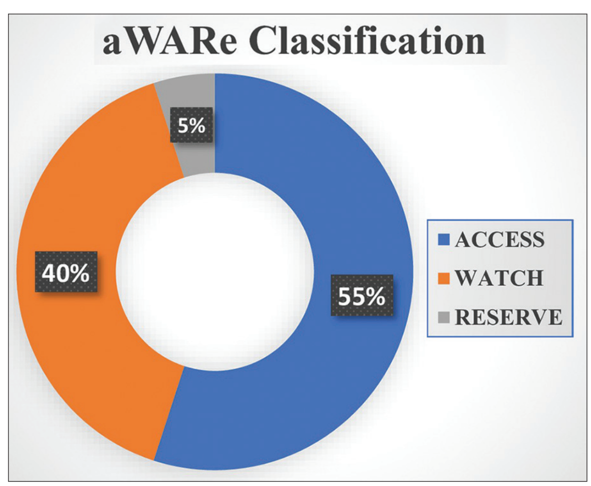

Figure 4: Consumption of antimicrobials using aware classification

requested cultures of interest tested positive for Gram-negative bacteria, 10% for Gram-positive bacteria, and 4% for fungi. The majority of detected species in the requested cultures were Gram-negative, with Klebsiella pneumoniae species found in 18.46% of the cultures (blood cultures: 3, tracheal secretions: 5, urine: 3, and pus: 1). However, 16.9% of all cultures had an identifiable Acinetobacter species. Enterococcus faecium was the most common species of Gram-positive bacteria, found in 7.69% of all cultures and 4% of tracheal secretion cultures. As for fungal species, Candidas albicans was the most common type and identified in 3% of cultures [Table 3].

Table 2: Distribution of microorganisms identified in cultures from patients admitted to the ICU

Table 3: Microbiological profile per ICU culture sample

Discussion

Gender disparities in healthcare and treatment practices have been well-documented in the literature, and such variations can impact antimicrobial prescribing patterns and contribute to the development of antimicrobial resistance. In our study, we observed differences in antimicrobial consumption among genders, with females (54%) demonstrating a higher likelihood of using antimicrobial drugs compared to males (46%). These findings align with previous studies that have reported similar disparities in antibiotic prescribing practices based on gender. For example, a study by Grigoryan *et al.*[11] found that females were more likely to receive antimicrobial prescriptions for respiratory infections compared to males. These results suggest that factors such as differences in immune response, underlying health conditions, and susceptibility to infections may contribute to increased antimicrobial consumption among female ICU patients. Additionally, hormonal influences and genetic factors could potentially play a role in the gender disparity observed in antibiotic usage within the critical care setting.[11] However, our study also revealed some contrasting results with previous research. For instance, a study by Liao *et al.*[12] reported no significant gender differences in antimicrobial consumption patterns. Studies by Peterson *et al.*[13] and Chang *et al.*[14] have also underscored gender-related differences in antimicrobial prescribing patterns and emphasized the need for gender-specific strategies to promote appropriate antibiotic use. These discrepancies may be attributed to variations in study populations, healthcare systems, and prescribing practices, highlighting the complexity of factors influencing antimicrobial use based on gender.[12]

Our study also revealed a higher antimicrobial consumption rate among the age group of 40–49 years (21.68%) followed by age groups of 50–59 years (19.27%) and 60–69 years (16.86%) with notable variations in prescribing practices between genders. The findings indicated that middle-aged individuals (40–60 years) were more likely to receive antibiotics as compared to younger and older age groups. This observation is consistent with previous research by Jones *et al.*[15] which reported a higher prevalence of infectious diseases and antibiotic prescribing rates among middle-aged women. The study highlighted the significance of

Table 1: Consumption of each antimicrobial [In defined daily dosage (DDD)] in ICU patients

Antimicrobial drug	Strength	Volume	DDD
Amikacin	500 mg	13	6.5
Amikacin	750 mg	92	69
Cefoperazone + sulbactam	1.5 mg	53	0.019
Cefotaxime	1 g	3	0.75
Ceftriaxone	1 g	217	108.5
Ceftriaxone	2 g	34	34
Cefuroxime	500 mg	20	3.33
Clindamycin	600 mg	6	2
Gentamycin	240 mg	12	12
Imipenem	1 g	144	72
Imipenem	1.5 g	32	24
Meropenem	1 g	101	33.66
Polymycin b	5 mu	4	6.66
Piperacillin + tazobactam	4.5 g	188	60.43
Piperacillin + tazobactam	2.25 g	12	1.93
Vancomycin	1 g	93	46.5
Colistin	2 mu	57	12.67
Levofloxacin	750 mg	63	94.5
Linezolid	200 mg	8	1.33
Metronidazole	400 mg	188	50.13
Azithromycin	500 mg	5	8.33
Cotrimoxazole	960 mg	3	None

Table 2: Distribution of microorganisms identified in cultures from patients admitted to the ICU

Microorganism	Frequency	Percentage
Gram-negative bacteria	43	86%
Gram-positive bacteria	5	10%
Fungi	2	4%

Table 3: Microbiological profile per ICU culture sample

Isolated microorganisms	Number of microorganisms isolated per type of sample				Total
	Blood	Tracheal Secretion	Urine	Pus	
Gram-negative bacteria					
Pseudomonas aeroginosa	6	3	1		10
Klebseilla pneumoniae	3	5	3	1	12
E. coli	5	1	2		8
Acinetobacter bamannii	2	3	3	3	11
Enterobacter species	1	1	1		3
Klebseilllaaerogens	1	3	1		5
Klebseillaoxytoca	1		2		3
Acinetobacter levoffi	2	1	2		5
Gram-Positive bacteria					
Enterococcus faecium	2		3		5
Staphylococcus species	1				1
Fungus					
Candida	1		1		2

the middle age group in terms of antimicrobial consumption, suggesting that factors such as lifestyle, comorbidities, and healthcare-seeking behavior may contribute to the increased antibiotic utilization in this age cohort.[15] Middle-aged individuals are often at a stage in life where they may have a higher prevalence of chronic conditions, which could necessitate antibiotic treatment for infections and other health issues.[15]

Understanding the specific reasons for antimicrobial prescribing in the ICU setting is crucial to optimize patient outcomes, prevent the spread of infections, and combat antimicrobial resistance. Our study findings revealed a variety of indications for antimicrobial therapy in the ICU, with antimicrobials prescribed for surgical prophylaxis (37.34%) being the most common indication followed by community-acquired infections (28.90%) such as sepsis and pneumonia. This aligns with previous studies by Khilnani *et al.* and Wilson *et al.*, which also identified surgical prophylaxis (to prevent surgical site infection), sepsis, and respiratory infections as leading indications for antimicrobial use in ICU patients.[16,17] Furthermore, our study highlighted the challenges associated with antimicrobial prescribing in the ICU, including the need for early and appropriate antibiotic therapy, the impact of multidrug-resistant pathogens, and the importance of de-escalation strategies to optimize treatment.[18] These findings resonate with the research by Kumar *et al.*[18] and Lopez *et al.*[19] which emphasizes the complex nature of antibiotic use in critically ill patients and the need for individualized treatment approaches.

The study on antimicrobial consumption in the ICU with regard to the consumption of each antimicrobial in DDD provides essential insights into the patterns of antibiotic use in critically ill patients and is crucial for optimizing treatment strategies, combating antimicrobial resistance, and improving patient outcomes.[20] Our study findings revealed varying levels of consumption (measured in terms of DDD) for different antimicrobial agents in the ICU, with antibiotics such as cephalosporins 1 g (108.5), Piperacillin + tazobactam 4.5 g (60.43) and metronidazole 400 mg (50.13) being among the most commonly prescribed antimicrobials. This aligns with previous studies by Smith *et al.*[20] and Johnson *et al.*,[21] which also reported high utilization rates of antibiotics like cephalosporins in critically ill patients in the ICU. Cephalosporins are frequently prescribed in ICU patients due to their broad-spectrum activity, providing coverage for a variety of potential pathogens in critically ill patients.[22] They are also generally well-tolerated and have a lower risk of adverse effects compared to other antibiotic classes.[23] Piperacillin + tazobactam have favorable pharmacokinetic properties with good tissue penetration and prolonged half-life making them suitable choices for treatment of severe infections in critically ill patients where achieving drug concentration is essential for treatment success.[24]

Second, understanding antimicrobial consumption through the lens of the Aware classification system allows for a more comprehensive analysis of antibiotic prescribing patterns and their impact on antimicrobial resistance.[25] The consumption of broad-spectrum antibiotics categorized under the Watch list was 55%. While the global goal is to have at least a 60% share of Access to antibiotics, we found a reversed Access-to-Watch ratio.[25] This may be related to the increase in infections already considered secondary caused by microorganisms from the hospital environment.[26] In our analysis, among the antimicrobials included in the watch list, broad-spectrum third-generation cephalosporins (Ceftriaxone - 108 DDD) were commonly prescribed specifically for cases of surgical prophylaxis. Ceftriaxone is beneficial in preventing post-operative infections, as they are effective against common pathogens and have a low risk of adverse effects compared to other antibiotics.[27] Our finding was consistent with previous studies, including a systematic review and spatial modeling.[28,29] Significant number of antimicrobials (45%) were also prescribed from drugs included in the access group (45%). This may be attributed to the fact that antimicrobials such as metronidazole (50.13 DDD) are frequently recommended in clinical guidelines for the treatment of anaerobic and Clostridioles difficle infection.[30] A Brazilian study conducted in an ICU evaluating antimicrobial consumption used the AWaRE classification and drew attention to an increase in the consumption of antimicrobials in the reserve group.[30] In contrast, our study shows a decrease in the consumption of antimicrobials in the reserve group, with a significant reduction in linezolid (1.33 DDDs) and other antibiotics in the reserve group. This is a positive point, as the high-priority pathogens on the WHO list, such as non-fermenting MDR Gram-negative bacilli, can only be treated with antibiotics from the Reserve group.[30] The increased consumption of these antibiotics unnecessarily raises concerns about the therapeutic options available for treating infections in the ICU.[30] However, we need more granular data to understand the healthcare settings where these medicines are used. Understanding the relationship between antimicrobial consumption and the types of microorganisms causing infections in the ICU is crucial for optimizing antibiotic use, preventing resistance, and improving treatment strategies. Our study revealed a diverse range of microorganisms identified in cultures from ICU patients. Gram-negative microorganisms were the most prevalent (86%) in patient infections and this is similarly seen in studies reported in other parts of the world that describe superinfections or secondary bacterial infections.[29] In our study, we found Klebsiella pneumoniae, Acinetobacter, and Pseudomonas species to be the predominant pathogens causing hospital-acquired infections. The Klebsiella pneumoniae and Acinetobacter isolates already had a high carbapenem resistance profile, >92% and >90%. Many carbapenem-resistant Acinetobacter infections (pneumonia, bloodstream among others) tend to occur in patients in ICUs and are of particular concern because they are often difficult to treat with available antibiotics, as well as increasing length of stay, costs, and increasing mortality.[29] The three isolates are real threats to public health that require urgent and aggressive action.

Conclusion

The study on antimicrobial consumption in the ICU has provided valuable insights into the patterns and indications for antimicrobial therapy in critically ill patients. Overall, the study findings underscore the importance of ongoing surveillance, monitoring, and evaluation of antimicrobial consumption in the ICU to ensure the appropriate use of antibiotics while minimizing the risk of adverse events and antimicrobial resistance. By implementing evidence-based strategies and promoting antimicrobial stewardship principles, healthcare facilities can enhance the quality of care for critically ill patients and contribute to the sustainability of effective antimicrobial therapy in the ICU setting.

List of Abbreviations

Abbreviation	Definition
WHO	World health Organisation
DDD	Defined Daily Dose
ICU	intensive care unit
MAT	moving average total
FDC	Fixed Drug combination
ATC	Anatomical Therapeutic Chemical
AMC	Antimicrobial consumption
MDR	Multi-drug resistant

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Nil.

Conflicts of interest

There are no conflicts of interest.

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