

## Antibiotic Resistance Pattern of the Clinical Isolates of *Klebsiella pneumoniae* in Lower Respiratory Tract Infections from a Tertiary Care Hospital of Tripura

Anup Saha<sup>1</sup>, Jayanta Debnath<sup>2\*</sup>, Pradip Kumar Das<sup>3</sup>, Niladri Sekhar Das<sup>4</sup><sup>1</sup>Assistant Professor, Department of Microbiology, Tripura Medical College & Dr. B.R. Ambedkar Memorial Teaching Hospital, Agartala, Tripura, India<sup>2</sup>Associate Professor, Department of Microbiology, Tripura Medical College & Dr. B.R. Ambedkar Memorial Teaching Hospital, Agartala, Tripura, India<sup>3</sup>Professor, Department of Microbiology, Tripura Medical College & Dr. B.R. Ambedkar Memorial Teaching Hospital, Agartala, Tripura, India<sup>4</sup>Assistant Professor, Department of Microbiology, Tripura Medical College & Dr. B.R. Ambedkar Memorial Teaching Hospital, Agartala, Tripura, India

\*Corresponding author: Jayanta Debnath

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## Abstract

## Original Research Article

*Klebsiella pneumoniae* has become one of the common causes of Lower Respiratory Tract infection, the most important aspect being emergence of drug resistant strains resulting in increased morbidity and mortality. This study was undertaken to analyze the Antimicrobial resistance pattern of *Klebsiella pneumoniae* isolated from adult patients with Lower Respiratory Tract Infection, so as to establish the current therapeutic options available for treatment in this geographical area of North East India. A total of 500 pulmonary samples were included in this study and processed for isolation & identification of *Klebsiella pneumoniae* by standard microbiological techniques. Antimicrobial susceptibility test of the isolated strains were performed by Kirby-Bauer Disc Diffusion method and interpreted as per CLSI guidelines. Culture positivity rate for *Klebsiella pneumoniae* was found to be 22.8% and were predominant in male and elderly patients. Only 8.77% isolates were resistant to Amikacin, followed by Gentamicin (15.78%), Levofloxacin (17.54%) and Imipenem (24.56%). Higher level of resistance was observed with Cefuroxime (75.43%), Ceftazidime (49.12%), Cefepime (45.61%) and Ciprofloxacin (37.28%). The Aminoglycosides and Levofloxacin may be considered as drugs of choice for treatment of infections caused by *Klebsiella pneumoniae* in our healthcare setting. As 61.4% of the isolates were recovered from hospitalized patients, more emphasis on strict adherence to hospital infection control guidelines and antibiotic policy is utmost recommended.

**Key words:** *Klebsiella pneumoniae*, Lower Respiratory Tract Infection, Antibiotic resistance.

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### INTRODUCTION

In 1883, Friedlander first isolated a capsulated bacillus from a patient with pneumonia and was named as Friedlander's bacillus. Later it was given the generic name of *Klebsiella* which is gram negative, nonmotile, lactose fermenting, facultative anaerobe belonging to *Enterobacteriaceae* family [1, 2]. Apart from various infections caused by *Klebsiella pneumoniae*, Lower Respiratory Tract Infection (LRTI) is an important one [1].

LRTI is not a single disease, but a group of specific infections which include pneumonia (infection of the lung alveoli), as well as infections affecting the airways such as acute bronchitis and bronchiolitis, influenza and whooping cough [3, 4]. LRTIs are responsible for 4.4% of all hospital admissions and 6% of all general practitioner consultations [5]. In western culture 3% to 5% of all community acquired pneumonia

is related to *Klebsiella pneumoniae* but in developing countries, it accounts for 15% of all cases of pneumonia. Overall 11.8% of all hospital acquired pneumonia is associated with *Klebsiella pneumoniae* [6].

Extensive use of broad spectrum antibiotics in hospitalized patients has led to both increased carriage of *Klebsiella pneumoniae* and development of multidrug resistant strains which causes serious nosocomial and community acquired infections that are hard to eradicate by using available antibiotics [7]. This study was conducted to analyze the antimicrobial resistance pattern of *Klebsiella pneumoniae* causing LRTI, in order to formulate proper antibiotic policy for treatment of patients in this region of North East India.

## MATERIALS AND METHODS

This Hospital based cross sectional study was carried out at Tripura Medical College & Dr. BR Ambedkar Memorial Teaching Hospital, a tertiary care Hospital of Tripura, from January 2016 to June 2016 following approval by Institutional Human Ethics Committee. A total of 500 samples including Sputum and Endotracheal (ET) aspirates were collected from clinically diagnosed adult patients with LRTI. Collection procedure and transportation of the sample from respective department was done following standard protocol[8]. Quality of the sputum samples were assessed based on direct microscopy by gram stain, in which 25 or more leucocytes and less than 10 squamous epithelial cells per low power field were considered as appropriate sample for processing in the Microbiology laboratory[9].

All accepted samples were inoculated onto Blood agar and Mac Conkey agar, followed by aerobic incubation at 37°C for 18 – 24 hrs. Growth of *Klebsiella pneumoniae* was recognized by their large, greyish white, mucoid colonies on Blood agar and Lactose fermenting, large, mucoid colonies on MacConkey agar[10]. Morphology of the bacteria was observed in gram stain from colony and described as short, stout

gram negative bacilli. Non-motile bacilli were detected in hanging drop preparation. Biochemical tests for confirmation of *Klebsiella pneumoniae* were based upon positive Catalase test, Voges-proskauer test, Citrate utilization test, Urease test and negative Indole production test, Methyl Red test and fermentation of Glucose, Lactose, Sucrose, maltose and mannitol with production of acid and gas[11].

Kirby-Bauer disc diffusion method was adopted for Antimicrobial susceptibility test of the isolated strains of *Klebsiella pneumoniae* and interpreted as sensitive or resistant based on the Clinical Laboratory and Standard Institute (CLSI) guidelines.[12] For quality control, *Klebsiella pneumoniae* ATCC 700603 was used.

## RESULTS

A total of 114 (22.8%) strains of *Klebsiella pneumoniae* were isolated out of 500 pulmonary samples including sputum and ET aspirates collected from clinically diagnosed patients with LRTI. The isolates were predominantly observed in infected male patients (66.66%) and in age group of more than 60 years (40.3%), as depicted in Figures 1 and 2 respectively.

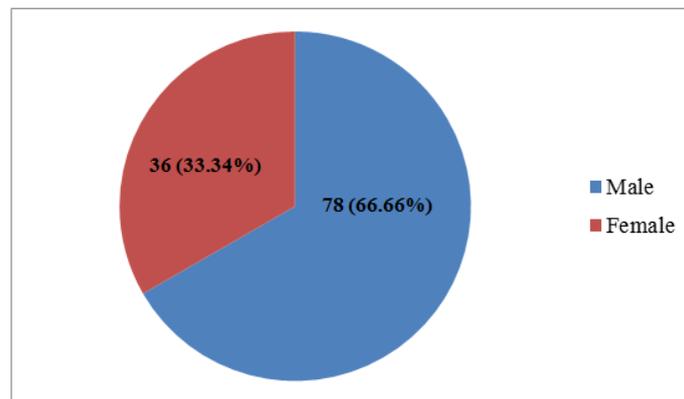


Fig-1: Gender wise Percentage of *K. pneumoniae* causing LRTI

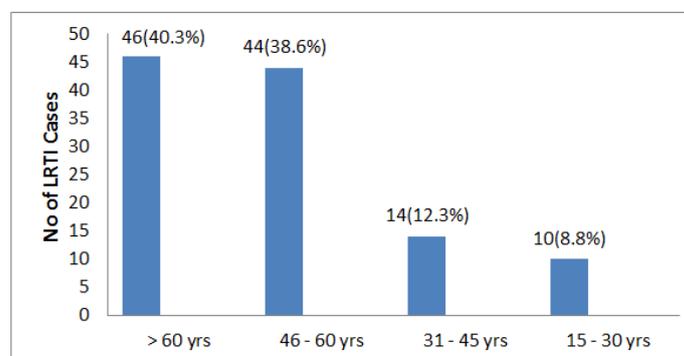
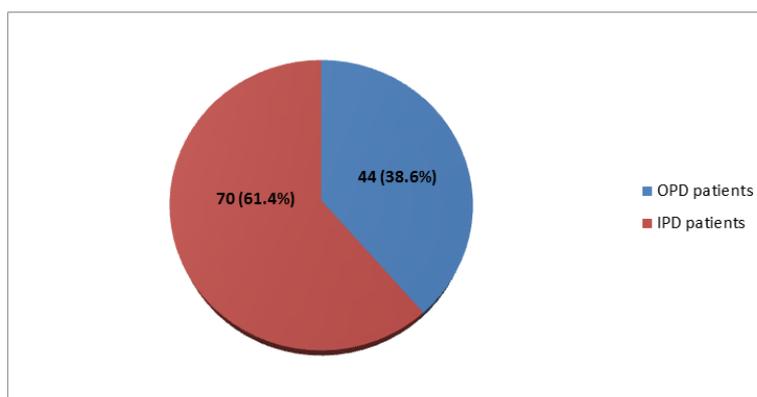


Fig-2: Age wise distribution of LRTI cases caused by *Klebsiella pneumoniae*



**Fig-3: Proportion of *Klebsiella pneumoniae* isolated from OPD and IPD patients**

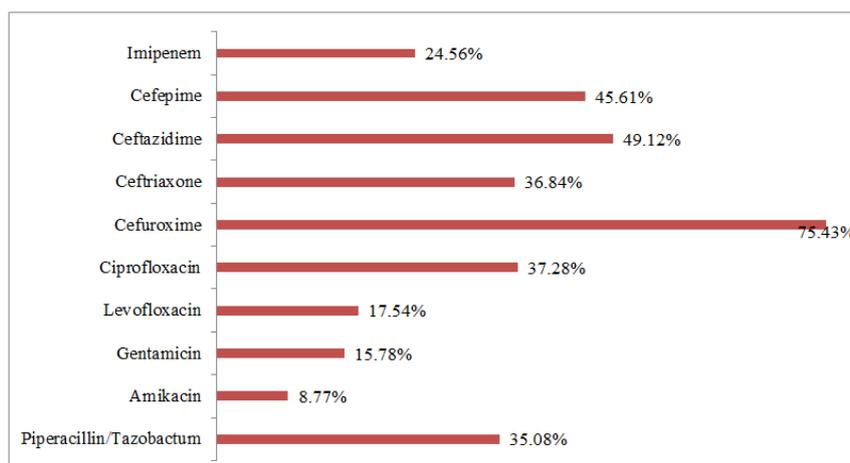
The isolated strains of *Klebsiella pneumoniae* were predominantly recovered from hospitalized patients (61.4%), as shown in Figure – 3.

On analysis of Antimicrobial susceptibility pattern of the isolated strains of *Klebsiella pneumoniae*, we observed that 86 (75.43%) isolates were resistant to Cefuroxime, followed by Ceftazidime (49.12%),

Cefepime (45.61%), Ciprofloxacin (37.28%), Ceftriaxone (36.84%) and Piperacillin Tazobactam (35.08%). Only 10 (8.77%) isolates were resistant to Amikacin, followed by Gentamicin (15.78%), Levofloxacin (17.54%) and Imipenem (24.56%). The observation has been depicted in Table 1 and Figure 4 below.

**Table-1: In vitro susceptibility pattern of *Klebsiella pneumoniae* isolates (N = 114)**

Antibiotics	Resistant Strains [% (N)]	Sensitive strains [% (N)]
Piperacillin Tazobactam	35.08% (40)	64.91% (74)
Amikacin	8.77% (10)	91.22% (104)
Gentamicin	15.78% (18)	84.21% (96)
Levofloxacin	17.54% (20)	82.45% (94)
Ciprofloxacin	37.28% (44)	61.40% (70)
Cefuroxime	75.43% (86)	24.56% (28)
Ceftriaxone	36.84% (42)	63.15% (72)
Ceftazidime	49.12% (56)	50.87% (58)
Cefepime	45.61% (52)	54.38% (62)
Imipenem	24.56% (28)	75.43% (86)



**Fig-3: Proportion of resistant strains of *Klebsiella pneumoniae* (N=114)**

**DISCUSSION**

In the present study, *Klebsiella pneumoniae* were isolated from 22.8% of the pulmonary samples, predominantly from male (66.66%) patients and in age

group of more than 60 years (40.3%). Our observation can be compared with a report from Bangalore stating 23.43% isolation rate of LRTI due to *Klebsiella pneumoniae* and predominantly isolated in age group more than 60 years [13]. However, in their observation,

females were predominant than males. Predominance of male patients with LRTI in our study could be due to associated co-morbid conditions like alcoholism, smoking, COPD and Diabetes and other immunosuppressive conditions which are prevalent in this geographical region.

We observed that, 61.4% of the isolated strains of *Klebsiella pneumoniae* were predominantly recovered from hospitalized patients. Most of the strains of *Klebsiella* spp. causing infections are associated with hospitalization and as opportunistic pathogens, *Klebsiella* spp. primarily attack immunocompromised individuals who are hospitalized and suffer from severe underlying diseases such as diabetes mellitus or chronic pulmonary obstruction [14]. A study from Pune reported that 72.81% clinical isolates of *Klebsiella pneumoniae* were from hospitalized patients [15].

On analysis of antimicrobial resistance pattern, we observed that, 8.77% of the isolates were resistant to Amikacin whereas 75.43% of the isolates were resistant to Cefuroxime, which accounted for the highest level of resistance. A similar study from Gujarat reported that 7.3% of their clinical isolates of *Klebsiella pneumoniae* were resistant to Amikacin whereas 66.4% isolates were resistant to Cefuroxime [16]. A study from Bangalore reported that, 33.33% of their isolates of were resistant to Amikacin [13].

In the present study, 35.08% isolates were resistant to Piperacillin tazobactam. A multicentric study in India, reported that more than 90% strains of *Klebsiella pneumoniae* were resistant to Piperacillin.[2] This observation indicates that combination of semisynthetic penicillin and beta lactamase inhibitors are more effective than semisynthetic penicillins alone.

Overall resistance to Cephalosporins were high in the present study, ranging from 36.84% to 75.43%, of which highest level of resistance was observed against Cefuroxime, which is a widely prescribed orally active second generation cephalosporin. This indicates the possibility of high prevalence of Beta lactamase producing strains of *Klebsiella pneumoniae* in this region, which needs to be explored by further studies. Similar observation was reported in a study from Gujarat stating resistance to Cephalosporins ranging from 51.1% to 73.2% [16].

Fluroquinolones are widely used to treat LRTI. Our observation reveals that the isolates showed considerable susceptibility to Levofloxacin with 17.54% resistance and can still be considered as drug of choice for treatment of infections caused by *Klebsiella pneumoniae* in this region. On the contrary, Ciprofloxacin was less susceptible to the isolates with 37.28% resistance. Authors from other Indian studies also reported high level of resistance of the isolates of

*Klebsiella pneumoniae* to Ciprofloxacin as 31.03% and 48.8% respectively [13,16].

Although Carbapenems are the reserved drugs to treat any gram negative bacterial infection, but our observation reveals that 24.56% strains of *Klebsiella pneumoniae* were resistant to Imipenem. This might be due to overuse and misuse of the antibiotic in our geographical area resulting in selection of mutant strains of *Klebsiella pneumoniae*. In a study reported from Bangalore, resistance of the isolates to Imipenem was as high as 43.33% [13].

## CONCLUSION

Microbiological confirmation of *Klebsiella pneumoniae* in LRTI and their antimicrobial susceptibility pattern is utmost necessary to minimize the mortality and morbidity due to drug resistant strains. On analysis of Antibiotic susceptibility pattern, we observed that Levofloxacin and Amikacin could be considered as current drugs of choice for treatment of infections caused by *Klebsiella pneumoniae* in our healthcare setting. As, majority of the isolates were recovered from hospitalized patients, we need to emphasize upon strict adherence to hospital infection control guidelines and antibiotic policy. Periodic antimicrobial surveillance is also recommended to keep a track on the development and spread of drug resistant strains, based on which antibiotic policy need to be formulated.

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