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Implementation and assessment of Antimicrobial Stewardship in tertiary care hospital in North India

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Abstract

Antimicrobial stewardship plays a vital role in the fight against antimicrobial resistance, a pressing global issue. Its significance in controlling and managing antimicrobial resistance is widely recognized and acknowledged by experts and healthcare professionals alike. The objective of this study was to acquire a comprehensive comprehension of the utilization of antimicrobial drugs within a medicine and surgery unit at a tertiary hospital in India. To achieve this, a qualitative case study methodology was employed. The study employed a qualitative case study design, focusing on a specific prospective audit and feedback process within the hospital. Data collection involved reviewing archival data and conducting expert interviews by approaching antimicrobial stewardship and surveillance. The collected data were analyzed using the WHO's AWaRe classification framework, which facilitated a structured analysis of antimicrobial usage. It also considered the perspectives of various stakeholders in developing guidelines for responsible antibiotic use. The research focused on the utilization of reserve antimicrobial drugs based on the AWaRe classification. The findings indicated a decrease in the utilization of these drugs over the study period, suggesting effective efforts to reduce unnecessary usage. The study contributes to promoting responsible antibiotic use and addressing antimicrobial resistance in Indian tertiary hospitals.

Keywords: Antimicrobial stewardship, AWaRe classification, Antimicrobial utilization, Prospective audit and feedback.

Introduction

Antimicrobial stewardship is recognized as a crucial tool in combating antimicrobial resistance. The importance of antimicrobial stewardship in controlling antimicrobial resistance is widely acknowledged [1, 2]. However, most evidence supporting the effectiveness of intervention studies in this field comes from developed countries [3]. In order to foster the establishment and growth of global antimicrobial stewardship programs, it is crucial for developing nations to initiate or enhance their existing initiatives in this area [4, 5]. While intervention studies have shown

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significant improvements in antimicrobial use, most evidence comes from developed countries [6-8].

To promote global antimicrobial stewardship programs, developing nations, including India, have formulated their own plans [1, 9-10]. However, resource limitations in healthcare settings pose challenges for implementing such programs. Despite this, tailoring antimicrobial stewardship to settings with limited resources has shown benefits, including reduced antimicrobial consumption [11].

The principles of AMS also extend to the use of antimicrobials in the animal and agriculture sectors, emphasizing wise usage of these agents [12]. Healthcare practitioners play a crucial role as frontline stewards in addressing the emerging health and economic concern of antimicrobial resistance [13]. By prescribing appropriately and educating patients and colleagues on responsible antimicrobial use, they can protect current and future patients from the challenges posed by decreasing antimicrobial effectiveness [14].

AMS interventions aim to create sustainable behavior change regarding antibiotic prescriptions, ensuring that antimicrobials are used optimally and that effective options for treating infectious agents remain available [15]. The main intention of this study is to emphasize the importance of responsible antimicrobial use to safeguard this valuable medical resource. In our work, we identified factors influencing antimicrobial use and implemented interventions such as audits, feedback, individualization and training. This study highlights the impact of these interventions on the pattern of antimicrobial use based on WHO’s AWaRe segmentation in the Medicine and surgical unit [16].

Material and Methods

Study Design

The current research was conducted using a qualitative case study approach, which offers the advantage of examining a medicine and surgery unit in depth and establishing connections between theoretical knowledge and real-world observations. By focusing on a specific case, researchers were able to gain a comprehensive understanding of the subject matter, considering various perspectives and contextual factors.

The present study employed a qualitative case study design specifically focused on

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a tertiary hospital in India. This approach allowed for a detailed examination of the specific prospective audit and providing feedback within the hospital setting. The data collection process involved systematically reviewing archival data and conducting in-depth expert interviews using qualitative methods [17, 18].

To interpret the collected data, a deductive thematic analysis framework designed by WHO as AWaRe classification of antimicrobial drugs was utilized, which facilitated a structured and comprehensive analysis of the information gathered from the hospital [17, 19]. The study sought to understand the unique challenges and dynamics within this specific hospital setting, considering factors such as patient demographics, resource availability, and healthcare practices [20]. Analyzing antimicrobial usage and practice was a key aspect of the study. These interests of study may serve as systematically developed recommendations to guide healthcare practitioners and patients in making informed decisions regarding appropriate healthcare in specific clinical circumstances [21]. Given the regional and institutional context, there may be specific factors influencing the use of antibiotics and the management of antimicrobial resistance. The study considered the local healthcare infrastructure, government policies, and available resources related to antibiotic use and surveillance [22]. Understanding these factors is crucial for promoting responsible antibiotic use and addressing the challenge of antimicrobial resistance in Indian tertiary hospitals [23].

The research also took into account the perspectives and experiences of various stakeholders, including healthcare professionals and patients, in assessing the acceptability and legitimacy of guidelines. They aimed to ensure that the development process of guidelines was perceived as fair, transparent, and based on relevant evidence and reasoning.

Result and Discussion

The WHO created the AWaRe Classification in 2017 to support antibiotic stewardship. It categorizes antibiotics into Access, Watch, and Reserve groups, considering their impact on antimicrobial resistance. The classification has been updated in 2021 with 78 new antibiotics, totaling 258. It serves as a monitoring tool for tracking antibiotic use, helping professionals and policy makers optimize usage

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and combat antimicrobial resistance.

The AWaRe Classification plays a crucial role in addressing antimicrobial resistance by promoting awareness and guiding the proper use of antibiotics [17, 24]. It serves as a comprehensive framework that promotes evidence-based decision-making and responsible prescribing practices, protecting the effectiveness of antibiotics for future generations. This study assesses the utilization of antibiotics based on the AWaRe Classification and evaluates its appropriateness.

Table - 1 illustrates the utilization of antimicrobial agents (AMAs) categorized as "Reserve" according to the WHO AWaRe classification. It presents data on their frequency of use, defined daily doses (DDDs), and DDDs per 1000 population per day across different study phases. The study discovered that all five listed antimicrobial drugs in the table are classified as"Reserve" agents according to the AWaRe classification. These antimicrobials should be used with caution and reserved for treating severe or life-threatening infections only, when alternative options have been exhausted or are not available.

ATC	Drugname	AWaRe Category	Phase1 LOT	Phase2 LOT	Phase3 LOT	Phase1 DDD	Phase2 DDD	Phase3 DDD	Phase1 DDD/100 OPD	Phase2 DDD/100 OPD	Phase3 DDD/100 OPD
J01XX08	Linezolid(gm)	R	109	60	37	130.8	86.4	46.2	118.48	108.60	46.05
J01DH51	Imipenem+Cilastatin(gm)	R	44	22	0	112	62	0	60.87	28.41	0
J01DI03	Faropenem(gm)	R	28	19	15	10.4	11.4	6	15.07	13.82	9.57
J01XB01	Colistin(MIU)	R	16	12	17	52	84	68	6.28	5.76	9.04
J01AA12	Tigecycline(gm)	R	0	0	3	0	0	3	0	0	35.89

Table - 1: Utilization of Reserve Antimicrobial drugs

DDD - Defined Daily Doses,
LOT - Length of Therapy,
ATC - Anatomical Therapeutic Classification as per W.H.O,
AwaRe - Access, Watch, Reserve classification by W.H.O

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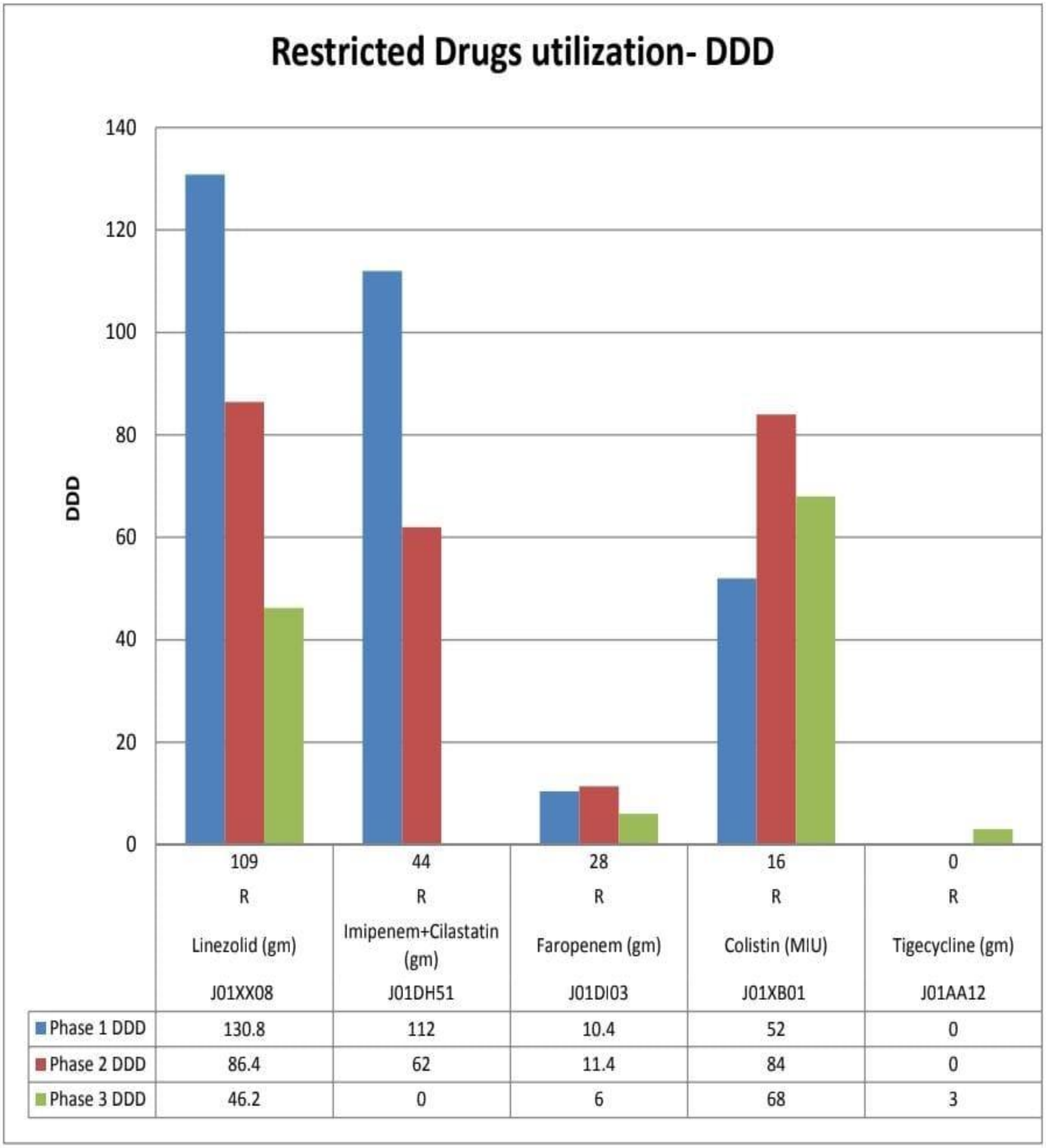

Figure - 1: Restricted Drugs utilization - DDD

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The AWaRe categorizations rely on the World Health Organization's Access, Watch, Reserve (AWaRe) classification system, which classifies antimicrobials according to their significance for human health, potential for antimicrobial resistance, and overall utility.

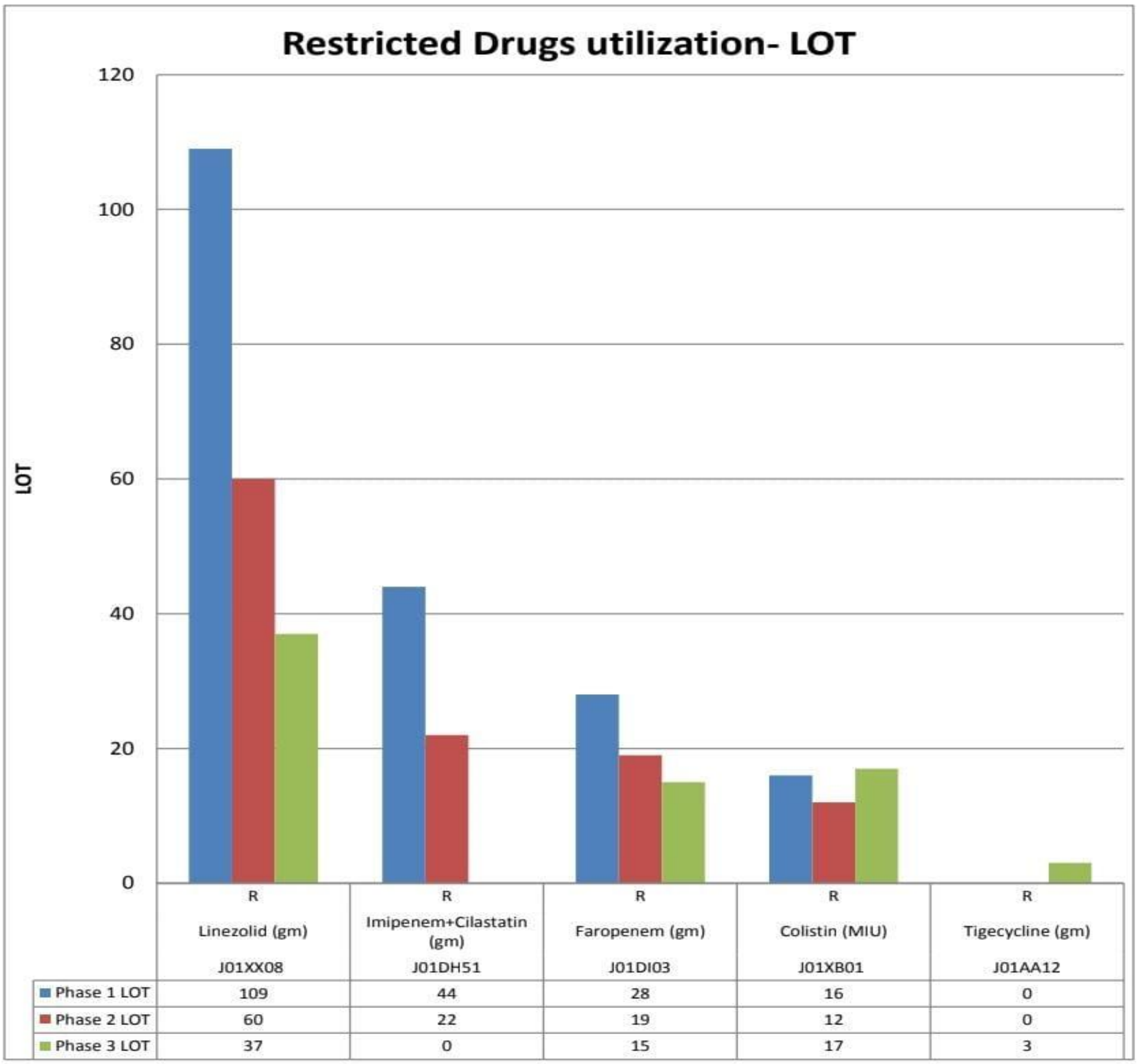

Figure - 2: Restricted Drugs utilization – Length of therapy

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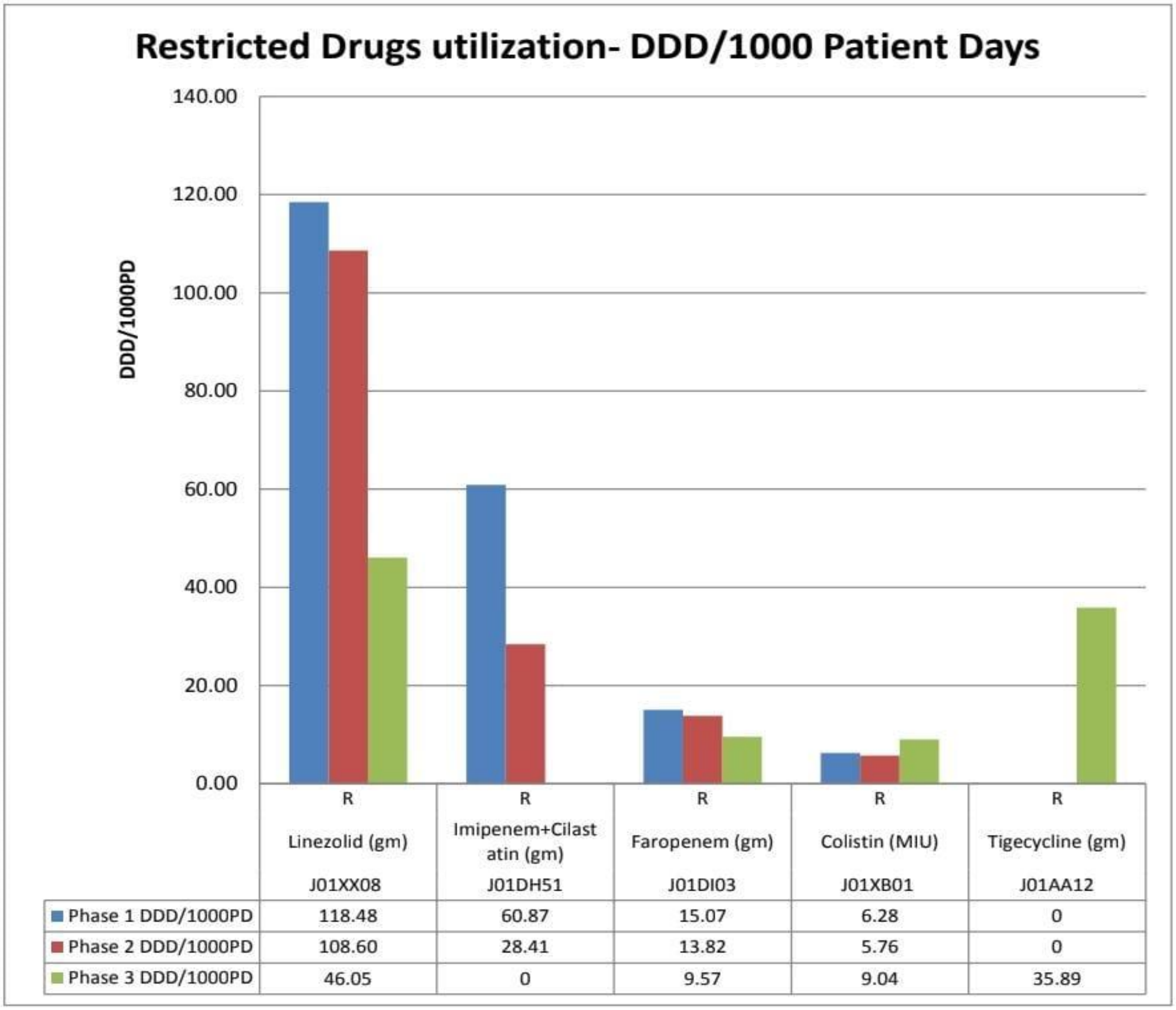
The table includes the Anatomical Therapeutic Chemical (ATC) code for each antimicrobial agent (AMA), which is a standardized code used to identify pharmaceutical substances. Additionally, it provides the LOT frequency, representing the number of lots of the respective AMA that were utilized [25, 26].



	R Linezolid (gm) J01XX08	R Imipenem+Cilastatin (gm) J01DH51	R Faropenem (gm) J01DI03	R Colistin (MIU) J01XB01	R Tigecycline (gm) J01AA12
Phase 1 DDD/1000PD	118.48	60.87	15.07	6.28	0
Phase 2 DDD/1000PD	108.60	28.41	13.82	5.76	0
Phase 3 DDD/1000PD	46.05	0	9.57	9.04	35.89

Figure - 3: Restricted Drugs utilization - DDD/1000 Patient Day

The table presents additional information, including the assumed average maintenance dose per day (DDD) for each drug's main indication in adults, as

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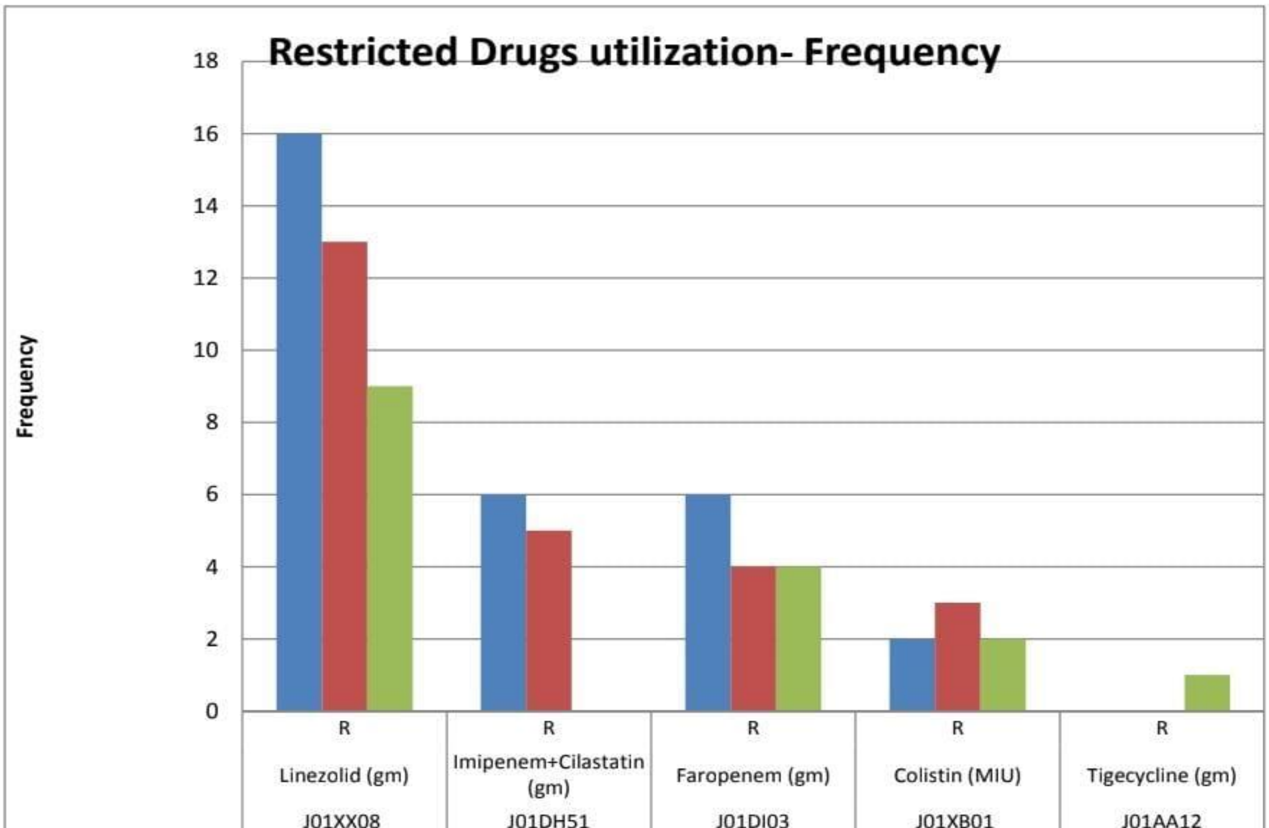
well as the DDDs per 1000 population per day.

According to the data, Linezolid (ATC code: J01XX08) was the most frequently utilized Reserve AMA, with 109 lots and a total of 130.8 DDDs. Meropenem (ATC code: J01DH02) and Imipenem+Cilastatin (ATC code: J01DH51) were also heavily used, with 111 lots and 44 lots respectively. Conversely, Colistin (ATC code: J01XB01) had the lowest utilization, with only 16 lots and a total of 52 million international units (MIU) of DDDs.



	R Linezolid (gm) J01XX08	R Imipenem+Cilastatin (gm) J01DH51	R Faropenem (gm) J01DI03	R Colistin (MIU) J01XB01	R Tigecycline (gm) J01AA12
Phase 1 Frequency	16	6	6	2	0
Phase 2 Frequency	13	5	4	3	0
Phase 3 Frequency	9	0	4	2	1

Figure - 4: Restricted Drugs utilization - Frequency

Profile plots display the Defined Daily Dose (DDD) of a Reserve antimicrobial drug, specifically Linezolid, in a graphical

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representation.

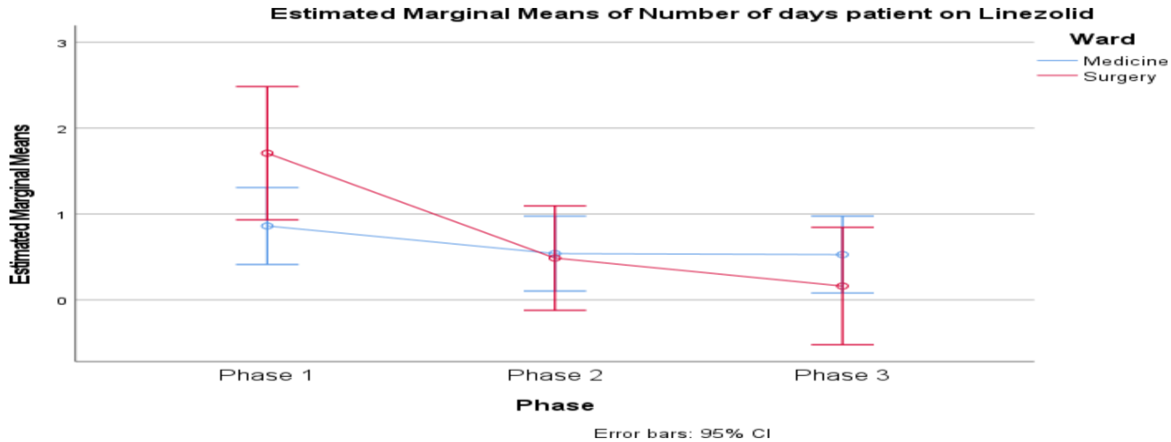

Figure - 5: Profile plot of estimated marginal means of number of days of Linezolid

The analysis of between-subjects effects examines the impact of Imipenem + Cilastatin on the dependent variable, which is the number of days a patient is on this drug. The results include the Type III sum of squares, degrees of freedom (df), mean square, F-value, significance level (Sig.), and partial eta squared (Partial Eta Squared) as a measure of effect size.

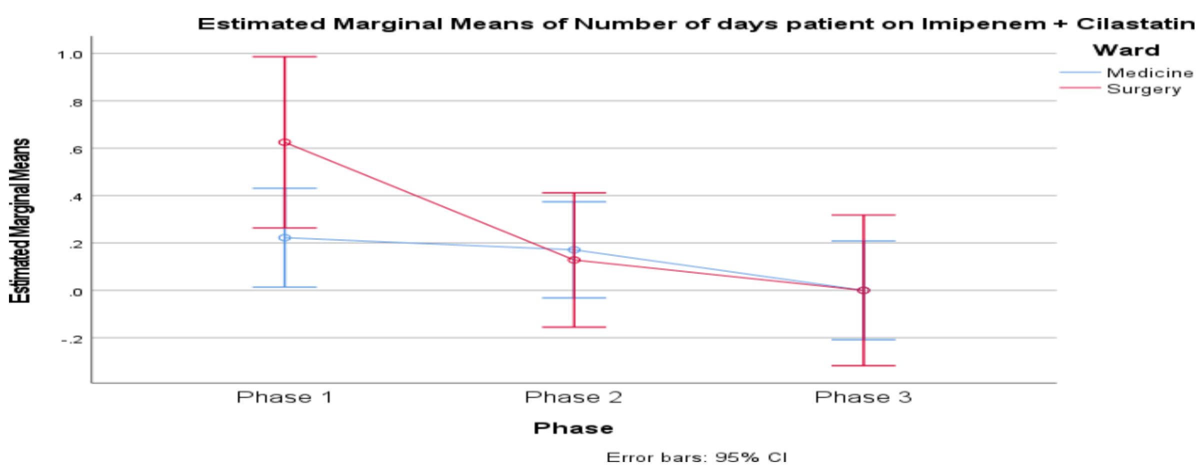

Figure - 6: Estimated marginal means of Number of days patient on Imipenem+Cilastatin

Overall, the data suggests that the utilization of these Reserve AMAs has decreased

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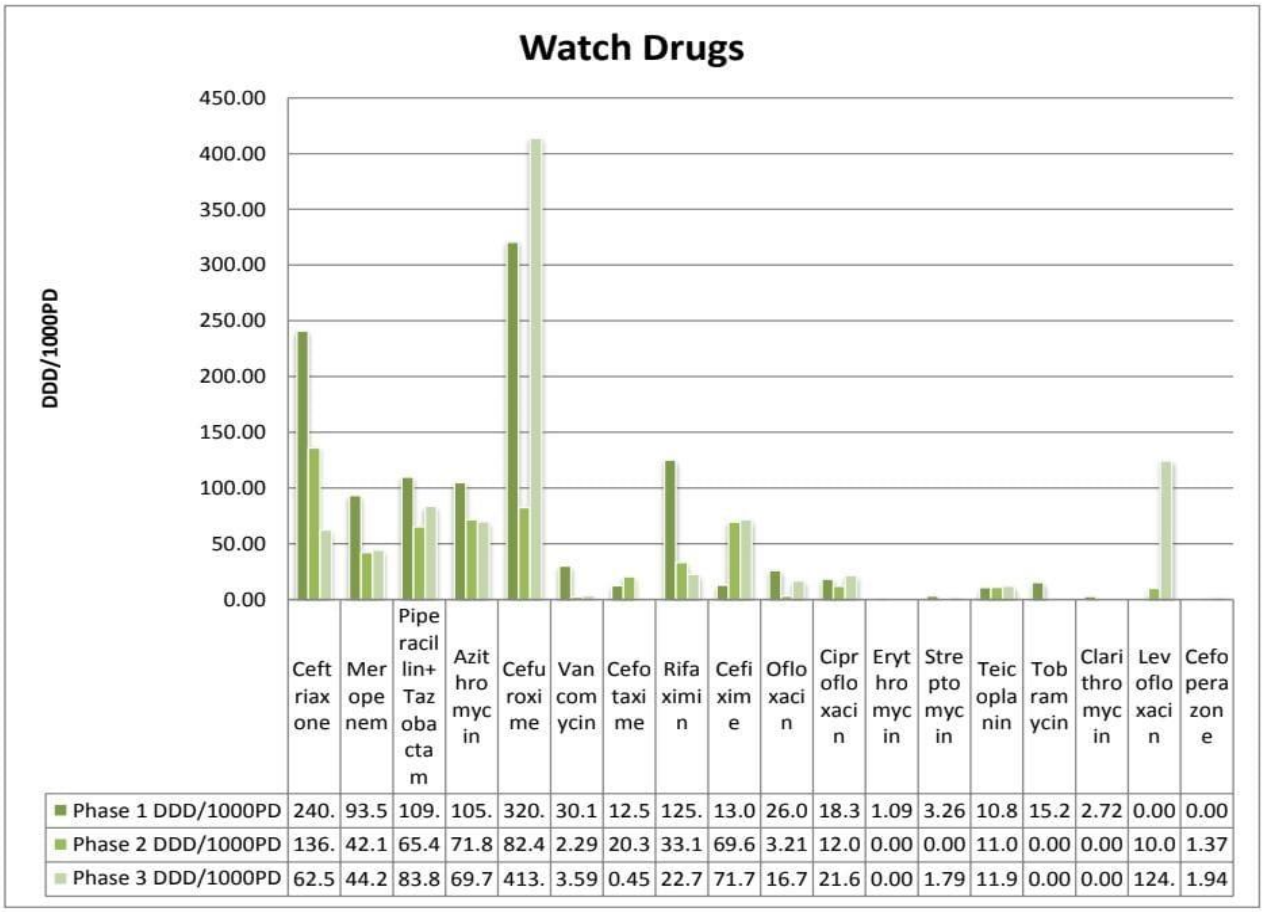
from Phase 1 to Phase 3, as indicated by the relatively low total LOT frequency and DDDs per 1000 population per day. This indicates that efforts to reduce unnecessary or inappropriate usage of these drugs have been effective.

The column labeled DDD/1000PD displays the ratio of the defined daily dose (DDD) used in the study period per 1000 patient days for each drug. The values were calculated based on the total milligrams of each drug utilized during the study period using the defined daily dose (DDD) for each drug and the W.H.O-defined daily dose (DDD) in milligrams. The table also indicates the relative significance of each drug used in the Watch category according to the AWaRE classification.



	Ceftriaxone	Meropenem	Piperacillin+Tazobactam	Azithromycin	Cefuroxime	Vancomycin	Cefotaxime	Rifaximin	Cefixime	Ofloxacin	Ciprofloxacin	Erythromycin	Streptomycin	Teicoplanin	Tobramycin	Clarithromycin	Levofloxacin	Cefoperazone
Phase 1 DDD/1000PD	240.	93.5	109.	105.	320.	30.1	12.5	125.	13.0	26.0	18.3	1.09	3.26	10.8	15.2	2.72	0.00	0.00
Phase 2 DDD/1000PD	136.	42.1	65.4	71.8	82.4	2.29	20.3	33.1	69.6	3.21	12.0	0.00	0.00	11.0	0.00	0.00	10.0	1.37
Phase 3 DDD/1000PD	62.5	44.2	83.8	69.7	413.	3.59	0.45	22.7	71.7	16.7	21.6	0.00	1.79	11.9	0.00	0.00	124.	1.94

Figure - 7: DDD/1000 PD of Watch drugs

The data provided in the table includes information on the number of AMAs used,

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the total frequency and amount of each drug used, their defined daily doses, and their ratios to the W.H.O-defined daily doses. This data is valuable for healthcare providers and policy makers in monitoring and improving the appropriate use of antibiotics to address the issue of antibiotic resistance.

Regarding the "Access" drugs, the table presents detailed frequencies for each drug based on their ATC code and AWaRe category in different phases. For example, Metronidazole (JO1XD01) was prescribed 22, 36, and 19 times during Phase 1, Phase 2, and Phase 3, respectively. Clindamycin (JO1FF01) had frequencies of 18, 15, and 4 in the corresponding phases, while Amoxicillin + Clavulanic acid (JO1CR02) had frequencies of 11, 26, and 11. These frequencies provide insights into the utilization patterns of these drugs throughout the study.

The text also provides information on specific AMA, their usage patterns, and their limitations. It highlights that Ceftriaxone/SB 1.5gm and Cefoperazone/SB 1.5gm are third-generation cephalosporins with beta-lactamase inhibitors commonly used for various bacterial infections. However, their overuse can lead to antibiotic resistance. Cefixime Clav. and Cefixime/Ofloxacin are combination antibiotics effective against specific bacterial strains, but not recommended as first-line agents. Ofloxacin/Ornidazole is another combination antibiotic, but its use is not recommended due to the development of antibiotic resistance. Lastly, Ampicillin/Cloxacillin is a combination antibiotic used for skin and soft tissue infections, but its use is limited due to antibiotic-resistant strains.

Conclusion

The study's conclusion highlights the effective utilization of Reserve antimicrobial agents (AMAs) in relatively low quantities, indicating successful efforts to reduce unnecessary or inappropriate usage. The data provides valuable insights into the patterns of AMA utilization and can aid healthcare providers and policymakers in monitoring and improving antibiotic usage. Furthermore, the study emphasizes the importance of appropriate AMA use to address the global challenge of antibiotic resistance. Overall, the findings contribute to the on-going efforts to optimize antimicrobial stewardship and safeguard the effectiveness of antibiotics for future generations.

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