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Antibiotic Susceptibility pattern of *Klebsiella pneumoniae* in a tertiary care hospital

Dr K.Shirisha[1], **Dr Lyra P R** [2], **Dr Swathi CM** [3]

[1]Assistant Professor, Department of Microbiology, Mallareddy Medical College for women, Suraram, Hyderabad.

[2]Associate Professor, Department of Microbiology, Kannur Medical College, Anjarakandy, Kannur, Kerala.

[3]Associate Professor, Department of Microbiology, Mallareddy Medical College for women, Suraram, Hyderabad

Corresponding Author: Dr. Lyra

Abstract

Klebsiella pneumoniae belongs to the Gram-negative bacterium family, commonly implicated in both hospital-acquired and community-acquired infections, particularly in individuals with compromised immune systems. Its range of infections includes those affecting the urinary tract, respiratory tract, lower biliary tract, soft tissues, bloodstream, surgical wounds, and liver. Notably, it exhibits resistance to various antibiotics, including penicillins, cephalosporins, and monobactams such as aztreonam, due to the presence of extended-spectrum β-lactamases (ESBLs). Moreover, it produces carbapenemases, a type of β-lactamase capable of hydrolyzing penicillins, cephalosporins, carbapenems, and monobactams, categorized under Ambler groups A and D. The emergence of these enzyme-producing bacteria significantly complicates treatment, rendering beta-lactam antibiotics ineffective in serious Enterobacteriaceae, lacking an outer envelope. It poses a significant threat as an opportunistic pathogen infections. Contributing to the challenge of combating drug resistance, factors such as antibiotic overuse and easy accessibility to antibiotics are prevalent issues, particularly in developing countries like India.

Keywords: *Klebsiella pneumoniae,* Antibiotic.

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Introduction

Klebsiella pneumoniae is a Gram-negative, non-enveloped bacterium belonging to the Enterobacteriaceae family. It is frequently present in the mouth, on the skin, and within the intestines, as well as in natural environments like water and soil[1].. This bacterium is a prevalent opportunistic pathogen responsible for both hospital-acquired and community-acquired infections, particularly in immunocompromised individuals. It commonly causes infections in the urinary tract, respiratory tract, lower biliary tract, soft tissue, bloodstream, surgical wounds, and liver[2]..

In recent years, multidrug-resistant *Klebsiella pneumoniae* (MDR-KP) has become a significant challenge for physicians treating infections. MDR *Klebsiella pneumoniae* has developed resistance to at least one antibiotic from three different classes. It shows resistance to all penicillins, cephalosporins, and monobactams such as aztreonam, due to the production of extended-spectrum beta-lactamases (ESBLs). Additionally, carbapenem-resistant strains of *Klebsiella pneumoniae* (CRKP) have been reported to cause severe infections in humans[3].. The emergence of ESBL-KP and CRKP has contributed to the rise of multidrug-resistant strains, severely limiting treatment options for patients. The production of ESBLs is plasmid-mediated and can be easily transferred within the Enterobacteriaceae family, leading to the accumulation of resistance genes in strains carrying multi-resistance plasmids. Carbapenemases are beta-lactamases capable of hydrolyzing penicillins, cephalosporins, carbapenems, and monobactams, belonging to the Ambler group A and D. Bacteria that produce these enzymes cause severe infections, where beta-lactam antibiotics are ineffective. In developing countries like India, drug resistance is exacerbated by the overuse and easy availability of antibiotics. The aim of this study was to determine the prevalence of MDR *Klebsiella pneumoniae*[4]. .

Study design

A Cross-sectional study was conducted at the Department of Microbiology, Mallareddy Narayana Multispeciality Hospital, Hyderabad, India, during over a period of one year April 2022 to April 2023. Ethical approval for this study was obtained from the Institutional Review Board (Approval No: MRMCWIEC/AP/84/2022). A total of 1600 Gram-negative bacilli strains were isolated from

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various clinical samples, including pus, urine, blood, and sputum. Among these, 283 *Klebsiella pneumoniae* isolates were included in this study after receiving approval from the Institutional Ethics Committee.

Inclusion criteria:

1. The clinical relevance of the isolate was determined based on the patient medical history in the study.
2. Participants aged over 18 years were considered eligible for inclusion.
3. Both male and female individuals were included in the study.
4. Only those who provided informed consent were enrolled in the study.

Exclusion criteria:

1. Participants below the age of 18 were excluded from the study.
2. Individuals who were uncooperative were not included in the study.

Klebsiella pneumoniae strains were identified using standard phenotypic methods, including Gram staining, growth characteristics on solid media, and biochemical tests [5]. Antimicrobial susceptibility testing was performed using the disc diffusion method on Mueller-Hinton agar as a lawn culture, following the Clinical and Laboratory Standards Institute (CLSI) guidelines. The antibiotic discs, provided by HiMedia The procedure involved preparing a bacterial suspension with turbidity adjusted to match the 0.5 McFarland turbidity standard. Five antibiotic discs were placed on each plate, and the plates were incubated at 37°C for 18-24 hours. The antibiotics tested included Amoxicillin–clavulanate (AMC), Amikacin (AK), Aztreonam (AT), Ceftazidime (CAZ), Cefixime (CXM), Cefazolin (CZ), Ciprofloxacin (CIP), Chloramphenicol (C), Colistin (CL), Ceftriaxone (CTR), Cefuroxime (CXM), Cefotaxime (CTX), Gentamicin (GEN), Imipenem (IPM), Meropenem (MRP), Nalidixic acid (NX), Nitrofurantoin (NIT), Piperacillin–Tazobactam (PIT), Cotrimoxazole (COT), Tobramycin (TOB), and Polymyxin-B (PB) [6].

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Results

A total of 1600 strains of gram-negative bacilli were identified from different clinical samples, including pus, urine, blood, and sputum. 283 isolates of *Klebsiella pneumoniae* were found among 1600 gram-negative bacteria.

Table 1: DISTRIBUTION OF *KLEBSIELLA PNEUMONIAE* FROM VARIOUS CLINICAL SPECIMENS (n = 283)

SAMPLE	TOTAL	POSITIVE		NEGATIVE	
		NUMBER	%	NUMBER	%
PUS	145	100	35.34	45	15.90
SPUTUM	58	51	18.02	7	2.47
URINE	51	43	15.19	8	2.83
BLOOD	29	25	8.83	4	1.41
TOTAL	283	219	77.39	64	22.61

Out of 283 *Klebsiella pneumoniae* isolates *100* were obtained from pus samples (35.34%), followed by sputum51 (18.02%), urine 43 isolates (14.49%), and less from blood 25 (8.83%).

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FIGURE 1: SEX WISE DISTRIBUTION OF *KLEBSIELLA PNEUMONIAE* (n = 283)

There was a male predominance with149 (52.66%) *Klebsiella pneumoniae* isolates were obtained from male patients where as only 70 (24.73%) *Klebsiella pneumoniae* isolates obtained were from female patients.

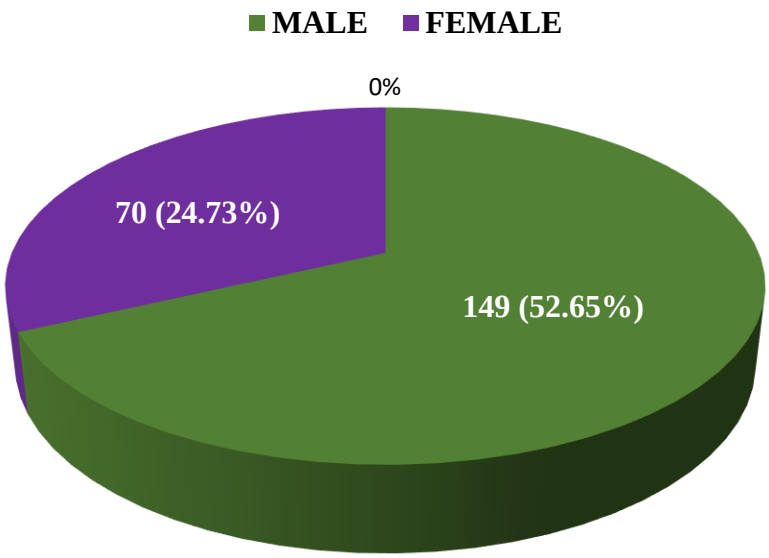

FIGURE 2: AGE WISE DISTRIBUTION OF *KLEBSIELLA PNEUMONIAE* (n = 283)

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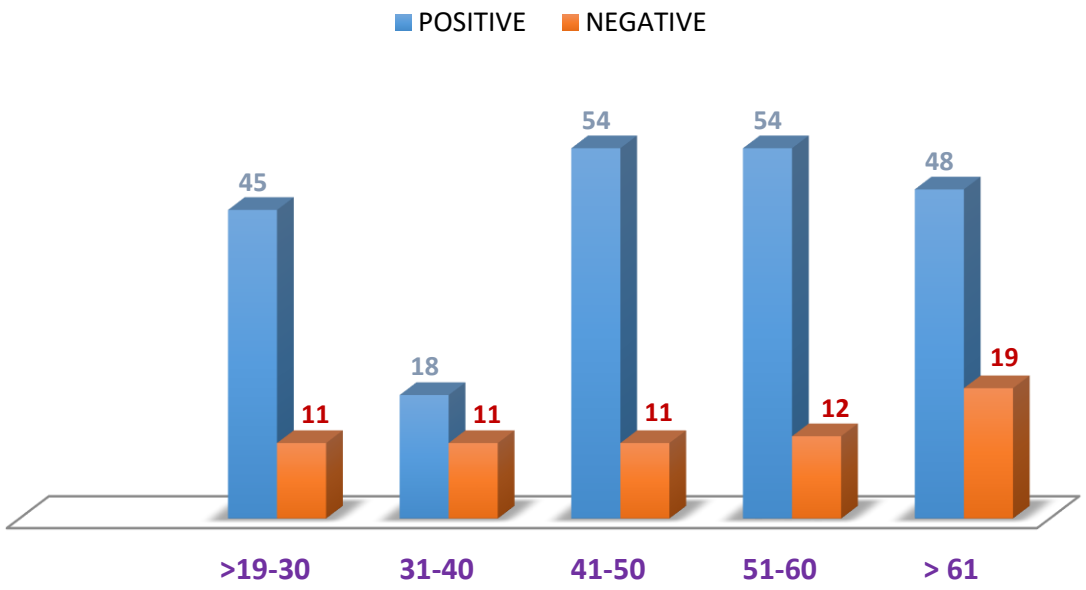
Positive isolates from patients aged 41–60 years accounted for the greatest number of isolates (19.08%), with >60 years coming in second (16.96%), and 31–40 years accounting for the least number of isolates (6.36%). The SPSS chi-square and Fisher exact tests were used to analyze the data using SPSS software version 20.0. The Significance level of P<0.05 was used.



AGE WISE DISTRIBUTION OF *KLEBSIELLA PNEUMONIAE*

TABLE-2 WARD WISE DISTRIBUTION IN *KLEBSIELLA PNEUMONIAE*.

WARD	TOTAL	POSITIVE		NEGATIVE	
		NUMBER	%	NUMBER	%
GENERAL MEDICINE	65	48	16.96	17	6.01
GENERAL SURGERY	28	21	7.42	7	2.47
ICU	92	77	27.21	15	5.30

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OBSTERTRIC &GYNAEC	45	36	12.72	9	3.18
ORTHO	38	26	9.19	12	4.24
OTHER WARDS	15	11	3.89	4	1.41
TOTAL	**283**	**219**	**77.39**	**64**	**22.61**

The majority of *Klebsiella pneumoniae*-positive isolates were from the intensive care unit 77 (27.21%), followed by general medicine ward 47 (16.96%), OBG ward 35 (12.72%), and Ortho ward 26 (9.19%), and a smaller number of isolates from other wards 11 (3.89%).

TABLE-3 *KLEBSIELLA PNEUMONIAE* ANTIBIOTIC SENSITIVITY PATTERN (n=283)

ANTIBIOTICS	**RESISTANT**		**SENSITIVE**	
	NUMBER	**%**	**NUMBER**	**%**
Cefazolin(CZ),	206	72.79	77	27.21
Ceftriaxone (CTR)	194	68.55	89	31.45
Gentamicin(GEN)	125	44.17	158	55.83
Tobramycin (TOB),	197	69.61	86	30.39
Cefuroxime(CXM)	198	69.96	85	30.04
Ceftazidime (CAZ)	217	76.68	66	23.32
Cefotaxime(CTX)	219	77.39	64	22.61
Meropenem (MRP)	133	47.00	150	53.00
Imipenem (IMP)	138	48.76	145	51.24
Amoxicillin-ClavulanicAcid (AMC)	170	60.07	113	39.93
Piperacillin-tazobactam (PIT)	139	49.12	144	50.88
Cefaperazone (CFS)	136	48.06	147	51.94
Amikacin (AK)	118	41.70	165	58.30

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Ciprofloxacin(CIP)	134	47.35	149	52.65
Cotrimoxazole (COT)	163	57.60	120	42.40
Aztreonam (AT)	139	49.12	144	50.88
Poymyxin-b (PB)	16	5.65	267	94.35
Colistin (CL)	20	7.07	263	92.93
Cefepime (CPM)	121	42.76	162	57.24
Nitrofurantion (NIT)	42	14.84	241	85.16

Out of 283 *Klebsiella pneumoniae* samples, the highest resistance found to Cefotaxime 219 (77.39%), followed by Ceftazidime 217 (76.68%), Cefazolin 206 (72.79%). Cefuroxime 198 (69.96%), Aztreonam 139 (49.12%), Imipenem 138 (48.76%), Meropenem 133 (47%), and the lowest-resistant found towards, Polymyxin-B16 (5.65%). In urine, there were a total of 51 samples. In which Nitrofurantion resistance was 42 (14.84%).

Discussion

Antimicrobial resistance has emerged as a significant obstacle for healthcare professionals striving to achieve positive patient outcomes within hospital environments. Among the noteworthy organisms contributing to these concerns is *Klebsiella pneumoniae*. This bacterium belongs to the Enterobacteriaceae and holds clinical significance due to its status as a leading opportunistic pathogen is the reason for a wide spectrum of infections. Alarmingly, it is becoming increasingly resistant to antibiotics. The genus *Klebsiella* can be found both as part of the natural flora and as transient inhabitants within the human body, and it ranks among the primary culprits behind nosocomial infections, particularly urinary tract infections, which, if not promptly diagnosed, can lead to renal failure.

In this study out of 1600 gram-negative bacterial isolates 283 isolates of *Klebsiella pneumoniae* were obtained. There is a 24.3% prevalence of *Klebsiella pneumonia*. In this study, the majority of isolates were isolated from pus (35.3%), followed by sputum (18.2%), urine (15.1%), and blood (8.8%). Similar studies were conducted where 50%

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and 21% *Klebsiella pneumoniae* isolates were obtained from pus and urine samples, respectively

In another study by **Bridal et al., (2015)** it was documented that 53% and 44% drug resistanat *Klebsiella pneumoniae* strains were isolated from urine and pus samples respectively and the prevalence of *Klebsiella pneumoniae* isolates was higher as compared to that of this study **Dahiya et al.,(2015**). In their study isolated 21.55% and 15.59% *Klebsiella pneumoniae* strains from pus and urine samples respectively.

In this study, the majority of the *Klebsiella pneumoniae* samples collected from the patients belonged to the age group between 21 and 70. This wide range of patients is because the study included all different clinical samples of MDR *Klebsiella pneumoniae* strains. This study is conducted in a tertiary care hospital where all age-group patients come for treatment. The increased number of patients observed in the old age group could be because of their decreased immunity, which makes them more susceptible to infections. In a similar study conducted by **Giri et al., (2021)** similar age distribution findings were found. In this study, it was observed that the maximum number of patients belonged to the age group of 40–70 years compared to other age groups.

Regarding gender distribution in this study, a male predominance, accounting for 52.66% of the isolates obtained from patients, while females accounted for 24.73%. In a study conducted by **Sathiya et al., (2018)** it was noted that approximately 71% of isolates were obtained from male patients, while roughly 29% were from female patients. In a study reported by **Offer et al. (1999)** where they demonstrated that the male gender represented a significant risk factor for major post-surgical infections.

In the present study, ESBL more isolates were acquired predominantly from the Intensive Care Unit (ICU) at a rate of 35.16%, with the subsequent highest numbers observed in general medicine (21.6%), Obstetrics and Gynecology (OBG) (16.44%), and surgery (10.5%). A study conducted by **Sinha et al., (2007)** reported a noteworthy proportion of

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Patients admitted to the intensive care unit (38%), surgical (22%), medical (18%), and burns (13%) were the most common causes of ESBL-producing isolates.

In this current investigation, we evaluated the resistance patterns of *Klebsiella pneumoniae* to diverse classes of antibiotics were assessed using the Kirby-Bauer disc diffusion method, adhering to CLSI guidelines. Among the total *Klebsiella pneumoniae* isolates studied, 45% demonstrated resistance to aminoglycosides, while 70–80% exhibited resistance to cephalosporins, and 47% displayed resistance to fluoroquinolones. These findings agree with a study conducted by **Beenet et al., (2009)**, reporting resistance rates of 77.46% for cephalosporins, 71.7% for fluoroquinolones, and 62.5% for aminoglycosides.

Conclusion

Timely and accurate diagnosis, coupled with effective treatment, is essential to battle multi-drug-resistant organisms. The latest research indicates a rising prevalence of multi-drug resistance in *Klebsiella pneumoniae*. This resistance primarily stems from the production of β-lactamase and carbapenemase enzymes, with a notably higher incidence among the elderly population. It underscores the importance of ongoing surveillance in monitoring these organisms, particularly in specimens like pus, where multi-drug-resistant organisms are more frequently isolated.

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