

## Original Research Article

### **Prevalence and Antibigram of Multidrug Resistant Klebsiella Species**

#### **Abstract**

**Aim:** To find out the prevalence and susceptibility of MDR klebsiella isolates in Karachi

**Study Design:** Pre-clinical in-vitro study

**Place and Duration of Study:** Study was conducted at the microbiology lab of the tertiary care hospital of Karachi during May to October 2021

**Methodology:** About 550 samples of blood, urine and wound swab were inoculated on blood agar and MacConkey agar and incubated at 37° Celsius for 24 hours. The antibiotic susceptibility was identified by Kirby Bauer's disc diffusion method. Antibiotic disc of Amoxicillin 20 µg, Fosfomycin 200 µg, Ciprofloxacin 5 µg, Moxifloxacin µg, Gentamicin 10 µg and Ceftolozane/tazobactam (30/10 µg) were placed on agar plate and then incubated at 35°C for 16-24 hours. Data was analyzed by using Statistical Package for Social Sciences (SPSS) version 20.

**Results:** Out of total 550 strains of Klebsiella 35% were multidrug resistant while 64% were not. Sensitivity and resistance pattern of multiple antibiotics against Klebsiella showed that majority of antibiotics were resistant to Klebsiella. The highest resistance was noted with amoxicillin that was 90%, followed by amoxiclave, nitrofurantoin, doxycycline, ceftazidime and ciprofloxacin with frequency of 86%, 75%, 64% 56% and 54% respectively. On the other hand, combination

of Ceftolozane and tazobactam were highly sensitive against klebsiella followed by fosfomycin, Imipenem and combination of piperacillin and tazobactam with frequency of 95%, 89%, 88% and 68% respectively.

**Conclusion:** It can be concluded that klebsiella species have developed high resistance against a number of antibiotics resulting in high morbidity and mortality. Currently combination of Ceftolozane and tazobactam is highly sensitive so it should be preserved as a future lifesaving drug. Beside this, fosfomycin, Imipenem and combination of piperacillin and tazobactam also reported high sensitivity.

**Keywords:** Klebsiella species, Multidrug resistance, Ceftolozane/tazobactam.

## **Introduction**

Bacterial infection caused by any type of bacteria is primarily treated with antibiotics (1). In medical science, the identification and formation of new antibiotics are the need of current era as these are the lifesaving drugs which fight against multiple infections (2). On the other hand, resistance against these antibiotics is also increasing day by day, which is developing a global threat. There are multiple reasons behind this rise in resistance these include excessive misuse, frequent intake in infections, delayed use and use in those infections where already antibiotics fails to respond (3). Current era is the challenging one for the medical physician to cure the infections because of development of antibiotic resistance.

Multi-drug resistance (MDR) is labelled when there is resistance for more than two antibiotics simultaneously. There are few underlying mechanisms including antimicrobial enzymes formation, mutated bacterial protein which bind with penicillin, extrusion of efflux pump, or mutated genes (4). MDR organisms are increasing rapidly in developing countries which is a troublesome condition, producing difficulty in treating infection and creating risk of patient's life (5).

The most common cause of hospital and community acquired infection is *Klebsiella pneumoniae*, which is an encapsulated, gram negative anaerobic bacteria. Most commonly it is involved in urinary tract infections, intraabdominal infections, wound infection, pneumonia, septicemia and many other pyogenic infections (6). *Klebsiella* specie is resistant to majority of antibiotics like ampicillin, quinolones and aminoglycosides. The mechanism of resistance by *klebsiella* is mediated by plasmids, transposons and gene mutation (7, 8). Carbapenems are used for treating MDR *klebsiella* but recently resistance against carbapenems are also reported leading to increase

in morbidity and mortality rates (9). So the aim of current study is to find out the prevalence and susceptibility of MDR klebsiella isolates in Karachi.

## **Material and Methods**

A pre-clinical in-vitro study was conducted at the microbiology lab of the tertiary care hospital of Karachi during May to October 2021. Study got approval from the ethical review committee of concerned hospital. About 550 samples of blood, urine and wound swab was collected and culture and sensitivity was performed as per guidelines.

The samples were inoculated on blood agar and MacConkey agar and incubated at 37° Celsius for 24 hours. On the basis of their dome-shaped colonies on blood agar and fermenting mucoid colonies on MacConkey agar, the Klebsiella species were identified. The antibiotic susceptibility was identified by Kirby Bauer's disc diffusion method. A bacterial inoculum lawn was created on a 150 mm Mueller Hinton Agar plate. Antibiotic disc of Amoxicillin 20 µg, Fosfomycin 200 µg, Ciprofloxacin 5 µg, Moxifloxacin µg, Gentamicin 10 µg and Ceftolozane/tazobactam (30/10 µg) were placed on agar plate and then incubated at 35°C for 16-24 hours. According to CLSI recommendations (2018), the zones of growth inhibition around each antibiotic disc were quantified and designated as either sensitive or resistant.

Data was analyzed by using Statistical Package for Social Sciences (SPSS) version 20. Categorical variables were presented as frequencies and percentages.

## **Results**

About 550 strains of Klebsiella were isolated out of which 35% (195) were MDR Klebsiella while 64% (355) were non-MDR. Gender wise distribution revealed that majority of strains were of female and mostly were having MDR Klebsiella as mentioned in Table I.

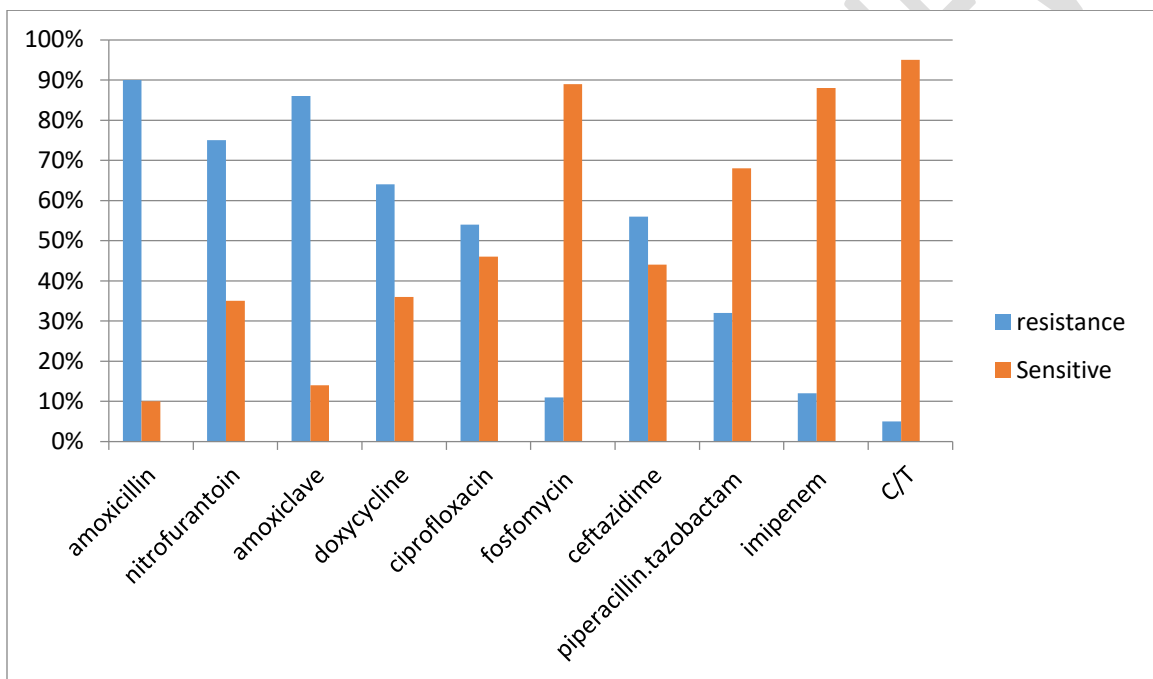
Table-I: Total samples of Klebsiella		
Total Sample	MDR	Non- MDR
550	195(35%)	355(64%)
Male 189	75 (39%)	114(60%)
Female 361	155 (42.9%)	206 (57%)

Blood, mucous and urine sample was used to isolate the Klebsiella species, majority were found in urine sample, out of which 80% were MDR. All the samples of blood, mucous and urine were predominantly having MDR strains with frequency of 65%, 56% and 80% respectively as reported in Table II.

Table-II: Frequency of MDR Klebsiella. in specimen.			
Source	Total Samples	MDR	Non- MDR
	550	195(35%)	355(64%)
Urine	235(42%)	190(80%)	45(20%)
Mucous	196 (35%)	110(56%)	86(43.8%)
Blood	119(22%)	78(65%)	41(35%)

Sensitivity and resistance pattern of multiple antibiotics against Klebsiella have been shown in Figure 1, among them majority of antibiotics were resistant to Klebsiella. The highest resistance

against *Klebsiella*, was noted with amoxicillin that was 90%, followed by amoxiclavate, nitrofurantoin, doxycycline, ceftazidime and ciprofloxacin with frequency of 86%, 75%, 64% 56% and 54% respectively. On the other hand, combination of Ceftolozane and tazobactam were highly sensitive against *klebsiella* followed by fosfomycin, Imipenem and combination of piperacillin and tazobactam with frequency of 95%, 89%, 88% and 68% respectively.



**Figure 1. Sensitivity and resistance pattern of multiple antibiotics against *Klebsiella***

## Discussion

*Klebsiella pneumoniae* is one of the most common cause of hospital or community acquired infections, as it is the second most common cause of urinary tract infection (10). The rate of morbidity and mortality is increasing day by day because of this specie along with increasing the resistance against antibiotics (11, 12). The current study found female predominance but the

literature contradict this finding by reporting higher prevalence of MDR klebsiella among males (13, 14). Current study reported that majority of MDR Klebsiella species were found in urine sample (80%), followed by blood (65%) and mucous (56%) but in India the majority of isolates were found in pus, then urine and then blood with frequency of 27.8%, 22% and 8% respectively (13, 15).

The current study highlights the increased prevalence of multidrug resistant klebsiella specie which is an alarming situation for not only the physician but for the community as well. Current study found 90% resistance against ampicillin while in North India 100% ampicillin resistance was noted (13). The reason for this high resistance might be the chromosomal mutation in  $\beta$ -lactamases (16). In India there is high resistance against few other antibiotics like amoxiclave and ciprofloxacin with frequency of 95% and 96% respectively (13, 17) but current study found amoxiclave with 86% resistance and ciprofloxacin with 54% resistance rate.

Current study reported Imipenem as a highly sensitive drugs, with 89% sensitivity against klebsiella species as majority of specimen responded well but in some regions of the world the resistance for carbapenem and Imipenem have been developed with rate of 81% and 89% respectively (13, 18, 19). The combination of Ceftolozane and tazobactam showed highest sensitivity against klebsiella specie in the current study with a rate of 95%. Randomized controlled trials revealed that this combination is 2 times more potent than any other antibiotic and having high clinical cure rates that is 97.4% (20).

## **Conclusion**

It can be concluded that klebsiella species have developed high resistance against a number of antibiotics resulting in high morbidity and mortality. Currently combination of Ceftolozane and

tazobactam is highly sensitive so it should be preserved as a future lifesaving drug. Beside this, fosfomycin, Imipenem and combination of piperacillin and tazobactam also reported high sensitivity.

UNDER PEER REVIEW

## Reference

1. Makabenta JMV, Nabawy A, Li C-H, Schmidt-Malan S, Patel R, Rotello VM. Nanomaterial-based therapeutics for antibiotic-resistant bacterial infections. *Nature Reviews Microbiology*. 2021;19(1):23-36.
2. Ventola CL. The antibiotic resistance crisis: part 1: causes and threats. *Pharmacy and therapeutics*. 2015;40(4):277.
3. Castro-Sánchez E, Moore LS, Husson F, Holmes AH. What are the factors driving antimicrobial resistance? Perspectives from a public event in London, England. *BMC infectious diseases*. 2016;16(1):1-5.
4. Hollis A, Ahmed Z. Preserving antibiotics, rationally. *New England Journal of Medicine*. 2013;369(26):2474-6.
5. Ayukekbong JA, Ntemgwa M, Atabe AN. The threat of antimicrobial resistance in developing countries: causes and control strategies. *Antimicrobial Resistance & Infection Control*. 2017;6(1):1-8.
6. Kapil A. Ananthanarayan & Paniker's Textbook of Microbiology. Published by Orient Black Swan Pvt Ltd (2013) ISBN. 2013;10:817371889X.
7. Borriello SP, Murray PR, Funke G. Topley & Wilson's Microbiology & Microbial Infections: Bacteriology: Wiley Online Library; 2005.
8. Kang HY, Jeong YS, Oh JY, Tae SH, Choi CH, Moon DC, et al. Characterization of antimicrobial resistance and class 1 integrons found in *Escherichia coli* isolates from humans and animals in Korea. *Journal of Antimicrobial Chemotherapy*. 2005;55(5):639-44.
9. Nordmann P, Cuzon G, Naas T. The real threat of *Klebsiella pneumoniae* carbapenemase-producing bacteria. *The Lancet infectious diseases*. 2009;9(4):228-36.
10. Peleg AY, Hooper DC. Hospital-acquired infections due to gram-negative bacteria. *New England Journal of Medicine*. 2010;362(19):1804-13.
11. Qin X, Wu S, Hao M, Zhu J, Ding B, Yang Y, et al. The colonization of carbapenem-resistant *Klebsiella pneumoniae*: epidemiology, resistance mechanisms, and risk factors in patients admitted to intensive care units in China. *The Journal of infectious diseases*. 2020;221(Supplement\_2):S206-S14.
12. Sarathbabu R, Ramani T, Rao KB, Panda S. Antibiotic susceptibility pattern of *Klebsiella pneumoniae* isolated from sputum, urine and pus samples. *IOSR J Pharm Biol Sci*. 2012;1(2):04-9.
13. Gupta S, Kashyap B. Bacteriological profile and antibiogram of blood culture isolates from a tertiary care hospital of North India. *Tropical Journal of Medical Research*. 2016;19(2):94-.
14. Sathyavathy K, Madhusudhan BK. Isolation, Identification, Speciation and Antibiotic Susceptibility Pattern of *Klebsiella* Species among Various Clinical Samples at Tertiary Care Hospital. *Journal of Pharmaceutical Research International*. 2021:78-87.
15. Biradar S, Roopa C. Isolation and antibiogram of *Klebsiella* species from various clinical specimens. *Int J Curr Microbiol App Sci*. 2015;4(9):991-5.
16. Sahly H, Aucken H, Benedi V, Forestier C, Fussing V, Hansen D, et al. Increased serum resistance in *Klebsiella pneumoniae* strains producing extended-spectrum  $\beta$ -lactamases. *Antimicrobial agents and chemotherapy*. 2004;48(9):3477-82.
17. Petri W. Penicillins, cephalosporins, and other  $\beta$ -lactam antibiotics. Goodman and Gilman's *The Pharmacological Basis of Therapeutics* 12th Ed McGraw-Hill, New York. 2011:1477-504.
18. Li Y, Shen H, Zhu C, Yu Y. Carbapenem-resistant *klebsiella pneumoniae* infections among ICU admission patients in Central China: prevalence and prediction model. *BioMed research international*. 2019;2019.
19. Nimer NA, Dayem SAA, AbouNouar GAK, Dakkah ANH. Evaluating antibiotic sensitivity patterns of *pseudomonas* in relation to specimen type in Jordanian Hospital. *JPMA*. 2019.

20. Popejoy MW, Paterson DL, Cloutier D, Huntington JA, Miller B, Bliss CA, et al. Efficacy of ceftolozane/tazobactam against urinary tract and intra-abdominal infections caused by ESBL-producing *Escherichia coli* and *Klebsiella pneumoniae*: a pooled analysis of Phase 3 clinical trials. *Journal of Antimicrobial Chemotherapy*. 2016;72(1):268-72.

UNDER PEER REVIEW