Original Research Article

Impact of Integrated Interventions of Prescriber Education and De-escalation Strategies on Implementing WHO Access: Insights from a South Indian Tertiary Care Setting

ABSTRACT

Aims: This study evaluates the effect of integrated interventions including prescriber education and de-escalation strategies on improving antibiotic prescribing practices, optimizing the Access: Watch ratio, reducing Reserve antibiotic use, and improving Length of Therapy (LOT) adherence in a South Indian tertiary care hospital.
Study design: Prospective Observational Study
Place and Duration of Study: The study was carried out in Fortis Healthcare, Adyar for a period of five months (March to July 2023).
Methodology: Data on Days of Therapy (DOT) and LOT were collected. Prescriber education and audit interventions were implemented, with pre- and post-intervention surveys to assess prescriber confidence in de-escalation.
Results: The Access: Watch ratio improved from 0.45 to 0.52, with a marked reduction in Watch antibiotic consumption. DOT for Cefoperazone-Sulbactam, a Watch antibiotic, decreased from 50.7 to 18.1, and Reserve antibiotics (e.g., Linezolid and Colistin) showed significant reductions. LOT adherence to WHO guidelines improved for various infections, and prescriber confidence in de-escalation increased from 88.9% to 100%.
Conclusion: Integrated interventions significantly optimized antibiotic use, achieved WHO Access: Watch targets, reduced Reserve antibiotic use, and enhanced prescriber practices. The study demonstrates the potential for similar strategies in other resource-limited settings to combat AMR.

Keywords: Antibiotic Stewardship Metrics, AMSP, Prescriber education, Antibiotic audit

1. INTRODUCTION

1.1 The Global Burden of Antimicrobial Resistance (AMR)

Antimicrobial resistance (AMR) remains one of the most critical global health challenges, leading to a rise in treatment failures and increased mortality rates. AMR has the potential to undermine decades of medical progress, including treatments for common infections and complex conditions like surgical interventions and cancer therapies. According to the World Health Organization (WHO), over 700,000 deaths occur annually due to AMR, with projections suggesting that this number could rise to 10 million by 2050, surpassing the mortality rates from cancer [1][2].

In countries like India, the issue is particularly pressing due to factors such as unregulated access to antibiotics, high rates of self-medication, and the over-prescription of broad-spectrum antibiotics in healthcare settings. The emergence of multi-drug-resistant (MDR)

pathogens like carbapenem-resistant e*nterobacteriaceae* (CRE) and vancomycin-resistant *enterococci* (VRE) is a major concern, with India reporting alarmingly high resistance rates [3]. The rising burden of AMR necessitates global cooperation and urgent action to limit the spread of resistance and preserve the effectiveness of antibiotics.

1.2 The Role of Antimicrobial Stewardship Programs (AMSPs)

AMSPs aim to optimize antibiotic prescribing practices by promoting the rational use of antibiotics, which is essential in reducing unnecessary exposure to broad-spectrum agents and preserving the effectiveness of existing antibiotics. Several studies have demonstrated that AMSPs, which incorporate prescriber education, audit and feedback, prospective monitoring, and de-escalation strategies, can significantly reduce antibiotic misuse [4][5].

In high-income settings, AMSPs have been highly effective, with reductions in antibiotic consumption of up to 40% and improved patient outcomes. However, the implementation of AMSPs in low- and middle-income countries (LMICs) faces challenges, including limited resources, inconsistent guideline adherence, and lack of trained personnel. A multi-center study in India showed that simple interventions, such as educating prescribers and conducting regular audits, resulted in a significant reduction in broad-spectrum antibiotic use [6]. Despite these challenges, studies have indicated that tailored AMSPs in LMICs can yield positive results, especially when they focus on education and engagement of the entire healthcare team [29-31].

1.3 WHO AWaRe Classification: A Framework for Rational Use of Antibiotics

The AWaRe classification was introduced by the WHO in 2017 to provide a framework for managing antibiotic use globally. By categorizing antibiotics into three groups based on their risk for resistance, AWaRe aims to promote appropriate antibiotic use and reduce antibiotic resistance.

- Access Antibiotics: These are first-line therapies recommended for common infections due to their low resistance potential (e.g., amoxicillin, penicillin) [7].
- Watch Antibiotics: These antibiotics are associated with higher resistance potential and should be used with caution, including cephalosporins and fluoroquinolones (e.g., Ceftriaxone, Ciprofloxacin) [8].
- Reserve Antibiotics: These are last-resort agents for multi-drug-resistant infections, such as colistin and Linezolid, and should only be used when absolutely necessary [9].

A study by Gandra et al. demonstrated that improving the Access: Watch ratio can significantly reduce the overuse of broad-spectrum antibiotics in hospital settings, helping to preserve the effectiveness of Watch and Reserve antibiotics for more critical cases [4].

1.4 Rationale for Integrated Interventions: Prescriber Education and De-escalation

Prescriber education plays a pivotal role in changing antibiotic prescribing behaviors. Several studies have shown that structured educational interventions result in improved adherence to guidelines, reduced inappropriate prescriptions, and increased knowledge about the importance of antibiotic stewardship. A study in Canada found that educational interventions improved adherence to antimicrobial guidelines by 35% in hospital settings, leading to a significant reduction in the use of fluoroquinolones [10].

De-escalation strategies, where broad-spectrum antibiotics are narrowed or switched to more specific agents once the pathogen is identified, also play a crucial role in minimizing AMR. Studies in Europe have shown that de-escalation can lead to reduced resistance

rates, while maintaining clinical efficacy. A meta-analysis of de-escalation studies found that patients who underwent de-escalation had similar outcomes to those treated with broad-spectrum antibiotics, but with significantly reduced rates of AMR [11].

2. MATERIAL AND METHODS

2.1 Study Design and Setting

This prospective observational study was conducted from March to July 2023 in a South Indian tertiary care hospital. The hospital serves a diverse patient population, with a wide array of infectious diseases, and operates in a resource-constrained setting. Patients included in the study were those prescribed antibiotics for common infections, while those receiving antibiotics for surgical prophylaxis or hospital-acquired infections were excluded.

2.2 Interventions

- **Prescriber Education:** Educational sessions were conducted for doctors, nurses, and clinical pharmacists, focusing on WHO AWaRe guidelines and the importance of rational antibiotic prescribing and de-escalation strategies.
- **Audit and Feedback:** Monthly antibiotic prescribing audits were conducted, with feedback provided to prescribers to encourage adherence to stewardship guidelines.
- **De-escalation Strategies:** The hospital implemented standardized protocols for narrowing the spectrum of antibiotics based on microbiological results and clinical progress.

2.3 Data Collection and Analysis

- **Days of Therapy (DOT):** DOT was calculated for each antibiotic class and standardized to 100 patient-beds to measure antibiotic consumption.
- **Length of Therapy (LOT):** LOT for common infections was compared to WHO-recommended durations to assess compliance with guidelines.
- **Prescriber Confidence:** Pre- and post-intervention surveys assessed changes in prescriber confidence regarding the implementation of de-escalation strategies.

2.4 Statistical Methods

Descriptive statistics were used to summarize demographic data and antibiotic prescribing patterns. The Access: Watch ratio was calculated by dividing DOT for Access antibiotics by DOT for Watch antibiotics. Paired statistical tests (e.g., paired t-tests) were used to evaluate differences prescriber confidence before and after the intervention.

3. RESULTS

3.1 Population distribution

A total of 360 cases were included for this study. The population consisted of patients from all age groups who had received at least one antibiotic during treatment, on discharge or both. In-patients that had received antibiotics on treatment but were not prescribed any antibiotics on discharge were also included in the study. The sample population was described demographically on the basis of these parameters,

- Age
- Gender
- Type of Infections

3.1.1 Age-wise distribution

Out of the 360 cases assessed, the largest group of patients belonged to the 71-80 age group with 18.9%, followed by 61 – 70 age group having 17.2 %, while patients of the 11 – 20 age group had the lowest frequency, with 5.3%, respectively (Table 1).

Table 1. Age-wise distribution of Population

Age (Years)	Number of patients	Percentage (%)
0 - 10	45	12.5
11-20	19	5.28
21-30	20	5.55
31-40	37	10.28
41-50	21	5.83
51-60	43	11.94
61 -70	62	17.2
71 -80	68	18.89
>80	45	12.5

3.1.2 Gender-wise distribution

The total number of male patients was found to be 168 (46.7%) whereas the female population was found to be 192 (53.3%) among the study population (Table 2). Hence the study population contained a greater percentage of females than the males.

Table 2. Gender-wise Distribution

Gender	Frequency	Percentage(%)
Male	168	46.7
Female	192	53.3

3.1.3 Infection-wise distribution

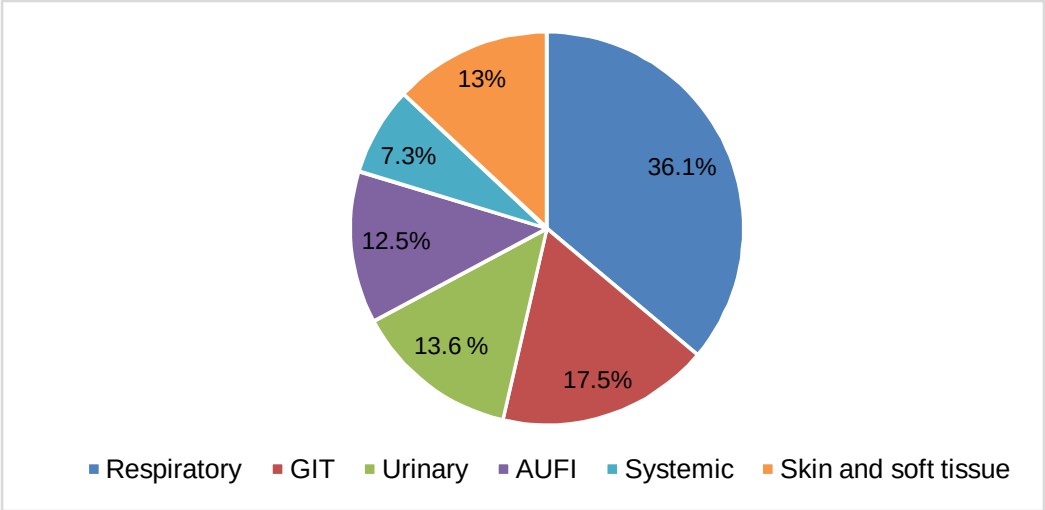
Among the study population, the occurrence of Respiratory tract infections (RTI) were highest, found in 130 patients (36.1%), Gastro-intestinal tract infections (GIT) were found in 63 (17.5%) of patients, Urinary tract infections (UTI) in 49 patients (13.6%), Acute undifferentiated febrile illness (AUFI) in 45 patients (12.5%), patients with Skin and Soft tissue infections (SSI) were 47 with 13 % and Systemic infections occurred in the lowest number of patients, 26 with 7.2% (Table 3, Figure 1).

Table 3. Infection-wise Distribution

Type of infection	Number of patients (n = 360)	Percentage (%)
Respiratory Tract Infection	130	36.1
Gastro-intestinal Tract Infection	63	17.5
Urinary Tract Infection	49	13.6
AUFI*	45	12.5
Systemic Infection	26	7.2
Skin And Soft Tissue Infection	47	13.0

**Acute Undifferentiated Febrile Illness*

Figure 1. Infection-wise Distribution



**Acute Undifferentiated Febrile Illness*

3.2 Trends in Antibiotic Usage

3.2.1 Watch Antibiotics: There was a noticeable reduction in DOT for cefoperazone-sulbactam (a Watch antibiotic), from 50.7 in April to 18.1 in July (Table 4).

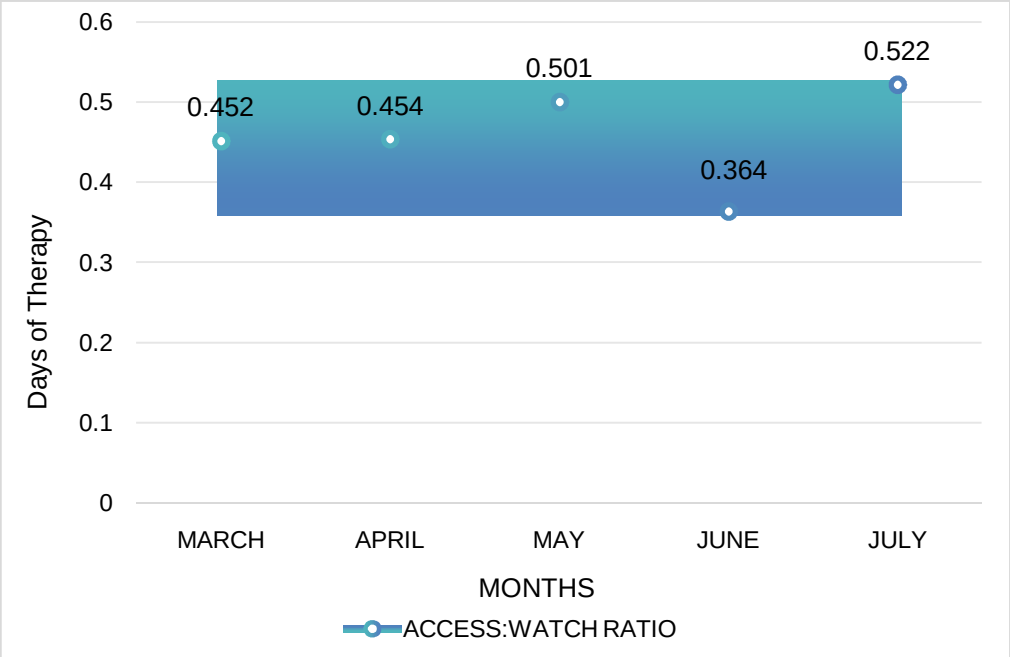
3.2.2 Access: Watch Ratio: The Access: Watch ratio improved from 0.45 in March to 0.52 in July, reflecting a shift towards decreased use of Watch antibiotics (Table 4, Figure 2). This improvement is consistent with similar findings from Europe, where targeted educational interventions led to improved Access: Watch ratios [12][13].

Table 4. Days of Therapy of Access, Watch and Reserve Antibiotics with Access: Watch Ratio

Class	Antibiotic	Days of Therapy (DOT)					
		March	April	May	June	July	Cumulative DOT
Access	Amikacin	3.1	5.5	8.9	3.8	6	**27.3**
	Amoxicillin-clavulanate	23.1	8.4	7	9.2	5.4	**53.1**
	Clindamycin	24.2	13.2	16	8	11.2	**72.6**
	Doxycycline	52	36.1	36.1	10.1	25.3	**159.6**
	Metronidazole	9.2	14.5	13.6	5.5	4.6	**47.4**
	Nitrofurantoin	12.6	10	14.5	1.7	6	**44.8**
	Ofloxacin	9.9	13.2	17.4	0	5.2	**45.7**
	Ofloxacin-Ornidazole	1.7	0	0	0.8	0	**2.5**
	Ofloxacin-Tinidazole	3.4	0	0	0	0	**3.4**

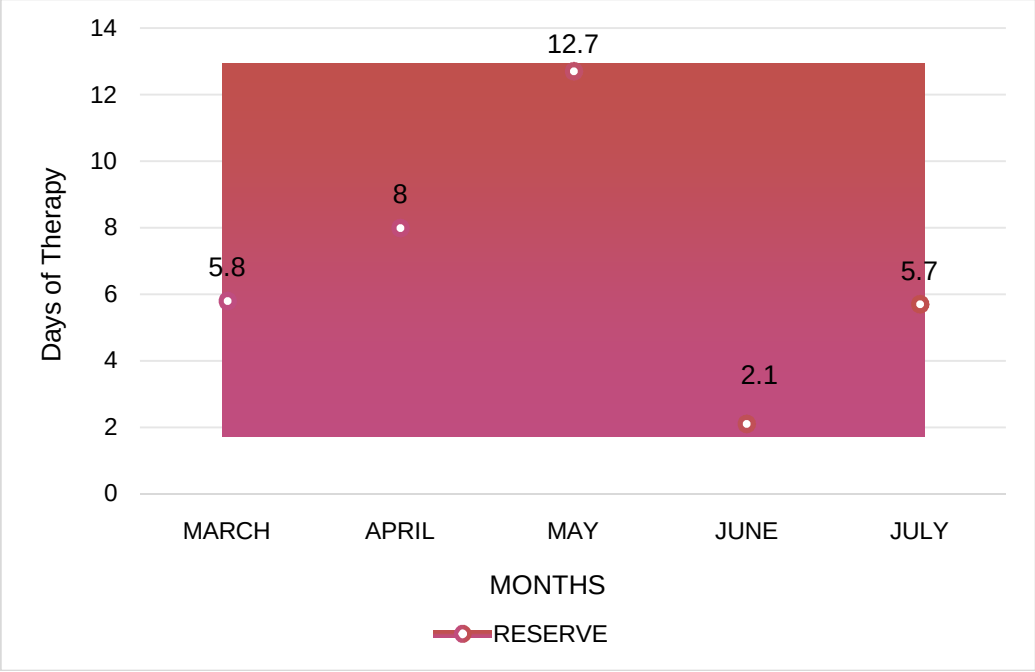
	Trimethoprim-sulfamethoxazole	0	0	6.1	2.9	0	**9**
	Total	**139.2**	**100.9**	**119.6**	**42**	**63.7**	**465.4**
Watch	Azithromycin	16.3	7.4	7.5	1.3	3.4	**35.9**
	Cefepime	27.5	8.7	15.5	2.1	7.2	**61**
	Cefixime	12.6	14.5	12.7	4.6	4.9	**49.3**
	Cefoperazone-sulbactam	50.7	48.7	50.7	19.3	18.1	**187.5**
	Cefotaxime	0	5.5	0	0	9	**14.5**
	Ceftriaxone	40.5	25.5	26.3	20.2	17.2	**129.7**
	Cefpodoxime	34.7	29.3	19.2	13.4	11.5	**108.1**
	Cefpodoxime-potassium clavulanate	0	0	0	0	1.4	**1.4**
	Cefuroxime	34.3	27.7	16.9	23.5	15.8	**118.2**
	Ciprofloxacin	13.3	10.3	17.8	15.1	1.4	**57.9**
	Ciprofloxacin-Tinidazole	7.1	0	3.3	0	1.4	**11.8**
	Clarithromycin	7.8	2.2	8.9	4.6	4.6	**28.1**
	Gatifloxacin	8.8	0	0	0	0	**8.8**
	Isepamicin	0.7	2.2	0	0	0	**2.9**
	Levofloxacin	3.4	0	7.5	4.6	3.2	**18.7**
	Meropenem	23.8	10.6	16	2.9	9.5	**62.8**
	Moxifloxacin	6.8	0	0	0	0	**6.8**
	Piperacillin-tazobactam	10.9	17.4	14.1	1.7	6	**50.1**
	Rifaximin	7.8	11.6	21.1	2.1	4.3	**46.9**
	Tobramycin	1	0	0	0	0	**1**
	Fosfomycin	0	0.6	1.4	0	1.4	**3.4**
	Ertapenem	0	0	0	0	1.7	**1.7**
	Total	**308**	**222.2**	**238.9**	**115.4**	**122**	**898.4**
Reserve	Linezolid	5.8	0	12.7	0	4.3	**22.8**
	Colistin	0	2.2	0	0	0	**2.2**
	Polymyxin B	0	2.9	0	0	0	**2.9**
	Tigecycline	0	2.9	0	0	0	**2.9**
	Faropenem	0	0	0	2.1	1.4	**3.5**
	Total	**5.8**	**8**	**12.7**	**2.1**	**5.7**	**34.3**
Access: Watch ratio	**Access ÷ Watch**	**0.452**	**0.454**	**0.501**	**0.364**	**0.522**	**0.518**

Figure 2. Trend of Access: Watch Ratio



3.2.3 Reserve Antibiotics: Reserve antibiotics, including Linezolid and colistin, had significant reductions in use over the five months (Table 4, Figure 3).

Figure 3. Trend of Reserve antibiotic use



3.3 Length of Therapy (LOT)

We have calculated the LOT during the period of our study and compared it with the recommended LOT as per the AWaRe guidelines of the WHO (Table 5). Among the selected 26 diagnoses, 7 conditions had their LOT decreased than recommended, 7 conditions matched the recommended LOT, 11 conditions were within the recommended LOT and only 1 condition had the LOT increased than recommended. The conditions with decreased LOT were Acute Viral Exanthematous fever, AUFI, Enterocolitis, Leptospirosis, RTI and Upper RTI. The conditions that were within recommended LOT were Acute infective exacerbation of Bronchial Asthma, Acute Gastroenteritis, Bronchiectasis, Dengue Fever, Enteric fever, Pharyngitis, Pneumonia, Pyelonephritis, Sinusitis, Urosepsis and Viral infections. The conditions that matched the recommended LOT were Acute infective exacerbation of COPD, Community acquired Pneumonia, Fungal pneumonia, GI infections, LRTI, SSI and UTI. Cellulitis was the only condition with increased LOT than recommended LOT compliance with WHO guidelines improved significantly, with many infections now treated for the recommended durations. For example, LRTI treatment durations were reduced from 14 days to 7 days, in accordance with WHO recommendations [14].

Table 5: Comparison of diagnosis-wise Length of Therapy (LOT)

S. No	Drug	Minimum LOT of drug	Maximum LOT of drug	Drug-wise mode	Diagnosis-wise mode	Recommended Length of Therapy (LOT)
1.	**Acute exacerbation of bronchial asthma**					
	Cefepime/ Tazobactam	4	7	5	**5 – 8 days**	**5-10 days**
	Cefoperazone/ Sulbactam	5	8	8		
	Cefpodoxime	5	5	5		
	Ceftriaxone	4	4			
	Cefuroxime	4	5			
	Doxycycline	4	10	5		
	Levofloxacin	10	10			
	Meropenem	5	5			
2.	**Acute exacerbation of COPD**					
	Azithromycin	4	4		**5 days**	**5 days**
	Cefepime/ Tazobactam	2	7	7		
	Cefoperazone/ Sulbactam	4	6			
	Cefpodoxime	3	5			
	Cefuroxime	2	5	5		
	Clarithromycin	6	7			
	Doxycycline	2	7	5, 7		
	Ertapenem	6	6			
	Meropenem	6	7	7		
	Nitrofurantoin	10	10			
	Ofloxacin	5	5	5		
	Piperacillin/ Tazobactam	2	3			
3.	**Acute viral Exanthematous fever**					
	Cefixime	2	5	3	**3 days**	**5 days**
	Ceftriaxone	3	4	3		
	Metronidazole	3	4	3		

4.	**Acute febrile illness**					
	Amikacin	3	3	3	**5 days**	**7 days**
	Amoxicillin/ Clavulanate	5	5	5		
	Azithromycin	3	5			
	Cefepime/ Tazobactam	2	5			
	Cefixime	3	5	3, 5		
	Cefoperazone/ Sulbactam	1	7	4		
	Cefotaxime	3	3			
	Cefpodoxime	2	7	5		
	Ceftriaxone	2	6	2		
	Cefuroxime	4	6	5		
	Ciprofloxacin	4	7			
	Clarithromycin	3	3			
	Clindamycin	5	5			
	Doxycycline	2	5	5		
	Gatifloxacin	7	7			
	Metronidazole	6	6			
	Nitrofurantoin	8	8			
	Ofloxacin	1	2	2		
	Ofloxacin/ Tinidazole	5	5			
	Piperacillin/ Tazobactam	5	5			
	Rifaximin	5	5			
5.	**Acute gastroenteritis**					
	Amikacin	2	5	5	**2 – 5 days**	**3-5 days**
	Amoxicillin/ Clavulanate	6	6			
	Azithromycin	2	2			
	Cefepime/ Tazobactam	1	9			
	Cefixime	2	5	2		
	Cefoperazone/ Sulbactam	2	3	3		
	Cefpodoxime	3	7	2, 3		
	Ceftriaxone	1	7	2		
	Cefuroxime	2	6	5		
	Ciprofloxacin	1	6	2		
	Ciprofloxacin/ Tinidazole	4	4			
	Doxycycline	3	10			
	Imipenem/ Cilastatin	2	2			
	Meropenem	2	2			
	Linezolid	2	2			
	Metronidazole	2	14	5		
	Ofloxacin	2	5	2		
	Ofloxacin/ Ornidazole	1	1			
	Ofloxacin/ Tinidazole	2	3			
	Rifaximin	2	12	3, 5		
6.	**Bronchiectasis**					
	Amikacin	6	7		**5 – 10 days**	**7-14 days**
	Cefepime/ Tazobactam	4	5	5		
	Cefoperazone/ Sulbactam	6	10			
	Cefuroxime	3	5			
	Doxycycline	3	7	3, 4, 5		
	Levofloxacin	6	10	10		

7.	**Community acquired pneumonia**					
	Amoxicillin/ Clavulanate	20	20		**3 – 5 days**	**3-5 days**
	Cefepime/ Tazobactam	5	5			
	Cefoperazone/ Sulbactam	2	9	3		
	Cefpodoxime	3	3			
	Ceftriaxone	4	4	4		
	Cefuroxime	5	5			
	Ciprofloxacin	7	7			
	Clarithromycin	6	10	9		
	Clindamycin	26	26			
	Doxycycline	3	5	5		
	Levofloxacin	5	5			
	Linezolid	7	7			
	Meropenem	12	12			
	Piperacillin/ Tazobactam	7	7			
8.	**Cellulitis**					
	Amoxicillin/ Clavulanate	7	15	7	**7 days**	**5 days**
	Cefixime	5	5			
	Cefoperazone/ Sulbactam	3	7	7		
	Cefpodoxime	5	5			
	Ceftriaxone	2	4			
	Cefuroxime	2	10			
	Clindamycin	5	11	5		
	Doxycycline	8	11			
	Linezolid	17	17			
	Metronidazole	4	7	4		
	Piperacillin/ Tazobactam	7	11			
	Rifaximin	7	7			
9.	**Dengue**					
	Amikacin	6	6		**3 – 5 days**	**5 -7 days**
	Amoxicillin/ Clavulanate	3	3			
	Cefixime	5	5			
	Cefoperazone/ Sulbactam	5	5			
	Cefpodoxime	3	5	4		
	Ceftriaxone	1	6	3, 4		
	Doxycycline	5	11	5		
	Ofloxacin	5	6			
10.	**Enteric fever**					
	Ceftriaxone	2	7		**5 – 7 days**	**7 - 10 days**
	Azithromycin	5	5	5		
	Cefepime/ Tazobactam	5	5			
	Cefixime	5	5	5		
	Ceftriaxone	2	4	2		
	Gatifloxacin	5	7	7		
	Moxifloxacin	6	7	7		
11.	**Enterocolitis**					
	Amikacin	3	3		**2 – 3 days**	**14 days**
	Cefotaxime	7	7			
	Cefpodoxime	2	2	2		
	Ceftriaxone	3	3	3		

	Meropenem	6	6			
	Metronidazole	6	6			
12.	**Fungal pneumonia**					
	Cefepime/ Tazobactam	4	8		**7 days**	**7 days**
	Amikacin	7	7			
	Cefoperazone/ Sulbactam	5	8			
	Cefuroxime	5	5			
	Doxycycline	5	10			
	Piperacillin/ Tazobactam	7	7			
13.	**Gastro-intestinal infections**					
	Amoxicillin/ Clavulanate	5	5		**5 – 7 days**	**5-7 days**
	Azithromycin	3	7			
	Cefoperazone/ Sulbactam	3	7	7		
	Cefpodoxime	5	5	5		
	Ceftriaxone	2	8			
	Cefuroxime	2	7	3		
	Ciprofloxacin	4	4			
	Doxycycline	2	2			
	Fosfomycin	5	5			
	Linezolid	5	5			
	Nitrofurantoin	8	8			
	Ofloxacin	13	13			
	Piperacillin/ Tazobactam	3	3			
	Rifaximin	4	6			
14.	**Leptospirosis**					
	Cefepime/ Tazobactam	6	6	6	**5 – 6 days**	**7-21 days**
	Cefoperazone/ Sulbactam	3	6			
	Cefpodoxime	5	5			
	Ceftriaxone	1	1			
	Ciprofloxacin/ Tinidazole	21	21			
	Doxycycline	2	8	5		
	Meropenem	8	8			
	Piperacillin/ Tazobactam	3	4			
	Rifaximin	7	7			
15.	**Lower respiratory tract infection (LRTI)**					
	Amikacin	5	6		**5 – 7 days**	**5-7 days**
	Amoxicillin/ Clavulanate	5	10			
	Azithromycin	5	15			
	Cefoperazone/ Sulbactam	2	6	3		
	Cefpodoxime	3	8	5		
	Ceftriaxone	2	9	2		
	Cefuroxime	3	5	5		
	Cefixime	5	5			
	Clarithromycin	14	14			
	Doxycycline	2	10	2, 5, 7		
	Levofloxacin	6	10			
	Meropenem	6	6			
	Nitrofurantoin	4	4			
	Ofloxacin	9	10			
	Rifaximin	7	7			

	Cotrimoxazole	2	4			
	Clindamycin	5	5			
	Linezolid	2	4			
16.	**Pharyngitis**					
	Amoxicillin/ Clavulanate	2	2			
	Azithromycin	5	6	5		
	Cefixime	6	6		**2 – 5 days**	**5 - 10 days**
	Cefpodoxime	3	4			
	Ceftriaxone	2	5	2, 3		
	Cefuroxime	1	5	2		
17.	**Pneumonia**					
	Amikacin	2	6	3		
	Amoxicillin/ Clavulanate	16	16			
	Azithromycin	2	5	2		
	Cefepime/ Tazobactam	2	6	6		
	Cefoperazone/ Sulbactam	1	13	7		
	Cefpodoxime	2	5	5		
	Ceftriaxone	3	4	3		
	Cefuroxime	5	5	5		
	Clindamycin	5	5		**5 days**	**5-14 days**
	Doxycycline	2	7	5		
	Linezolid	5	5			
	Meropenem	2	10			
	Metronidazole	2	9			
	Ofloxacin	5	5	5		
	Piperacillin/ Tazobactam	5	5			
	Rifaximin	3	3			
18.	**Pyelonephritis**					
	Cefoperazone/ Sulbactam	1	5			
	Cefpodoxime	5	5	5		
	Ciprofloxacin	7	7	7		
	Fosfomycin	3	3		**4 – 7 days**	**7 days**
	Linezolid	4	4	4		
	Meropenem	2	6			
	Piperacillin/ Tazobactam	4	10			
19.	**Respiratory tract infection**					
	Amikacin	3	7			
	Amoxicillin/ Clavulanate	4	5			
	Azithromycin	4	7			
	Cefepime/ Tazobactam	4	4			
	Cefoperazone/ Sulbactam	2	4	3, 4		
	Cefpodoxime	3	5	5		
	Ceftriaxone	2	6	3	**5 days**	**7 days**
	Cefuroxime	1	4			
	Ciprofloxacin	10	10			
	Clarithromycin	5	5			
	Doxycycline	3	14			
	Imipenem/ Cilastatin	5	5			
	Levofloxacin	6	6			
	Metronidazole	5	5			

20.	**Sepsis and related syndrome**					
	Amoxicillin/ Clavulanate	7	7		**5 days**	**7-21 days**
	Cefoperazone/ Sulbactam	1	7	7		
	Cefotaxime	5	5	5		
	Cefpodoxime	5	5	5		
	Ceftriaxone	3	5			
	Cefuroxime	5	5			
	Clindamycin	10	10			
	Colistin	7	7			
	Doxycycline	9	9			
	Faropenem	5	5	5		
	Fosfomycin	2	2			
	Linezolid	17	17			
	Meropenem	2	11	6		
	Metronidazole	2	8			
	Nitrofurantoin	14	14			
	Piperacillin/ Tazobactam	4	8			
	Polymyxin B	9	9			
	Rifaximin	2	4			
	Tigecycline	9	9			
21.	**Sinusitis**					
	Amoxicillin/ Clavulanate	1	2		**4 days**	**5 days**
	Azithromycin	2	3			
	Cefoperazone/ Sulbactam	3	4			
	Cefpodoxime	4	4			
	Ceftriaxone	4	4			
	Cefuroxime	5	5	5		
	Ciprofloxacin	6	7			
	Ciprofloxacin	10	10			
22.	**Skin and soft tissue infection**					
	Amikacin	1	1		**5 days**	**5 days**
	Amoxicillin/ Clavulanate	5	8	7		
	Cefoperazone/ Sulbactam	3	5			
	Cefpodoxime	3	5	5		
	Ceftriaxone	3	6	6, 5		
	Cefuroxime	1	10	5		
	Ciprofloxacin	2	10			
	Clindamycin	3	10	5		
	Doxycycline	5	5			
	Isepamicin	2	7			
	Linezolid	10	10			
	Meropenem	6	6			
	Metronidazole	4	5			
	Nitrofurantoin	5	5	5		
	Ofloxacin	2	5	4		
	Piperacillin/ Tazobactam	2	8			
	Rifaximin	3	3			
	Tobramycin	3	3			
23.	**Urosepsis**					

	Amikacin	1	4		**4 days**	**3-5 days**
	Azithromycin	1	1			
	Cefoperazone/ Sulbactam	6	6			
	Ceftriaxone	3	4			
	Cefuroxime	5	5			
	Clindamycin	4	4			
	Cotrimoxazole	7	7			
	Linezolid	5	5			
	Meropenem	4	9			
	Nitrofurantoin	4	5			
	Piperacillin/ Tazobactam	6	6			
24.	**Upper respiratory tract infection**					
	Cefepime/ Tazobactam	5	5		**3 days**	**10 days**
	Cefixime	3	3			
	Cefoperazone/ Sulbactam	1	3			
	Ceftriaxone	2	6	3		
	Cefuroxime	4	4			
	Ciprofloxacin/ Tinidazole	5	5			
	Clarithromycin	3	3			
	Metronidazole	3	3			
25.	**Urinary tract infection**					
	Amikacin	1	7		**3 – 5 days**	**3-5 days**
	Amoxicillin/ Clavulanate	5	15			
	Azithromycin	3	3			
	Cefepime/ Tazobactam	4	4			
	Cefixime	4	11	5		
	Cefoperazone/ Sulbactam	2	13	3		
	Cefpodoxime	2	7	5		
	Ceftriaxone	2	6	3		
	Cefuroxime	2	7	5		
	Ciprofloxacin	4	7			
	Clindamycin	5	7	5		
	Doxycycline	2	11	5		
	Ertapenem	6	6			
	Meropenem	5	5			
	Fosfomycin	5	5			
	Imipenem/ Cilastatin	5	5			
	Linezolid	2	4			
	Meropenem	2	11			
	Metronidazole	5	7			
	Nitrofurantoin	2	14	5, 10		
	Ofloxacin	5	13	5		
	Piperacillin/ Tazobactam	2	7	6, 4		
	Cotrimoxazole	7	7			
26.	**Viral infections**					
	Azithromycin	15	15		**3 days**	**7-14 days**
	Cefixime	3	4	3		
	Cefpodoxime	5	5			
	Ceftriaxone	3	5			
	Metronidazole	3	3			

3.4 Pre-Post survey on Strategies, Situations & Safety of Antimicrobial De-escalation

A Continuing Medical Education session on the topic 'Strategies, Situations & Safety of Antimicrobial De-escalation' was conducted for 25 healthcare professionals including Duty Medical Officers, Microbiologist, Clinical Pharmacist, Infection Control Nurse, Intensive Care Unit Nurses and Clinical Educator. Questions regarding antimicrobial de-escalation were asked before and after the session and responses were collected using a live polling software (Figure 4). Question regarding the definition of de-escalation was raised in which, 50% of the healthcare professionals were able to select the most appropriate definition for de-escalation inclusive of narrowing antimicrobial spectrum of activity, IV to PO conversion and reduction in number of antibiotics used. The remaining 50% of them selected the option which missed IV to PO conversion, but included narrowing the spectrum and reduction in number of antibiotics. After the session, 100% of the health care professionals selected the option inclusive of narrowing antimicrobial spectrum of activity, IV to PO conversion and reduction in number of antibiotics used. A case scenario was given, for which, 62.5% of the healthcare professionals selected the near appropriate empiric antibiotic and after the session, 83.3% of them chose the most appropriate antibiotics. Only 88.9% of the healthcare professionals felt that antimicrobial de-escalation was safe, before the session. 100% of the healthcare professionals felt that antimicrobial de-escalation supported by microbiological evidence and clinical stability was safe, after the session, on explaining the impact of using overly-broad spectrum antibiotics for a relatively longer period. On provision of appropriate microbiological evidence in clinically stable patients, 33.3% of healthcare professionals decided to de-escalate for the above-mentioned case-scenario, before the session. After the session 57.1% of healthcare professionals chose to de-escalate from Cefoperazone-Sulbactam to Cefazolin, on provision of evidence for sensitivity of both the drugs in Methicillin-sensitive Staphylococcus aureus associated Skin and Soft tissue infection.

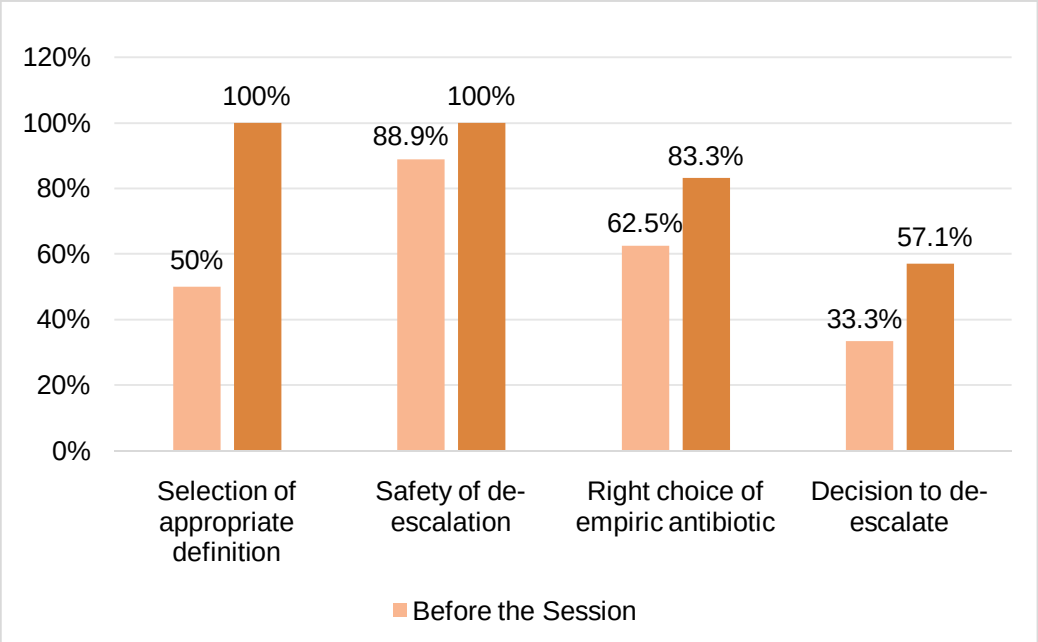
Paired t-test for the Pre-Post survey

The paired t-test was performed for the pre- and post-intervention data such as:

- Confidence in de-escalation strategies (pre: 88.9%, post: 100%).
- Selection of appropriate antibiotics in a case scenario (pre: 62.5%, post: 83.3%).
- Decision to de-escalate based on microbiological evidence (pre: 33.3%, post: 57.1%).

The paired t-test results show a t-statistic of 4.84 and a p-value of 0.04. This indicates a statistically significant improvement ($p < 0.05$) in the outcomes post-intervention, suggesting that the session effectively enhanced participants' knowledge and decision-making related to antimicrobial de-escalation. It led to improved recognition of a comprehensive definition of de-escalation, better empiric antibiotic selection, and increased confidence in the safety of de-escalation supported by evidence. The session also reinforced the importance of using microbiological data and clinical stability to guide de-escalation decisions, highlighting its critical role in antimicrobial stewardship.

Figure 4. Pre-post survey results



4. DISCUSSION

4.1 Effectiveness of Prescriber Education

The study demonstrates that prescriber education can significantly improve antibiotic prescribing practices. After the educational intervention, there was a marked reduction in the use of Watch antibiotics. This aligns with findings from studies conducted in the US and UK, where structured educational interventions led to significant improvements in adherence to antibiotic prescribing guidelines [15][16].

4.2 Improvement in the Access: Watch Ratio

The improvement in the Access: Watch ratio from 0.45 to 0.52 indicates a positive shift towards rational antibiotic use. This is in line with a study in Brazil, where the Access: Watch ratio improved by 0.10 after a series of prescriber education sessions [17]. The shift towards Access antibiotics is crucial in preventing the overuse of fluoroquinolones and third-generation cephalosporins, which contribute significantly to AMR.

4.3 Reduction in Reserve Antibiotic Usage

The reduction in the use of Reserve antibiotics, such as colistin and Linezolid, reflects the success of stewardship interventions in preserving last-resort agents. In a US study, Reserve antibiotics were reduced by 40% following a similar AMSP intervention [18]. Preserving these antibiotics is crucial for managing multidrug-resistant infections, which have been increasing in India and other countries [19].

4.4 Length of Therapy- Compliance with WHO Guidelines

LOT compliance showed significant improvement, with many infections treated in line with WHO-recommended durations. Studies conducted in Europe and the Middle East have shown that reducing LOT for infections like community-acquired pneumonia and urinary tract

infections not only minimizes resistance but also reduces hospital costs and treatment complications [20][21].

4.5 Prescriber Confidence in De-escalation

A major finding of this study was the increase in prescriber confidence from 88.9% to 100% in implementing de-escalation strategies. This finding aligns with studies in Canada and South Africa, where educational interventions led to a significant increase in the confidence of prescribers to narrow the spectrum of antibiotics once microbiological results were available [22][23].

4.6 Long-term Impact of Prescriber Education

Prescriber education not only improves immediate compliance with antibiotic guidelines but also fosters lasting changes in prescribing behaviors. Repeated and updated training ensures sustained reductions in inappropriate prescriptions. A longitudinal study in Canada showed a 25% sustained reduction in the use of broad-spectrum antibiotics over five years after the introduction of periodic educational modules [24]. Incorporating real-time feedback and ongoing education as part of continuous professional development can help institutionalize rational antibiotic prescribing.

4.7 Addressing Barriers in Low-resource Settings

The implementation of AMSPs in resource-constrained settings poses unique challenges. These include limited diagnostic capabilities, restricted access to essential antibiotics, and insufficient training in stewardship principles. A study conducted in sub-Saharan Africa revealed that 70% of healthcare facilities lacked the infrastructure necessary for effective AMSP implementation [25]. Addressing these barriers requires investments in diagnostic technology, better resource allocation, and tailored training programs that consider the specific needs of these settings.

4.8 The Role of Multidisciplinary Teams (MDTs)

Multidisciplinary teams are crucial to the success of AMSPs. Teams comprising physicians, microbiologists, pharmacists, and infection control specialists can facilitate more informed and effective prescribing decisions. For example, a study in the Philippines found that MDT-led AMSPs reduced inappropriate antibiotic prescriptions by 35% within one year [26]. These teams also play a key role in mentoring staff, monitoring antibiotic usage, and ensuring compliance with stewardship guidelines.

4.9 Incorporating Technology into AMSPs

Technology, such as electronic health records (EHRs) and clinical decision support systems (CDSS), is increasingly being used to enhance AMSPs. EHRs allow for better tracking of antibiotic use, while CDSS can provide prescribers with real-time guidance based on patient-specific factors. A randomized trial in Australia demonstrated that hospitals using CDSS experienced a 20% reduction in broad-spectrum antibiotic use [27]. Scaling such technologies in low-resource settings could be transformative, although initial costs and infrastructure needs remain barriers.

4.10 Global Collaboration in Combating AMR

Tackling antimicrobial resistance (AMR) requires a concerted global effort. Initiatives such as the WHO's Global Action Plan on AMR provide frameworks for countries to align their stewardship efforts. Collaborative networks that share data, best practices, and resources have shown promise. For instance, the Fleming Fund has helped several LMICs develop surveillance systems for AMR, improving their capacity to implement effective AMSPs [28]. Continued international support is essential to ensure equitable access to the tools and knowledge needed to combat AMR worldwide.

5. LIMITATIONS OF THE STUDY

- Single-Center Design: The findings are based on data from a single tertiary care hospital, which may limit the generalizability to other healthcare settings, particularly those with different resource levels and patient demographics.

- Short Study Duration: The five-month period of observation may not capture long-term trends or seasonal variations in antibiotic prescribing practices and resistance patterns.

These limitations should be considered when interpreting the findings of the study and in the planning of future research.

6. CONCLUSION

This study highlights the effectiveness of integrated interventions, including prescriber education and de-escalation strategies, in optimizing antibiotic prescribing practices and improving adherence to the WHO AWaRe guidelines. The improvement in the Access: Watch ratio, reduction in Reserve antibiotic use, and enhanced prescriber confidence are promising results for AMSPs in resource-limited settings. Ongoing stewardship efforts are crucial for combating AMR globally.

ETHICAL APPROVAL

Authors got ethical clearance from the faculty of Ethics Committee of the Fortis Healthcare.

Disclaimer (Artificial intelligence)

Option 1:

We the Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.) and text-to-image generators have been used during the writing or editing of this manuscript.

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