

Multidrug Resistance (MDR), Extensive Drug Resistance (XDR), And Pan Drug Resistance (PDR) *Klebsiella Pneumoniae* From Clinical Samples

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Abstract

Background: The spectrum of resistance to antibiotics by *Klebsiella pneumoniae* is gradually increasing. **Aim:** The objective of the study is to detect the resistance pattern of *Klebsiella pneumoniae* in patients attending general hospitals, Azare Bauchi state Nigeria. **Method:** An antimicrobial sensitivity test was carried out to detect the susceptibility of *Klebsiella pneumoniae* to different classes of antibiotics as recommended by the CLSI guidelines. Basic culture techniques, Gram Staining, and biochemical tests were used to identify the isolates and the patterns of resistance to different classes of antibiotics were determined using the disc Antibiotic Susceptibility Test. **Results:** Fifty-two (52) bacterial isolates were identified from 60 urine samples, *Klebsiella pneumoniae* recorded the highest occurrences rate with 32 (61.5%) followed by *Escherichia coli* 8(15.4%), *Staphylococcus aureus* 7(13.5%) then *Streptococcus species* 5(9.6%). However, the identified isolates were higher in male patients with 30(69.7%) and 22 (42.3%) in female patients out of 52(100%). Amoxicillin and penicillin were resistant to Beta-lactam with 12 mm and 10 mm zone of inhibition, Levofloxacin is resistant to Fluoroquinolones with 5 mm zone of inhibition, Gentamycin and Streptomycin were resistant to Aminoglycoside were with 8mm and 2mm zone of inhibition and Erythromycin is resistant to Macrolide with 8 mm zone of inhibition. *K. pneumoniae* resistant to almost all classes of antibiotics was recorded, this implies that the rate of mortality and virulence of the pathogen is increasing thus; further research should be conducted on hypervirulent strain to compare virulence with resistivity.

Keywords: *Klebsiella pneumonia*, MDR, XDR, PDR.

1. Introduction

Antibiotic-resistant bacteria have become one of the main threats to human health. Reckless use and misuse of antimicrobials (WHO, 2021), includes the use of antibiotics in animal feed (Timothy *et al.*, 2012), over-prescription of antibiotics, poor infection control in health care, hygiene, and sanitation (Maillard *et al.*, 2020). These and the ability of bacteria to acquire multiple resistance genes by bacteria may lead to the development of Extensive and Pan drug-resistant strains. Hudson *et al.*, (2014) categorize this drug-resistant into three and define them as follow: Multi-Drug Resistance (MDR) defined as non-susceptibility to at least two or more antimicrobial agent in a particular family, Extensive Drug Resistance (XDR) is non-susceptibility to at least one agent in two or fewer antimicrobial families while Pan Drug resistance (PDR) refers to isolate that is nonsusceptible to one or two agents in all the antimicrobial families.

Classic *Klebsiella pneumoniae* strains are opportunistic bacteria infecting immune-compromised individuals in both community and hospital settings (Pamakova, 2012). CKp acquires resistance genes through plasmid transfer, some encode multiple antibiotics resistance. Recent evidence implicates human misuse and plasmids as the primary source of the resistance genes (Ma *et al.*, 2021).

The concepts of PDR and XDR are dynamic and changing as a result of the available antimicrobial categories, which vary with time and country (Sahah *et al.*, 2021). Drug Resistance usually emerges among gram-negative bacilli, especially *Enterobacteriaceae* because of their prevalence in hospital settings (Ruppé, 2015). Antimicrobial monotherapy, including the old drug such as polymyxin, may no longer provide satisfactory efficacy to cure bacterial infection (WHO, 2021). These resistances have contributed to the development of hypervirulent *Klebsiella pneumonia* (hvKp) which can infect both immunocompetent and immunosuppressed individuals (Pamakova, 2012).

HvKp strain has been discovered all around the globe resisting almost all recurrent use antimicrobial agents most especially in Africa and China (Reshman *et al.*, 2020) Considering the danger force by hvKp and its resistance to the available antibiotics, this study seeks to isolate, identify and categories the susceptibility profile of Hyper-virulent *Klebsiella pneumonia* to the available drugs. This and scarce literature on multiple-drug-resistant *Klebsiella pneumoniae* in Azare and its environs necessitate this study.

2.0 Materials and method

2.1 Study Area

The general hospital Azare is located in Azare Bauchi state Nigeria on latitudes 11°40'27"N, 100°11'28"E and longitude 11.67417° N, 10.191110E. The hospital has a pathology unit with microbiology, parasitological, and chemical pathology laboratory saddle with diagnosing many patients from the metropolis and environs.

2.2 Sample Size

The sample size for this research was determined using Sarmukaddam and Gerald, 2006 formula for sample size determination. The sample was calculated at a 95% confidence level and a previous prevalence rate of 4.2% for *Klebsiella pneumonia* in the study area

$$N = \frac{Z^2 (P) Q}{L^2}$$

Where N= Sample size

Z= Statistics for a level of 95% confidence interval = 1.96

P= Prevalence rate of multidrug resistant *Klebsiella pneumoniae* from previous studies = 4.2%.

L = level of significance (allowable error) = 5% or 0.05

Q= 1-p

$$N = \frac{(1.96^2) \times 0.04 \times (1-0.02)}{(0.05)^2}$$

$$= \frac{3.8416 \times 0.04 \times 0.98}{0.0025}$$

$$N = 60.24$$

2.3 Sample Collection

Midstream urine samples were collected in sterile wide mouth containers from both male and female patients within all age groups attending General Hospital Azare and immediately transported to the Bauchi state university, Microbiology laboratory for further processing.

2.4 Gram staining

A drop of sterile distilled water was placed on a clean grease-free slide. The inoculated loop is heated until it becomes red. The loop was allowed to cool and bacterial isolates were picked and smeared on the drop of water on the slide. The slide was air dry and fixed by gentle heating. The slide was then flooded with crystal violet for 1 min. The stain was washed off with an excess of distilled water. Gram's iodine was poured over the slide for 1 min. The slide was then washed and stained with ethyl alcohol. Finally, counterstaining was done with safranin for the 30s. Slides were washed again and observed under the microscope oil immersion X100 objective lens. The gram-positive organisms appear purple while the gram-negative organisms appear red.

2.5 Biochemical Test

2.5.1 Catalase Test

A small amount of overnight pure isolate was transferred to the surface of a clean, dry glass slide using a sterile loop; a drop of 3% H₂O₂ was placed on the slide and mixed. A positive result was identified by the rapid rise of oxygen within 10 seconds as evidenced by bubbling.

2.5.2 Coagulase Test

An overnight culture was placed using a sterile wire loop in a test tube containing 2mls of serum, coagulase-positive bacteria secrete Coagulase enzyme which coagulates the serum by activating prothrombin.

2.5.3 Indole Test

Using a sterile wire loop a peck of an overnight pure culture was transferred on Tryptone broth and incubated at 37°C for 24 hours. After incubation, 5 drops of Kovac's reagent were placed into the test tube, Indole production is indicated by the production of pink to red color. The result was compared with the control test tube.

2.5.4 Methyl red and Voges Proskauer Test

Two test tubes containing MR-VP Broth were inoculated with overnight pure culture and were incubated at 35 °C for 24 hours. A few drops of the methyl red indicator solution (C.I. Acid Red 2 or methyl red reagent) were added to the first tube for the Methyl Red test while Barrett's A and Barrett's B reagents. (5% alpha-naphthol, followed by 0.2 mL of 40% KOH) were added to the second tube for the Voges-Proskauer test following the method of Lautenbach *et al.*, (2002).

2.5.5 Citrate Test

Koser's citrate medium was prepared by weighing 2.5g of Sodium citrate, 1.5g of Ammonium Phosphate, 0.2g of Magnesium sulfate, 1g of Potassium Dehydrogenate Phosphate, and 0.1g of Bromothymolblue and dissolved in 1 liter of distilled water, homogenized and dispensed into test tubes then, the test tubes were corked with cotton wool. A peck of each isolate was inoculated into Koser's citrate medium and incubated at 37°C for 72 hours.

2.6 Antimicrobial Susceptibility Test

Klebsiella pneumoniae isolates were subjected to an antibiotic susceptibility test using the Kirby-Bauer disc diffusion method as per the CLSI guidelines. The turbidity of inoculums was adjusted to 0.5 McFarland's standard. Then isolates were inoculated on a Muller-Hinton agar plate.

2.6.1 Multidrug-Resistant Assay for *Klebsiella pneumoniae*

Amoxicillin, Penicillin, Rocephin Antibiotic discs from Beta-lactam class were placed using sterile forceps and pressed gently to confirm proper contact with the medium and incubated at 37 for 24 hrs. The zone of inhibition was measured and interpreted.

2.6.2 Extensive drug Resistant Assay for *Klebsiella pneumoniae*

Antibiotic discs, three each from Beta-lactam, Fluoroquinolones, and Aminoglycoside classes were placed using sterile forceps and pressed gently to confirm proper contact with the medium and incubated at 37 for 24 hrs. The zone of inhibition was measured and interpreted.

2.6.3 Pan drug Resistant Assay for *Klebsiella pneumoniae*

Antibiotic discs, three each from Beta-lactam, Fluoroquinolones, Aminoglycoside, and Macrolides classes were placed using sterile forceps and pressed gently to confirm proper contact with the medium and incubated at 37 for 24 hrs. The zone of inhibition was measured and interpreted.

Categorize using Hudson *et al.*; (2014) establish a definition for MDR, XDR, and PDR

3.0 Results

3.1 Characteristics of the sampled population

Out of the Sixty (60), samples collected 22(36.7%) were male while 38(63.3%) were female, most of the patients were from age group 31-40 years and above 41 years however, there were few patients in the age group 11-20 year and not in the age group below 10 years as presented in table 1.

Table 1: Characteristics of the test population

Age	Sex		Frequency
	Male	Female	
≤ 10	0	0	0(0%)
11-20	6	1	7(11.7)
21-30	7	8	15(25%)
31-40	7	12	19(31.7%)
≥ 41	2	17	19(31.7%)
Total	22	38	60(100%)

3.2 Distribution of positive isolates by Age and Sex of the patients

Fifty-two (52) bacterial isolates were identified from 60 urine samples, *Klebsiella pneumoniae* recorded the highest occurrences rate with 32 (61.5%) followed by *Escherichia coli* 8(15.4%), *Staphylococcus aureus* 7(13.5%) then *Streptococcus species* 5(9.6%). However, the identified isolates were higher in male patients with 30(69.7%) and 22 (42.3%) in female patients out of 52(100%) as shown in table 2.

Table 2: Distribution of positive isolates by Age and Sex of the patients

Isolates	Sex		Frequency (%)
	Male	Female	
<i>Staph. Aureus</i>	4	3	7(13.5%)
<i>Escherichia coli</i>	2	6	8(15.4%)
<i>Klebsiella pneumonia</i>	22	10	32(61.5%)
<i>Streptococcus species</i>	2	3	5(9.6%)
Total	30	22	52(100%)

3.3 Distribution of *Klebsiella pneumoniae* by type of Resistance

Figure 1, shows a distribution of 32 *Klebsiella pneumoniae* isolates by the types of resistance, 3 (9.4%) are pan-drug resistant strain, 10(31.2%) were extended-drug resistant strain while 19 (59.3%) were multidrug-resistant strain out of the 32(100%) positive *Klebsiella pneumoniae*.

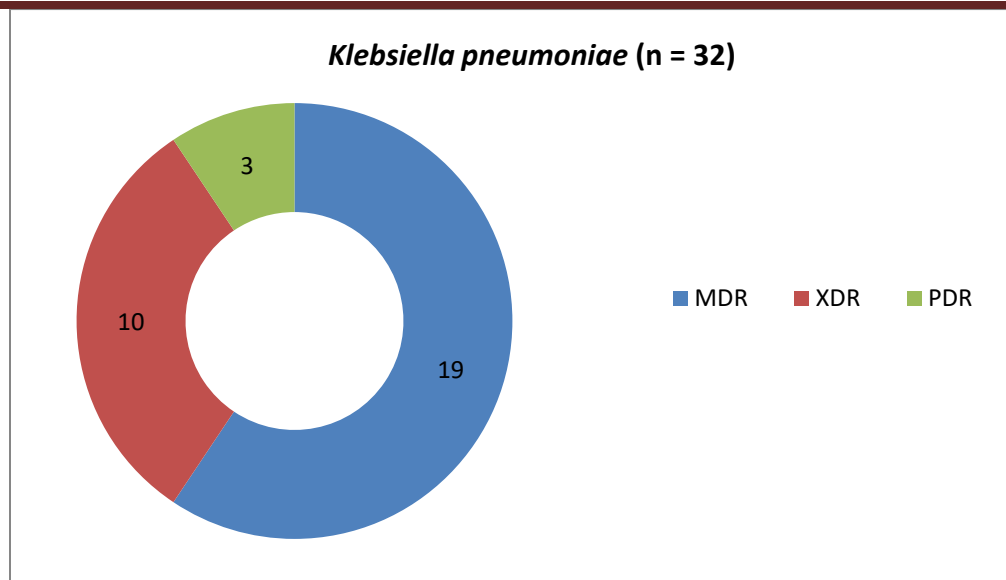


Figure 1: Distribution of *Klebsiella pneumoniae* by type of Resistance

Key:

MDR Multi-Drug Resistance
XDR Extended-Drug Resistance
PDR Pan-Drug Resistance

3.4 Antibiotic Susceptibility pattern *Klebsiella pneumoniae* by different classes of antibiotics

Out of the thirty-two (32), *Klebsiella pneumoniae* isolates tested for susceptibility to Beta-Lactam class of antibiotics, Amoxicillin and penicillin were resistant with 12 mm and 10 mm zone of inhibition while Rocephin was intermediate with 16mm zone of inhibition as presented in table 3. From table 4, Levofloxacin is resistant to fluoroquinolones with a 5 mm zone of inhibition, while Ofloxacin and Ciprofloxacin were intermediate with 14mm and 15 mm zone of inhibition. Gentamycin and Streptomycin were resistant to Aminoglycoside were with 8mm and 2mm zone of inhibition and Erythromycin is resistant to Macrolide with 8 mm zone of inhibition. The antibiotics were resistant to most of the *Klebsiella pneumoniae* isolates. The pattern of the resistance is reported based on the CLSI standard as shown in table 5. However, *Klebsiella pneumoniae* resist almost all the antibiotics whereas Rocephin with 16mm, Ofloxacin with 15mm, and Ciprofloxacin 14mm zone of inhibition were Intermediate while Streptomycin shows a high resistance susceptibility pattern. The equal resistant pattern was recorded in Beta-Lactams, Fluoroquinolones, Aminoglycoside, and Macrolide.

Table 3. Antibacterial activity of one class antibiotic on *Klebsiella pneumoniae* (MDR)

S/N	Antibiotic	Efficacy	Class	Zone Of Inhibition	Susceptibility
1	Amoxicillin	30 µg	Beta Lactams	12mm	Resistance
2	Penicillin	10 µg	Beta Lactams	10mm	Resistance
3	Rocephin	25 µg	Beta Lactams	16mm	Intermediate

Keys: Keys:

Based on CLSI Guideline:
Resistance <14mm,
Intermediate 14-18mm
Sensitive 19mm>

Table 4: Antibacterial activity of more than two classes of antibiotics on *Klebsiella pneumoniae* (XDR)

S/N	Antibiotic	Efficacy	Class	Zone of Inhibition	Susceptibility
1	Amoxicillin	30 µg	Beta Lactams	12mm	Resistance
2	Penicillin	10 µg	Beta Lactams	10mm	Resistance
3	Rocephin	25 µg	Beta Lactams	16mm	Intermediate
4	Ciprofloxacin	10 µg	Fluoroquinolones	14mm	Intermediate
5	Levofloxacin	30 µg	Fluoroquinolones	5mm	Resistance
6	Ofloxacin	10 µg	Fluoroquinolones	15mm	Intermediate
7	Gentamycin	10 µg	Aminoglycoside	8mm	Resistance
8	Streptomycin	10 µg	Aminoglycoside	2mm	Resistance

Keys:

Based on CLSI Guideline:

Resistance <14mm,

Intermediate 14-18mm

Sensitive 19mm>

Table 5: Antimicrobial activity of almost all classes of antibiotics on *Klebsiella pneumoniae* (PDR)

S/N	Antibiotic	Efficacy	Classes	Zone Of Inhibition	Susceptibility Pattern
1	Amoxicillin	30 µg	Beta Lactams	12mm	Resistance
2	Penicillin	10 µg	Beta Lactams	10mm	Resistance
3	Rocephin	25 µg	Beta Lactams	16mm	Intermediate
4	Ciprofloxacin	10 µg	Fluoroquinolones	14mm	Intermediate
5	Levofloxacin	30 µg	Fluoroquinolones	5mm	Resistance
6	Ofloxacin	10 µg	Fluoroquinolones	15mm	Intermediate
7	Gentamycin	10 µg	Aminoglycoside	8mm	Resistance
8	Streptomycin	30 µg	Aminoglycoside	2mm	Resistance
9	Erythromycin	10 µg	Macrolide	8mm	Resistance

Keys:

Based on CLSI Guideline:

Resistance <14mm,

Intermediate 14-18mm

Sensitive 19mm>

4.0 Discussion

4.1 Multidrug-Resistant *Klebsiella pneumoniae* (MDR-KP)

Resistant to commonly used antibiotics within the same class by *Klebsiella pneumoniae* is quite frequent in this part of the country. This study recorded a resistance to amoxicillin and penicillin which are the most prescribed antibiotics within the Beta-lactam class. A similar pattern was reported (Tugal *et al*; 2015). MDR-KP, when contracted, may be very difficult to treat or get rid of, Ireland factsheet on MDR-KP report that Taking antibiotics can encourage MDR-KP to multiply in the body, so they should only be taken for a much more serious reason. Antibiotics are available to treat MDR-KP infection but they probably will not clear MDR-KP entirely from the body. (Arena *et al*; 2021, Lemmen *et al*; 2014) report MDR-KP was treated using a combination of Ertapenem/meropenem on multiple occasions despite the elevated MICs.

4.2 Extended Drug-Resistant *Klebsiella pneumoniae* (XDR-KP)

This study utilizes frequently prescribed drugs from the classes of antibiotics tested, this drug might have been ineffective in the treatment of the most prevalent etiological agent causing community-acquired infection most especially enteric bacteria like *Klebsiella pneumoniae*, the resistance pattern recorded in this study is similar to what was reported by Silpi, *et al* (2016). Recent studies (Sahah *et al.*, 2021) report a case of XDR-KP in the united stated and, (Giovanni *et al.*, 2022, Yang *et al.*, 2007) in China which corroborates with this study, enteric bacteria resistant to an antibiotic within two or more classes have been increasing rapidly in many countries. The trend in the occurrences of XDR –KP indicates that they are most prevalent in nosocomial and pneumonia patients as reported (Wu *et al.*, 2021).

4.3 Pan Drug-Resistant *Klebsiella pneumoniae* (PDR-KP)

The quest in search of an effective drug for the treatment of excessive resistant strain might have been led to mismanagement of broad-spectrum antibiotics; this is creating bacterial strains that are resisting one or two antibiotics in almost every class of antibiotics. This trend is reported in India by Silpi, *et al.*, (2016) and, Anna *et al.*, (2021) in China. Ma *et al.*, (2021) and Zowawi *et al.*, (2015 explain that immunocompromised and drug addicts are at risk of harbouring pan-drug resistant bacterial strains because of their recurrent use of a drug or toxic substances.

5.0 Conclusion

Based on the findings of this study, we can conclude that out of every 60 clinical urine samples there are 50% enteric bacteria likewise out of every 30 nosocomial bacterial isolates there is 3 (9.4%) Pan-Drug resistant (PDR) strain. Thus, there is a need to search for other alternative treatments for Multidrug-resistant strains. This also justifies those resistant strains are becoming more difficult to cure. With Pan drug-resistant *Klebsiella pneumoniae*, almost all diseases caused by this bacterium will become life-threatening with increased mortality.

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References

- Arena, F., Coda, A.R.D., Meschini, V. (2021). Droplets generated from toilets during urination as a possible vehicle of carbapenem-resistant *Klebsiella pneumoniae*. *Antimicrob Resist Infect Control* 10, 149 <https://doi.org/10.1186/s13756-021-01023-5>
- Annie J Browne, Michael G Chipeta, Georgina Haines-Woodhouse, Emmanuelle P A Kumaran, Bahar H Kashef Hamadani, Sabra Zarea, Nathaniel J Henry, Aniruddha Deshpande, Robert C Reiner, Nicholas P J Day, Alan D Lopez, Susanna Dunachie, Catrin E Moore, Andy Stergachis, Simon I Hay, Christiane Dolecek (2021). Global antibiotic consumption and usage in humans, 2000–18: a spatial modelling study, *The Lancet Planetary Health*, 5(12) e893-e904, [https://doi.org/10.1016/S2542-5196\(21\)00280-1](https://doi.org/10.1016/S2542-5196(21)00280-1).



- Giovanni Lorenzin, Floriana Gona, Simone Battaglia, Andrea Spitaleri, Francesca Saluzzo, Alberto Trovato, Federico di Marco, Paola Cichero, Anna Biancardi, Paola Nizzero, Barbara Castiglione, Paolo Scarpellini, Matteo Moro, Daniela Maria Cirillo, (2022). Detection of NDM-1/5 and OXA-48 co-producing extensively drug-resistant hypervirulent *Klebsiella pneumoniae* in Northern Italy. *Journal of Global Antimicrobial Resistance*, 28, 146-150, <https://doi.org/10.1016/j.jgar.2022.01.001>.
- Lee, S. S., Chen, Y. S., Tsai, H. C., Wann, S. R., Lin, H. H., Huang, C. K., & Liu, Y. C. (2008). Predictors of septic metastatic infection and mortality among patients with *Klebsiella pneumoniae* liver abscess. *Clinical infectious diseases: an official publication of the Infectious Diseases Society of America*, 47(5), 642–650. <https://doi.org/10.1086/590932>
- Lemmen, S. W., Heffner, H., Zolldann, D., Stanzel, S., & Lütticken, R. (2004). Distribution of multi-resistant Gram-negative versus Gram-positive bacteria in the hospital inanimate environment. *The Journal of hospital infection*, 56(3), 191–197. <https://doi.org/10.1016/j.jhin.2003.12.004>
- Lin, Y. T., Wang, F. D., Wu, P. F., & Fung, C. P. (2013). *Klebsiella pneumoniae* liver abscess in diabetic patients: association of glycaemic control with the clinical characteristics. *BMC infectious diseases*, 13, 56. <https://doi.org/10.1186/1471-2334-13-56>
- Ma, F., Xu, S., Tang, Z., Li, Z., & Zhang, L. (2021). Use of antimicrobials in food animals and impact of transmission of antimicrobial resistance on humans. *Biosafety and Health*, 3(1), 32–38. <https://doi.org/https://doi.org/10.1016/j.bsheal.2020.09.004>
- Maillard, J. Y., Bloomfield, S. F., Courvalin, P., Essack, S. Y., Gandra, S., Gerba, C. P., Rubino, J. R., & Scott, E. A. (2020). Reducing antibiotic prescribing and addressing the global problem of antibiotic resistance by targeted hygiene in the home and everyday life settings: A position paper. *American journal of infection control*, 48(9), 1090–1099. <https://doi.org/10.1016/j.ajic.2020.04.011>
- Pamakova, D. (2012). Clinical and phenotypic differences between classic and hypervirulent *Klebsiella pneumoniae*. *European Journal of Clinical Microbiology*, 981-9.
- Ruppé, É. W. (2015). Mechanisms of antimicrobial resistance in Gram-negative bacilli. . *Annals of intensive care*, 5(1), 61.
- Reshma Silvester, Ajin Madhavan, Aswin Kokkat, Ajilesh Parolla, Adarsh B.M., Harikrishnan M., Mohamed Hatha Abdulla (2022). Global surveillance of antimicrobial resistance and hypervirulence in *Klebsiella pneumoniae* from LMICs: An in-silico approach, *Science of The Total Environment*, 802, 149859, <https://doi.org/10.1016/j.scitotenv.2021.149859>.
- Saha, M., & Sarkar, A. (2021). Review on Multiple Facets of Drug Resistance: A Rising Challenge in the 21st Century. *Journal of Xenobiotics*, 11(4), 197–214. MDPI AG. Retrieved from <http://dx.doi.org/10.3390/jox11040013>
- Sarmukaddam and Gerald, (2010). Functional classification of beta-lactamases. *Antimicrobial Agents Chemotherapy*. 54(3):969-76. <https://doi: 10.1128/ AAC.01009-09>.
- Silpi Basak, Priyanka Singh, and Monali Rajurkar, (2016). Multidrug-Resistant and Extensively Drug-Resistant Bacteria: A Study. Volume 2016, Article ID 4065603, 5 pages <http://dx.doi.org/10.1155/2016/4065603>.
- Tugal, D., Lynch, M., Hujer, A. M., Rudin, S., Perez, F., & Bonomo, R. A. (2015). Multi-drug-resistant *Klebsiella pneumoniae* pancreatitis: a new challenge in a serious surgical infection. *Surgical infections*, 16(2), 188-93.



- Timothy F. Landers, B. C. (2012). A review of antibiotic Use in Food Animals, perspective, Policy, and Potential. *Public Health Report*, 4_22.
- WHO. (2021, 11 17). *Antimicrobial resistance* . Retrieved 3 19, 2022, from World Health Organisation : https://www.who.int/news_room/fact_sheet/antimicrobial_resistance
- Wu, X., Shi, Q., Shen, S., Huang, C., & Wu, H. (2021). Clinical and Bacterial Characteristics of *Klebsiella pneumoniae* Affecting 30-Day Mortality in Patients With Bloodstream Infection. *Frontiers in Cellular and Infection Microbiology*, 11. <https://doi.org/10.3389/fcimb.2021.688989>
- Yang CS, Tsai HY, Sung CS, Lin KH, Lee FL, Hsu WM (2007). “Endogenous *Klebsiella* endophthalmitis associated with pyogenic liver abscess”. *Ophthalmology*; 114:876–80.
- Zowawi HM, Forde BM, Alfaresi M, Alzarouni A, Farahat Y, Chong TM, Yin WF, Chan KG, Li J, Schembri MA (2015)“Stepwise evolution of pan-drug- resistance in *Klebsiella pneumoniae*”. *Sci Rep*. 5: 15082