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Original article:

Recent Trends in Bacteriological Profile of Lower Respiratory Tract Infections (LRTIs) in Outdoor, Indoor and Critical Care Settings of a Tertiary Care Centre in Pune

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Abstract:

According to the Global Burden of Disease 2015 study Chronic Obstructive Pulmonary Disease (COPD) and Lower respiratory tract infection (LRTI) represent the third and fourth most common cause of death respectively after ischemic heart disease and cerebrovascular diseases (1). Annual incidence of Pneumonia, one of the most important (LRTIs) is reported to be 24.8 per 10,000 adults. The rate, etiology and symptomology of respiratory disease vary with age, gender, season, type of population at risk and other factors (1). "Pneumonia" is defined as New lung infiltrates plus clinical evidence that the infiltrate is of infectious origin which includes new onset of fever, purulent sputum, leukocytosis and decline in oxygenation". The present study provides prevalence of lower respiratory tract infection pathogens and their antibiotic sensitivity patterns in different hospital setting of a tertiary care centre of Western India. If injudicious use of antibiotics continues, we will face problem of pan-drug resistance in near future. Thus, by formulating antibiogram for respiratory isolates helps in implementing antibiotic stewardship program restricting antibiotic usage, promoting combination therapy ultimately contributing to reduction of drug resistance.

Keywords: Bacteriological Profile , Chronic Obstructive Pulmonary Disease

Introduction:

According to the Global Burden of Disease 2015 study Chronic Obstructive Pulmonary Disease (COPD) and Lower respiratory tract infection (LRTI) represent the third and fourth most common cause of death respectively after ischemic heart disease and cerebrovascular diseases (1). Annual incidence of Pneumonia, one of the most important (LRTIs) is reported to be 24.8 per 10,000 adults. The rate, etiology and symptomology of respiratory disease vary with age, gender, season, type of population at risk and other factors (1). "Pneumonia" is defined as New lung infiltrates plus clinical evidence that the infiltrate is of infectious origin which includes new onset of fever, purulent sputum, leukocytosis and decline in oxygenation".

American Thoracic Society / Infectious Diseases Society of America (IDSA) guidelines until 2016 in addition to Community acquired pneumonia (CAP), Hospital acquired Pneumonia (HAP), Ventilator associated Pneumonia (VAP) had fourth type of pneumonia, Health care associated pneumonia (HCAP) (2, 3). HCAP included any patient who acquired pneumonia in community but had following risk factors, hospitalized in an acute care hospital for two days or more within 90 days of the infection, received recent intravenous antibiotic therapy, chemotherapy, or wound care within past 30 days of current infection, or resided in nursing home or long-term care facility, or attended hospital or hemodialysis clinic. HCAP due to risk factors were believed to be at increased risk of acquiring infection with multi drug resistant bacteria (MDR) and were to be treated as nosocomial pneumonia. Community acquired Pneumonia (CAP) was defined as Pneumonia acquired outside

Hospital setting without above risk factors. However, in 2016 updated guidelines by ATS/IDSA, terminology of Health care associated pneumonia (HCAP) was removed/eliminated and it is recommended that these patients are be treated as CAP patients and need not be treated as nosocomial pneumonias with additional coverage of MRSA and *Pseudomonas aeruginosa* unless they meet criteria for locally validated risk factors for antibiotic-resistant bacteria (2, 3).

HAP is defined as pneumonia that develops at least 48 hours following hospitalization in patients without mechanical ventilation, while VAP is defined as pneumonia that develops at least 48 hours after endotracheal intubation (2, 3).

Key changes of present guidelines (2016 ATS/IDSA guidelines) from the previous guidelines (2005 ATS/IDSA guidelines) include: 1) removal of the health care-associated pneumonia (HCAP) entity; 2) emphasis on developing local antibiograms to aid health care providers in selecting empiric antibiotics; 3) new indications for empiric dual gram-negative and methicillin-resistant *Staphylococcus aureus* (MRSA) therapy, and 4) a seven-day duration of antibiotic therapy (2,3).

Thus, our study aims at formulating antibiogram for lower respiratory tract infections in outpatient department patients (OPD representative of mainly community acquired pneumonia), Inpatient department/ Wards patients (IPD representing mainly Hospital acquired pneumonia) and Intensive Care Unit patients (ICUs representing mainly Ventilator associated pneumonia).

Aims and objective:

1) To determine the current trends in bacterial etiology (five predominant bacteria) and susceptibility of lower respiratory tract bacterial isolates from OPD, IPD and ICU set up of a tertiary care hospital.
2) To formulate an antibiotic policy for effective empirical management of the same.

Material and Methods:

Study Design: Retrospective descriptive record-based study.

Duration of study: Two-year study from January 2017- December 2018

Study setting: Department of Microbiology of a Tertiary Care Centre in Pune.

Specimen collection - Respiratory samples like Sputum, Endotracheal aspirate (ETA) and Bronchoalveolar lavage (BAL) from clinically suspected pneumonia patients avoiding oral contamination.

Specimen processing: a) Sputum: Quality of sputum was assessed by Murray Washington grading scheme. Only good quality samples were processed as per conventional standard microbiology methods. Pure growth or 2 types of colonies with moderate to heavy growth were considered pathogens (4).

BAL and ETA samples were processed by aerobic conventional semiquantitative method using calibrated loop technique as per standard microbiological methods.

b) For ETA:10^4 CFU/ml and c) BAL:10^3 CFU/ml were considered as pathogens (4, 5).

Identification and antimicrobial susceptibility testing by following standard and CLSI guidelines (6).

Data analysis: Data was entered and analyzed by using WHONET software and only 1st isolate of each patient was considered for formulation of antibiogram as per CLSI guidelines for formulation of Antibiogram (7, 8).

Classification of LRTIs/Pneumonias: All isolates from respiratory samples of Outpatient department were representative of Community acquired pneumonia, samples from wards without mechanical ventilation were representative of Hospital acquired pneumonia and ICU isolates with mechanical ventilation represented mostly Ventilator associated pneumonia (VAP).

Results:

A total of 3576 respiratory samples were received from different OPDs, IPDs and ICUs of the hospital, however 825 (23%) were rejected due to oral contamination and 2751 were processed. Of the 2751 processed respiratory samples, pathogens were isolated from 1552 samples (56%) and 1192 samples (44%) had no pathogen grown, thus Culture positivity was 56% in present study. As per CLSI guidelines M39 for formulation of antibiogram, only 1st isolate was considered, hence 1452 isolates from 1452 patients were considered for formulation of antibiogram and repeat isolates from same patient were ignored (7, 8). Out of 1452 patients, 891 (61%) were males and 561 (39%) were females. Maximum patients were in the age group 41-60 years followed by 21-40 years (Table no. 1). Gender-wise ratio of 1.59 :1 was observed and skewed in favor of males (Table no. 2)

Table No. 1: Distribution based on Age

Sr. No	Age group	No. of patients
1	<1 year	31
2	1-20	161
3	21-40	452
4	41-60	468
5	61-80	319
6	81-100	21

Table no.2: Distribution based on sex

Gender	No. of Patients
Male	891 (61%)
Female	561 (39%)

Table no.3: Distribution of Isolates of patients from OPD, Wards and ICUs

Organisms	Medicine ward	TB ward	MICU	TICU	OPD	Other wards	Overall prevalence
Type of LRTI	**HAP**		**VAP**		**CAP**	**HAP**	
Klebsiella pneumoniae (Kpn)	126	82	90	38	15	37	388 (27%)
Pseudomonas aeruginosa (Pae)	78	54	41	23	11	11	218 (15%)
Acinetobacter species *(Aci.)*	47	14	66	33	2	38	200 (14%)
Citrobacter species *(Citr.)*	61	20	49	28	6	19	183 (13%)
Escherichia coli (E. coli)	53	32	27	27	4	1	144 (10%)
Enterobacter (Enter.)	51	16	22	7	3	16	115 (8%)

Non fermenter Gram negative bacilli (NFGNB)	28	11	22	12	1	7	81 (5%)
Staphylococcus aureus (Sau)	19	18	5	3	5	0	50 (3.44%)
Streptococci species *(Str.)*	14	6	4	3	15	6	48 (3.30%)
Proteus species (Prot.)	7	1	6	7	0	4	25 (2%)
Total	**484**	**254**	**332**	**181**	**62**	**139**	**1452**

There is overall predominance of Gram-negative bacilli (1354/1452 isolates i.e., 94%) as cause of LRTI with *Klebsiella pneumoniae* (27%) being the most common pathogen followed by *Pseudomonas aeruginosa* (15%), *Acinetobacter* species (14%), Other Enterobacteriaceae and other Gram-positive isolates like Staphylococcus aureus (3%) and Streptococci species (3%).

Maximum isolates were from Medicine ward (484), followed by MICU (332), TB (254) and TICU (181) other wards (139) and OPD (62).

Five predominant CAP pathogens from OPD were *Klebsiella pneumoniae* (15/62), *Streptococci* species (15/62), *Pseudomonas aeruginosa* (11/62), *Citrobacter* species (6/62), *Staphylococcus aureus* (5/62).

Five predominant HAP pathogens from wards were *Klebsiella pneumoniae* (245/877) followed by *Pseudomonas aeruginosa* (143/877), *Citrobacter* species (100/877), *Acinetobacter* species (99/877) and *Escherichia coli* (86/877).

Predominant HAP and VAP pathogens from ICUs were *Klebsiella pneumoniae* (128/513), Acinetobacter species (99/513), *Citrobacter* species (77/513), *Pseudomonas aeruginosa* (64/513) and *Escherichia coli* (54/513) (Table no. 3)

Antimicrobial susceptibility pattern of Gram-negative bacilli and Gram-positive cocci from OPDs, IPDs and ICUs are shown in graph 1 and 2, respectively.

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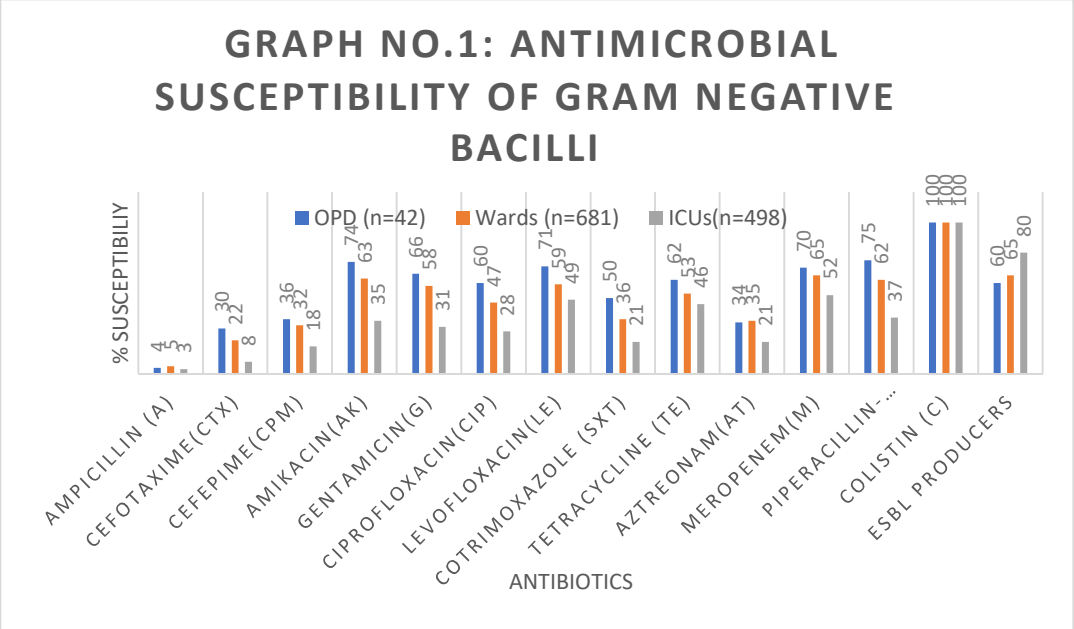
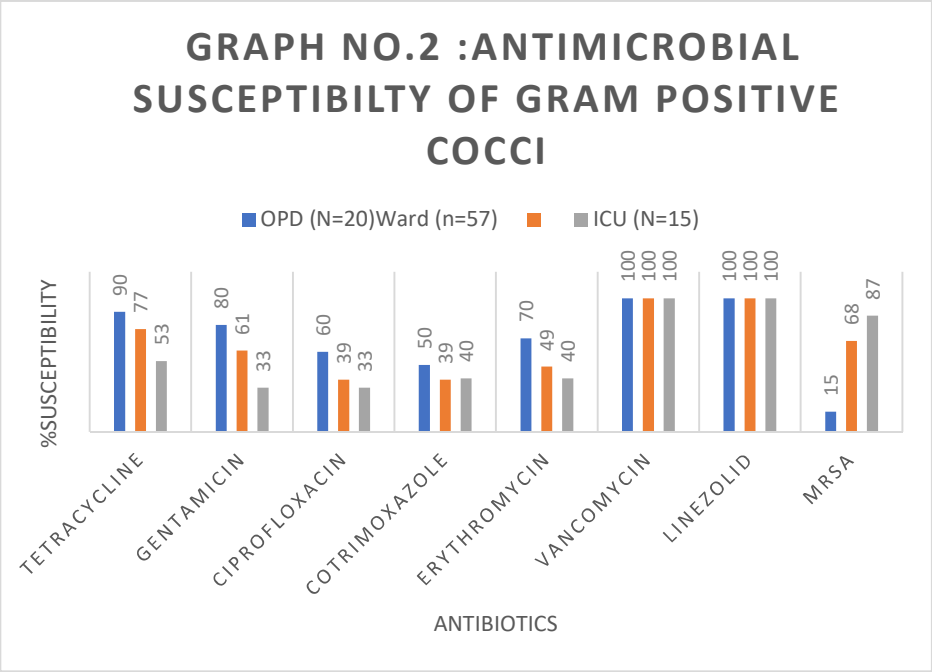


Gram-negative bacilli had exceptionally low susceptibility to Ampicillin, Cephalosporins like Cefotaxime, Cefepime, in all three settings. Susceptibility of OPD isolates to oral drugs was 71% for Levofloxacin, 62% for Tetracycline, 60% for Ciprofloxacin and 50% for Cotrimoxazole. But use of fluroquinolones being reserve drug for Tuberculosis is not recommended. Gram-negative bacilli respiratory isolates from ward show comparatively higher susceptibility to aminoglycosides like Amikacin (63%) and Gentamicin (58%), Piperacillin-Tazobactam (62%), Meropenem (65%) and Colistin (100%). ICU respiratory isolates were multi-drug resistant and had high resistance to almost all antibiotics. They showed sensitivity to Meropenem and Colistin as 52% and 100%, respectively. Prevalence of ESBL producers in OPD, IPD and ICU isolates were 60%, 65% and 80 % respectively. (Graph no.1)



Amongst respiratory Gram-positive isolates, OPD isolates had high susceptibility to oral drugs like Tetracycline (90%), followed by Erythromycin (70%), Ciprofloxacin (60%) and Cotrimoxazole (50%). Prevalence of MRSA infection was 15%, 68% and 87% in OPD, IPD and ICU respiratory isolates. Ward isolates also had high susceptibility to Tetracyclines (77%) followed by Gentamicin (61%). In suspected MRSA patients Vancomycin and Linezolid, be used as they were 100% susceptible to both antimicrobials. ICU isolates had high resistance to 1st and 2nd line treatment antibiotics. Prevalence of MRSA was 87% hence Vancomycin (100% susceptible) and Linezolid (100% susceptible) preferred as effective treatment. (Graph No.2)

Discussion:

Management of Respiratory Tract Infections has been a challenge to the physicians, most recently due to the emergence of multi drug resistance. This study is an attempt to analyze the bacterial profile of respiratory culture isolates, assess antimicrobial trends, and to formulate antibiogram and empirical treatment of Lower respiratory tract infections in different hospital settings.

In our study, the bacterial etiology for LRTI was noticed in 56% of samples. The isolation rates by Ramana et al (9) (Andhra Pradesh 2013), Mishra et al (10) (Nepal 2012), Nayanjyoti Sarmah et al (11) (Assam 2016), Borkot Ullah (12) (Bangladesh 2016) were 52.83%, 44.4%, 50%, and 64%, respectively. The difference in prevalence rates may be explained by the differences in study designs and geographical areas. Spread of respiratory infections varies between populations and countries depending on differences in geography, climate, and socioeconomic conditions.

Gender-wise ratio of 1.59:1 was observed skewed in favor of males in our study. It 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 (12). Maximum patients were in the age group 41-60 years followed by 21-40 years. From the present study, it was observed that the young adults and middle aged were most at risk of acquiring respiratory infection may be due to smoking/drinking habit and occupational hazard.

In our study Gram-negative bacteria predominated over Gram-positive bacteria as cause of lower respiratory tract infections contributing to 94% of the isolates. A similar finding was observed by a recent study from Nepal by SK Mishra et al (10) who reported 84.1% occurrence and from Kerala by Regha IR et al (13) as 84.7%. In studies by Veena Kumari et al, (14) and Goel et al (15) lower respiratory tract infections in Intensive care units showed Gram-negative bacilli prevalence as 92.2% and 97.4%, respectively. This predominance might be due to unequal distribution of patients with Community-acquired and Hospital-acquired infections and due to spreading antimicrobial resistance in hospital settings (13). Amongst Gram-negative bacilli *Klebsiella pneumoniae* (27%) predominated followed by *Pseudomonas aeruginosa* (15%) and *Acinetobacter* species (14%) and other members of Enterobacteriaceae family. This trend of pathogens is similar to other Indian and south east Asian countries (9, 10, 13, 14). Amongst Gram-positive isolates overall prevalence of *Staphylococcus aureus* (3.44%) and *Streptococcus pneumoniae* (3.30%) contributed equally and were more predominant in OPD patients (20 of 62 isolates i.e., contributing to 32.25% of total infections).

In the present study, Gram-negative respiratory isolates showed low susceptibility to Ampicillin (4%, 5%, 3%) and cephalosporins like Cefotaxime (30%, 22%, 8%), Cefepime (36%, 32%, 18%), Aztreonam (34%, 35%, 21%) in OPD, IPD and ICU isolates, respectively. Beta-lactam drugs are rapidly becoming ineffective for

treating BSIs due to indiscriminate and non-judicious usage. The fact that cephalosporins are one of the most used antibiotics for in-patients as well as for out-patients could be the reason for such high degree of resistance.

All GNBs showed moderate sensitivity to Levofloxacin (71%, 59%, 49%), Ciprofloxacin (60%, 47%, 28%), Tetracycline (62%, 53%,4 6%), Trimethoprim-sulfamethoxazole (50%, 36%, 21%). But use of fluroquinolones is restricted being reserve drug for tuberculosis treatment.

Comparatively higher sensitivity to Aminoglycosides, Amikacin, Gentamicin; Piperacillin-Tazobactam, Meropenem, Chloramphenicol and Colistin. These findings match with other Indian studies (9, 10, 11, 12, 13).

Gram-negative isolates had comparatively higher susceptibility to Amikacin (74%, 63%, 35%), Gentamicin (66%, 58%, 31%), Piperacillin-Tazobactam (75%, 62%, 37%) and Meropenem (70%, 65%, 52%) in OPD, IPD and ICU isolates, respectively. ICU isolates showed lower susceptibility to almost all antibiotics, with comparatively higher susceptibility to Meropenem (52%) and Colistin (100%). These findings are consistent with other Indian studies (9, 10, 11, 12, 13).

In present study, Gram-positive isolates showed higher sensitivity to Vancomycin (100%), Linezolid (100%) in all 3 settings. High susceptibility to tetracycline (90%, 77%, 53%) moderate sensitivity to Gentamicin (80%, 61%, 33%) and Erythromycin (60%, 49%, 40%) in OPD, IPD and ICU settings. Low susceptibility to Cotrimoxazole (50%, 39%, 40%) and Ciprofloxacin (60%, 39%, 33%) which is comparable to other Indian studies [9, 10, 11, 12]. ICU isolates had high percentage of drug resistance.

Conclusion:

The present study provides prevalence of lower respiratory tract infection pathogens and their antibiotic sensitivity patterns in different hospital setting of a tertiary care centre of Western India. If injudicious use of antibiotics continues, we will face problem of pan-drug resistance in near future. Thus, by formulating antibiogram for respiratory isolates helps in implementing antibiotic stewardship program restricting antibiotic usage, promoting combination therapy ultimately contributing to reduction of drug resistance.

We recommend the following empirical treatment based on antibiogram at our set up:

Type of Pneumonia		**Antibiotics**	**Remark**
Community acquired Pneumonia	Mild (Not hospitalized)	Oral tetracycline, Erythromycin	Use oral drugs
	Moderate (Hospitalized, not in ICU)	Gentamicin/ Amikacin Or Piperacillin-Tazobactam	Use injectables Switch to oral earliest
	Severe (ICU)	Gentamicin, Piperacillin-Tazobactam or Meropenem. Add Vancomycin (if MRSA suspected)	Escalate/deescalate after Culture and Sensitivity report
Hospital Acquired Pneumonia		Amikacin/ Gentamicin and Piperacillin-Tazobactam / Meropenem (Add Vancomycin if MRSA sis uspected)	Escalate/deescalate after Culture and Sensitivity report

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