The study of Non-Tuberculous Aerobic bacterial and fungal profile of Lower Respiratory tract infection in Tertiary Care Centre

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Abstract

Lower respiratory tract infections (LRTIs) cause significant morbidity and mortality, complicated by rising antimicrobial resistance and fungal co-infections. This prospective study at a tertiary care centre in Chennai analyzed 200 LRTI specimens for aerobic bacterial and fungal pathogens and antimicrobial susceptibility. Klebsiella pneumoniae (57.5%) was the predominant bacterium, followed by Acinetobacter baumannii (19.8%) and Pseudomonas aeruginosa (17.9%). Carbapenem resistance occurred in 34% of Gram-negative isolates, with Acinetobacter showing the highest rates.

Colistin resistance was found in 2.5% of carbapenem-resistant Klebsiella. Carbapenemase production was confirmed in 60% and metallo-β-lactamase in 40% of Klebsiella tested. Fungal growth was detected in 15.5% of samples, mainly Aspergillus fumigatus among filamentous fungi. Eight cases had bacterial-fungal co-infections. The study underscores the urgent need for antimicrobial stewardship and accurate microbial diagnosis to improve LRTI management and control multidrug resistance.

Keywords: Lower Respiratory Tract Infection (LRTI), non-tuberculous bacteria, fungal co-infection, antimicrobial resistance, *Klebsiella pneumoniae, Acinetobacter baumannii, Carbapenem resistance,* ESBL, *Colistin resistance, Aspergillus fumigatus*.

Introduction

Lower respiratory tract infections (LRTIs) remain a significant cause of morbidity and mortality globally. In India, they account for nearly 20% of deaths due to infectious diseases, while in the United States, they rank sixth among leading causes of death.[1,2] In tertiary care settings, LRTIs constitute a notable proportion of outpatient visits and hospital admissions. Chronic respiratory conditions alone contribute to around 5% of global deaths each year.[3] LRTIs encompass pneumonia, bronchitis, bronchiolitis, bronchiectasis and lung abscesses. Pneumonia poses a major burden, particularly in developing countries where challenges such as delayed pathogen identification and irrational antibiotic use hindered effective management.[4] While bacterial infections are predominant, there is a growing prevalence of fungal infections, even among immunocompetent individuals.[5]

LRTIs are broadly categorized as community-acquired pneumonia (CAP) or healthcare-associated pneumonia (HCAP), with the latter being more common in patients with chronic illnesses or prolonged hospital stays. These settings often lead to infections with multidrug-resistant (MDR) organisms due to asymptomatic colonization and aspiration.[6] The global rise in antimicrobial resistance is a growing concern, often fueled by indiscriminate antibiotic use without culture confirmation, lack of de-escalation based on results and overuse in viral infections like acute bronchitis. Azole resistance in Aspergillus species is another emerging threat that complicates treatment decisions and outcomes.[7,8]

In this context, the present study aims to evaluate the nontuberculous aerobic bacterial and fungal profile of lower respiratory tract infections in a tertiary care centre. It focuses on isolating the causative organisms and determining the antimicrobial susceptibility patterns of the bacterial isolates, thereby aiding in appropriate and timely therapeutic interventions.

Material and Methods

A prospective cross-sectional study was conducted over a period of one year in a tertiary care hospital in Chennai. After obtaining Instituional ethics committee approval NO: 15082018, a total of 200 non-repetitive, nontuberculous clinical isolates were obtained from lower respiratory tract specimens including sputum, bronchoalveolar lavage (BAL), endotracheal aspirates (ETA) and pleural fluid, collected from both outpatient and hospitalized patients with clinical suspicion of lower respiratory tract infections (LRTIs). Samples were processed as per standard microbiological techniques.[9]

Sample Processing and Identification: Specimens were subjected to Gram staining and cultured on blood agar, MacConkey agar and Sabouraud dextrose agar (for fungal isolates). The plates were incubated at 37°C for 24–48 hours aerobically. Fungal cultures were incubated for up to 7 days.

Bacterial isolates were identified based on colony morphology, Gram staining and a series of biochemical reactions. Fungal isolates were identified by conventional methods including lactophenol cotton blue mount and slide culture for mold differentiation.[9,10]

Antimicrobial Susceptibility Testing (AST): All aerobic bacterial isolates were subjected to antimicrobial susceptibility testing using the Kirby-Bauer disc diffusion method on Mueller-Hinton agar, following CLSI guidelines[5]. Antibiotics tested included gentamicin, imipenem, meropenem and piperacillin-tazobactam. Zone diameters were interpreted using CLSI breakpoints specific for Enterobacteriaceae, *Pseudomonas aeruginosa* and Acinetobacter species.[11]

Detection of Extended Spectrum Beta-Lactamase (ESBL) Production: Initial ESBL screening was performed using ceftazidime (30 µg) and cefotaxime (30 µg). Isolates showing zone diameters <22 mm for ceftazidime and <27 mm for cefotaxime were subjected to the phenotypic confirmatory test using the combination disc method. Cefotaxime and cefotaxime–clavulanic acid (30/10 µg) discs were placed on Mueller-Hinton agar inoculated with the test organism. An increase of ≥3 mm in the inhibition zone in the presence of clavulanic acid confirmed ESBL production.[12]

Detection of Carbapenemase Production (mCIM and eCIM): The modified Carbapenem inactivation method (mCIM) was used for phenotypic detection of carbapenemase-producing isolates. A 10 µL loopful of test organism was emulsified in 2 mL trypticase soy broth (TSB) and incubated with a meropenem (10 µg) disc at 35°C for 4 hours. The disc was then transferred onto a Mueller-Hinton agar plate inoculated with a standard suspension of *E. coli* ATCC 25922. After incubation for 18–24 hours, zones of inhibition were measured. A zone ≤15 mm or pinpoint colonies within a zone of 16–18 mm indicated carbapenemase production.[13]

To differentiate metallo-β-lactamases (MBLs) from serine carbapenemases, the EDTA-modified CIM (eCIM) was employed. A second TSB tube containing 5 mM EDTA and a meropenem disc was processed alongside the mCIM. Both discs were placed on the same MHA plate inoculated with *E. coli* ATCC 25922. An increase of ≥5 mm in the eCIM zone diameter was compared to mCIM indicating MBL production.[14]

Detection of Colistin Resistance – Colistin Broth Disc Elution (CBDE) Method: Colistin susceptibility testing was performed by the CBDE method for Enterobacterales isolates, as per CLSI guidelines[5]. Four tubes of cation-adjusted Mueller-Hinton broth were labeled as 1, 2 and 4 µg/mL and control. Corresponding numbers of 10 µg colistin discs were added, vortexed and allowed to elute for 30 minutes. A standard 0.5 McFarland suspension of the test isolate was prepared and 50 µL was inoculated into each tube. After incubation at 35–37°C for 18–24 hours, turbidity was assessed for growth. Subcultures were performed on blood agar for purity.[15]

Fungal Isolation and Processing: Samples showing fungal growth were further processed with LPCB mount and slide culture for morphological identification. Only clinically significant fungal isolates (excluding contaminants or commensals) were included.[16]

Quality Control: Quality control was ensured using standard ATCC strains: *E. coli* ATCC 25922, *Klebsiella pneumoniae* ATCC BAA-1705 (carbapenemase-positive) and ATCC BAA-1706 (carbapenemase-negative). All reagents and media were prepared and tested according to quality assurance protocols.[17]

Results

Out of 200 lower respiratory tract specimens processed, 106 (53%) yielded significant bacterial growth. Among these, *Klebsiella* species were the most frequently isolated (61/106, 57.5%) followed by *Acinetobacter baumannii* (21/106, 19.8%), *Pseudomonas aeruginosa* (19/106, 17.9%) and *Escherichia coli* (5/106, 4.7%).[18]

Carbapenem Resistance Pattern: Among the Gram-negative isolates (n=106), carbapenem resistance was observed in 37 isolates (34%). *Acinetobacter baumannii* showed the highest resistance (47.6%, 10/21) followed by *Klebsiella* species (36%, 22/61), *Pseudomonas aeruginosa* (21%, 4/19) and *E. coli* (20%, 1/5).[15,16]

Colistin Resistance Pattern: Of the 22 carbapenem-resistant *Klebsiella* isolates tested by the Colistin Broth Disc Elution (CBDE) method, 5 isolates (2.5%) were found to be colistin-resistant.[14]

Phenotypic Detection of Carbapenemase and MBL Production: Fifteen *Klebsiella* isolates underwent phenotypic testing by modified Carbapenem inactivation method (mCIM) and EDTA-modified CIM (eCIM). Nine (60%) were positive for carbapenemase production by mCIM alone, while six isolates (40%) showed positivity for both mCIM and eCIM, indicating metallo-β-lactamase (MBL) production.[13]

Fungal Culture Positivity: Of the 200 respiratory samples, 31 (15.5%) yielded fungal growth. The highest positivity was seen in bronchoalveolar lavage samples (6/31, 20%), followed by endotracheal aspirates (13/68, 19%) and sputum (12/109, 11%).[17]

Distribution of Fungal Isolates: Among sputum isolates (n=12), *Aspergillus fumigatus* (33.5%) and *Aspergillus flavus* (25%) were predominant followed by *Candida tropicalis*, *C. albicans*, *C. krusei* and *Aspergillus niger*[17]. From endotracheal aspirates (n=13), *Aspergillus fumigatus* (46%) and *A. flavus* (22%) were most common, along with *Candida tropicalis*, *C. albicans* and *C. glabrata*.

BAL cultures (n=6) predominantly yielded *Aspergillus fumigatus* (50%) and *C. albicans* (33%).[17]

Growth Pattern of Yeast vs. Filamentous Fungi: Out of 31 fungal isolates, 21 (67.7%) were filamentous fungi while 10

(32.3%) were yeasts. Filamentous fungi predominated across all specimen types: sputum (8/12), ETA (9/13) and BAL (4/6).[17]

Bacterial and Fungal Co-infections: Co-infections were identified in 8 cases. In sputum samples (n=2), combinations included *Klebsiella oxytoca* + *Candida tropicalis* and *Pseudomonas aeruginosa* + *Candida krusei*. In endotracheal aspirates (n=3), co-isolated organisms were *Acinetobacter baumannii* + *Candida glabrata*, *A. baumannii* + *Aspergillus fumigatus* and *Klebsiella aerogenes* + *C. albicans*. BAL specimens (n=3) revealed combinations such as *Klebsiella pneumoniae* + *Aspergillus fumigatus*, *P. aeruginosa* + *C. albicans* and *P. aeruginosa* + *Aspergillus fumigatus*. Overall, *Klebsiella* species were the most frequent bacterial partners in co-infections.[17]

Discussion

Lower respiratory tract infections (LRTIs) continue to pose a major public health challenge globally, particularly among the elderly and immunocompromised patients. In the present study, conducted on 200 clinically suspected LRTI cases at Rajiv Gandhi Government General Hospital, Chennai, a comprehensive analysis of bacterial and fungal pathogens was performed, including antibiotic resistance patterns and coinfections.

Demographic and Clinical Profile: The majority of LRTI cases were reported in males (69%) and in patients aged above 60 years (29%). Diabetes mellitus (52.5%) emerged as the most common comorbidity, followed by chronic obstructive pulmonary disease (COPD) (33%). These findings are in agreement with previous studies that emphasize the vulnerability of elderly, diabetic and COPD patients to respiratory infections.[18] Cough (96%) was the most frequent symptom reported.

Specimen and Pathogen Distribution: Among the collected specimens, sputum (50.5%) was the most common followed by endotracheal aspirates (34%) and bronchoalveolar lavage (BAL) (15.5%).

- In sputum samples, *Klebsiella pneumoniae* was the most prevalent pathogen (63.7%) followed by *Pseudomonas aeruginosa* (12.8%)[19]. These findings are consistent with the study by Nisha et al[19], who reported *Klebsiella pneumoniae* in 57% of cases and also correlate with findings by Nithya Chinnusamy et al[4].
- In endotracheal aspirates, *Acinetobacter baumannii* was predominant (35.7%) followed by *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* (21.4% each)[22]. These findings align with studies by Kiranjeet Kaur et al[12] and Zorgani et al[32], though in contrast with studies reporting *Klebsiella* as predominant.
- In BAL samples, *Klebsiella pneumoniae* (50%) and *Pseudomonas aeruginosa* (25%) were the leading isolates. This correlates well with results reported by Madhavi et al[17], Veena et al[28] and Vishwanath et al.[29]

Across all samples, *Klebsiella* species (30.5%) was the most commonly isolated Gram-negative organism followed by *Acinetobacter baumannii* (10.5%) and *Pseudomonas aeruginosa* (9.5%).[15]

Antibiotic Susceptibility Patterns:

- Among Enterobacteriaceae, *Klebsiella* species and *E. coli* showed highest sensitivity to amikacin, followed by piperacillin-tazobactam and meropenem. Both exhibited poor sensitivity to third-generation cephalosporins in concordance with Regha et al.[22]
- Among non-fermenters:
  - *Pseudomonas aeruginosa* showed 100% sensitivity to amikacin and 84.2% to both gentamicin and piperacillin-tazobactam.
  - *Acinetobacter baumannii* was more sensitive to piperacillin-tazobactam (61.9%) and meropenem (52.3%) but was completely resistant to ceftazidime.

These results highlight the rising resistance to cephalosporins and underline the empirical utility of amikacin and piperacillin-tazobactam in managing LRTIs.

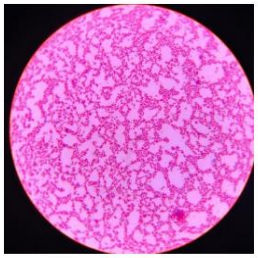
Resistance Mechanisms:

- ESBL production was observed in 53% of Enterobacteriaceae isolates, with *Klebsiella* (48%) being the predominant ESBL producer. This is similar to the study by Assudani et al[1] while slightly lower than the prevalence was reported by Govidaswamy et al[8] (88.3%).
- Carbapenem resistance was seen in 34% of Gram-negative isolates, with *Acinetobacter baumannii* (47.6%) and *Klebsiella* species (36%) showing the highest resistance. These findings correlate with Jinsha et al[11]and Manojkumar et al[18] as in table 1.
- Among carbapenem-resistant *Klebsiella*, 2.5% showed colistin resistance. Additionally, 60% were carbapenemase producers by mCIM, with 40% confirmed as MBL producers using eCIM. These results emphasize the growing concern of multidrug resistance including last-resort drug resistance.

Fungal Profile: Fungal culture positivity was highest in BAL (20%), followed by endotracheal aspirates (19%) and sputum (11%). Filamentous fungi (n=21), particularly *Aspergillus fumigatus*, were more prevalent than yeasts (n=10). *Aspergillus* species were the predominant isolates across all specimen types, especially BAL, which is consistent with the findings of Sripriya et al[25] as in table 2. In contrast to the findings by Dhivya et al[7] who reported *Candida albicans* as the predominant fungus, our study identified *Aspergillus fumigatus* as the leading fungal pathogen, indicating a regional shift in fungal etiology of LRTIs.

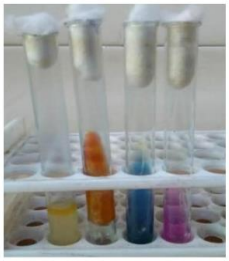
Bacterial-Fungal Coinfections: A total of eight coinfections were reported, with *Klebsiella* species frequently co-isolated with fungal pathogens such as *Candida* and *Aspergillus*.

1.Gram staining – Gram negative bacilli



2.Lactose fermenting colonies of Klebsiella pneumoniae on MAC

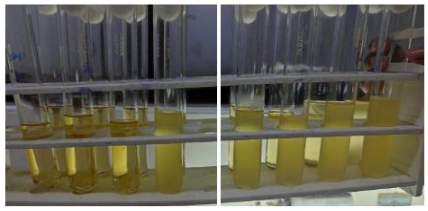
3. Biochemical Reactions : Klebsiella pneumoniae



4.ESBL producing Klebsiella pneumoniae

5. mCIM and eCIM for Carbapenamase detection in Klebsiella species

6. Phenotypic detection of Colistin resistance by colistin broth disc elution method in Klebsiella species

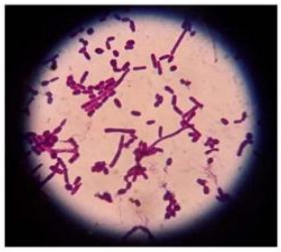


INTERMEDIATE SENSITIVE RESISTANT

7. BAP showing non hemolytic greyish white colonies of Pseudomonas aeruginosa

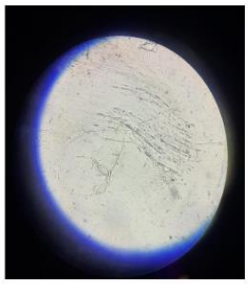
8. Antibiogram of Pseudomonas aeruginosa

9.. Gram stain – Candida albicans with Pseudo hyphae



10.. SDA agar- creamy colonies suggestive of Candida species

11.. Sputum KOH mount showing Budding yeast cells with pseudohyphae



12. Candida species – CHROM Agar

Fig. 1

Table 1
Distribution of Carbapenem and Colistin Resistance among Gram-Negative Bacterial Isolates (N=106)

Organism	Total Isolates (n)	Carbapenem-Resistant (n, %)	Colistin-Resistant among CR isolates (n, %)
Klebsiella spp.	61	22 (36%)	5 (2.5%)
Acinetobacter baumannii	21	10 (47.6%)	Not tested
Pseudomonas aeruginosa	19	4 (21%)	Not tested
Escherichia coli	5	1 (20%)	Not tested
Total	106	37 (34%)	

*Colistin resistance was tested only in carbapenem-resistant Klebsiella isolates using the Colistin Broth Disc Elution (CBDE) method.

Table 2
Distribution of Fungal Isolates by Sample Type and Morphology (N=31)

Specimen Type	Total Fungal Isolates (n)	Filamentous Fungi (n)	Yeasts (n)	Predominant Species
Sputum	12	8	4	*Aspergillus fumigatus, A. flavus*
Endotracheal Aspirate	13	9	4	*A. fumigatus, A. flavus*
BAL	6	4	2	*A. fumigatus, C. albicans*
Total	31	21 (67.7%)	10 (32.3%)	

Note: Aspergillus species were the predominant filamentous fungi across all respiratory specimens, while Candida tropicalis and C. albicans were the most common yeasts.

Table 3
Distribution of Bacterial and Fungal Coinfections in Respiratory Samples

Specimen Type	Organism Isolated	Remarks
Sputum (n=2)	*Klebsiella oxytoca* + *Candida tropicalis* *Pseudomonas aeruginosa* + *Candida krusei*	—
Endotracheal aspirate (n=3)	*Acinetobacter baumannii* + *Candida glabrata* *Acinetobacter baumannii* + *Aspergillus fumigatus* *Klebsiella aerogenes* + *Candida albicans*	—
Bronchial wash (n=3)	*Klebsiella pneumoniae* + *Aspergillus fumigatus* *Pseudomonas aeruginosa* + *Candida albicans* *P. aeruginosa* + *Aspergillus fumigatus* *Klebsiella pneumoniae* + *Aspergillus flavus*	Klebsiella species were most frequent in co-infections

These findings stress the importance of dual screening for bacterial and fungal infections in severe LRTI cases, particularly in ICU settings[29] as in table 3.

Conclusion

This study demonstrated a higher prevalence of Gram-negative bacteria as the primary pathogens causing lower respiratory tract infections, with *Klebsiella pneumoniae* being the predominant isolate across all respiratory samples. Extended-spectrum beta-lactamase (ESBL) production was notably common among *Klebsiella pneumoniae* while most Gram-negative isolates exhibited higher sensitivity to amikacin and piperacillin-tazobactam.

A concerning level of carbapenem resistance was observed, with *Acinetobacter baumannii* as the leading carbapenem-resistant pathogen. Carbapenemase production was the principal resistance mechanism among carbapenem-resistant *Klebsiella* species. Alarmingly, significant colistin resistance was also detected in *Klebsiella* isolates, highlighting a critical threat to last-resort antimicrobial efficacy.

The findings emphasize that indiscriminate and inappropriate uses of antibacterial agents in both community and hospital settings drive the emergence of antimicrobial resistance. Rising carbapenem and colistin resistance patterns call for urgent and strict antimicrobial stewardship including vigilant antibiotic prescription monitoring, active microbiology department involvement in policy formulation and rigorous infection control measures to curb resistance escalation. Additionally, filamentous fungi, predominantly *Aspergillus* species, were more frequently isolated than yeasts among respiratory samples. Accurate identification of both bacterial and fungal pathogens is essential to guide appropriate clinical management and improve patient outcomes in lower respiratory tract infections.

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