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Original Research Article

Respiratory Tract Infections and Antibiotic Stewardship: Examine microbiology, antibiotic use, and outcomes in pneumonia and other RTIs

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Abstract

Background: Respiratory Tract Infections (RTIs) have been identified as one of the major causes of morbidity, mortality and hospitalization globally. The prevalence of antimicrobial resistance has made the management of these infections more difficult and has made it even more important to ensure optimal use of antimicrobials and patient outcomes through antibiotic stewardship.

Methods: Cross sectional observational Study was done on 100 adult patients admitted to hospital for RTI. Standard microbiological techniques were used to process clinical specimens such as sputum, endotracheal aspirate, Bronchoalveolar Lavage (BAL) fluid, blood and pleural fluid. Bacterial isolates were identified by traditional methods and antibiotic resistance testing was done by the Kirby–Bauer disk diffusion method as per Clinical and Laboratory Standards Institute (CLSI) guidelines.

Results: 74% of patients were culture-positive in a total of 100 patients. The most common isolates were Klebsiella pneumoniae (28.4%), Pseudomonas aeruginosa (21.6%) and Acinetobacter baumannii (17.6%). The most commonly prescribed antibiotics were ceftriaxone (52%) followed by piperacillin–tazobactam (44%). The majority of patients made a recovery (72%), 6% were admitted to the ICU and 4% were dead. The most resistant was third generation cephalosporins.

Conclusion: The clinical burden of respiratory tract infections remains high. Optimizing antibiotic use, achieving better clinical results, and reducing the risk of antimicrobial resistance is critical and requires culture-guided antimicrobial therapy and the implementation of an effective antibiotic stewardship program.

Keywords: Respiratory Tract Infection, Pneumonia, Antibiotic Stewardship, Antimicrobial Resistance, Culture, Antibiotic Susceptibility, PMCH Patna.

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Introduction

RTIs are one of the most common causes of morbidity and mortality in the world and remain a health problem of great importance, especially in low and middle-income countries [1]. World health estimates that Lower Respiratory Tract Infections (LRTIs) are one of the most frequent causes of hospitalisation and mortality in people of all ages with a higher impact in older adults, young children and immunocompromised people [2].

RTIs makes a significant proportion of the outpatient visits, hospital admissions and Intensive Care Unit (ICU) admissions in India resulting in increased healthcare costs, longer hospital stays and poor clinical outcomes [3]. The increasing antimicrobial resistance has also made the management of these infections more complex, and the need for early diagnosis and appropriate antimicrobial treatment is increasingly important [4]. RTIs are a wide range of infectious diseases including community-acquired pneumonia (CAP), Hospital-Acquired Pneumonia (HAP), Ventilator-Associated Pneumonia (VAP), Acute Bronchitis, Chronic Obstructive Pulmonary Disease (COPD) exacerbations and other LRTI [5]. HAP and VAP are often associated with multidrug resistant organisms and typically acquired in the hospital, while CAP is acquired outside the hospital [6]. COPD exacerbation and acute bronchitis are also important drivers of use of health services, especially in elderly persons and those with chronic respiratory conditions [7].

The bacterial and viral composition of RTIs varies with patient characteristics, health care exposure and the epidemiology of the area [8]. Typical

Gram-positive pathogens are Streptococcus pneumoniae and Staphylococcus aureus, and emerging Gram-negative pathogens like Klebsiella pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii and Escherichia coli are associated, especially with hospital-acquired infections [9]. Other respiratory pathogens, such as atypical organisms (Mycoplasma pneumoniae, Chlamydia pneumoniae, Legionella pneumophila) also cause respiratory infections, but their diagnosis may be more difficult [10].

Antibiotic stewardship has become a key approach to ensure the careful use of antimicrobials and combating antimicrobial resistance [11]. Stewardship programs aim to increase the rates of appropriate antibiotic selection, correct dosing, optimal treatment duration, timely de-escalation based on the microbiological results, and culture-guided therapy, all of which contribute to better patient outcomes and reduction of the emergence of resistant organisms [12]. These interventions increase the efficacy of treatment, decrease unnecessary antibiotic use and facilitate evidence-based clinical practice.

In spite of the high burden of RTIs, limited information are available from Bihar on microbiological spectrum, antibiotic prescription pattern, antibiotic resistance pattern and outcome of the patients. Hence, the present study has been conducted at Patna Medical College and Hospital (PMCH), Patna on 100 patients with respiratory tract infection.

Objective:

- To identify the microbiological profile of the RTIs
- To gauge the antibiotic prescribing patterns, antimicrobial susceptibility profile, clinical outcome and the role of antibiotic stewardship in improving the management of RTIs.

Materials and Methods

Study Design: The current study is a cross-sectional observational study done in the hospital setting to assess the microbiological pattern, antibiotic prescribing practices, antimicrobial susceptibility and clinical outcomes of patients admitted with RTIs. The study was an observational design and had no interventions to influence patient management, so it was possible to evaluate the standard clinical and microbiological practices around antibiotic stewardship.

Study Area and Duration: The study was carried out in the Departments of Microbiology and General Medicine at PMCH, Patna, Bihar, a tertiary care teaching hospital that caters to a large number of patients from Bihar and neighbouring states. The data was collected for six months (January 26 – June 26).

Study Population and Sample Size: Hospitalized adult patients with RTIs, such as CAP, HAP, VAP, COPD exacerbation and other LRTIs were included in the study population. With consecutive sampling technique 100 patients were included who were eligible according to the selection criteria.

Inclusion Criteria

- Age ≥18 years.
- Had been admitted to hospital with a clinical diagnosis of a respiratory tract infection.
- Radiological signs of respiratory infection, if clinically relevant (chest X-ray or computed tomography).
- Providing suitable clinical samples for microbiological testing.
- Familiarity with the process and informed consent signed by patient or legal guardian.

Exclusion Criteria

- Not having a complete clinical or laboratory record.
- Antibiotic history for over 72 hours prior to admission to hospital (if applicable).
- Failure to give informed consent.
- Clinical specimens that were inadequate or contaminated for microbiological analysis.

Clinical Specimens and Laboratory Procedures: Clinical samples (sputum, endotracheal aspirates, bronchoalveolar lavage fluid, blood and pleural fluid) were collected using standard aseptic collection procedures. Samples were immediately analyzed in the Department of Microbiology. Initial examination consisted of Gram staining and then the culture of the appropriate bacteriological media. Isolation was achieved by colony morphology and Gram stain characteristics, and by conventional biochemical tests. When available, automated identification systems were used to confirm the identification of bacteria.

Antibiotic Susceptibility Testing: The antimicrobial susceptibility testing was done by using the Kirby-Bauer disk diffusion method based on the standard CLSI guidelines. Various antibiotics were tested, including those from major classes of commonly used drugs, including penicillins, cephalosporins, carbapenems, macrolides, fluoroquinolones, aminoglycosides, colistin, linezolid and vancomycin. The susceptibility results were reported as susceptible, intermediate, or resistant, using the most recent CLSI breakpoints. The data were collected and analyzed using a statistical approach.

Data Collection and Statistical Analysis: A structured data collection form was used to gather data on patient demographic, clinical diagnosis,

comorbid conditions, microbiological findings, antibiotics prescribed, treatment outcomes and length of hospital stay. All the collected data were analysed using SPSS software version 26.0. Categorical and continuous variables were described using descriptive statistics.

The Chi-square test was used to determine the association between categorical variables and the independent t-test to determine any differences between continuous variables. A p value of < 0.05 was considered statistically significant.

Results

Demographic Characteristics of the Study Population: The total number of patients with RTIs admitted to hospitals included were 100. Most of the patients were in the age group 41-60 years (38%) followed by above 60 years (34%). The average age for the population in the study was 54.8 ± 16.2 years. Sixty-two percent of the participants were males and 38% were females.

The majority of the patients were from the rural areas (58%). 42% of the patients were reported as being smokers, while 28% were observed to be drinkers of alcohol. The most prevalent comorbidities were diabetes mellitus (36%), hypertension (32%), COPD (24%) and chronic kidney disease (CKD) (12%).

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

Variable	Frequency (n)	Percentage (%)
Age Group (years)		
18–40	28	28.0
41–60	38	38.0
>60	34	34.0
Gender		
Male	62	62.0
Female	38	38.0
Residence		
Rural	58	58.0
Urban	42	42.0
Smoking	42	42.0
Alcohol consumption	28	28.0
Diabetes mellitus	36	36.0
Hypertension	32	32.0
COPD	24	24.0
CKD	12	12.0

Clinical Diagnosis: Community-acquired pneumonia was the common type of respiratory infection diagnosed (44%). HAP accounted for 20% of the cases and VAP accounted for 10% of the cases. 14% of cases were due to COPD exacerbations, 8% to acute bronchitis and 4% to other LRTIs.

Table 2: Clinical Diagnosis of Respiratory Tract Infections

Diagnosis	Frequency (n)	Percentage (%)
Community-acquired pneumonia	44	44.0
Hospital-acquired pneumonia	20	20.0
Ventilator-associated pneumonia	10	10.0
Acute bronchitis	8	8.0
COPD exacerbation	14	14.0
Others	4	4.0

Distribution of Clinical Specimens: Sputum (56%), blood samples (18%) and endotracheal aspirates (14%) were the most commonly collected samples. Bronchoalveolar lavage and pleural fluid specimens were obtained in 8% and 4% of cases, respectively.

Table 3: Distribution of Clinical Specimens

Specimen	Frequency (n)	Percentage (%)
Sputum	56	56.0
Endotracheal aspirate	14	14.0
Bronchoalveolar lavage	8	8.0
Blood	18	18.0
Pleural fluid	4	4.0

Culture Positivity: A total of 74 out of 100 clinical samples positive bacterial growth and 22 showed no bacterial growth. Four specimens were positive for mixed bacterial growth.

Table 4: Culture Positivity of Clinical Specimens

Culture Result	Frequency (n)	Percentage (%)
Positive	74	74.0
Negative	22	22.0
Mixed growth	4	4.0

Microbiological Profile: The microorganisms isolated were mainly gram-negative bacteria. The most prevalent pathogen was Klebsiella pneumoniae (28.4%) followed by Pseudomonas aeruginosa (21.6%) and Acinetobacter baumannii (17.6%). Staphylococcus aureus (14.9%) and Streptococcus pneumoniae (10.8%) were the Gram-positive organisms. Escherichia coli constituted 4.1% of the isolates and Candida species were isolated in 2.7% of the samples.

Table 5: Microbiological Profile of Culture-Positive Isolates (n = 74)

Organism	Frequency (n)	Percentage (%)
Klebsiella pneumoniae	21	28.4
Pseudomonas aeruginosa	16	21.6
Acinetobacter baumannii	13	17.6
Staphylococcus aureus	11	14.9
Streptococcus pneumoniae	8	10.8
Escherichia coli	3	4.1
Candida species	2	2.7

Antibiotic Prescribing Pattern: All patients received empirical antibiotic treatment at admission. Ceftriaxone was the most commonly prescribed empirical antibiotic with 52%, followed by piperacillin–tazobactam (44%) and azithromycin (38%). In 46% of patients therapy was changed after culture and susceptibility reports were available.

The commonly used culture-guided antibiotics based on the microbiological findings were meropenem, linezolid, vancomycin and levofloxacin.

Table 6: Antibiotic Prescribing Pattern

Antibiotic	Empirical Use n (%)	Culture-Guided Use n (%)
Ceftriaxone	52 (52.0)	18 (18.0)
Piperacillin–Tazobactam	44 (44.0)	32 (32.0)
Meropenem	18 (18.0)	30 (30.0)
Azithromycin	38 (38.0)	10 (10.0)
Levofloxacin	26 (26.0)	20 (20.0)
Vancomycin	8 (8.0)	14 (14.0)
Linezolid	6 (6.0)	12 (12.0)

Antibiotic Susceptibility Pattern: High sensitivity to carbapenems and colistin was realized in most Gram-negative isolates while resistance to third generation cephalosporins was common. Gram-positive isolates continued to be mostly susceptible to vancomycin and linezolid.

Table 7: Overall Antibiotic Susceptibility Pattern

Organism	Sensitive n (%)	Intermediate n (%)	Resistant n (%)
Klebsiella pneumoniae	14 (66.7)	2 (9.5)	5 (23.8)
Pseudomonas aeruginosa	11 (68.8)	2 (12.5)	3 (18.7)
Acinetobacter baumannii	7 (53.8)	2 (15.4)	4 (30.8)
Staphylococcus aureus	9 (81.8)	1 (9.1)	1 (9.1)
Streptococcus pneumoniae	7 (87.5)	0	1 (12.5)

Clinical Outcomes: A total of 100 patients were included in the study, and 72 of them recovered completely, and 18 had clinical improvement at the time of discharge. Six patients had to be transferred to the intensive care unit and four patient's morality in the hospital. The mean length of hospital stay was 8.6 ± 3.4 days.

Table 8: Clinical Outcomes of Patients

Outcome	Frequency (n)	Percentage (%)
Recovered	72	72.0
Improved	18	18.0
ICU transfer	6	6.0
Mortality	4	4.0
Mean hospital stays (days)	**8.6 ± 3.4**	—

Association between Culture Positivity and Clinical Outcome: A chi-square analysis showed that there was a statistically significant relation between culture positivity and adverse clinical outcomes. Microbiologically confirmed infections were associated with higher rates of ICU admission and mortality ($\chi^2 = 7.84$, $p = 0.020$), respectively. Patients with culture-positive infections had higher rates of ICU admission and mortality, respectively, compared with those with negative cultures ($\chi^2 = 7.84$, $p = 0.020$), indicating poorer clinical outcomes in those with microbiologically confirmed infections.

Table 9: Association between Culture Positivity and Clinical Outcome

Clinical Outcome	Culture Positive (n=74)	Culture Negative (n=26)	Total	p-value
Recovered	50	22	72	
Improved	16	2	18	
ICU transfer	5	1	6	
Mortality	3	1	4	
Chi-square (χ^2)	**7.84**			**0.020***

***Statistically significant at $p < 0.05$.**

Discussion

Burden of Respiratory Tract Infections: RTIs remain a significant source of global morbidity, mortality and health care utilization. The most common clinical diagnosis in the present study would be community-acquired pneumonia followed by HAP and COPD exacerbations [13]. The results are similar to recent studies in India that showed pneumonia as the primary cause for hospitalization in adults with LRTI. This is consistent with other countries around the world, where LRTIs are still one of the main causes of hospitalisation, especially older adults and those with chronic diseases. The high prevalence of diabetes mellitus, hypertension, and COPD among study participants further underscores the role of underlying comorbidities on disease severity and hospitalization. These observations illustrate the ongoing clinical and economic impact of RTIs, and the need for timely diagnosis, timely appropriate antimicrobial therapy, and prevention.

Microbiological Profile: Microbiological results of the present study represent a predominance of Gram-negative bacteria, Klebsiella pneumoniae, Pseudomonas aeruginosa and Acinetobacter baumannii were the most common pathogens isolated. This distribution is similar to the microbiological profile observed in tertiary care hospitals with a higher prevalence of healthcare associated infections and long hospital stays, leading to exposure to higher prevalence of multidrug resistant organisms. These pathogens were more commonly encountered because of the relatively large number of hospital-acquired and VAP cases, and admissions to the ICU [14]. These microbiological findings are similar to the one reported in some of the Indian studies which consistently report Gram-negative bacilli as the main etiological agents of severe respiratory infections in hospitalised patients. Increase in Klebsiella and Acinetobacter spp. has also been reported in international studies done in tertiary care hospitals, and Streptococcus pneumoniae is still a major pathogen in many community-based studies. The results highlight the need for ongoing local microbiological monitoring to support the appropriate use of empirical antibiotic therapy.

Antibiotic Prescribing Pattern: Consistent with the guidelines for early antibiotic treatment of bacterial respiratory infection, empirical antibiotic therapy was started in all patients as soon as clinical diagnosis was made. Most commonly used empirical drugs were the 3rd generation cephalosporins, piperacillin–tazobactam and macrolides. There was a significant change in antibiotic therapy in the majority of patients after receiving microbiological culture and susceptibility reports, indicating culture-based treatment. This practice helps with the principles of antibiotic stewardship and optimises antimicrobial use based on microbiological data. Previous stewardship initiatives from India and other countries have demonstrated that de-escalation from broad-spectrum antibiotics to narrower-spectrum at the right time will help limit the unnecessary use of antimicrobials, reduce adverse effects of antimicrobials, cut down on treatment costs and decrease the risk of resistance [15]. Thus, periodic

cultures and antibiotic adjustments continue to play an important part in quality clinical care.

Antibiotic Resistance: RTI are one of the main problems in the management of antimicrobial resistance. Resistance to third generation cephalosporins was found among some gram-negative isolates, with relatively good activity against carbapenems, but at a lesser extent with resistance noted in a certain proportion of isolates especially for A. baumannii. With the appearance of multidrug-resistant organisms and the emergence of extended-spectrum β-lactamase (ESBL) producing Enterobacterales, there is a therapeutic problem with a lack of effective treatment options. Moreover, although most Gram-positive isolates were found to be susceptible to vancomycin and linezolid, these were still considered important causes of HAP in this study. These results are similar to recent national and international surveillance reports that have reported a rise in the prevalence of antimicrobial resistance in respiratory pathogens. Overall, the findings highlight the critical importance of implementing antibiotic stewardship measures, optimizing antibiotic use, and regular surveillance of antimicrobial resistance to ensure the continued effectiveness of available antibiotics.

Strengths: This study represents the few studies conducted at PMCH to assess the microbiological pattern of RTI and antibiotic usage along with clinical outcomes of the study. Extensive culture, antimicrobial susceptibility and stewardship data are useful regional data to support evidence informed antibiotic policies and better management of patients in tertiary care hospitals.

Limitations: The present study has a number of limitations. It was done in a single tertiary care center with a small number of participants which might restrict the generalizability of the results. A study of the cross-sectional design was not able to assess long-term outcomes and causal relationships. Microbiological characterization of the mechanism of antimicrobial resistance was not done and discharge follow-up was not available, which did not allow for long-term treatment success and recurrence to be evaluated.

Conclusion

RTIs continue to be a significant cause of hospitalization and a significant source of morbidity and health care utilization. The present study highlighted predominance of Gram negative bacterial pathogens among the hospitalized patients highlighting the changing microbiological pattern observed in tertiary care hospitals. With the increasing rate of antimicrobial resistance, it is important to have timely microbiological diagnosis and culture-directed antibiotic therapy for proper patient management. ASPs can encourage rational use of antibiotics, assist in appropriate antibiotic de-escalation, enhance the clinical outcomes, and help to prevent emergence of resistant organisms. To achieve optimal management of respiratory tract infections and combat antimicrobial resistance, there is a need for continuous microbiological surveillance and complying with the institution's antibiotic policies.

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