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Research Article

Cost Variation and Cost per Defined Daily Dose of WHO Aware Category Oral Antibiotics in India: Implications for Rational Antimicrobial Therapy

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ABSTRACT

Background: Economic factors significantly influence antibiotic prescribing and use in low- and middle-income countries such as India, where healthcare expenditure is largely out-of-pocket. The World Health Organization (WHO) introduced the AWaRe classification—comprising 'Access', 'Watch', and 'Reserve' categories—to guide rational antibiotic use and support antimicrobial stewardship. However, data on price variation and cost per Defined Daily Dose (DDD) of AWaRe-classified oral antibiotics in India remain limited.

Objectives: To assess cost variation and cost per DDD of WHO AWaRe category oral antibiotics available in the Indian market and to examine their implications for rational antimicrobial therapy.

Methods: A cross-sectional cost analysis was performed using publicly available Indian drug price databases and standard pharmaceutical compendia. Antibiotics were categorized according to the WHO AWaRe framework. Cost per DDD was calculated using WHO ATC (Anatomical Therapeutic Chemical)/DDD methodology, while cost variation was assessed using maximum–minimum price ratios. Fixed-dose combinations, parenteral formulations, oral syrups or suspensions and antibiotics without an assigned WHO DDD were excluded. Data was analyzed using descriptive statistics.

Results: Nineteen oral antibiotic formulations were included in the analysis. Antibiotics in the 'Watch' category exhibited the greatest price variability when compared with 'Access' antibiotics, with several commonly prescribed agents showing multi-fold differences in cost across brands. Reserve category antibiotic linezolid was associated with substantially high cost per DDD.

Conclusion: Marked cost variation exists among WHO AWaRe category oral antibiotics in India, particularly within the 'Watch' group. Integrating cost per DDD into prescribing practices and antimicrobial stewardship policies may enhance treatment adherence and support rational antibiotic use.

Keywords*: AWaRe classification, Antibiotic cost, Defined daily dose, Drug price variation, Antimicrobial stewardship, India.*

INTRODUCTION

Antimicrobial resistance (AMR) has emerged as a major global public health concern, driven by the inappropriate and excessive use of antibiotics. [1] To address AMR, the World Health Organization (WHO) introduced the AWaRe (Access, Watch, and Reserve) classification system as a stewardship tool to monitor antibiotic consumption and promote rational use of antibiotics. [2] This framework encourages the preferential use of 'Access' antibiotics for common infections and recommends judicious use of Watch and Reserve agents for specific, well-defined indications. [3] Treatment decisions in countries such as India where healthcare spending is predominantly out-of-pocket are guided not only by clinical efficacy and resistance patterns but economic considerations as well. The financial aspects play a crucial role in real-world prescribing and patient adherence. [4]

India is one of the largest pharmaceutical markets globally. The Indian market is characterized by widespread availability of branded generics for most antibiotics. [4] Along with enhanced availability, this also leads to substantial price variation

between different brands of the same drug. Such variability may influence prescribing decisions, contribute to irrational antibiotic use, and can impose an unwarranted financial burden on patients. [5,6] The cost per Defined Daily Dose (DDD) is a standardized measure developed by the WHO. It offers a useful approach for comparison of the economic burden of antibiotics across different drugs and formulations, independent of dosing schedules. [7,8]

Although several studies from India have explored price variation among antibiotics, relatively few have examined these costs within the context of the WHO AWaRe classification, and even fewer have assessed cost per DDD. [9,10] Evaluating these economic dimensions is crucial in bridging the gap between principles of antimicrobial stewardship and routine clinical practice. Against this background, the present study aimed to assess cost variation and cost per DDD of WHO AWaRe category oral antibiotics available in the Indian market and to explore their implications for rational antimicrobial therapy.

MATERIALS AND METHODS

A cross-sectional, descriptive cost analysis was conducted to evaluate oral antibiotics available in the Indian pharmaceutical market.Antibiotics were included in the study if they met the following criteria:availability in oral solid dosage forms (tablets or capsules), classification under the World Health Organization (WHO) AWaRe framework, assignment of an Anatomical Therapeutic Chemical (ATC) code and a Defined Daily Dose (DDD) by the WHO and marketing in India at the time of data collection.The following were excluded from the analysis: fixed-dose combinations (FDCs), oral syrups or suspensions, parenteral formulations, and antibiotics without an assigned WHO DDD. These exclusions were applied to ensure methodological uniformity and to enable accurate and comparable cost per DDD calculations.

A total of 19 oral antibiotics were included in the analysis, comprising 9 ‘Access’, 9 ‘Watch’, and 1 ‘Reserve’ category antibiotics. The selected agents represent commonly prescribed oral antimicrobials in outpatient clinical practice in India. *[3-6]*Price data were obtained from the Current Index of Medical Specialties (CIMS), a widely used and publicly accessible Indian drug price database and pharmaceutical compendium. *[11]* For each antibiotic, multiple marketed brands were identified. As a large number of brands were available, the analysis was restricted to the first ten listed brands to ensure feasibility and consistency. For antibiotics with fewer than ten available brands, all listed brands were included.

Each antibiotic was categorized as Access, Watch, or Reserve according to the WHO AWaRe classification. Classification was applied at the drug level and not at the formulation level. *[2]*The cost per Defined Daily Dose (DDD) was calculated by multiplying Cost per unit with Number of units required to meet the WHO-defined DDD *[7]*Unit cost was derived from the retail price of each brand. For each antibiotic, the minimum and maximum cost per DDD across brands were identified.Cost variation for each antibiotic was assessed using the maximum-minimum price ratio, by dividing Maximum cost per DDD by Minimum cost per DDD.

The data was entered in MS excel and was analyzed using the SPSS version 16. Continuous variables were summarized as means with standard deviations or medians, while categorical variables were expressed as proportions with 95% confidence intervals.

RESULTS

A total of 19 oral antibiotics were included in this study. Antibiotics were categorized according to the WHO AWaRe classification. (Table 1) ‘Access’ and ‘Watch’ antibiotics were equally represented (9 each), while the ‘Reserve’ category was represented by a single drug. There was substantial variability between the minimum- and maximum-priced brands available for the same antibiotic, demonstrating meaningful dispersion in prices within the market. (Table 2) For ‘Access’ antibiotics, the *minimum* cost per unit ranged from INR 0.622 to INR 16.33, while the *maximum* cost per unit ranged from INR 3.30 to INR 46.88. For ‘Watch’ antibiotics, minimum unit costs ranged from INR 3.60 to INR 37.19, and maximum unit costs ranged from INR 5.90 to INR 104.00. The single ‘Reserve’ antibiotic, linezolid, had a minimum unit cost of INR 29.431 and maximum unit cost of INR 80.505.Across all included antibiotics, the lowest observed minimum unit cost was for metronidazole (Access) at INR 0.622, while the highest observed maximum unit cost was for cefuroxime (Watch) at INR 104.00.

When comparing ‘Access’ vs ‘Watch’ antibiotics on minimum cost per unit, ‘Watch’ antibiotics showed higher average minimum unit prices than ‘Access’ antibiotics. This difference was statistically significant. (Mann–Whitney U test $p = 0.022$). This suggests that ‘Watch’ antibiotics tended to have higher floor prices. For maximum cost per unit, ‘Watch’ antibiotics also had higher mean values than ‘Access’ antibiotics, but the between-group difference was not statistically significant. (Mann–Whitney testing $p = 0.14$) This indicates that while ‘Watch’ drugs tended to be more expensive, the upper-end brand prices were highly variable across drugs.

When standardized using WHO DDD values, marked cost variability persisted. (Table 3) Among ‘Access’ antibiotics, minimum cost per DDD ranged from INR 0.93 to INR 54.00, and maximum cost per DDD ranged from INR 3.30 to INR 187.52. Among ‘Watch’ antibiotics, minimum cost per DDD ranged from INR 6.54 to INR 37.19, and maximum cost per

DDD ranged from INR 10.40 to INR 104.00. For the 'Reserve' antibiotic (linezolid), minimum and maximum costs per DDD were INR 58.862 and INR 161.01, respectively.The lowest minimum cost per DDD was for doxycycline (Access) at INR 0.93, whereas the highest maximum cost per DDD was for ampicillin (Access) at INR 187.52. There was no significant difference between 'Access' and 'Watch' groups for either minimum cost per DDD or maximum cost per DDD. (Mann-Whitney U)

Across antibiotics, price dispersion measures such as the price ratio and percent cost variation indicated substantial within-drug variability between the cheapest and most expensive brands. This pattern was observed across both 'Access' and 'Watch' groups, consistent with heterogeneous pricing across manufacturers and formulations. The median unit-cost price ratio was 3.55 in the 'Access' group, with ratios ranging from 1.64 to 18.03. The largest between-brand price dispersion was observed for ampicillin (Access), which showed a price ratio of 18.03 and percent cost variation of 1703.08 percent, followed by metronidazole (Access) with a price ratio of 12.06 and percent cost variation of 1105.79 percent

Across drugs, there was a strong positive relationship between minimum and maximum prices, both at the unit-cost level and at the DDD-cost level. Pearson and Spearman correlations were high and statistically significant $p < 0.001$, indicating that antibiotics that were expensive even at their lowest-priced brands also tended to have higher maximum-priced brands. This suggests that pricing tiers move together across the market rather than reflecting isolated extremes.

Table 1. Characteristics of WHO AWaRe Category Oral Antibiotics Included in the Study

Drug name	Dosage form	Strength	AWaRe category	ATC code	WHO DDD (g)	DPCO status	NLEM status
Amoxicillin	Capsule	500 mg	Access	J01CA04	1.5	Yes	Yes
Amoxicillin + clavulanic acid	Tablet	500/125 mg	Access	J01CR02	1.5 (amoxicillin component)	Yes	Yes
Ampicillin	Capsule	500 mg	Access	J01CA01	2	Yes	Yes
Azithromycin	Tablet	500 mg	Watch	J01FA10	0.3	Yes	Yes
Cefadroxil	Tablet	500 mg	Access	J01DB05	2	Yes	Yes
Cefalexin	Capsule	500 mg	Access	J01DB01	2	Yes	No
Cefixime	Tablet	200 mg	Watch	J01DD08	0.4	Yes	Yes
Cefpodoxime proxetil	Tablet	200 mg	Watch	J01DD13	0.4	Yes	No
Cefuroxime	Tablet	500 mg	Watch	J01DC02	0.5	Yes	Yes
Ciprofloxacin	Tablet	500 mg	Watch	J01MA02	1	Yes	Yes
Clarithromycin	Tablet	500 mg	Watch	J01FA09	0.5	Yes	Yes
Clindamycin	Capsule	300 mg	Access	J01FF01	1.2	Yes	Yes
Doxycycline	Capsule/ Tablet	100 mg	Access	J01AA02	0.1	Yes	Yes
Levofloxacin	Tablet	500 mg	Watch	J01MA12	0.5	Yes	Yes
Linezolid	Tablet	600 mg	Reserve	J01XX08	1.2	Yes	Yes
Metronidazole	Tablet	400 mg	Access	P01AB01	2	Yes	Yes
Moxifloxacin	Tablet	400 mg	Watch	J01MA14	0.4	Yes	Yes
Nitrofurantoin	Tablet	100 mg	Access	J01XE01	0.2	Yes	Yes
Ofloxacin	Tablet	200 mg	Watch	J01MA01	0.4	Yes	No

NLEM-National List of Essential Medicines 2022

Table 2. Cost Variation among WHO AWaRe Category Oral Antibiotics in India

Drug name	Strength	Number of brands analyzed	Minimum cost per unit (INR)	Maximum cost per unit (INR)	Price ratio (Max/Min)	Percent cost variation
Amoxicillin	500 mg	10	5.49	9.00	1.64	63.93
Amoxicillin + clavulanic acid	500/125 mg	10	16.33	28.38	1.74	73.78
Ampicillin	500 mg	10	2.60	46.88	18.01	1700.81
Azithromycin	500 mg	10	18.00	26.00	1.44	44.44
Cefadroxil	500 mg	10	3.30	7.29	2.21	120.91
Cefalexin	500 mg	10	4.43	22.61	5.10	410.38
Cefixime	200 mg	10	9.70	20.02	2.06	106.37
Cefpodoxime proxetil	200 mg	10	5.60	25.44	4.54	354.29
Cefuroxime	500 mg	10	37.19	104.00	2.80	179.67
Ciprofloxacin	500 mg	10	4.05	7.50	1.85	85.19
Clarithromycin	500 mg	10	19.25	97.37	5.06	405.82
Clindamycin	300 mg	10	13.50	36.00	2.67	166.67
Doxycycline	100 mg	10	0.93	3.30	3.55	254.84
Levofloxacin	500 mg	10	6.54	10.40	1.59	59.02
Linezolid	600 mg	10	29.43	80.51	2.74	173.54
Metronidazole	400 mg	7	0.62	7.50	12.06	1105.79
Moxifloxacin	400 mg	10	24.04	75.00	3.12	211.99
Nitrofurantoin	100 mg	10	1.00	8.17	8.17	717.00
Ofloxacin	200 mg	10	3.60	5.90	1.64	63.89

INR- Indian Rupee ,Max=Maximum ,Min=Minimum

Table 3. Cost per Defined Daily Dose (DDD) of WHO AWaRe Category Oral Antibiotics in India

Drug name	AWaRe category	Minimum cost per DDD (INR)	Maximum cost per DDD (INR)
Amoxicillin	Access	16.47	27.00
Amoxicillin + clavulanic acid	Access	48.99	85.14
Ampicillin	Access	10.40	187.52
Cefadroxil	Access	13.20	29.16
Cefalexin	Access	17.72	90.44
Clindamycin	Access	54.00	144.00
Doxycycline	Access	0.93	3.30
Metronidazole	Access	3.11	37.50
Nitrofurantoin	Access	2.00	16.34
Azithromycin	Watch	10.80	15.60
Cefixime	Watch	19.40	40.04
Cefpodoxime proxetil	Watch	11.20	50.88
Cefuroxime	Watch	37.19	104.00
Ciprofloxacin	Watch	8.10	15.00
Clarithromycin	Watch	19.25	97.37
Levofloxacin	Watch	6.54	10.40
Moxifloxacin	Watch	24.04	75.00

Ofloxacin	Watch	7.20	11.80
Linezolid	Reserve	58.86	161.02

INR- Indian Rupee , DDD- Defined Daily Dose

DISCUSSION

This study offers a focused assessment of the affordability of oral antibiotics in India by examining cost per defined daily dose (DDD) across WHO Access and Watch categories. By shifting attention from brand-level price differences to molecule-level treatment costs, the analysis provides a practical perspective on the economic burden faced by patients in routine outpatient care. The findings indicate that Access antibiotics are generally associated with lower and more predictable costs per DDD compared with Watch antibiotics, supporting their role as preferred first-line agents.

Affordability is a critical determinant of antibiotic use in India, where out-of-pocket expenditure remains substantial. [12,13] Even small increases in daily treatment cost can influence whether patients initiate therapy promptly or complete the prescribed course. [14,15,16] The higher median costs and wider cost dispersion observed among Watch antibiotics suggest that economic factors may unintentionally shape prescribing decisions and patient adherence. From a stewardship standpoint, this raises concerns, as incomplete treatment or cost-driven substitutions can compromise clinical outcomes and potentially contribute to antimicrobial resistance. [17,18]

An important observation from this analysis is that affordability is not uniform within AWaRe categories. Although Access antibiotics were generally less expensive, a small number were associated with relatively higher costs per DDD. This finding highlights that classification within the Access group does not automatically translate into affordability at the point of care. Market forces and pricing structures may influence treatment costs, underscoring the need for continuous monitoring of affordability even among antibiotics recommended for widespread use. [19,20]

The use of cost per DDD as an outcome measure offers several advantages. Unlike unit-based pricing, cost per DDD reflects the actual daily cost of therapy and allows meaningful comparison across antibiotics with different dosing schedules. Incorporating such pharmacoeconomic indicators into clinical decision-making could help prescribers evaluate therapeutic alternatives within the same AWaRe category, balancing effectiveness with affordability. This approach is particularly relevant in resource-constrained settings, where cost considerations strongly influence both prescribing behavior and patient adherence. [21,22]

The findings also have implications for antimicrobial stewardship programs. While stewardship efforts traditionally focus on resistance patterns and appropriateness of use, integrating affordability considerations may strengthen their effectiveness. Promoting the rational use of affordable Access antibiotics, where clinically appropriate, could support adherence, reduce unnecessary reliance on higher-cost Watch antibiotics, and enhance equity in access to essential medicines.

From a broader health system perspective, molecule-level affordability data can inform formulary decisions and guide procurement strategies in public healthcare settings. Identifying antibiotics associated with higher treatment costs may help prioritize cost-effective options without compromising clinical efficacy.

Overall, this study underscores the importance of incorporating economic evaluation into antimicrobial stewardship and policy frameworks. By highlighting differences in affordability between Access and Watch antibiotics, the analysis supports a more holistic approach to rational antibiotic use—one that aligns clinical effectiveness, resistance containment, and patient-centered affordability.

LIMITATIONS

This study has several limitations. The cross-sectional design of this study captured prices at a single time point and thus does not account for temporal price fluctuations. We restricted our analysis to a maximum of ten brands, which may have resulted in underestimation of true market price variability for antibiotics with extensive brand price variability. We excluded fixed dose combinations and parenteral formulations. This was necessary for methodological consistency but can limit generalizability. Also, there might be variability in actual procurement prices and listed retailed prices in CIMS.

CONCLUSION

Significant cost variation exists among WHO AWaRe category oral antibiotics in India, particularly within the ‘Watch’ group. Cost per DDD analysis should be incorporated into antimicrobial stewardship initiatives as it can provide valuable insight into the economic burden of antibiotic therapy. Policy measures should aim at reducing extensive price variation and promoting use of ‘Access’ antibiotics. This can enhance rational antimicrobial use and improve patient outcomes.

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Informed Consent Statement: This study did not involve human participants, and therefore, informed consent was not required.

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