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Microbiological Profile of Lower Respiratory Tract Infections in MICU in a Tertiary Care Hospital

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ABSTRACT

Lower respiratory tract infections (LRTI's) are the most frequent infections among patients in intensive care units. The consequences of increased drug resistance are far reaching since bacterial infection of the lower respiratory tract is a major cause of death from infectious disease. This was a prospective study of clinically suspected cases of LRTI's over a period of 6 months from Jan 2019 to June 2019. Lower respiratory tract samples were inoculated on BA, CA, MAC agar and incubated overnight & AST was performed after identification. 124 (88.5%) of total 140 samples were positive for bacterial culture. 118 (84.28%) were gram negative bacilli (GNB) and 6 (4.2%) were gram positive cocci (GPC). Occurrence of LRTI was 71.4% with dominance of males and age group of 20-65 years. *Klebsiella spp.* (59.28%) was the most common isolate followed by *Pseudomonas aeruginosa* (11.4%), *E. coli* (7.1%), *Acinetobacter baumannii* (6.4%), *Staphylococcus aureus* (4%). Susceptibility of GNB was highest towards Imipenem followed by Piperacillin-tazobactam. Gram positive organisms exhibited highest susceptibility towards Vancomycin and Linezolid. The resistance pattern of these pathogens can help to formulate effective antimicrobial policy. Therefore, an ultimate and detailed bacteriological diagnosis and susceptible testing is required to overcome global problem of antibiotic resistance.

Keywords

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Introduction

Lower respiratory tract infection is defined as an acute illness usually for a period of 1-3 weeks, presenting with symptoms of cough, expectoration, dyspnoea, wheeze & chest pain/discomfort. Various predisposing factors which may lead to LRTI are smoking, alcohol,

immunosuppressive conditions, Diabetes mellitus, COPD, Bronchial asthma etc.¹

Acute lower respiratory tract (ALRI) infections are among the most common infectious diseases affecting humans worldwide causing significant morbidity and mortality for all age groups. It is liable for

4.4% of all hospital admissions and 6% of GP consultations. It accounts for 3 to 5% of deaths in adults globally, about 4.2 million ALRI deaths are estimated to occur among all age groups. The problem is much greater in developing countries where pneumonia is the most common cause of hospital attendance in adults.⁴

Age, gender and season can affect the occurrence of LRTIs. Pneumonia in adults occurs in 4% of Indians with male to female ratio of 1.56:1.14 and an annual incidence rate of (1.12–3.16 per 1000 people), which is increased as age advances.²

The aetiological agents of LRTIs vary from area to area, so the susceptibility profile will also differ between geographical locations.⁶

The dramatic rise in the antimicrobial resistance among the respiratory pathogens, presumably due to the prophylactic administration of antibacterial therapy even before the availability of the culture reports, is a matter of potential concern worldwide.⁷

This study has reviewed our current understanding on lower respiratory tract infections and it has emphasized the changing trends in their occurrence and therefore the antimicrobial susceptibility pattern of the respiratory pathogens which were isolated during a government hospital of western India, thus enabling the clinicians to appropriately formulate and endorse a competent and rational antibacterial policy, to further curb the incidence of the disease.⁸

Materials and Methods

The Prospective study was conducted in the Department of Microbiology in Government Medical College and Hospital during Jan 2019 to June 2019. A total of 140 patients admitted in Medicine Intensive Care Unit (MICU), who were provisionally diagnosed as Lower

Respiratory Tract Infection were enrolled in the study. Lower Respiratory Tract samples (Endotracheal aspirate) were collected & transported immediately to Microbiology Laboratory and processed further.

The samples were inoculated onto Blood Agar (BA), Chocolate Agar (CA) & MacConkey Agar (MAC) and incubated at 37°C for 24 hours. After incubation, identification of bacterium from positive cultures was done with standard microbiological techniques which include Gram staining, motility testing by hanging drop preparation and various biochemical reactions such as Catalase, Coagulase, Indole, Methylred, Voges-Proskauer, Citrate, Urease and Oxidase test etc.

The bacterial isolates were put up for susceptibility testing by standard Kirby Bauer disc diffusion methods on Muller Hinton Agar. The susceptibility patterns of the bacterial pathogens were determined following the panel of antimicrobial agents as recommended by Clinical Laboratory Standard Institute (CLSI) guidelines, 2019.

Depending on the isolate, antibiotic discs were applied and Zone diameter was measured in millimetres and interpreted as per CLSI guidelines. The entire testing was done under strict quality control and American Type Culture Collection (ATCC) strains were used as control strains.

Results and Discussion

A total of 140 samples were processed based on the standard microbiological methods. The results of the study revealed that out of the 140 samples tested, significant pathogens were isolated from 124 (88.57%) samples and 16 (11.4%) showed no growth (Graph 1). Of these 100 (71.4%) samples were of males and 40 (28.5%) samples of female's (Graph 2). The highest isolation rates were observed in the

age group of 20-40 years followed by 40-60 years of age group (Table 1).

Out of 140 cases of LRTI's, maximum number of cases were from Organophosphorus poisoning (OPP) with respiratory failure (n = 77), Pneumonia (n =20), Pneumothorax (n =17), TB (n =10), Chronic Obstructive Pulmonary Disease (COPD) (n=9), GBS with respiratory failure (n=3) in which *Klebsiella pneumoniae* cause the highest no. of cases of LRTI's followed by *Pseudomonas aeruginosa*, *E.coli*, *Acinetobacter baumannii* and *Staphylococcus aureus* (Table 2).

Among the Culture positive isolates 118(84.2%), the predominant pathogen isolated was *Klebsiella pneumoniae* (59.28%), followed by *Pseudomonas aeruginosa* (11.4%), *Escherichia coli* (7.1%), *Acinetobacter baumannii* (6.4%) and *Staphylococcus aureus* (4.2%) respectively (Table 3).

Out of the 140 samples tested, 124 showed significant growth in which, 18 samples (14.5%) showed Polymicrobial infection (mostly by *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*) and 106 samples (85.4%) showed Monomicrobial infection (Table 4).

Gram positive isolates were 100% resistance to Penicillin G followed by Ciprofloxacin (83.3%), Trimethoprim/ Sulfamethoxazole (66.7%) (Table 5).

Most of the gram-negative bacterial isolates showed resistance to commonly used Cephalosporins. *Klebsiella pneumoniae* showed resistance to most of the drugs like Cefotaxime (100%), Cefuroxime (99.4%), Ampicillin (97.4%), Amikacin (81.3%), Ciprofloxacin (92.9%), Gentamicin (71.4%), Meropenem (81.8%), Trimethoprim/

Sulfamethoxazole (86.5%), Piperacillin/Tazobactam (87.1%).

Pseudomonas aeruginosa showed relatively more resistance to Cephalosporins, Ciprofloxacin (45.5%), Ceftazidime (42.4%), Meropenem (37.5%), Amikacin (46.9%), Gentamycin 936.4%), Tobramycin (52.9%), Piperacillin/Tazobactam (33.3%).

E. coli showed resistance to most of the Cephalosporins, Fluoroquinolones and Meropenem (60%), Piperacillin/Tazobactam (60%), Amikacin (60%), Gentamycin (53%), Trimethoprim/Sulfamethoxazole (73%).

Acinetobacter baumannii showed resistance to most of the Cephalosporins followed by Ciprofloxacin (91%), Amikacin, Gentamycin (87%), Meropenem (77.3), Piperacillin/Tazobactam (87%) (Table 6).

Confirmed LRTI cases were associated with either single risk factor or multiple comorbidities i.e. more than one risk factor. Out of which Multiple comorbidities (28%) followed by Hypertension (13%), Diabetes (17%), Smoking (19%) and Alcohol (10%), Kidney disease (9%).(Graph 3)

The present study provides an insight on the prevalence and antibiogram of the respiratory pathogens which were isolated from cases of Lower Respiratory Tract Infection (LRTI) admitted in MICU in Government Medical College, Aurangabad.

Lower Respiratory Tract samples (Endotracheal aspirate) culture positivity was found to be 88.5% (124outof140). The isolation rates reported by Ratna et al.,⁷Amutha et al.,² and Elumalai et al.,⁶ were 39.77%, 51% and 65.14% respectively. The remaining 16 (11.4%) Lower Respiratory Tract samples (Endotracheal aspirate) which yielded no growth in culture could be due to

due to previous antibiotic therapy or viral aetiology.

Among the culture positive isolates, the predominant organism were *Klebsiella pneumonia* followed by *Pseudomonas aeruginosa* similar to a study done by Amarasinghe *et al.*,¹⁴

Males were found to be more affected than females which was in concordance to a similar study by Dsouza *et al.*,⁵ and Rana *et al.*,⁹. This may be explained by male behaviour of more outdoor stay exposing them to air pollution than the female counterparts.

Moreover smoking habits are more pronounced in males that constitute one of the predisposing factors for the development of LRTIs. Smoking and pollution are responsible for decrease in mucociliary clearance and innate immunity. It leads to increased bacterial colonization that can give rise to increased airway inflammation and thus exacerbations.⁷

The age range in our study varies between 20-60 years of age which was similar to Okesola *et al.*,¹¹ Kalgo *et al.*,¹² and Srivastav *et al.*,¹³

Out of the culture positive samples, in 18 cases (14.5%), more than two organisms were isolated. The isolation rates by Saha *et al.*,¹ Bajpai *et al.*,¹⁰ Agmy *et al.*,¹⁵ were 2.04%, 24.24%, 12% respectively.

In the current study Gram positive organisms showed 100% susceptibility to Linezolid & Vancomycin while possessing good susceptibility to Doxycycline, Trimethoprim/Sulphamethoxazole, Tetracycline and followed by their reduced susceptibility to Penicillin, Ciprofloxacin, and Gentamycin. Out of 4% of the *Staphylococcus aureus*, four isolates were found to be Methicillin resistant (MRSA).

Vancomycin Susceptibility in *Staphylococcus aureus* was checked by using Vancomycin screen agar.²³

For Gram positive bacterial infections, Aminoglycosides and Levofloxacin are widely recommended as first line drugs for empirical treatment reserving Vancomycin and Linezolid for resistant cases.

Similar findings were reported from some other investigators as well like Sarmah *et al.*,³ Regha *et al.*,⁴ Panda *et al.*,¹⁹

There were also reports from India regarding increase prevalence of drug resistance among gram negative bacilli strains from LRTI¹⁸.

In our study also *K. pneumoniae*, *E. coli*, *Acinetobacter baumannii* strains have shown 95 to 100% resistance to Cephalosporins and Fluroquinolone's and *P. aeruginosa* was comparatively more susceptible to antibiotics.

P. aeruginosa had 60% susceptibility to Meropenem and Imipenem each, whereas all the 9 *Acinetobacter baumannii* were resistant to Carbapenems.

There were several antibiotic- resistance mechanisms working in *P. aeruginosa* and *Acinetobacter spp.* Moreover, high colonisation rates have been observed in the ICU setting, particularly in the respiratory tract. Thomas *et al.*,¹⁷ conducted a detailed study on MDR Gram negative bacilli causing lower respiratory infections. They had *K.pneumonia*, *Acinetobacter species* as the commonest MDR isolates.

High rates of resistance to Cephalosporins was not noticed in several studies Tripathi *et al.*,¹⁶ Nepal *et al.*,²⁰. Our observation about Cephalosporins match with their findings. This might be due to the extensive use of 3rd generation Cephalosporins in hospitals.

Table.1 Age wise distribution of cases of LRTI

Age in years	Male	Female	Total
1-20	8	7	15
20-40	46	20	66
40-60	42	13	55
60-80	2	1	3
80-100	0	1	1

p =0.248NS (since $p > 0.05$, there is no association exist between age and sex of the patients, it is not statistically significant)

Table.2 Correlation of cases of LRTI with microorganisms isolated in cases of LRTI's

Diagnosis	Number of cases	<i>Klebsiella pneumoniae</i>	<i>Pseudomonas aeruginosa</i>	<i>Escherichia coli</i>	<i>Acinetobacter baumannii</i>	<i>Staph. aureus</i>
OPP With Respiratory Failure	77	40	20	11	6	0
Acute Respiratory Distress Syndrome	4	2	2	0	0	0
Pneumonia	20	8	4	2	4	2
GBS with Respiratory Failure	3	1	2	0	0	0
COPD	9	7	2	0	0	0
Pneumothorax	17	7	4	2	3	1
Tuberculosis	10	3	4	2	0	1

p=0.43NS (Since $p > 0.05$, distribution of organisms with respect to diagnosis to diagnosis is natural and no significant difference exist i.e. a particular organism had no association with type of diagnosis so it is not statistically significant)

Table.3 Organism wise distribution of cases of LRTI's

Name of Organism	Total No. of Isolation	Percentage
<i>Klebsiella pneumoniae</i>	83	59.28%
<i>Pseudomonas aeruginosa</i>	16	11.4%
<i>Escherichia coli</i>	10	7.1%
<i>Acinetobacter baumannii</i>	9	6.4%
<i>Staph.aureus</i>	6	4%

Table.4 Type of Infection in cases of LRTI's

Type of Infection	No. of isolation	%
Polymicrobial infection	18	14.5
Monomicrobial infection	106	85.4

Table.5 Gram positive cocci (*Staphylococcus aureus*) antibiogram pattern in cases of LRTI's

Drugs	Resistance pattern (%)	Sensitivity pattern (%)
Ciprofloxacin	83.3	16.7
Clindamycin	72.2	27.8
Doxycycline	27.8	66.7
Erythromycin	55.6	27.8
Cefoxitin	83.3	16.7
Gentamicin	72.2	27.8
Linezolid	0	100
Penicillin G	100	0
Trimethoprim/Sulfamethoxazole	66.7	33.3
Tetracycline	27.3	54.5
Vancomycin*	0.0	100

(*For *Staphylococcus aureus*, Vancomycin susceptibility was tested by Vancomycin screen agar)

Table.6 Gram negative bacilli antibiogram pattern in cases of LRTI's

Drugs	Organism							
	<i>Pseudomonas aeruginosa</i>		<i>Klebsiella pneumoniae</i>		<i>Escherichia coli</i>		<i>Acinetobacterbaumannii</i>	
	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)
Amikacin	46.9	53.1	81.3	5.8	60	40	87	8.7
Ampicillin	100	0	97.4	0.6	93.3	6.7	-	-
Ciprofloxacin	45.5	48.5	92.9	3.2	80	6.7	91.3	8.7
Cefotaxime	-	-	99.4	0.6	86.7	6.7	100	0
Cefepime	42.4	57.6	95.5	1.3	86.7	13.3	95.7	4.3
Gentamycin	36.4	63.6	74.8	23.9	53.3	46.7	87	8.7
Imipenem	40	60	81.8	15.5	60	40	80	20
Levofloxacin	41.2	58.8	89.3	3.9	62.5	37.5	-	-
Meropenem	37.5	62.5	81.8	15.5	60	33.3	77.3	22.7
Trimethoprim/Sulfamethoxazole	-	-	86.5	12.3	73.3	26.7	82.6	17.4
Piperacillin/ Tazobactam	33.3	60.6	87.1	9.7	60	26.7	87	13
Ceftazidime	42.4	57.6	-	-	-	-	87	13
Ceftriaxone	100	0	99.4	0.6	-	-	100	0
Minocycline	-	-	-	-	-	-	59.1	40.9
Ampicillin/ Sulbactam	-	-	-	-	-	-	95.7	4.3
Tetracycline	-	-	-	-	-	-	68.2	31.8
Tobramycin	52.9	47.1	-	-	-	-	72.7	27.3
Aztreonam	-	-	-	-	-	-	-	-
Cefuroxime	-	-	100	-	100	-	-	-
Colistin*	-	100	-	100	-	100	-	-

(* Colistin susceptibility was tested by Microbroth dilution, MBD)

Graph.1 Isolation distribution in cases of LRTI

Graph.2 Sex wise distribution of cases of LRTI's

Graph.3 Risk factors associated with LRTI

Against GNB, the most active antibiotics were Colistin, Imipenem, Meropenem followed by Amikacin, Gentamycin and Piperacillin/tazobactam. Carbapenems had been used as the last resort for infections caused by resistant Enterobacteriaceae.

But Carbapenem-Resistant Enterobacteriaceae (CRE) have now been increasingly reported worldwide.²¹ *Kanj et al.*,²² pointed that Aminoglycosides, Fluoroquinolones and Cotrimoxazole must be used with caution in serious infections even when they are active in

vitro. The risk factors associated with LRTI cases were Diabetes, Hypertension, Smoking, Alcohol, Kidney disease and multiple comorbidities. On further analysis of the associated risk factors, it had been found that multipleco-morbidities i.e. patient having more than one risk factor was showing highly prevalent among LRTI cases.

The highest rates of MDR bacteria were found in ICUs and selective pressures from intense antimicrobial exposure contributes to the emergence of MDR bacteria. De-escalation after receiving the culture and sensitivity reports is also not done in many ICUs, thus compounding the problem.

High prevalence of multidrug-resistance were observed in respiratory isolates. For effective management of lower respiratory tract infections, an ultimate and detailed microbiological diagnosis and antibiotic susceptibility testing is required.

In intensive care units and critical care units, antibiotic resistance rates are escalating to the point of complete resistance. With strategies like 'antibiotic cycling' and 'antibiotic stewardship' gaining much importance now, it 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 curb the issue of antibiotic resistance worldwide. Moreover, determination of the type of bacterial pathogens and their antibiotic resistance trends aid in better patient management by helping the clinician in the judicious use of antibiotics.

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