

Bacterial Profile, Antibiotic Sensitivity and Resistance of Lower Respiratory Tract Infections in RIMS, Ranchi: A Tertiary Care Hospital

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ABSTRACT

Introduction: Lower respiratory tract infections (LRTI) account for a considerable proportion of morbidity and mortality. Moreover these infections result in high use of antibiotics.

Aims: We aimed to identify the causative bacteria, antibiotic sensitivity and resistance of hospitalized adult patients due to LRTI in RIMS, Ranchi.

Materials and Methods: A prospective study of patients admitted in the department of Medicine was performed during January 2013 to September 2015 in the department of Microbiology RIMS, Ranchi. Samples included sputum or bronchoalveolar lavage (BAL) for staining and culture, and serum for serology.

Results: The predominant isolates in 225 patients with community acquired pneumonia (CAP) were *S. pneumoniae* (36%), *C. pneumoniae* (18.22%), and *M. pneumoniae* (12%). A higher sensitivity was recorded for moxifloxacin, levofloxacin, macrolides, and cefepime. A higher of resistance was recorded for doxycycline, cephalosporins, and β -lactam- β -lactamase inhibitors. The predominant isolates in 176 patients with HAP were, methicillin-resistant *Staphylococcus aureus*; MRSA (23.29%), *K. pneumoniae* (14.20%), and polymicrobial in 12.5%. A higher sensitivity was recorded for vancomycin, ciprofloxacin, and moxifloxacin. Very high resistance was recorded for β -lactam- β -lactamase inhibitors and cephalosporins. The predominant organisms in 210 patients with acute exacerbation of chronic obstructive pulmonary diseases (AECOPD) were *H. influenzae* (30%), *S. pneumoniae* (25.23%), and *M. catarrhalis* (17.61%).

Conclusions: The most predominant bacteria for CAP in RIMS, Ranchi were *S. pneumoniae* and atypical organisms, while that for HAP were MRSA and Gram negative bacteria. For acute exacerbation of COPD, *H. influenzae* was the commonest organism. Respiratory quinolones, macrolides, and cefepime are the most efficient antibiotics in treatment of LRTI in our hospital.

KEYWORDS: Lower Respiratory Tract Infections, Resistance, Methicillin Resistant *Staphylococcus Aureus* (MRSA), Community Acquired Pneumonia (CAP), Hospital Acquired Pneumonia.

INTRODUCTION

Acute respiratory tract infections, such as bacterial pneumonia and acute exacerbations of chronic bronchitis, account for a considerable proportion of morbidity and antibiotic use. Moreover, these infections result in high mortality rates.¹ Unfortunately, the three major bacterial respiratory pathogens; *Streptococcus pneumoniae*, *Moraxella catarrhalis* and *Haemophilus influenzae*; have a worldwide increasing prevalence of

antibiotic resistance.²⁻⁴ The importance of monitoring the progress of such resistance has led to numerous international, regional and national surveillance programmes. However, results from surveillance studies show wide variations in susceptibility rates, both geographically and over time.^{1,5} Prevalent flora and antimicrobial resistance pattern may vary from region to region depending upon the antibiotic pressure in that

locality.⁶ Thus, there is a great need for local resistance prevalence data in order to guide empirical prescription and to identify areas in which medical need for new agents is greater. Therefore, the present study was designed to identify the bacterial profile of lower respiratory tract infections (LRTIs) in RIMS, Ranchi and to determine the antibiotic susceptibility and resistance patterns among these pathogens in the hospital.

MATERIALS AND METHODS

A prospective study of patients admitted in the department of Medicine was performed during January 2013 to September 2015. The study included 225 patients with community-acquired pneumonia (CAP), 176 patient with hospital-acquired pneumonia (HAP) and 210 patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD). Samples collected from all patients were sent to the Department of Microbiology, RIMS, Ranchi. Samples included sputum and /or bronchoalveolar lavage (BAL), for Gram stain and culture, blood samples for blood cultures and serum sample for serology. One morning spontaneously produced or induced sputum sample was obtained from the majority of patients. The valid sputum originating from the lower respiratory tract was defined as that containing squamous epithelial cell less than 10/high power field and polymorphonucleocytes more than 25/high power field. One BAL was taken from each patient under anesthesia. For blood samples; 5to10 ml of venous blood was collected from each patient using sterile syringes. Blood samples were inoculated immediately under complete aseptic conditions into bottles containing 50 ml of brain heart infusion broth.⁸ Such validated sputum as well as BAL samples were cultured on three bacteriological media (Nutrient, Chocolate and Mac Conkey's) agar plates. Plates were incubated aerobically at 37°C with 5% CO₂ for 24-48 hours. For blood samples; the blood culture bottles were incubated aerobically at 37°C for 7 days. The bottles were examined daily for evidence of bacterial growth as hemolysis, gas production or turbidity above the red cell line. Subcultures using sterile syringes were done on

blood agar, chocolate agar, Mac Conkey's agar and Bile Esculin Azide agar on alternate days before reporting blood cultures as negative.⁸ Isolation of anaerobes was not considered. Bacterial isolates were identified by their biochemical characteristics. PNEUMOSLIDE IgM which is an indirect immunofluorescent assay (IFA) kit (VIRCELL PNEUMOSLIDE; VIRCELL, GRANADA, Spain) for the simultaneous diagnosis in human serum of IgM antibodies of the main infectious agents of the respiratory tract was used for detection of atypical pathogens.⁹

Antimicrobial Susceptibility Testing

Susceptibility testing was done by Kirby Bauer disc diffusion method.¹⁰ Zone diameter was measured and interpreted as per the Clinical and Laboratory Standards Institute (CLSI) guidelines.¹⁰ The following antibiotics were tested: B-lactams (Ampicillin-sulbactam, Amoxicillin/clavulanic acid, Oxacillin), Cephalosporins (Ceftriaxone, Cefuroxime, Cefotaxime, Ceftazidime, Cefepime), Carbapenems (Imipenem), Macrolides (Erythromycin, Azithromycin, Clarithromycin), Aminoglycosides (Amikacin, Gentamicin), Quinolones (Ciprofloxacin, Levofloxacin, Moxifloxacin), and others (Vancomycin, Doxycycline).

Statistical Analysis

Statistical analysis was carried out using the SPSS software (Ver.16).

RESULTS

Patients with CAP

The predominant isolates in 225 patients with CAP were *S. pneumoniae* (36%), *C. pneumoniae* (18.22%), *M. pneumoniae* (12%) and *K. pneumoniae* (10.22%). (Table 1) The sensitivity and resistance rates of *S. pneumoniae* and *K. pneumoniae* against tested antibiotics are depicted in Table 2. A higher sensitivity was recorded for moxifloxacin, levofloxacin, macrolides, and cefepime; whereas, a higher rate of resistance was recorded for doxycycline, cephalosporins, ampicillin-sulbactam, and amoxicillin-clavulinate.

Table 1: Bacterial profile of lower respiratory tract infection

Common bacterial pathogens No. %		
CAP (n=225)	HAP (n=176)	AECOPD (n=210)
<i>S. pneumoniae</i> (n=81, 36%)	MRSA (n=41, 23.29%)	<i>H. influenzae</i> (n=63, 30%)
<i>C. pneumoniae</i> (n=41, 18.22%)	<i>K. pneumoniae</i> (n=25, 14.20%)	<i>S. pneumoniae</i> (n=53, 25.23%)
<i>M. pneumoniae</i> (n=27, 12%)	<i>E. coli</i> (n=19, 10.79%)	<i>M. catarrhalis</i> (n=37, 17.61%)
<i>K. pneumoniae</i> (n=23, 10.22%)	<i>P. aeruginosa</i> (n=16, 9.09%)	<i>K. pneumoniae</i> (n=26, 12.38%)
	MSSA (n=11, 6.25%)	<i>C. pneumoniae</i> (n=17, 8.09%)
	Polymicrobial (n=22, 12.5%)	

Table 2: Antibiotic sensitivity and resistance rates (%) S. pneumonie and K.pneumonie patients with CAP*

		S. pneumonie	K.pneumonie
Moxifloxacin	S	97.1	84.2
	MS	0.9	4
	R	2	11.8
Levofloxacin	S	89.5	93
	MS	4.3	2.7
	R	6.2	4.3
Doxycycline	S	39.9	84.4
	MS	12.1	11.6
	R	48	4
Cephalosporins	S	56.3	50
	MS	11.2	8.6
	R	31.5	41.4
Macrolides	S	82.4	87.8
	MS	7.6	5.2
	R	10	7
Ampicilin/Salbactum	S	52.7	53.5
	MS	7.2	9.9
	R	40.1	36.6
Amoxicillin/Clavulinic acid	S	66.7	60
	MS	12.8	12
	R	20.5	28
Cefepime	S	73.3	76.3
	MS	6.7	5
	R	20	18.7

*Percentage of the number with respect to the total number of bacterial isolates of each pathogen.
CAP- Community acquired pneumonia, S - Sensitive, MS – Moderately sensitive, R - Resistant

Table 3: Antibiotic sensitivity and resistance rates (%) of common pathogens of HAP**

		MRSA	H. influenzae	M. catarrhalis	K. pneumoniae	MSSA
Moxifloxacin	S	44.7	74.6	73	69.5	58.9
	MS	15	3.8	2.6	8	11
	R	40.3	21.6	24.4	22.5	30.1
Vancomycin	S	67.8	ND	ND	ND	80.1
	MS	12				8
	R					11.9
Cephalosporin	S	20.2	33.3	27.2	15.5	16.7
	MS	8	6	2	10	9
	R	11.3	60.7	70.8	74.5	74.3
Ciprofloxacin	S	33.3	78.4	80	75.3	42.7
	MS	11	9.6	2.3	5	12.3
	R	55.7	12	17.7	19.7	45
Cefapime	S	44.3	61.7	65	59.9	56.6
	MS	18	11.3	8.3	13.1	10
	R	37.7	26.7	26.7	27	33.4
Amoxicillin/Sulbactum	S	0	36.6	48.4	ND	51.6
	MS	0	11.4	9.8		14.4
	R	100	52	41.8		34
Amoxicillin/Clavulinic acid	S	0	41.2	52.7	ND	72.2
	MS	0	22.7	18.3		15.4
	R	100	36.1	29		12.4
Amikacin	S	54.2	67.4	78	76.6	64
	MS	17	8.7	10	3.4	12.6
	R	28.8	23.9	12	20	23.4

**Percentage of the number with respect to the total number of bacterial isolates of each pathogen.
HAP- hospital acquired pneumonia, MRSA-Methicillin resistant Staphylococcus aureus,
MSSA- Methicillin sensitive Staphylococcus aureus, S - Sensitive, MS – Moderately sensitive, R - Resistant

Patients with HAP

The predominant isolates in 176 patients with HAP were, *methicillin-resistant Staphylococcus aureus*; MRSA (23.29%), *K. pneumoniae* (14.20%), *E. coli* (10.79%), *P. aeruginosa* (9.09%), *methicillin-sensitive Staphylococcus aureus*; MSSA (6.25%), and polymicrobial in 11.93%. (Table 1) No growth was demonstrated in 25%. Table 3 shows the sensitivity and resistance rates of common pathogens causative of HAP against tested antibiotics. Higher sensitivity rates were recorded for vancomycin, amikacin, moxifloxacin, levofloxacin, and cefepime. Characteristically, MRSA showed an absolute resistance (100%) for β -lactam- β -lactamase inhibitors, and high resistance rate (92%) for cephalosporins. The predominant isolates in 210 patients with AECOPD were *H. influenzae* (30%), *S. pneumoniae* (25.23%), *M. catarrhalis* (17.61%), and *K. pneumoniae* (12.38%). (Table 1)

DISCUSSION

The increasing antibiotic resistance problems, largely due to wide spread and irrational use of antimicrobial agents in hospitals and community, is of great concern, especially in developing countries. Reliable statistics on antibiotic resistance that are mandatory to control spread of resistant pathogens. Hospital antibiograms are commonly used to help guide empiric antimicrobial therapy and are an important component of detecting and monitoring trends in antimicrobial resistance.⁶ International guidelines for CAP strongly recommend that locally adapted guidelines should be implemented to improve process of care variables and relevant clinical outcomes.⁴

For patients with CAP, our results showed similar bacterial profiles to those reported by the international studies.⁴ However, our results showed higher prevalence of the so-called atypical organisms. This pattern of predominance should be taken into consideration upon prescribing antimicrobials in our hospital. Fortunately, this higher prevalence was closely-related to the susceptibility pattern; hence we found the highest rates for respiratory quinolones and macrolides. Over the past 3 decades, antimicrobial resistance among *S. pneumoniae* has escalated dramatically worldwide. By the early 1990s, penicillin-resistant clones of *S. pneumoniae* spread rapidly across worldwide. Additionally, resistance to macrolides and other antibiotic classes escalated in tandem with penicillin resistance. Recently, it was reported that 15 to 30% of *S. pneumoniae* worldwide are multidrug-resistant (MDR).¹¹ Our data revealed high resistance rates for doxycycline, cephalosporins, and the β -lactam- β -lactamase inhibitors. These findings are in agreement with the increasing prevalence of resistance of *S. pneumoniae* to those antimicrobial groups, demonstrated by regional,^{5,12} and world-wide^{4,5} studies. Moreover, our results highlight the

increasing problem of MDR *S. pneumoniae* in CAP, a problem that was extensively addressed in the literature.^{11,12} This, alarms us for the need for judicious use of different antimicrobial groups, particularly in our resource-limited country. With regards to patients with HAP, the problem of antibiotic resistance seems to be more important; hence the situation is more complicated than that in CAP. Nosocomial pneumonias result in high morbidity and mortality especially among ICU patients.⁷ In most clinical situations, there is a need to initiate empirical antimicrobial therapy before obtaining the microbial results. However, the situation is further complicated by the emergence of multiple beta lactamase producers and MDR pathogens.^{12,13}

The current study revealed the predominance of MRSA, Gram-negative organisms, and *P. aeruginosa* among patients with HAP. This is clearly different from the results obtained by Goel and co-workers.¹³ Although the later study addressed the problem of HAP in 75 cases of ICU patients at Assiut University Hospital, the predominant pathogens were *S. aureus* (32%), *P. aeruginosa* (30%), and *S. pneumoniae* (15%). Interestingly, our data showed polymicrobial etiology in 12.5% of cases; that was concordant to that reported by other studies.^{13,16}

Our results revealed very high rates of resistance for β -lactam- β -lactamase inhibitors and cephalosporins. Goel and co-workers observed 100% and 96.9% resistance to ceftazidime against *A. baumannii*, and *Klebsiella* spp., respectively.¹³ This, again adds to the complex scenario of antimicrobial resistance found usually in nosocomial infections; particularly in developing countries.^{13,14} On the other hand, high susceptibility rates for respiratory quinolones still confirms the importance of these agents for management of HAP.¹³ Morbidity and mortality in COPD patients are, for the most part, related to their acute exacerbations, which occur one to three times a year on average.³ The most common causes of these exacerbations are infection of the tracheobronchial tree and air pollution.¹⁵

Several studies have shown an association between the presence of certain bacterial species, such as *S. pneumoniae*, *M. catarrhalis* and *H. influenzae*, and AECOPD.¹⁷ The profile of causative pathogens observed in the current study is very similar to that published in the literature.³ Again, very high susceptibility rates for the respiratory quinolones confirm the importance of using such agents for AECOPD. It also represents an agreement with the international recommendations for antibiotics indicated for mild and moderate COPD exacerbations.³

Moreover, our reported resistance rates for aminoglycosides, cephalosporins, and doxycycline further encourage using respiratory quinolones for AECOPD. At the end, our results in three patterns of lower respiratory tract infections have many similarities

and differences to other studies. To conclude, data from this study can be very useful. A master antibiogram would allow tertiary care institutions to consider resistance patterns in hospitals referring patients and to select appropriate antimicrobial therapy or change drugs in non-responding patients.

CONCLUSIONS

The most predominant bacteria for CAP in RIMS, Ranchi are *S. pneumoniae* and atypical organisms, while that for HAP are MRSA and Gram negative bacteria. For acute exacerbation of COPD, *H. influenzae* and *S. pneumoniae* were the commonest responsible organisms. Respiratory quinolones, macrolides, and cefepime are the most efficient antibiotics in treatment of lower bacterial respiratory tract infections.

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