Introduction

Lower respiratory tract infections (LRTI) are among the most common infectious diseases affecting humans worldwide causing significant morbidity and mortality for all age groups. It is responsible for 4.4% of all hospital admissions and 6% of physicians’ consultation. It accounts for 3%–5% of deaths in adults. LRTI are often misdiagnosed, mistreated, and underestimated due to its nonspecific presentation in community or hospital-setting. Etiological agents of LRTI vary geographically and timely. The problem is much greater in developing countries. Recognition of the possible existence of lung microbiome has been a major recent revelation in medicine. The increase in antibiotic-resistance has compromised selection of empirical treatment and choice of effective-antibiotic.

Objectives

The objective of the present study was to identify the bacterial aetiology of LRTI among patients who attended AIIMS, Jodhpur from January 2017 to December 2018 and to ascertain the current scenario of bacterial susceptibility in respiratory tract infections in order to optimize empiric therapy in patients presenting with...
cases of community acquired pneumonia (CAP), hospital acquired pneumonia (HAP), ventilator-associated pneumonia (VAP), chronic obstructive pulmonary disease (COPD), and cystic fibrosis in various healthcare centers.

Materials and Methods

Setting
This is a retrospective study conducted at the Department of Microbiology, All India Institute of Medical Sciences, Jodhpur, for the duration January 2017 to December 2018. The study was approved by Institutional Ethics Committee wide letter number AIIMS/IEC/2019/1767 (06.04.2019).

Patient’s enrolment
All the patients enrolled in the study were from Out-Patient Department (OPD), In-Patient Department (IPD), and Intensive Care Unit (ICU). The respiratory tract samples (sputum, bronchoalveolar lavage [BAL], endotracheal aspirate, gastric lavage, etc.) were obtained from the patients of all the age and sex groups, with clinical presentation of COPD, cystic fibrosis, CAP, VAP, HAP, post-influenza, old tuberculosis, cavitatory lesions, lung abscess, neoplasm, prolonged hospital stay, etc.; suggestive of LRTI. History of antibiotic consumption was also noted.

Sample collection and processing
In total, 1,775 samples of sputum, BAL, endotracheal aspirate, gastric lavage, etc., were obtained.

Sample selection was done: sputum-quality of sample was assessed based on Bartlett’s scoring. Satisfactory sputum samples were further processed. BAL-microscopically percentage of neutrophils with engulfed bacteria was determined, and semiquantitative analysis ≥10⁶ colony forming unit (CFU)/mL was done. Endotracheal aspirate: semi quantitative analysis ≥10⁴ CFU/ml was done.

Samples were further processed for routine bacterial culture and sensitivity. Following culture, the isolated organisms were identified and antimicrobial sensitivity was performed as per laboratory standards and antibiotic interpretation was done as per Clinical and Laboratory Standard Institute (CLSI) guidelines.

Results
In total, 1,775 respiratory specimens were received during the study period out of which 769 cultures yielded a significant pathogen and 1,006 cultures had growth of normal oropharyngeal flora.

It was realized that almost 50% of these isolates were in poorly collected samples. Swabs from endotracheal tubes were refused as it represents only colonization. Many a times, tracheal aspirates were mislabelled as BAL sample.

Among 769 positive cultures, 112 samples showed polymicrobial infection. Pseudomonas species 31.2% (275) was the most common isolate followed by Klebsiella pneumoniae 21.3% (188), Acinetobacter baumanii 17.5% (154), Escherichia coli 15.4% (136), and Staphylococcus aureus 5% (44). Others were as follows: Group A β-hemolytic Streptococcus 3.2% (28), Burkholderia cenocepacia complex 1.1% (10), Stenotrophomonas maltophilia 0.4% (4), and Nocardia 0.2% (2) [Table 1].

Oxacillin (1 μg) disc was used as surrogate marker to identify penicillin resistance in Streptococcus pneumoniae. Group A β-hemolytic Streptococci was identified presumptively with Bacitracin (0.04 U) disc. Demographic and clinical details (age, sex, location of patients, sample distribution) of the patients are provided in Table 2. Antibiotic resistance pattern of Gram-negative bacteria and Gram-positive bacteria are shown in Tables 3 and 4, respectively.

Discussion
In our study, LRTI were more common in males 73% than in females 27%. Male prevalence of LRTI may be due to their exposure to different group of population and due to some associated risk factors of respiratory tract infection, such as smoking, alcohol consumption, and COPD. Similar to other studies, our findings corroborated with the results accomplished by Shah et al., Panda et al., Saha et al., and Akingbade et al.5-9 It was observed that adults and the elderly males were most at risk of a severe respiratory condition. Almost one-third of cases were of pulmonary Kochs.

In this study, single and multiple organisms were isolated in 86.67% and 13.33%, respectively, of study population. These findings are similar with the study conducted by Saxena et al. and Narayanagowda et al.10,11

Table 1: Distribution of organisms presenting to OPD, IPD, and ICU

| Organism name                        | OPD | IPD | ICU | Number, n=769 (%) |
|--------------------------------------|-----|-----|-----|-------------------|
| Pseudomonas aeruginosa               | 79  | 103 | 44  | 226 (25.6)       |
| Pseudomonas species                  | 22  | 18  | 9   | 49 (5.6)         |
| Acinetobacter species                | 21  | 60  | 73  | 154 (17.5)       |
| Burkholderia cenocepacia Complex     | 0   | 7   | 3   | 10 (1.1)         |
| Stenotrophomonas maltophilia         | 0   | 2   | 2   | 4 (0.5)          |
| Klebsiella species                   | 41  | 88  | 59  | 188 (21.3)       |
| Escherichia coli                     | 31  | 81  | 24  | 136 (15.4)       |
| Citrobacter freundii                 | 0   | 3   | 2   | 5 (0.6)          |
| Enterobacter aerogenes               | 2   | 8   | 4   | 14 (1.6)         |
| Proteus species                      | 0   | 3   | 1   | 4 (0.5)          |
| Serratia marcescens                  | 0   | 2   | 0   | 2 (0.2)          |
| Staphylococcus aureus                | 13  | 23  | 8   | 44 (5)           |
| Streptococcus pneumonia              | 14  | 1   | 0   | 15 (1.7)         |
| Group A β-Hemolytic - Streptococci   | 22  | 6   | 0   | 28 (3.2)         |
| Nocardia                             | 0   | 2   | 0   | 2 (0.2)          |
In this study, Gram-positive 10.1% (89) and Gram-negative 89.9% (792) organisms were isolated. Similar observations have been shown in other studies as shown in Table 5. Among which nonfermenting Gram-negative bacilli (NFGNB) were isolated in 50.3% (443/881) of respiratory samples. The importance of isolation of nonfermenters has increased in last decade, after more and more reports are correlating them with the infection outbreaks in hospitals or healthcare-associated infections. Most of the patients were having prolonged hospital stay for more than a week. It supports the fact that these patients may have acquired some of these multidrug resistant pathogens in hospital settings as HAP and VAP. Identification of nonfermenters used to be considered as commensal flora, but due to increased awareness of their pathogenicity in certain patient population and improvement in diagnostic criteria, they are increasingly being reported.

Antimicrobial susceptibility pattern of 

**Antimicrobial susceptibility pattern of Pseudomonas aeruginosa**, Acinetobacter species, Klebsiella species and Staphylococcus aureus are depicted in Figures 1-4 respectively.

In this study, 28.3% bacterial strains were isolated from ICU, whereas 51.7% were isolated from wards from which most isolates were *Acinetobacter baumannii* 73 (47.4%), followed by *Klebsiella pneumoniae* 59 (31.4%) and *Pseudomonas aeruginosa* 44 (19.4%) similar to that seen in Ullah *et al.* In other Study by Nishat *et al.*, nonfermenters (61.11%) were the predominant isolates from Surgical ICU, whereas in the medical ICU, along with nonfermenters (47.91%), enterobacteriaceae (41.66%) was the most common organisms isolated.

*Pseudomonas aeruginosa* is more commonly found in patients with chronic lung cavities or as a complication of treatment with immunosuppressive drugs. *Pseudomonas aeruginosa* was isolated in 25.6% (226) cases, similar to Saha *et al.*, Sethi...
et al., Sethi et al., and ElKorashy et al.\cite{8,16,17}  
Pseudomonas was found to be sensitive to amikacin, piperacillin–tazobactam, ceftazidime–tazobactam, cefepime, gentamicin, levofloxacin, and ciprofloxacin. Similar findings were observed by Narayanagowda et al. and Vishwanath et al.\cite{11,13}  

In this study, \textit{K. pneumoniae} was the second most common Gram-negative isolate and was tested to be sensitive to piperacillin–tazobactam, amikacin, ceftazidime, ceftazidime–tazobactam, cefepime, levofloxacin, gentamicin, ciprofloxacin, and amoxiclav. These findings are same as observed in the study carried out by Regha et al., Saha et al., Saxena et al., Vishwanath et al., and Kulkarni et al.\cite{1,8,9,13,14}  

Malini et al.\cite{18} from Kolar in India, have documented the isolation of 6.8% (25 of 365) of NFGNB in respiratory samples. \textit{Stenotrophomonas maltophilia} is considered as a common

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**Table 4: Antibiotic resistant (%) gram positive organism**

| Organism                        | No. | Pn  | AMP | OX  | CX  | COT | TOB | GEN | AK  | CIP | LE  | E   | CD  |
|---------------------------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| \textit{Staphylococcus aureus}  | 44  | 40  | 91  | -   | -   | 25  | 56  | 9   | 10  | 22  | 5   | 11  | 4.5 |
| Group A B-Hemolytic-Streptococci| 28  | 1   | 3.6 | 1   | 3.6 | -   | -   | -   | -   | -   | -   | 1   |
| \textit{Streptococcus pneumonia}| 15  | -   | 13.3| 6   | 40  | -   | 33  | -   | -   | -   | -   | 13  |

P=Tetaillin, AMP=Ampicillin, OX=Oxacillin, CX=Cefoxitin, COT=Cefotaxime, TOB=Tobramycin, GEN=Gentamicin, AK=Amikacin, CIP=Ciprofloxacin, LE=Levofloxacin, E=Erythromycin, CD=Clindamycin

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**Table 5: Comparison with other similar studies**

| Year       | Gram-positive cocci | Gram-negative bacilli | Nonfermenter Gram-negative bacilli (NFGNB) | Enterobacteriaceae | n |
|------------|---------------------|-----------------------|--------------------------------------------|-------------------|---|
| This study (Jodhpur) 2018 | 89 (10.1%) | 792 (89.9%) | 443 (50.3%) | 349 (39.6%) | 881 |
| Regha et al.\cite{1} (Kerala) 2018 | 44 (15.3%) | 244 (84.7%) | 136 (55.7%) | 108 (37.5%) | 288 |
| Anup Saha et al.\cite{8} (Tripura) 2018 | 510% | 92.86% | 35 (10.1%) | 191 (55.4%) | 345 (58.9%) |
| Ravichitra et al.\cite{2} (Andhra Pradesh) 2016 | - | 65.5% | - | - | 100 |
| Sarmah et al.\cite{12} (Guwahati) 2016 | 13 | 407 | 80 | 327 | 597 (49.4%) |
| Vishwanath et al.\cite{3} (Karnataka) 2013 | - | - | 830 (16.4%) | - | 5056 (54%) |
| Ullah et al.\cite{4} (Bangladesh) 2015 | 57 (80.06%) | 7 (10.92%) | 2 (3.12%) | 5 (7.80%) | 64 |
| Kulkarni et al.\cite{14} (Nashik) 2014 | 29% | 71% | 26.7% | 20% | 45 |

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**Figure 1:** \textit{Pseudomonas aeruginosa} antimicrobial susceptibility pattern

**Figure 2:** \textit{Acinetobacter} species antimicrobial susceptibility pattern

**Figure 3:** \textit{Klebsiella} species antimicrobial susceptibility testing

**Figure 4:** \textit{Staphylococcus aureus} antimicrobial susceptibility testing
nonfermży to causa infection in hospital settings. Correct identification of this NFGNB assumes importance as it shows inherent resistance to commonly used broad spectrum β-lactam group antibiotics and even to imipenem.[6] Our study has shown the isolation of this bacterium in four cases. *Burkholderia cepacia* complex is another NFGNB colonizing and infecting patients with chronic respiratory illness. It is known to cause disease in cystic fibrosis patients, and once infected, it is very difficult to treat due to multiple intrinsic resistance to many β-lactam drugs, aminoglycosides, colistin and polymyxin B, the first-line therapeutics of choice against serious pseudomonal infections.[5]

In our study, *Burkholderia cepacia* complex was isolated in 10 cases from IPD (7) and ICU (2). Rahbar et al.[19] have shown the isolation of *Burkholderia cepacia* complexas 4.66% of all the nonfermenters isolated from different types of specimens (respiratory, blood, urine, wound, etc).

NFGNB have shown resistance to amikacin, gentamicin, imipenem, cefepime, ceftriaxone, and piperacillin–tazobactam [Table 3]. The aminoglycosides that are considered as good option for life-threatening lower respiratory infections have shown high resistance in the present study for these nonfermenters wherever tested. There is poor penetration of aminoglycosides from blood into infected respiratory tissues so as to reach the local drug concentration above the minimum inhibitory concentration necessary for the infecting organisms. This observation has also been discussed by earlier studies. All these nonfermenters are known for their inherent resistance to multiple groups of antibiotics. Hence, correct identification of these nonfermenters is very important for choosing correct antibiotic so as to reduce the morbidity and mortality. Any NFGNB culture isolate from respiratory tract infection should not be ignored as just contaminant but correlated clinically for its pathogenic potential and identified using standard methods, so as to institute appropriate and timely antibiotic coverage. It is equally important not to treat commensal NFGNBs.

In this study, among Gram-positive organisms, *S. aureus* 5% (44) was the most common pathogen isolated followed by Group A β-hemolytic *Streptococci* from OPD patients and *Streptococcus pneumoniae*. *Staphylococcus aureus* was sensitive to tobramycin, ceftriaxone, and gentamicin, 56.9% were Methicillin Resistant *Staphylococcus aureus* (MRSA). All isolates were vancomycin and linezolid sensitive. Similarly in the study conducted by Narayanagowda et al.,[31] β-Hemolytic *Streptococci* was second frequently identified Gram positive organism and was sensitive to penicillin group of antibiotics, erythromycin, clindamycin, and levofloxacin. *Staphylococcus aureus* and Aspergilli are known to cause secondary infections post-influenza. Increasingly fungal pathogens are being reported as cause of LRTIs from ICU.[20]

It is necessary to have policies regarding restrictive use of antibiotics such as carbapenems and colistin. Regular monitoring of such resistant isolates would be important for infection control in critical units.[21]

Strict implementation of the concept of ‘antibiotic stewardship’ has become necessary to conserve the already available antibiotics. Hospitals should have an “antibiotic policy” and facilities for proper monitoring of antibiotic usage along with effective infection control practices to check the issue of antibiotic resistance worldwide. Periodic analysis of types of respiratory pathogens and regular updation of their antibiograms should be done in every healthcare setting, so that changing trends can be identified and therapy adjusted accordingly.[1]

The trend towards increased use of molecular diagnostic tools will probably continue with increased availability of point of care testing.[4]

**Conclusion**

This study reveals that a variety of pathogens are responsible for LRTI and antibiotics resistance has become a great public health issue. Gram-negative organisms showed increased resistance to routinely used antibiotics. Gram-positive organisms showed 100% susceptibility to vancomycin, linezolid, and clindamycin.

Proper identification of the probable pathogens and their antibiotic susceptibility pattern can help our health professionals to choose the right antibiotic therapy and improve the outcome. Do not report everything that grows, knowledge of colonizers and contaminants in different clinical conditions is important. This year CDC (Center for Disease Control) has proposed theme during Fungal Disease Awareness week (September 23–27, 2019) think fungus if a case of pneumonia does not improve with appropriate antibiotics.

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**Conflicts of interest**

There are no conflicts of interest.

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