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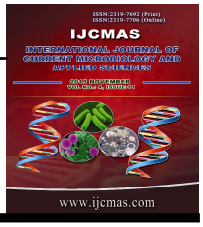

Original Research Article

A Surveillance Study of Microbial Pathogens and their Antibiotic Sensitivity of Respiratory Tract Infections in a Tertiary Care Hospital

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Keywords

Respiratory tract infections (RTI), Antibiotic sensitivity, Polymicrobial, Vancomycin, *Esherichia coli*, Imipenem

A B S T R A C T

We evaluated the etiological agents causing respiratory tract infections (RTI), risk factors, seasonal distribution and antibiotic sensitivity testing in all patients attending the out patients departments with signs and symptoms of respiratory tract infections. A total of 1268 aged above 15 years with clear diagnosis of RTI confirmed by the clinician, who have not taken any kind of antibiotics for past one week duration were included in the study. The specimens included throat swab, sputum, endotracheal secretions and broncheo alveolar lavage (BAL). The growth on the media was observed after incubation and processed as per standard CLSI guidelines. All the bacterial isolates were identified and confirmed by standard Biochemical tests and procedures. 1576 pathogens were isolated of which 668 (42.39%) were gram positive bacterial pathogens, 712 (45.18%) were gram negative bacterial pathogens and 196 (12.44%) were fungal. Among them gram negative isolates were *Escherichia coli* 288 (18.27%) > *Klebsiella pneumoniae* 198 (12.56%) > *Pseudomonas aeruginosa* 128 (8.12%) > *Acinetobacter* 98 (6.22%). The gram positive bacterial pathogens isolated were *Staphylococcus aureus* 148 (9.39%) >Coagulase negative *Staphylococci* 122(7.74%) > *Streptococcus pyogenes* 128 (8.12%) > *Pneumococci* 248 (15.74%) > *Nocardia* sp 22(1.4%). Among the fungal pathogens *Candida* Species were 158 (10.03%) > *Aspergillus* sp 38 (2.41%). *Escherichia coli* exhibited maximum sensitivity to imipenem (95.83%) followed by meropenem (93.06%). *Klebsiella pneumoniae* demonstrated maximum sensitivity to imipenem (91.41%) followed by meropenem (87.88%). *Pseudomonas aeruginosa* was maximum sensitive to Imipenem (87.50%) followed by meropenem and cefoperazone+sulbactum (84.38%), whereas, all Gram positive pathogens exhibited maximum sensitivity to vancomycin and linezolid. The level of antibiotic resistance in this study is alarming and brings to light the timely and proper diagnosis of the major microbial causes of RTI and appropriate antibiotic administration based on susceptibility test. The ongoing surveillance of AM susceptibility pattern helps in the preparation and regular review of local guidelines for the empirical selection of anti-microbial agents.

Introduction

Respiratory tract infections (RTI) are one of the most common infections which cause morbidity and mortality if untreated (Bipin Prajapati *et al.,* 2011; Jacobs *et al.,* 2009; Sharma *et al.,* 2005). They account for one of major global problem which accounts for 50 million deaths worldwide every year and reported in both community and health care settings (Zafar *et al.,* 2008). Tuberculosis and Acute respiratory infections were two of the six leading causes of death across all ages (WHO, 2003). The Age, gender and season are the factors that have been implicated in causation of RTI. Environmental sources and cross-infection from other people have been implicated in RTI. Microorganisms larger than 10µm are trapped by nasal hair and cilia lining the epithelium. Coughing and sneezing are the reflexes that expel the microorganisms from nose and mouth respectively (Prescott *et al.,* 2005). Most of the infections of respiratory tract are limited to upper tract and only 5% involve the lower respiratory tract. LRTI's have been attributed to account for almost 20% mortality among the infectious disease deaths in India as reported by World Health Organization (WHO, 2013). Upper respiratory tract involves the nasal passages, pharynx, tonsils and epiglottis. Lower respiratory tract involve the bronchi and alveoli. These infections have a significant impact on economy in terms of productivity and make the physicians to prescribe unnecessary antibiotics even in case of viral etiology.

The most common bacteria implicated in causing RTI are *Staphylococcus aureus, Streptococcus pneumonia, Streptococcus pyogenes, Klebsiella pneumoniae, Pseudomonas aeruginosa, Acinetobacter* sp. (Riley and Riley, 2003; Rudan *et al.,* 2008). A logical approach to treatment requires better understanding of the pathogens and there resistance pattern In the last three decades, there have been a lot of reports in the scientific literature on the inappropriate use of antimicrobial agents and the spread of bacterial resistance among microorganisms causing respiratory tract infections (Imani *et al.,* 2007; Tenever and McGowan Jr, 1996). Most of the RTI in India are often treated empirically without any sensitivity testing. Emergence of antibiotic resistance in management is a serious public health issue because of poverty, ignorance and also high prevalence of fake and spurious drugs in the community (Mahmoud Aly and Balkhy, 2012).

The present study was conducted to find the etiological agents causing respiratory tract infections and possible risk factors and seasonal distribution of the infections. Antibiotic sensitivity testing was performed to determine the resistance pattern of the bacterial pathogens. The sensitivity testing would help us to formulate policies for rationale and effective use of antimicrobial agents.

Materials and Methods

The present study was a prospective study conducted at Narayana General and super speciality Hospital, Nellore a tertiary care hospital. The period of the study was from July 2013 to September 2014 for a period of 15 months. Institutional ethical committee clearance was obtained for the study.

Study population: All patients attending the OPD and in patients of General Medicine and Department of TB & RD of the Hospital with signs and symptoms of RTI were enrolled in the study.

Inclusion criteria: Patients above 15 yrs of age with clear diagnosis of RTI confirmed

by the clinician were included in the study. Patients who have not taken any kind of antibiotics for past one week duration were included in the study. Old history of any RTI, Pre existing lung disorders were also included in the study.

Exclusion criteria: Patients with H/O of antibiotic administration for past one week were not included in the study.

Specimen collection: The specimens included Throat swab, Sputum, Endotracheal secretions and Broncheoalveolar lavage (BAL). Appropriate instructions were given to the patients regarding sputum collection. The sputum was collected in a wide mouthed, sterile, disposable plastic container with screw cap tops as described by Kolawale *et al.* (2009). A sterile cotton swab moistened with peptone water was swabbed over the infected portion of the throat and sent to laboratory for immediate processing. The endotracheal secretions and broncheoalveolar lavage were collected under aseptic precautions by the clinician and send to laboratory for immediate processing (Cheesbrough, 2006).

Processing of specimens:

The Specimens received to the laboratory were performed gram stain, and acid fast staining. Inappropriate sputum specimens with saliva were not processed and requested for another sample. Throat swabs were done Albert's staining also. Modified acid fast staining was done for specimens suspecting *Nocardia* sp. KOH wet mount was also done in cases of Aspergillosis.

All the specimens were inoculated on sheep blood agar, chocolate agar, Mac Conkey's agar, Sabouraud's dextrose agar and incubated at 37°C for overnight.

The growth on the media was observed after incubation and processed as per standard CLSI guidelines (CLSI, 2011). All the bacterial isolates were identified and confirmed by standard Biochemical tests and procedures. All the bacterial isolates except *Nocardia* species were subjected to Antibiotic susceptibility by Kirby- Bauer Disc diffusion method (Kirby *et al.,* 1966) and interpreted as per CLSI guidelines.

Escherichia coli ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853 was used as quality control strains for disc diffusion tests. However antifungal susceptibility was not performed due to technical reasons.

Results and Discussion

During the study period data of 1268 culture positive cases patients of which 696 patients from the general medicine dept and 882 from department of TB& RD were evaluated. Culture negative cases were suspected as viral etiology and tuberculosis patients. The data included inclusion of risk factors, age group, coexisting lung disorders, diabetes, smoking etc. Out of 1268 culture positive cases 796 (62.78%) were males and 472 (37.22%) were females (Table 1). The predominant age group affected was >65 years with 452 cases (35.65%) followed by 51–65yrs, 333 (26.26%) cases, 31–50 yrs 262 (20.66%) cases and least age group was 15–30 yrs with 221 (17.43%) cases (Table 2). The cases predominance was mostly seen between October to December 424/1268 (33.44%) indicating more during cold season followed by July–September (26.58%) (Table 3). Smoking was identified as the dominant risk factor 758 (59.78%) followed in order by diabetes 689 (54.34%), coexisting lung order 654 (51.58%), alcoholism 550 (43.38%) and last

immunosuppressive states 166 (13.09%) (Table 4). Majority of the culture positive cases were diagnosed as pneumonia 342 (26.97%) followed by asthma 277 (21.85%), COPD 210 (16.56%), bronchiectasis 156 (12.30%), Bronchitis 154 (12.15%) and last pharyngitis 129 (10.17%).

From total 1268 culture positive cases, 1576 pathogens were isolated of which 668 (42.39%) were gram positive bacterial pathogens, 712 (45.18%) were Gram negative bacterial pathogens and 196 (12.44%) were fungal (Table 5). In 444 (35%) of culture positive cases two and more than two isolates were recovered (Polymicrobial) and rest 824 (65%) yielded single isolate (monomirobial) growth.

Gram negative bacteria were the predominant pathogens 712 (45.18%) of the total study. The most common GNB was *Escherichia coli* 288 (18.27%) followed in order by *Klebsiella pneumoniae* 198 (12.56%), *Pseudomonas aeruginosa* 128 (8.12%) and *Acinetobacter* 98 (6.22%). The gram positive bacterial pathogens isolated were *Staphylococcus aureus* 148 (9.39%), Coagulase negative *Staphylococci* 122 (7.74%), *Streptococcus pyogenes* 128 (8.12%), *Pneumococci* 248 (15.74%) and *Nocardia* sp 22 (1.4%). Among the fungal pathogens *Candida* sp were 158 (10.03%) followed by *Aspergillus* sp 38 (2.41%) (Table 6).

Escherichia coli exhibited maximum sensitivity to Imipenem (95.83%) followed by meropenem (93.06%) followed by cefoperazone + sulbactam (86.11%), sparfloxacin (80.56%), netilmycin (84.03%) and least to amoxycillin (16.67%).

Klebsiella pneumoniae demonstrated maximum sensitivity to imipenem (91.41%) followed by meropenem (87.88%) and least sensitivity to amoxycillin (22.22%). *Pseudomonas aeruginosa* was maximum sensitive to imipenem (87.50%) followed by meropenem and cefoperazone + sulbactum (84.38%). *Acinetobacter* sp also exhibited the same pattern of sensitivity of *Pseudomonas* with maximum sensitivity to imipenem and meropenem followed by cefoperazone+sulbactam (Table 7).

With regard to Gram positive pathogens all exhibited maximum sensitivity to vancomycin and linezolid. However CONS has shown maximum sensitivity to cefoperazone + sulbactum (100%). *S. pneumoniae* and *S. pyogenes* demonstrated >95% sensitivity to cefoperazone + sulbactam (Table 8).

The present study was conducted in Narayana general and super specialty hospital, Nellore for a period of 15 months. Out of the total 1578 patients included in the study 1268(80.35%) were culture positive which coincides with the studies of El-Mohamed *et al.*, Okesola and Oni, Ezgi Ozilmaz *et al.* (El-Mahmood *et al.*, 2010; Okesola and Oni, 2009; Ezgi Ozyilmaz *et al.*, 2005).

Out of total 1268 culture positive cases males formed 62.78% whereas females around 37.22% which show RTI are more frequent in males than females. According to Doddann-Navar as reported by Gauchan *et al.* (2006), smoking, alcohol consumption, use of tobacco which causes reduction in local respiratory tract makes them more vulnerable to RTI. As mentioned in various studies worldwide smoking appears as the main risk factor for RTI which is followed by diabetes and any significant coexisting lung disorder. With regard to seasonal distribution of RTI in India, most of the cases were seen during October- December because of more incidences of viral infections in cold season favouring secondary bacterial infections as mentioned

by Kumari *et al.* (2007). This study also recovered the highest prevalence 35.65% among age group more than 65 years. Similar studies indicate that pneumococcal infections are more common after 55 years due to decreased immune system and degenerative diseases like diabetes etc. Most of the cases were seen after 65 years indicating that debilitated and old age are more prone to develop RTI as wading immune system make more vulnerable for infections (MacFarlane *et al.,* 1993).

The most common isolate throughout the study was *Escherichia coli* followed by *Klebsiella pneumoniae* and the other isolates were *Pseudomonas aeruginosa* and *Acinetobacter* sp. Among the gram positive pathogens Streptococcus pneumoniae was the predominant isolate followed by *Staphylococcus aureus, Streptococcus pyogenes* and CONS. The findings in our study were similar to studies of Akingbade *et al.* (2012), Riley and Riley (2003), Rudan *et al.* (2012). However studies of Gauchan *et al.* (2006), Jafari *et al.* (2009) and Kousalya *et al.* (2010) from south india reported *Klebsiella pneumoniae* as the predominant isolate followed by *Staphylococcus aureus* which are in contrast to our study (Jafari *et al.,* 2009; Kousalya *et al.,* 2010). The reason is respiratory pathogens are variable from place to place based on geographic distribution.

The present study clearly states that gram negative pathogens shows maximum sensitivity to carbapenems and variable sensitivity to other cephalosporins and fluoroquinolones. Findings of our study correlate with the studies in India & abroad. However studies done by Watnabe *et al.* (1995). Sarathbabu *et al.* (2012) indicate cephalosporin + sulbactam, piperacillin + tazobactam with maximum sensitivity to gram negative respiratory pathogens. The present study clearly indicated gram positive respiratory pathogens exhibited maximum sensitivity to vancomycin, linezolid followed by cefoperazone + sulbactam which is similar to findings in various other studies. Streptococci pneumoniae and Streptococci pyogenes also demonstrated good sensitivity to azithromycin (85.48%, 87.50%) and least sensitive to amoxycillin.

Table.1 Gender wise distribution of cases

Gender	No	%
MALE	796	62.78
FEMALE	472	37.22
TOTAL	1268	

Table.2 Age wise distribution of cases

Age Group	Male	Female	Total (%)
15-30 YRS	123	98	221 (17.43%)
31-5+0 YRS	188	74	262 (20.66%)
51-65 YRS	231	102	333 (26.26%)
>65 YRS	254	198	452 (35.65%)
TOTAL	796	472	1268

Table.3 Seasonal distribution of cases

	Male	Female	Total (%)
Jan-Mar	175	113	288 (22.71%)
Apr-Jun	143	76	219 (17.27%)
Jul-Sep	212	125	337 (26.58%)
Oct-Dec	266	158	424 (33.44%)
TOTAL	796	472	1268

Table.4 Data of risk factors distribution

	Male	Female	Total	%
Smoking	672	86	758	59.78
Alcoholism	452	98	550	43.38
Diabetes	426	263	689	54.34
Coexisting lung disorder	376	278	654	51.58
Immunosuppressive state	98	68	166	13.09

Table.5 Grams pattern of isolates

	No	%
Gram positive	668	42.39
Gram negative	712	45.18
Fungal	196	12.44
Total	1576	

Table.6 Distribution of isolates from specimens

Pathogen	**No**	**%**
Staphylococcus aureus	148	9.39
Coagulase Negative Staphylococcus	122	7.74
Streptococcus pneumoniae	248	15.74
Streptococcus pyogenes	128	8.12
Esherichia coli	288	18.27
Pseudomonas aeruginosa	128	8.12
Klebsiella pneumoniae	198	12.56
Acinetobacter Sp	98	6.22
Nocardia sp	22	1.40
Candida sp	158	10.03
Aspergillus sp	38	2.41
Total	1576	

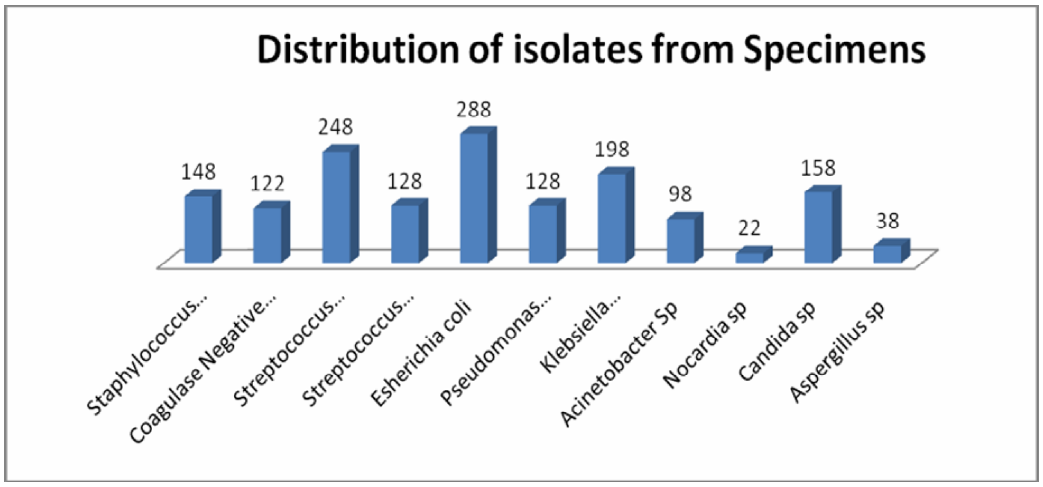
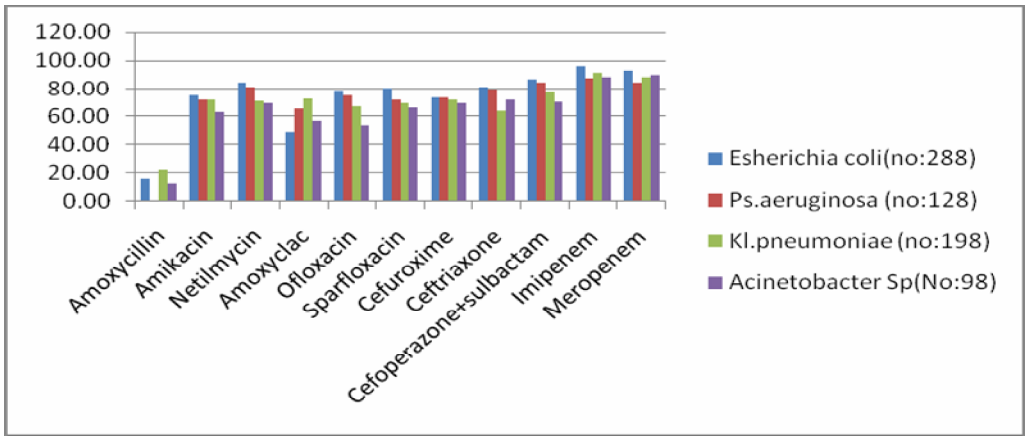


Table.7 Antibiogram of Gram negative respiratory pathogens (sensitivity %)

Antibiotic	*Esherichia coli(no:288)*	*Ps.aeruginosa (no:128)*	*Kl.pneumoniae (no:198)*	*Acinetobacter Sp(no:98)*
Amoxycillin	16.67	NA	22.22	12.24
Amikacin	75.00	71.88	71.72	63.27
Netilmycin	84.03	81.25	70.71	69.39
Amoxyclac	49.31	65.63	72.22	57.14
Ofloxacin	78.47	75.00	66.67	54.08
Sparfloxacin	80.56	71.88	69.70	66.33
Cefuroxime	73.61	73.44	71.72	69.39
Ceftriaxone	81.25	79.69	63.64	71.43
Cefoperazone+sulbactam	86.11	84.38	77.78	70.41
Imipenem	95.83	87.50	91.41	87.76
Meropenem	93.06	84.38	87.88	89.80

Table.8 Antibiogram of Gram positive respiratory pathogens (Sensitivity %)

Antibiotic	***S.aureus***	**CONS**	***S.pneumoniae***	***S.pyogenes***
Pencillin	29.73	54.10	65.32	54.69
Amoxycillin	39.19	72.13	27.42	67.19
Erythromycin	60.14	80.33	58.06	51.56
Azithromycin	82.43	88.52	85.48	87.50
Amoxyclac	72.97	96.72	75.00	76.56
Ofloxacin	59.46	77.05	75.81	60.94
Sparfloxacin	75.68	80.33	79.84	65.63
Cefuroxime	66.22	91.80	78.23	87.50
Ceftriaxone	70.27	86.89	89.52	79.69
Cefoperazone+sulbactam	62.16	100.00	95.97	96.88
Vancomycin	100.00	95.08	99.19	100.00
Linezolid	100.00	94.26	100.00	100.00



The pattern of sensitivity obtained in our study against *Klebsiella, E. coli, Acinetobacter* and *Staphylococcus aureus, S. pneumoniae* was consistent with results obtained from different studies in India and abroad Amin *et al.* (2009), Akpan *et al.* (2011). Differences in the prevalence of antimicrobial resistance in countries may be due to several factors such as different patterns of antimicrobial usage, which lead to variable selective pressure on resistance (Wilson, 2001). Distribution of specific serotypes and spread of resistant clones among different regions may be other factors.

B-lactamase and Meta-B-lacatmase mediated resistance is increasingly reported from all the isolates. The clinical relevance of these enzymes is in causing therapeutic failures. In our study isolates have shown good sensitivity with combination of B-lactam inhibitors.

Global surveillance studies conducted by Morissey *et al.* (2002) indicate the levels of resistance are alarmingly rising and needs to be effectively monitored.

The possible explanation of increasing antibiotic resistance is indiscriminate and promiscuous use of higher generation antibiotics. Further frequent prescription by the physicians even when the agent is not clear, use of suboptimal and long duration regimens increases the opportunity for acquisition or amplification of resistant strains.

In conclusion, this study indicates that there is no major significant change in the pattern of pathogens of RTI. The level of antibiotic resistance in the study is alarming and brings to light the timely and proper diagnosis of the major microbial causes of RTI and appropriate antibiotic administration based on susceptibility test. Ongoing surveillance of AM susceptibility pattern helps in the preparation and regular review of local guidelines for the empirical selection of anti microbial agents.

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