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# The Burden of Empirical Therapy: Analyzing the Predominance of Broad-Spectrum Antibiotic Usage in Lower Respiratory Tract Infections

**Jeuti Talukdar[1], Syed Mufeed Ahmad[2,*] and Arun Walia[3]**

[1]Department of Pharmacy Practice, CT Institute of Pharmaceutical Sciences, Shahpur, Jalandhar (Punjab), India
[2]Department of Pharmacy Practice, CT Institute of Pharmaceutical Sciences, Shahpur, Jalandhar (Punjab), India
[3]Department of Pulmonary, Sleep & Critical Care, Innocent Hearts Superspeciality Hospital, Jalandhar (Punjab), India

[*]**Corresponding Author:** Dr. Syed Mufeed Ahmad, Assistant Professor, Department of Pharmacy Practice, CT Institute of Pharmaceutical Sciences, Jalandhar (Punjab), India, Tel no: +7099751348, E-mail: jeutitalukdar93@gmail.com

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## Abstract

**Background:** Lower respiratory tract infections (LRTIs) frequently require immediate empirical antibiotic therapy due to diagnostic delays and clinical severity. Empirical regimens commonly rely on broad-spectrum agents, which can increase selective pressure for antimicrobial resistance. This study quantifies the predominance of broad-spectrum antibiotic use among hospitalized respiratory tract infection (RTI) patients, with an emphasis on the LRTI burden and subsequent antibiotic modification practices (escalation/de-escalation).

**Methods:** A prospective observational study was conducted at Innocent Hearts Superspeciality Hospital in collaboration with CT Institute of Pharmaceutical Sciences (Jalandhar, Punjab, India) over January 2025 to May 2025. A total of 100 hospitalized patients with RTIs were enrolled. Data were collected using a structured case record form and included demographics, RTI diagnosis and type (URTI/LRTI), microbiological culture results, antibiotic route and class, spectrum category (narrow/broad/extended), and therapy modifications during admission.

**Results:** LRTIs constituted 87% of RTIs, and pneumonia was the most common diagnosis (30%). Culture yield was low, with no organism identified in 80% of cases. Broad-spectrum antibiotics predominated (89% of prescriptions), and injectables were used in 76% of patients. Beta-lactams were the most frequently prescribed class (82 patients), followed by macrolides (40 patients). Antibiotic de-escalation occurred in 46% of patients, predominantly by dose reduction (47.82%) or switching to narrower-spectrum agents (45.65%). Escalation occurred in 31% of patients, most often by addition of another antibiotic (64.5% of escalations).

**Conclusions:** Hospitalized RTI care in this setting was characterized by a high LRTI burden, a substantial diagnostic gap, and near-universal reliance on broad-spectrum empirical therapy. Nevertheless, de-escalation was implemented in almost half of patients, underscoring the importance of systematic review-and-revise practices and antimicrobial stewardship to balance timely empirical coverage with resistance prevention.

**Keywords:** Empirical Therapy; Broad-Spectrum Antibiotics; Lower Respiratory Tract Infection; Antibiotic Stewardship; De-Escalation; Tertiary Care Hospital

**Abbreviations**

ADE, Antibiotic De-Escalation; AMR; Antimicrobial Resistance; CAP; Community-Acquired Pneumonia; HAP; Hospital-Acquired Pneumonia; LRTI; Lower Respiratory Tract Infection; MDR, Multidrug Resistant; RTI, Respiratory Tract Infection; URTI; Upper Respiratory Tract Infection; VAP; Ventilator-Associated Pneumonia

## Introduction

Respiratory tract infections (RTIs) are among the most frequent causes of healthcare consultation worldwide. The respiratory tract is traditionally separated into upper and lower segments, with the larynx being the anatomical demarcation [30]. This separation has clinical relevance since infections in various segments have different symptoms, etiologic pathogens, and treatment strategies [31]. The COVID-19 pandemic has dramatically altered the landscape of respiratory infection research and clinical practice since early 2020, stimulating unprecedented research into respiratory viral transmission, pathogenesis, and management [32].

### Types of Respiratory Tract Infection

Upper Respiratory Tract Infections (URTIs): Upper respiratory tract infections affect the structures above the larynx, such as the nasal passages, pharynx, larynx, sinuses, and middle ear.

Depending on the anatomical location of the predominant involvement, URTIs are divided into the following distinct clinical entities :

- Rhinitis (Common Cold): Nasal mucosal inflammation with nasal congestion, rhinorrhea, and sneezing.
- Pharyngitis/Tonsillopharyngitis: Pharyngeal and tonsillar inflammation with predominant presentation as sore throat.
- Sinusitis/Rhinosinusitis: Inflammation of paranasal sinuses, usually accompanied by nasal inflammation.
- Otitis Media: Middle ear space infection, most prevalent in children. Ø Laryngitis: Inflamed larynx resulting in hoarseness and voice change.
- Epiglottitis: Epiglottis inflammation with risk of airway obstruction [33].

A 2022 study analyzing electronic health records across five countries found that rhinitis accounts for approximately 50% of all URTIs, followed by pharyngitis (23%), sinusitis (15%), otitis media (10%), and laryngitis (2%) [34]

1.2 Lower Respiratory Tract Infections (LRTIs): Lower respiratory tract infections include the below-laryngeal structures, such as the trachea, bronchi, bronchioles, and alveoli.

LRTIs are divided into a few distinct clinical syndromes depending upon the anatomical location and pathophysiologic features:

- Acute Bronchitis: Bronchial inflammation with productive cough but in the absence of evidence for pneumonia.
- Bronchiolitis: Bronchiolar inflammation, which is most common in infants and preschool children.
- Pneumonia: Lung parenchymal inflammation with consolidation, graded by:
- Community-acquired pneumonia (CAP): Acquired outside of healthcare facilities
- Hospital-acquired pneumonia (HAP): Occurring ≥48 hours after hospital admission
- Ventilator-associated pneumonia after endotracheal intubation. (VAP): Occurring ≥48 hours
- Healthcare-associated pneumonia (HCAP): Occurring in non-hospitalized patients with extensive healthcare contact
- Lung Abscess: Focal accumulation of pus in the lung parenchyma secondary to microbial infection.
- Emphysema: Accumulation of infected material in the pleural space [40].

### Antibiotics - Empiric Therapy

Severe acute respiratory infections (SARI) and sepsis are major global causes of death, with hundreds of millions of SARI cases and over 19 million sepsis cases each year. Delayed initiation of appropriate antibiotics in suspected bacterial infections increases the risk of poor outcomes, including death that leads to implementation of empirical therapy[73].

Although early empirical antibiotic therapy improves outcomes in patients with sepsis and septic shock, the use of broad-spectrum antibiotics can lead to harmful effects. These include the emergence and selection of multidrug-resistant organisms and disruption of normal gut microbiota. Frequent and excessive antibiotic use creates strong selective pressure that promotes bacterial resistance [73].

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### Study Objectives

- To quantify the prevalence of LRTIs versus URTIs among hospitalized RTI patients.
- To describe empirical antibiotic prescribing patterns, including spectrum category, class distribution, and route of administration.
- To characterize the frequency and methods of antibiotic modification (escalation and de-escalation) during hospitalization.
- To summarize microbiological culture yield and its relationship to empirical broad-spectrum prescribing.

## Materials and Methods

### Study Design and Setting

This was a prospective observational study conducted over six months (January 2025 to May 2025) at Innocent Hearts Superspeciality Hospital in collaboration with CT Institute of Pharmaceutical Sciences, Jalandhar (Punjab), India.

### Participants

A total of 100 hospitalized patients diagnosed with RTIs were included. Inclusion criteria comprised patients of all ages and genders, including pregnant women, admitted with a clinical diagnosis of RTI. Patients with cancer, immunocompromised conditions, or psychotic illness were excluded.

### Data Collection and Variables

Data were collected from inpatient case records and, where required, patient interviews using a pre-structured case record form. Variables included demographics (age, sex), RTI diagnosis, comorbidities, microbiological culture results, antibiotic prescriptions (agent, class, dose, route, frequency), spectrum category (narrow, broad, extended), and antibiotic modification during admission (no change, escalation, de-escalation).

### Operational Definitions

**LRTI/URTI Classification:** RTIs were categorized as URTI or LRTI based on the documented clinical diagnosis.

**Spectrum Category:** Antibiotics were classified as narrow-, broad-, or extended-spectrum according to their usual range of activity as recorded in the study dataset.

**Empirical Therapy:** Initial antibiotic therapy prescribed before microbiological confirmation was considered empirical.

**Escalation:** A change to a broader-spectrum agent, an increase in dose, or addition of another antibiotic to expand coverage.

**De-escalation:** A reduction in antibiotic intensity via dose reduction, spectrum narrowing, or discontinuation of one or more antibiotics.

### Outcomes

The primary outcome was the proportion of antibiotic prescriptions categorized as broad-spectrum. Secondary outcomes included the prevalence of LRTIs, microbiological culture yield, the frequency of antibiotic escalation/de-escalation, and the methods by which escalation/de-escalation were implemented.

### Statistical Analysis

Descriptive statistics were used to summarize distributions of diagnoses and prescribing patterns. Analyses were performed using SPSS (version 16) and Microsoft Excel.

### Ethics Approval

The study protocol was approved by the Institutional Ethics Committee of the Punjab Institute of Medical Sciences and Hospital (IEC/24/49). Patient confidentiality was maintained throughout data collection and reporting.

## Results

### Patient Demographics

The study included 100 hospitalized RTI patients. The age distribution was skewed toward older adults, with the highest proportion in the 68-77 year group (26%). Females comprised 53% of the cohort, males 43%, and pregnant women (reported as a distinct subgroup) accounted for 4%.

**Table 1:** Demographic Characteristics of the Study Population (N=100)

| Characteristic | n | % |
|---|---|---|
| **Age group (years)** | | |
| 8-17 | 2 | 2% |
| 18-27 | 8 | 8% |
| 28-37 | 11 | 11% |
| 38-47 | 9 | 9% |
| 48-57 | 13 | 13% |
| 58-67 | 17 | 17% |
| 68-77 | 26 | 26% |
| 78-87 | 12 | 12% |
| 88-97 | 2 | 2% |
| **Sex** | | |
| Male | 43 | 43% |
| Female | 53 | 53% |
| Pregnant women | 4 | 4% |

## Clinical Diagnosis and Infection Type

LRTIs accounted for 87% of RTI cases (Figure 1). Pneumonia was the most frequent diagnosis (30%), followed by respiratory failure (13%), bronchitis (8%), and pharyngitis (5%); other RTI-related diagnoses comprised 44% (Table 2).

**Table 2:** RTI Diagnosis and Type Among Hospitalized Patients (N=100)

| Category | Subcategory | n | % |
|---|---|---|---|
| Diagnosis | Pneumonia | 30 | 30% |
| Diagnosis | Respiratory failure | 13 | 13% |
| Diagnosis | Bronchitis | 8 | 8% |
| Diagnosis | Pharyngitis | 5 | 5% |
| Diagnosis | Other RTI diagnoses | 44 | 44% |
| RTI type | LRTI | 87 | 87% |
| RTI type | URTI | 13 | 13% |

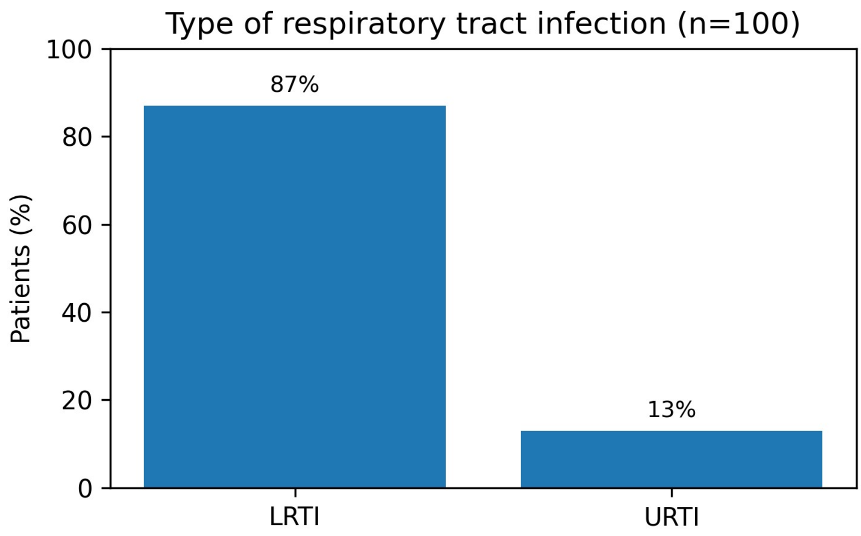


**Figure 1:** Distribution of Respiratory Tract Infection Type (N=100)

## Microbiological Findings and the Diagnostic Gap

Microbiological confirmation was limited. No microorganism was identified in 80% of patients, indicating a large culture-negative burden (Table 3 and Figure 2). Among identified pathogens, Streptococcus pneumoniae and Mycobacterium tuberculosis were most frequent (7% each).

**Table 3:** Microorganisms Identified From Cultures (N=100)

| Result | n | % |
|---|---|---|
| No growth | 80 | 80% |
| S. pneumoniae | 7 | 7% |
| M. tuberculosis | 7 | 7% |
| A. baumannii | 2 | 2% |
| Pseudo hyphae | 2 | 2% |
| Orthopneumovirus | 1 | 1% |
| Other | 2 | 2% |

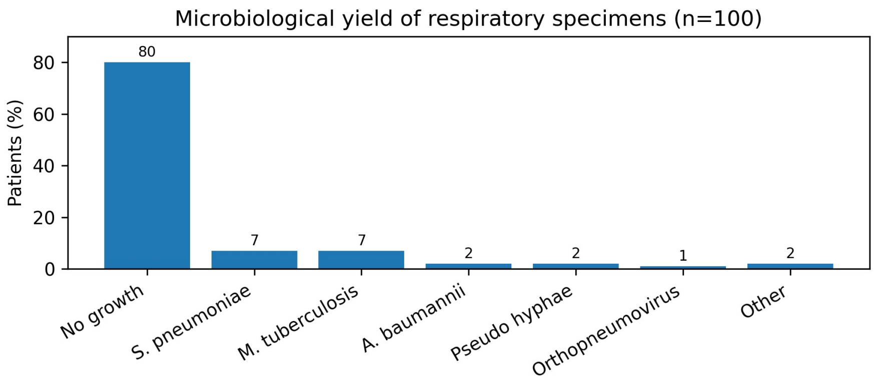


**Figure 2:** Microbiological Yield of Respiratory Specimens (N=100)

### Antibiotic Prescribing Patterns

Empirical therapy was predominantly broad-spectrum: 89% of antibiotic prescriptions were categorized as broad-spectrum (Figure 3). Injectable formulations were used in 76% of patients, indicating a preference for parenteral therapy in hospitalized RTI care. Beta-lactams were the most frequently prescribed class (82 patients), followed by macrolides (40 patients) (Table 4 and Figure 4).

**Table 4:** Empirical Antibiotic Use Characteristics (N=100)

| Domain | Category | n | %/Notes |
|---|---|---|---|
| Route of administration | Injectables | 76 | 76% |
| Route of administration | Oral | 24 | 24% |
| Antibiotic spectrum | Broad-spectrum | 89 | 89% of prescriptions |
| Antibiotic spectrum | Narrow-spectrum | 8 | 8% of prescriptions |
| Antibiotic spectrum | Extended-spectrum | 3 | 3% of prescriptions |
| Combination therapy | Two antibiotics | 63 | 63% of patients received two antibiotics |
| Antibiotic class (patients may receive >1 class) | Beta-lactams | 82 | n=82 |
| Antibiotic class (patients may receive >1 class) | Macrolides | 40 | n=40 |
| Antibiotic class (patients may receive >1 class) | Fluoroquinolones | 17 | n=17 |
| Antibiotic class (patients may receive >1 class) | Tetracyclines | 9 | n=9 |
| Antibiotic class (patients may receive >1 class) | Aminoglycosides | 5 | n=5 |
| Antibiotic class (patients may receive >1 class) | Other | 6 | n=6 |

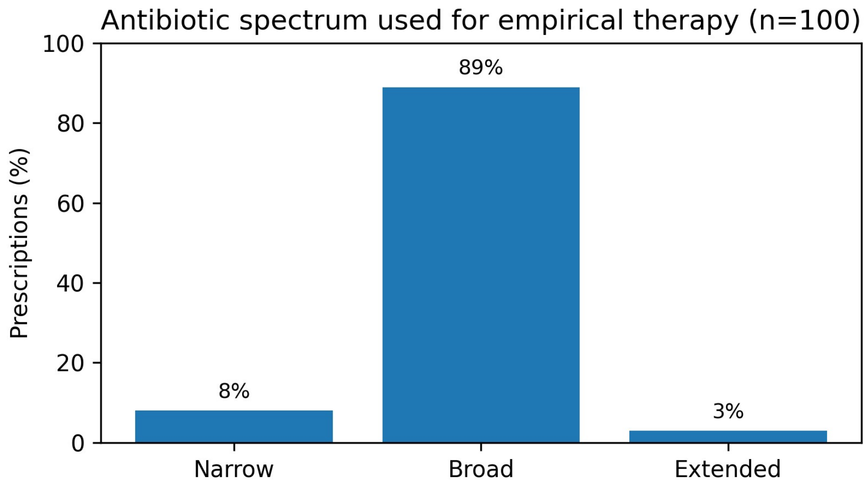


**Figure 3:** Distribution of Antibiotic Spectrum Categories (N=100)

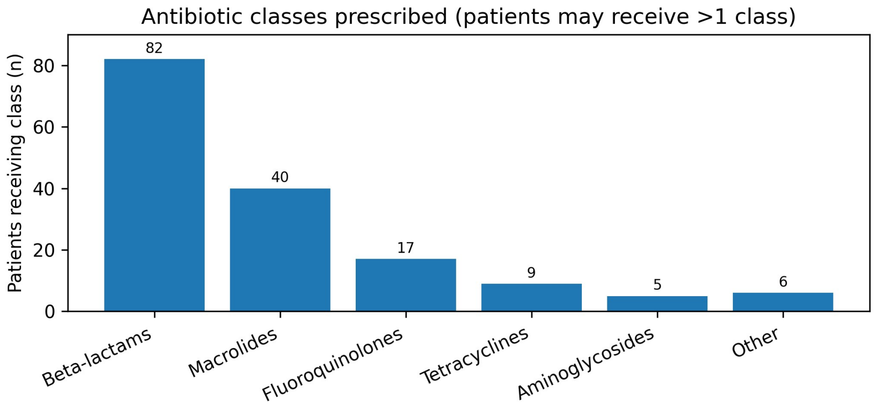


**Figure 4:** Antibiotic Classes Prescribed (Patients May Receive More Than One Class)

### Antibiotic Modification: Escalation and De-Escalation

Antibiotic therapy was modified during admission in the majority of cases. De-escalation occurred in 46% of patients, escalation in 31%, and no change in 23% (Figure 5). Among escalations, adding another antibiotic was most common (64.5%), followed by switching to a broader-spectrum antibiotic (19.35%) and dose escalation (16.12%). Among de-escalations, dose de-escalation (47.82%) and switching to narrower-spectrum therapy (45.65%) predominated; discontinuation occurred in 6.50%.

**Table 5:** Antibiotic Regimen Modifications and Methods (N=100)

| Modification | Category | Value | Notes |
|---|---|---|---|
| Overall change | De-escalation | 46% | Patients in whom therapy was de-escalated |
| Overall change | Escalation | 31% | Patients in whom therapy was escalated |
| Overall change | No change | 23% | No modification |
| Escalation method | Add another antibiotic | 64.50% | Among escalated cases |
| Escalation method | Shift to broader spectrum | 19.35% | Among escalated cases |
| Escalation method | Dose escalation | 16.12% | Among escalated cases |
| De-escalation method | Dose de-escalation | 47.82% | Among de-escalated cases |
| De-escalation method | Shift to narrower spectrum | 45.65% | Among de-escalated cases |
| De-escalation method | Discontinue antibiotic | 6.50% | Among de-escalated cases |

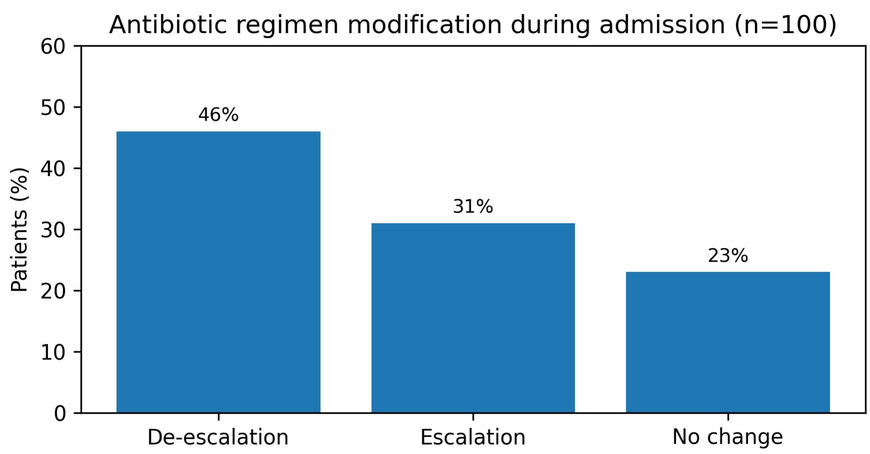


**Figure 5:** Frequency of Antibiotic Regimen Modification during Admission (N=100)

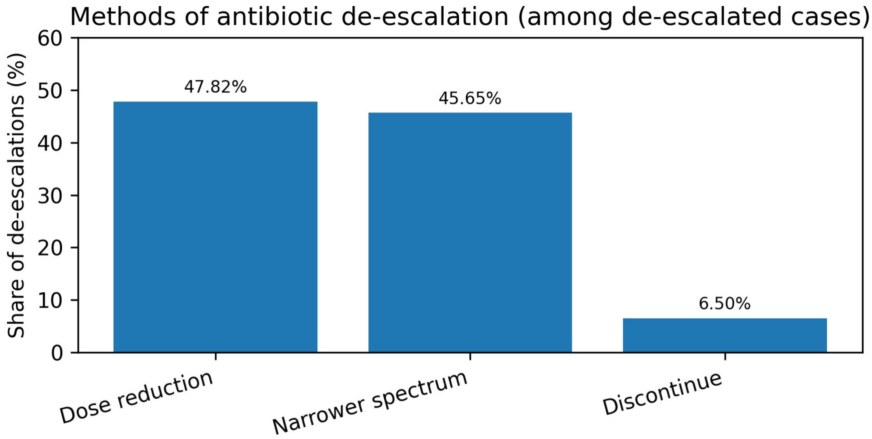


**Figure 6:** Methods of Antibiotic De-Escalation (Among De-Escalated Cases)

## Discussion

This study demonstrates a high burden of LRTIs among hospitalized RTI patients (87%), with pneumonia as the leading documented diagnosis. In such populations, delayed initiation of effective therapy is clinically undesirable, which likely contributes to the observed reliance on broad-spectrum empirical regimens.

A central finding is the large diagnostic gap: 80% of cultures yielded no organism. Culture-negative LRTI is common and may reflect prior antibiotic exposure, limited specimen quality, viral infections with bacterial rule-out, or diagnostic limitations of conventional culture. In this context, clinicians often maintain broad initial coverage to mitigate the risk of undertreatment.

Broad-spectrum antibiotics accounted for 89% of prescriptions, and parenteral therapy predominated (76%). Beta-lactams and macrolides were the most frequent classes used, consistent with common empirical strategies for pneumonia and severe LRTI presentations. While this approach may be justified early in severe disease, continued broad-spectrum exposure is a recognized driver of AMR and can increase adverse events.

Importantly, de-escalation was implemented in 46% of patients, most commonly via dose reduction and spectrum narrowing. This indicates that empirical broad-spectrum therapy can be managed as a time-limited intervention, provided there is deliberate reassessment. Conversely, escalation in 31% of patients highlights clinical complexity, possible initial undercoverage, or deterioration requiring expanded antimicrobial therapy.

From a stewardship perspective, these results support a practical model of 'start broad when necessary, then reassess early.' Strategies to reduce the diagnostic gap could further lower unnecessary broad-spectrum exposure, including optimizing specimen collection before antibiotics, strengthening microbiology workflows, and incorporating rapid diagnostics and biomarkers where feasible.

## Limitations

- Single-center design and modest sample size (n=100) may limit generalizability.
- The analysis is descriptive and does not evaluate clinical endpoints such as mortality, length of stay, or cost.
- Pathogen identification and susceptibility results were limited due to a high rate of culture-negative cases, which

restricts assessment of appropriateness of empirical regimens.

- Spectrum categorization was based on standard activity ranges recorded in the dataset; antibiotic-level granularity and guideline concordance were not assessed.

## Conclusions

In this tertiary care cohort, hospitalized RTI management was dominated by LRTIs and characterized by heavy reliance on broad-spectrum empirical antibiotics in the setting of limited microbiological confirmation. Despite this high initial burden, de-escalation occurred in nearly half of patients, demonstrating an opportunity to mitigate broad-spectrum exposure through structured review, culture optimization, and stewardship practices.

## Declarations

## Funding

No external funding was reported.

## Conflicts of Interest

The authors declare no competing interests.

## Author Contributions

Jeuti Talukdar: data collection, analysis, and manuscript drafting. Syed Mufeed Ahmad: study supervision and manuscript review. Arun Walia: clinical supervision and manuscript review.

## Data Availability

Data are available from the corresponding author on reasonable request.

## Ethics Approval and Consent to Participate

Approved by the Institutional Ethics Committee of the Punjab Institute of Medical Sciences and Hospital (IEC/24/49).

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## References


1. Murray CJ, Ikuta KS, Sharara F (2022) Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. The Lancet, 399: 629-55.

2. Tan SY, Tatsumura Y (2021) Alexander Fleming (1881–1955): Discoverer of penicillin. Singapore Medical Journal, 62: 409-10.

3. Aminov RI (2022) The role of antibiotics and antibiotic resistance in nature. FEMS Microbiology Reviews, 46: fuab040.

4. Hutchings MI, Truman AW, Wilkinson B (2023) Antibiotics: past, present and future. Current Opinion in Microbiology, 71: 102249.

5. Bush K, Bradford PA (2021) Interplay between β-lactamases and new β-lactamase inhibitors. Nature Reviews Microbiology, 19: 557-77.

6. Wilson DN (2021) Targeting translation as an antibacterial strategy. Nature Reviews Microbiology, 19: 767-84.

7. Klempner MS, Chopra I, Fauci AS (2021) The Need for New Approaches in Antibiotic Research and Development. The Journal of Infectious Diseases, 223: 553-555.

8. Duarte AG, Guarino C, Berg B (2022) The membrane potential: Molecular basis and physiological role in antimicrobial resistance. Biochimica et Biophysica Acta - Biomembranes, 1864: 183809.

9. Yoneyama H, Katsumata R (2023) Antibiotic resistance in bacteria and its future for clinical practice. The Lancet Infectious Diseases, 23: e147-e156.

10. Lee SY, Park YJ, Yu JK (2022) Mechanisms and molecular epidemiology of Beta-lactam resistance in clinical isolates. Infection & Chemotherapy, 54: 89-103.

11. Krause KM, Serio AW, Kane TR (2021) Aminoglycosides: old friends and new advances. Microbiology Spectrum, 9: e0018321.

12. Grossman TH (2022) Tetracycline antibiotics and resistance. Current Opinion in Microbiology, 64: 189-95.

13. Dinos GP (2021) The macrolide antibiotic renaissance. British Journal of Pharmacology, 178: 169-75.

14. Bisacchi GS, Manchester JI (2023) Quinolone antibiotics: challenges and opportunities.ACS Infectious Diseases, 9: 316-36.

15. Wencewicz TA (2022) New antibiotics from nature's chemical inventory. Bioorganic & Medicinal Chemistry, 69: 116833.

16. Karakonstantis S, Saridakis I (2021) Narrow vs broad spectrum antimicrobial therapy for common infections. Clinical Microbiology and Infection, 27: 826-27.

17. Peterson E, Kaur P (2021) Antibiotic resistance mechanisms in bacteria: relationships between resistance determinants of antibiotic producers, environmental bacteria, and clinical pathogens. Frontiers in Microbiology, 12: 640648.

18. Kohanski MA, Dwyer DJ, Collins JJ (2022) How antibiotics kill bacteria: from targets to networks. Nature Reviews Microbi-

ology, 20: 382-96.

19. Pankey GA, Sabath LD (2021) Clinical relevance of bacteriostatic versus bactericidal mechanisms of action in the treatment of gram-positive bacterial infections. Clinical Infectious Diseases, 73: 120-127.

20. World Health Organization (2023) Global antimicrobial resistance and use surveillance system (GLASS) report 2023. Geneva: World Health Organization.

21. Bush K (2022) Past and Present Perspectives on β-Lactamases. Antimicrobial Agents and Chemotherapy, 66: e01076-21.

22. Fisher JF, Mobashery S (2021) Constructing and deconstructing the bacterial cell wall. Protein Science, 30: 251-69.

23. Henderson JC, Zimmerman SM (2022) Molecular mechanisms of antibiotic permeability across the bacterial outer membrane. Nature Chemical Biology, 18: 1189-96.

24. Chueca B, Pagán R, García-Gonzalo D (2021) Mechanisms and role of bacterial efflux pump inhibition by essential oils. Critical Reviews in Food Science and Nutrition, 61: 2328-42.

25. Luo Y, Luo R, Ding C (2023) Bacterial horizontal gene transfer networks constrain the spread of antibiotic resistance. Nature Communications, 14: 2351.

26. Ashiru-Oredope D (2023) Global antimicrobial stewardship strategies: progress, challenges and ways forward. JAC-Antimicrobial Resistance, 5: dlad026.

27. Banerjee R (2021) The impact of the COVID-19 pandemic on outpatient antibiotic prescriptions in Ontario, Canada: an interrupted time series analysis. Open Forum Infectious Diseases, 8: ofab533.

28. Charani E (2023) Antibiotic prescribing in general dental practice: a systematic review and meta-analysis. Journal of Dental Research, 102: 856-66.

29. Tartari E (2022) The global hand hygiene self-assessment framework: a systematic review and meta-analysis. Antimicrobial Resistance & Infection Control, 11: 168.

30. Jamal A, Khan SA, Mubarak R (2021) Classification and clinical presentations of respiratory tract infections: an updated review. J Infect Public Health. 14: 596-603.

31. Mackenzie G, Lipsitch M (2021) The burden of respiratory infections: a global perspective. JAMA. 326: 1410-12.

32. Wiersinga WJ, Rhodes A, Cheng AC (2020) Pathophysiology, transmission, diagnosis, and treatment of coronavirus disease 2019 (COVID-19): A review. JAMA. 324:782-793.

33. Zoorob R, Sidani MA, Fremont RD (2021) Antibiotic use in acute upper respiratory tract infections. Am Fam Physician. 104: 395-400.

34. Johnson KM, Smith SM, Butler CC (2022) The burden of respiratory tract infections in primary care: a multinational study. Fam Pract. 39: 472-80.

35. Ison MG, Hayden FG, Hay AJ (2023) Respiratory virus surveillance and pathogen discovery in the 21st century. Nat Rev Microbiol. 21: 294-307.

36. Bessen DE, Smeesters PR, Beall BW (2023) Molecular epidemiology of group A streptococci. Microbiol Spectr. 11: e0247422.

37. Eccles R, Turner RB, Dicpinigaitis PV (2021) Natural history and duration of the common cold. J Clin Virol. 142: 104916.

38. Little P, Stuart B, Francis N (2021) Effect of communication skills training for clinicians on antibiotic prescribing for respiratory tract infections. JAMA. 326: 526-34.

39. De Sutter AI, van Driel ML, Kumar AA (2022) Oral antihistamine-decongestant-analgesic combinations for the common cold. Cochrane Database Syst Rev. 7: CD004976.

40. Metlay JP, Waterer GW (2023) Update in adult community-acquired pneumonia: key points from the 2019 ATS/IDSA guidelines and 2023 updates. Ann Intern Med. 176: 669-79.

41. LRTI (2024) Investigators GBD. Global burden of lower respiratory infections and the effect of COVID-19 in 204 countries and territories, 2000–24. Lancet Respir Med. 12: 115-35.

42. Lo SW, Gladstone RA, van Tonder AJ (2023) Global spread of new pneumococcal serotypes following introduction of conjugate vaccines. Lancet Microbe. 4: e156-e168.

43. Huang DT, Yealy DM, Filbin MR (2021) Procalcitonin-guided use of antibiotics for lower respiratory tract infection. N Engl J Med. 384: 2004-15.

44. WHO (2023) Global antimicrobial resistance surveillance system report: 2022. World Health Organization.

45. Czaplewski L, Bax R, Clokie M (2022) Alternatives to antibiotics—a pipeline portfolio review. Lancet Infect Dis. 22.

46. Walsh EE, Falsey AR, Scott DA (2023) Safety and immunogenicity of mRNA-1345, a respiratory syncytial virus vaccine in older adults. N Engl J Med. 388: 911-23.

47. Bagheri G, Thiede B, Hejazi B (2022) An upper bound on one-to-one exposure to infectious human respiratory particles. Proc Natl Acad Sci USA. 119.

48. Wunderink RG, Srinivasan A, Barie PS, Chastre J, Dela Cruz CS, et al. (2020) Antibiotic stewardship in the intensive care unit : An official American Thoracic Society workshop report in collaboration with the AACN, chest, CDC, and SCCM. Ann Am Thorac Soc. 17: 531-40.

49. Alanazi A, Almuhaya R, Almohaimeed M, Alahmari N, Abdulrahim N, et al. (2023) Impact of Antibiotic De-Escalation on Antibiotic Consumption, Length of Hospitalization, Mortality, and Cost: A Systematic Review and Meta-Analysis. Pharmacoepidemiology [Internet]. 2: 289-306.

50. Vu Quoc Dat, Tran Tat Dat (2022) Antibiotic use for empirical therapy in the critical care units in primary and secondary hospitals in Vietnam: a multicenter cross-sectional study. The Lancet Regional Health - Western Pacific, 18: 100306.