



Research Article

Isolation, Characterization and antibiotic susceptibility of *Klebsiella* species in urine samples of UTI patients visiting DHQ Hospital D.I. Khan Nameera Attiq¹| Zain ul Zahidin¹| Areeba Alizai²| Laiba Rasheed³| Hikmat Ullah¹| Anila Khan⁴| Saqib Ali Rustam¹| Sana Ullah¹| Aftab Ahmad Jan⁵| AttaUr Rehman^{1*}

¹Institute of Microbiology, Faculty of Veterinary and Animal Sciences Gomal University Dera Ismail Khan
Email: nameeraattiq002@gmail.com, zahidingul@gmail.com; hikmatullahdikhan@gmail.com dralirustam555@gmail.com dsm.lajpal@gmail.com arehman@gu.edu.pk

²Gomal Medical College Dera Ismail Khan
Email: alizaiareeba@gmail.com

³University of Agriculture Dera Ismail Khan
Email: rasheedlaiba61@gmail.com

⁴Institute of Biological Sciences Gomal University Dera Ismail Khan
Email: anila2638@gmail.com

⁵Lecture department of pharmacy Qurtuba University of science and information technology Dera Ismail Khan
Email: doctoraftab1989@gmail.com

Correspondence

Atta Ur Rehman
Email: arehman@gu.edu.pk

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1 | INTRODUCTION

A common health issue emerging across the globe, caused by pathogenic bacteria in the urinary tract of humans is Urinary Tract infection. The most common UTI causing pathogen is *E. coli* which is the cause of 75% of all bacterial UTI cases followed by other bacteria such as *Klebsiella*, *Proteus*, *Staphylococcus aureus*, *Pseudomonas*

ABSTRACT:

Background A gram-negative rod-shaped pathogenic bacterium-*Klebsiella*, repeatedly causing Urinary Tract Infection. **Objectives:** Isolation, Characterization and antibiotic susceptibility of *Klebsiella* species in urine samples of UTI patients. **Methodology:** For this purpose, a total of 105 samples were randomly collected from the patients with urinary tract complications visiting District Head Quarter Hospital D.I. Khan, Pakistan. **Results:** Urine samples with pus cells were inoculated on Cystine-lactose-electrolyte-deficient (CLED) agar and it was revealed that only 12 out of 105 samples were *Klebsiella* positive on the basis of cultural characteristics. Further confirmation was done using biochemical characterization through Analytical Profile Index (API 10) and out of 12 all the isolates were *Klebsiella pneumoniae*. Disc diffusion method was used to test the antibacterial susceptibility on Muller Hinton Agar. *Klebsiella* isolates showed 100% resistance to Cefepime, Cotrimoxazole and Ceftriaxone, 91% to Ampicillin, Doxycycline and Cefazoline and 83% to Piperacillin/Tazobactam, Imipenem, Ciprofloxacin and Gentamycin. Only two antibiotics Fosfomycin and Nitrofurantoin were two antibiotics *Klebsiella* isolates showing sensitivity. **Conclusion:** It is assumed that excessive use of antibiotics without proper diagnosis is among one of the main reasons responsible for antibiotic resistance.

KEYWORDS:

API 10E, CLED Agar, Disc Diffusion method, *Klebsiella* isolates, Urine samples

Aeruginosa and *Enterococcus* ¹. After *E.coli* cases of UTI by *Klebsiella* species are increasing very rapidly in health care settings ². Above 150 million people have UTIs each year across the globe. A positive urine culture, pyuria along with relevant sign and symptoms are needed to diagnose the presence of UTIs ³. Socio economic Factors play a vital role in risk of UTI ⁴ poverty and overcrowded living increase the likelihood of bacterial transmission, and untreated UTI and limited access to healthcare increase the risk of UTI ⁵ demographic factors may also make individuals more likely to cause UTI. Women are more vulnerable to UTIs than men due to Anatomical differences such as shorter urethra which allow the bacteria to colonize bladder more easily ⁶.

Klebsiella is a gram negative rod shaped bacterium, infecting multiple sites ⁷ of human body resulting into septicemia, UTIs and respiratory tract ailments ⁸. The bacterium was first identified by Edwin Klebs from the lungs of patients died from pneumonia ⁹. Most pathogenic *Klebsiella* species are *Klebsiella pneumoniae* and *Klebsiella Oxycota* with UTI causing rate of 68 % and 32% respectively ¹⁰. The multi drug resistant *Klebsiella* is causing UTI and nosocomial infections. By nature, *Klebsiella* species showing resistance to some classes of antibiotics known as intrinsic resistance ¹¹ such as production of beta lactam enzyme which resist the beta lactam antibiotics including penicillin and carbapenems ¹². Some important characteristics that help uropathogenic *Klebsiella* to colonize the human body are the production of adhesions, siderophores and toxins. Also, the bacterium sticks to the medical devices such as catheters and form biofilms, invading the host immune system and cause antibiotic resistance. Eighty percent of the population in Pakistan lacks access to laboratory microbiological diagnosis, thus doctors there often administer many antibiotics, contributing to the rise in antibiotic resistance. Examining the frequency of *Klebsiella* strains in medical centers is crucial, as ailments brought on by resistant organisms are far more common there. The incidence of *Klebsiella* species in UTIs is rising in Pakistan especially in the area like Dera Ismail Khanas documented by ¹³. The present study was conducted to find out and characterize *Klebsiella* species in UTI patients and the associated UTI patients and to evaluate the efficacy of routinely used antibiotics against the *Klebsiella* species.

2 | MATERIAL AND METHODS

2.1 | Study Area

The study was conducted at Dera Ismail Khan, Khyber Pakhtunkhwa. Samples were collected from patients visiting District Head Quarter (DHQ) Hospital Dera Ismail Khan from November 2023 to March 2024. The samples were collected in the sterile container with the age and name of patients labeled on it. The samples were transported to the Institute of Microbiology in an iced box for further processing. The samples were collected on various demographic parameters as under.

Table 1: Urine Sample Distribution on the basis of Gender, Age, Area and Educational Status

No. of samples	Gender		Age			Area based		Education based	
	Male	Female	<20	21-50	51-90	Urban	Rural	Literate	Illiterate
	42	63	10	63	32	64	41	64	41
Grand Total	105		105			105		105	

Table 1 shows that a total (N=105 samples) was collected from the patients, based on age, gender, residential area and level of education. Based on age, 10 samples were collected from <20 years, 63 from of 20-50 and 32 were collected from 51-90 years. Similarly, gender wise 64 samples collected from females and 41 from males based. Likewise, 64 and 41 samples were collected in urban and rural areas of District D.I. Khan respectively. On literacy basis 61 samples were collected from literate people and 44 were collected from illiterate people.

2.2 | Processing of Samples

The microscopic examination of each urine sample was performed for the presence of pus cells. Each urine sample having pus cells was further processed and inoculated on Cystine-lactose-electrolyte-deficient (CLED Oxoid Catalogue No. CM0423) media and placed in incubator for 24 hours. Large yellow and mucoid colonies indicated *Klebsiella* species which was further confirmed by Gram staining ¹⁴. The Gram stain (Microscope Catalogue No. IM57684) was used in this study. Following gram staining, the colonies were inoculated on MacConkey agar with the help of wire loop. Pink, mucoid, sticky colonies indicate the presence of gram-negative lactose fermenting *Klebsiella* species ¹⁴.

2.3 | Catalase Test and Oxidase Activity

With the help of a sterile loop a droplet of hydrogen peroxide (3%) was dropped on the bacterial colony and bubbles production indicated a positive reaction. A loopful culture from the selected a colony from a pure culture was placed wet filter paper and no color change on filter paper indicated the negative reaction.

2.4 | Analytical Profile Index (API)

A commercially available biochemical tests kit named as API 10E Kit was used differentiate various species of *Klebsiella isolates* on the basis their biochemical attribute including indole, lysine, citrate, urease, ONPG and other tests specific for specific bacterial species, are usually included in the API 10E Kit testing.

2.5 | Procedure

The selected colony from the media plate was suspended in an appropriate quantity of sterile water filled every well on the API 10E strip with the suspension following the instructions of the kit leaflet and strip was incubated for 24 hours. The change of color was noticed in every well and data was collected by repeating the procedure with each colony on MacConkey agar plate. The color change pattern on kit was read to get a profile number. To identify the organism, cross-reference the profile number with those found in a commercial codebook.

2.6 | Antibiotic Susceptibility Test

After the characterization of *Klebsiella* isolates through biochemical test, the antibiotic susceptibility of the bacteria was carried out by using the Kirby Bauer disc diffusion method on Muller Hinton Agar medium. Following 24-hour incubation at 37C, the zone of inhibition was determined through the recommended methodology of Clinical and Laboratory Standard Institute (CLSI). The antibiotics used in the current study are nitrofurantoin (300µg), imipenem (10µg), amikacin (30µg), gentamycin (10µg) and ceftriaxone (30µg)¹⁵. Piperacillin tazobactam (110µg), cefepime (30 µg), cefazolin (30 µg), cotrimoxazole (25 µg), ampicillin (10 µg)¹⁶ Fosfomycin (50 µg), ciprofloxacin (5 µg)¹⁷.

2.7 | Antibiotic Used

Following antibiotics are used in the current study to check the antimicrobial susceptibility of *Klebsiella* isolates.

Table 2: List of Antibiotics

Antibiotic group	Antibiotics	Abbreviation	Disc content
Penicillin	Pipra-Tazobactam	TZP	110µg
	Ampicillin	AMP	10µg
Cephalosporin	Ceftriaxone	CRO	30µg
	Cefepime	FEP	30µg
	Cefazoline	KZ	30µg
Aminoglycoside	Fosfomycin	FOS	50µg
	Amikacin	AK	30µg
	Gentamicin	CN	10µg
Nitrofurantoin	Nitrofurantoin	F	300µg
Tetracycline	Doxycycline	DO	30µg
Sulfonamide	Co-trimoxazole	CRO	25µg
Carbapenem	Imipenem	IMP	30µg
Fluoroquinolones	Ciprofloxacin	CIP	5 µg

3 | RESULTS AND DISCUSSION

Table 3 indicates the overall percentage of pus cell in the urine samples as 64.8% (68/105) and the prevalence of *Klebsiella* isolates as 17% (12/68) which is statistically significant (p = 0.007) as given below.

Table 3: Percentage of Pus Cells and *Klebsiella* Isolates through Biochemical Characterization

Variable	Response	Frequency (%)	<i>Klebsiella</i> +ve (%)	<i>Klebsiella</i> -ve (%)	X ²	Df	p-value
Pus cells presence	Yes	68(64.8)	12(17)	56(83)	7.372	1	0.007
	No	37(35.2)	0(0)	37(100)			
	Total	105(100)	12(11.4)	93(88.6)			

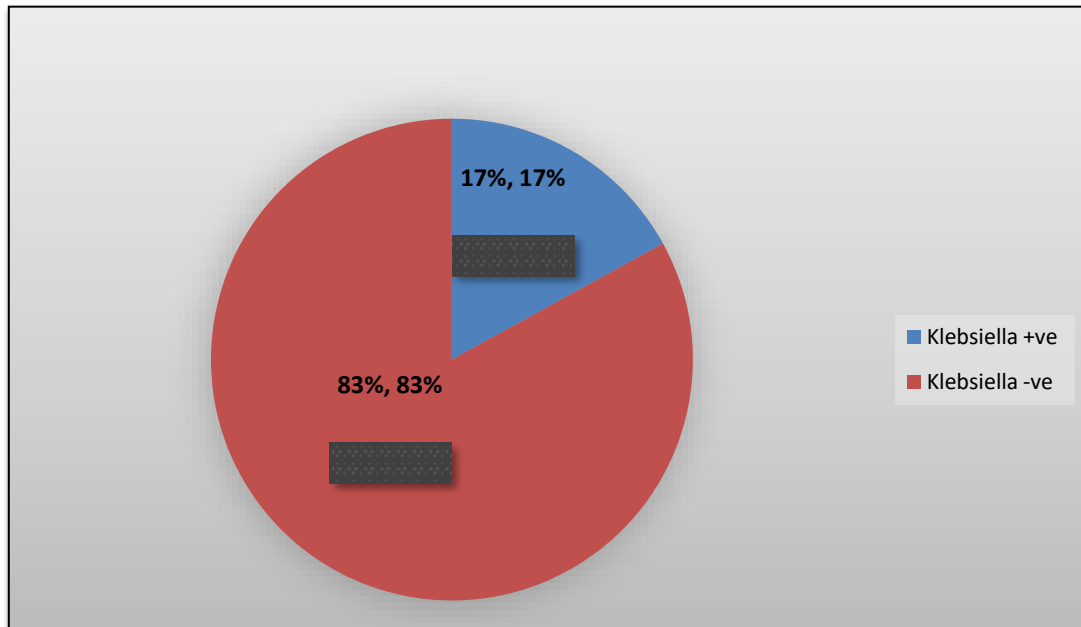


Figure 1: Prevalence of *Klebsiella* in UTIs

Results of Gram Staining

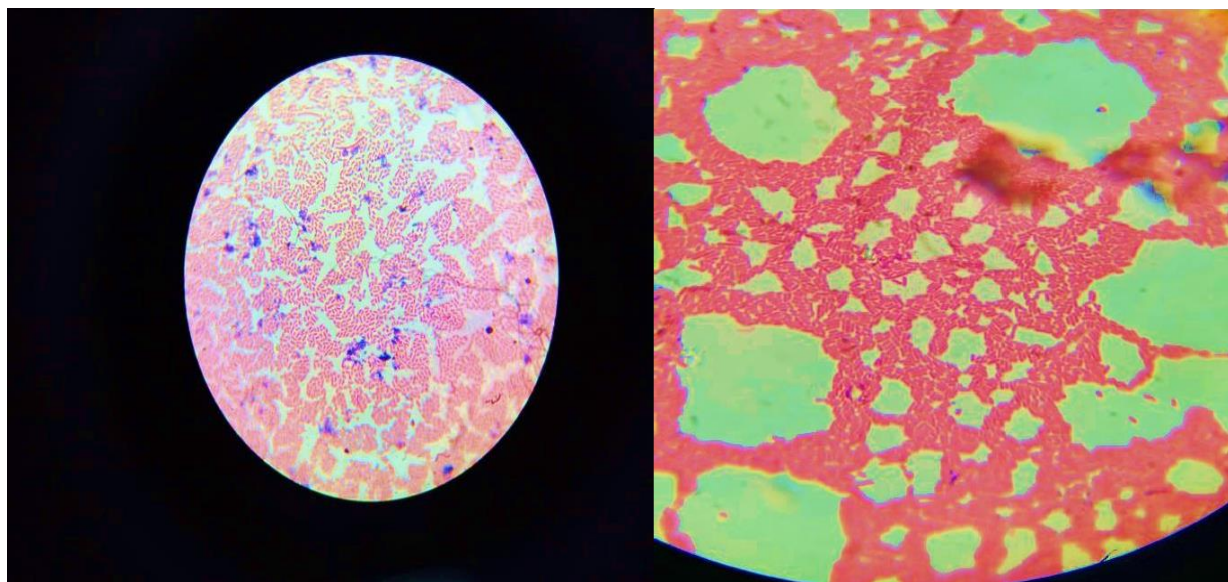


Fig 2: Showing the presence of Gram-Negative rod-shaped bacteria

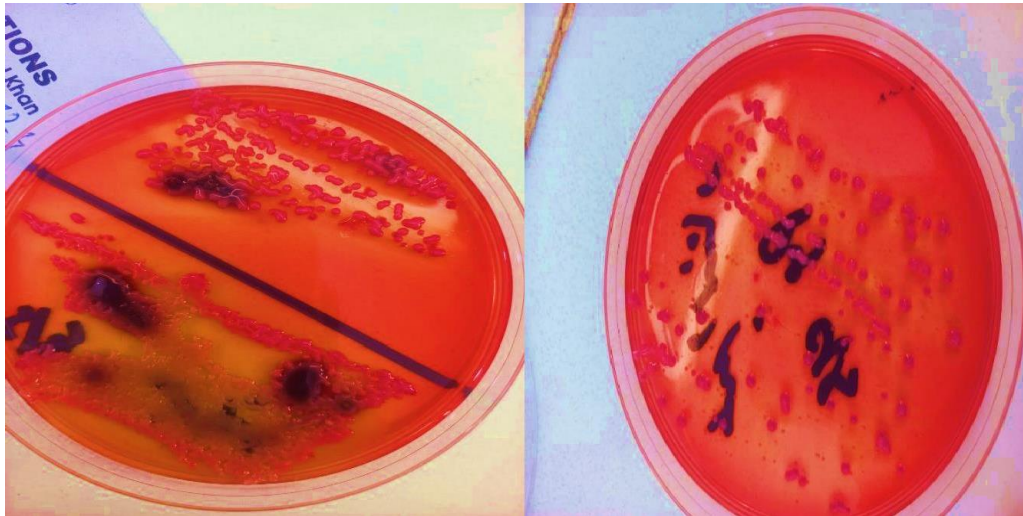


Fig 3: Typical colonies of *Klebsiella* on MacConkey Agar

3.1 | Biochemical Identification

Biochemical tests on the API 10E kit showed the following results which indicated that the isolated bacteria are *Klebsiella* isolates after cross checking the profile number given in the commercially available codebook.

Table 4: Indication of Biochemical Test results

Biochemical Tests	Results	Color Indication
ONPG	+ve	Yellow
GLU	+ve	Yellow
ARA	+ve	Yellow
LDC	+ve	Red
ODC	-ve	Yellow
CIT	+ve	Blue
H ₂ S	-ve	Colorless
URE	-ve	Yellow
TDA	-ve	Yellow
IND	-ve	Colorless
OX	-ve	No change in color
NO ₂	+ve	Bubble production



Figure 4: API 10E results

Table 4 shows the presence of pus cells in variables based on age, gender, area of residence and level of education. In age group under 20 years the population having pus cells is 40% (4/10), in age group 20-50 years the population having pus cells is 66% (42/63) and in age group 51- 90 years there is the prevalence of pus cells is 69% (22/32). Based on gender, the population having the higher prevalence of pus cells in their urine were female which is 72% (46/64) and the prevalence of UTI in male is 54% (22/41) having the significant difference (p=0.05).Likewise, based on area of residence the higher prevalence of 78% (32/41) in rural areas having the significant value (p=0.023) while in urban areas the prevalence of UTI is low as 56% (36/64).On the basis of level of education, the prevalence of UTI is 65% (40/61) and 64% (28/44) in literate and illiterate patients respectively.

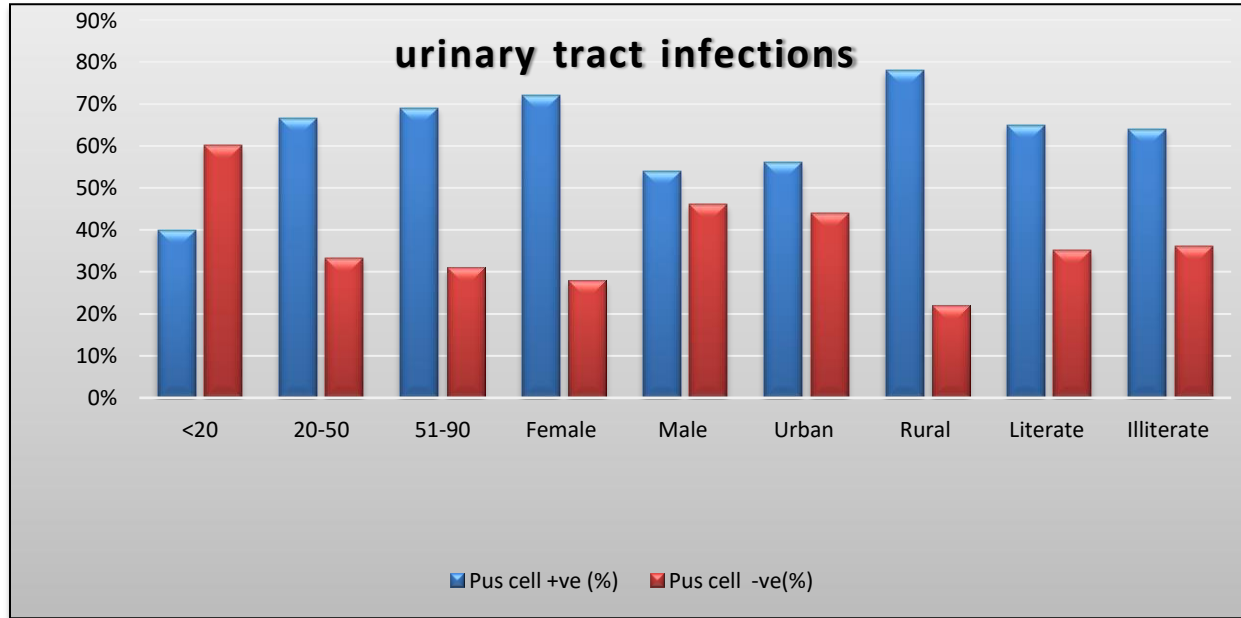


Figure 5: Prevalence of pus cells in the urine samples of various groups of patients

Table 5: Prevalence of *Klebsiella* in District D.I. Khan

Variable	Response	Positive (%)	Negative (%)	Total (%)	X2	Df	P-Value
Age	<20	1 (10)	9(90)	10 (100)	0.063	2	0.969
	20-50	7(11.11)	56(88.88)	63(100)			
	51-90	4(12.5)	28(87.5)	32(100)			
Gender	Female	9(14)	55(86)	64(100)	1.123	1	0.289
	Male	3(7.3)	38(92.6)	41(100)			
Area of Residence	Urban	9(14)	55(86)	64(100)	1.123	1	0.289
	Rural	3(7.3)	38(92.6)	41(100)			
Level of Education	Literate	6 (10)	55(90)	61(100)	0.365	1	0.546
	Illiterate	6(14)	38 (86)	44(100)			

Table 5 shows the prevalence of *Klebsiella* isolates in different demographic characteristics based on age, gender, area of residence and level of education, the results shows that presence of *Klebsiella* isolates in age groups as 10%, 11.11% and 12.5% in <20, 20-50 and 51-90 respectively. Based on gender the presence of *Klebsiella* isolates in female is 14% and in male is 7.3%. The prevalence of *Klebsiella* isolates in urban and rural areas was 14% and 7.3% respectively. The prevalence of *Klebsiella* isolates was as 10% (6/61) and 14% (6/44) in literate and illiterate patients respectively. The results of antibiotic susceptibility test indicate that *Klebsiella* isolates shows higher resistance against Cefepime, co-trimoxazole and ceftriaxone (100% resistance) having the significant p-value (p<0.001). *Klebsiella* isolates also shows higher resistance of 91% against Ampicillin, cefazoline and doxycycline. And 83% resistance against ciprofloxacin, gentamycin, piperacillin/tazobactam and imipenem with the significant p-value (<0.001). The results shows that *Klebsiella* is sensitive to Fosfomycin (83%), nitrofurantoin (58%) and amikacin (58%) with the significant p-value (<0.001).

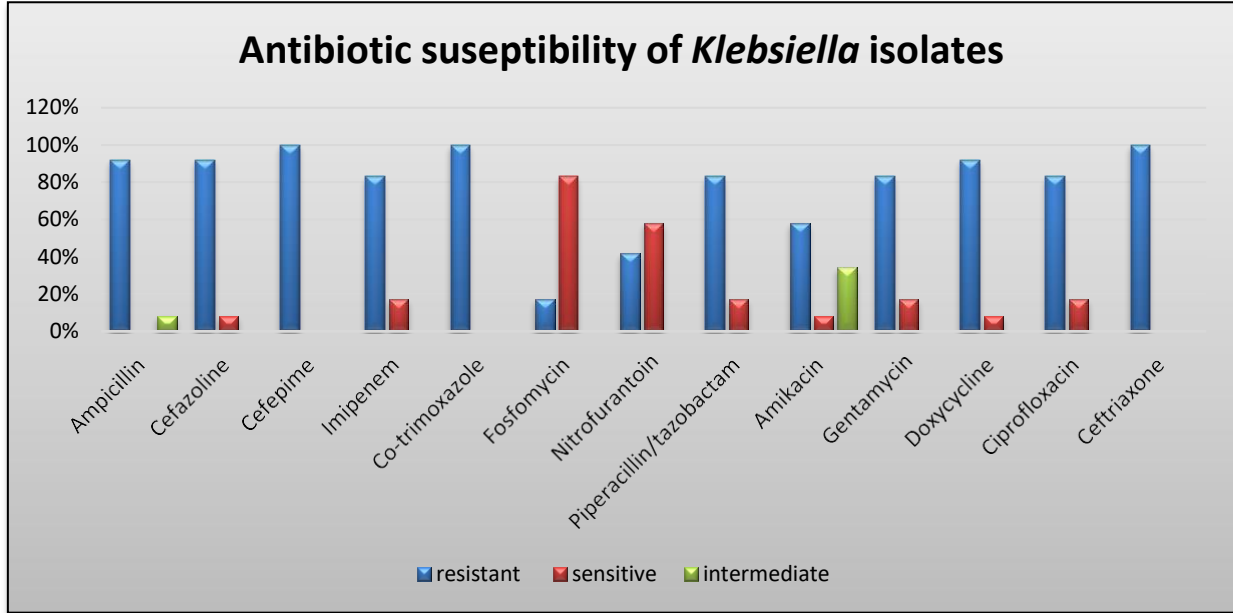


Figure 6: Results of antibiotic susceptibility against *Klebsiella* Isolates

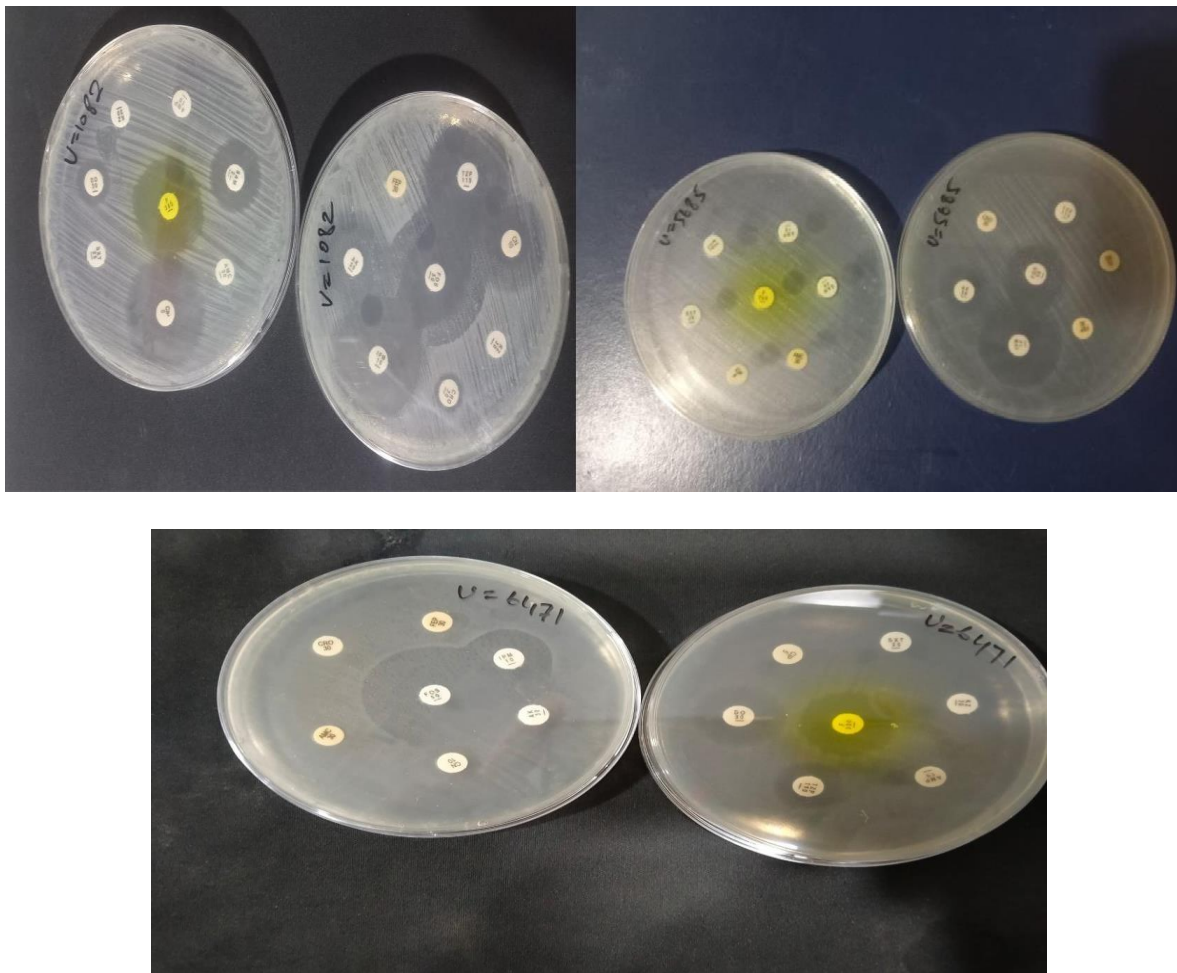


Figure 7: showing Antibiotic sensitivity of *Klebsiella* isolates

Common ailments caused by bacteria, in human beings, mostly Enterobacteriaceae, is UTIs. In direct microscopy the existence of pus cells also points out urinary tract infection. The primary aim of conducting the study was to determine the urinary tract infection (UTIs) incidence as well as the prevalence of *Klebsiella* spp: from the samples isolated from district D.I. Khan. The results indicated the abundance of UTI as 64.8% (68/105) and *Klebsiella* isolates as in the study area with a significant value ($p=0.007$) as indicated in Table 2 which is like the results documented by Plose *et al*; 2020¹⁵ as 61.9% UTI prevalence in Iraq. Table 2 also indicates the overall incidence of *Klebsiella* (in samples having pyuria), in the recent study is 17% (12/68). Similar results (16.86%) documented by Bobbadi *et al*; 2021¹⁸ in India. Another study by Plose *et al*; 2020¹⁵ showed the incidence of *Klebsiella* isolates in UTI is 16.17%. Research in Nigeria also indicated the 16% occurrence of *Klebsiella* in UTIs Mike-Ogburia *et al*; 2023¹⁹. In present investigation, the age group with the higher rate of UTI is 51-90 years which is 69% ($n=22/32$) and the least one 40% ($n=4/10$) in age group <20 years. The UTI occurrence in the age group 20-50 years is 66.6% ($n=42/63$), suggested that UTI can occur in any age but mostly it occurs in old age because the Immunity of the patients is low in elderly people. The findings of Kolawole *et al*;2009²⁰ in India also indicated 60% UTI prevalence in old age which coincides with present study. Wang *et al*; 2023²¹ also found similar type of results in Chaina indicated that the old age is the risk factor of UTIs. The results are parallel with the findings of Prakash and Saxena, 2013²² and Manzoor *et al*; 2020²³. Gender based findings in the recent study showed that UTI cases in female was higher (72%) with the significant P value ($p=0.05$) in comparison to male (54%).

These results are almost relatable to a study in Nigeria which indicated the incidence of UTI in female and male was 57% and 42% respectively Mike-Ogburia *et al*; 2023¹⁹. This study also comparable to a study of Kolawole *et al*;2009²⁰ from Nigeria showed 80% and 40% ratio in female and male respectively. A study in Lahore Pakistan also indicated female (69%) having UTI was at higher risk than males (30%) Manzoor *et al*; 2020²³. In same way, residence based prevalence of UTI in the current study showed that UTI is more prevalent in rural areas (78%) with the significant p value ($p=0.023$) than in the urban areas (56%) of the district D.I. Khan. the high number of UTI cases in rural areas may be due to poor sanitation or low standard of living, the result of this study is evident to the study conducted in Lahore, Pakistan which confirms that UTIs are mostly common in the rural areas Manzoor *et al*; 2020²³. Likewise, education-based results indicated no significant statistics in the occurrence of UTI in literate (65%) or illiterate (64%) population ($p=0.838$) the findings coincide with the findings of Mike-Ogburia *et al*; 2023¹⁹. But a study in India is unparallel to our research showing significant statistic in UTI prevalence in literate (53%) and illiterate (47%) Muthulakshmi and Gopalakrishnan, 2017²⁴. Table: 3 indicated that age-based frequency of *Klebsiella* isolates was 10% 11.11% and 12.5% in age groups <20 , 20-50 and 50 -90 years respectively, which is not significant statistically ($p=0.969$), showed that infection by *Klebsiella* can be occur in any age but the slightly difference in the percentage shows that it may infect elderly because the immunity in this age is lower. This result is identical to the study of Mike-Ogburia *et al*; 2023¹⁹ performed in the teaching Hospital in Nigeria. This result is also like the analysis of²⁵ in India which reveals that, prevalence of *Klebsiella* was higher at the old age. Individuals in this age have many ailments like diabetes which increases the risk of UTIs Devrari *et al*; 2018²⁵. The outcomes are relatable to the outcomes of comparative study of Jalal *et al*; 2023²⁶ conducted in the hospitals of Saudia Arabia.

Likewise, the intensity of *Klebsiella* isolates in female subjects is higher as 14% as compared to male as 7.5%, however, the percentage in the current study is not significant statistically ($p=0.289$) but results indicates that infection by *Klebsiella* isolates is most likely to cause in female the difference is due to the differences in anatomy of male and females, or *Klebsiella* infection is higher in female during pregnancy this study is comparable with the study conducted in hospitals at Najaf city, Iraq which also indicated the large number of *Klebsiella* isolates cases in female compared to male Hasan *et al*; 2021²⁷. In India research revealed that the *Klebsiella* isolates is high in female in contrast to male counterparts Rizwan *et al*; 2018¹⁶ the reason behind this may be the vaginal colonization with uropathogens or entry of pathogen into the bladder through urethra Rizwan *et al*; 2018¹⁶. Moreover, in the present study *Klebsiella* isolates showed higher ratio in Urban areas as 14% ($n=9$) in comparison with rural areas 7% ($n=3$), the result was not statistically significant ($p=0.546$), this investigation confirms previous study conducted in Pakistan by Mustafai *et al*; 2023²⁸ which shown 16.9% and 9.1% ratio of *Klebsiella* in urban and rural areas respectively. The reason behind the difference may be due to the exposure of antibiotics in the urban population is more than in rural population which can increase the risk of prolonged bacterial infection. Additionally, on literacy level, the incidence of *Klebsiella* isolates was 10% and 14% in literate and illiterate population respectively, not significant statistically ($p=0.546$). the study in India also showed the higher incidence of *Klebsiella* isolates in literate compared to illiterate Muthulakshmi and Gopalakrishnan, 2017²⁴. The conclusion also aligned with the outcomes of Mike-Ogburia *et al*; 2023¹⁹.

The antibiotic susceptibility pattern of *Klebsiella* isolates disclosed that the higher number as 100% isolates showed resistance to Ampicillin, cefepime, ceftazidime and doxycycline followed by ciprofloxacin, gentamycin, piperacillin/tazobactam and imipenem (83%). The antibiotic against which *Klebsiella* showed sensitivity were Fosfomycin (83%), nitrofurantoin (58%) and amikacin (58%) with the significant p-value (<0.001). The current findings regarding the susceptibility pattern displayed that *Klebsiella* isolates is multidrug resistance defined as opposing one antimicrobial agent at least in more than three antibiotic classes. The result complements to the data of Manjula *et al*; 2014²⁹, conducted a study in India to find the antimicrobial resistance pattern of *Klebsiella* isolates. A study in Saudia Arabia showed a significant increase in the resistance of *Klebsiella* isolates up to 84% against amoxicillin and Tazobactam and cefepime and imipenem Jalal *et al*; 2023²⁶. Another study in a hospital of Saudia Arabia by Al Bshabshe *et al*; 2020³⁰ finds out that *Klebsiella* shown 100% resistance against ampicillin and piperacillin. Simon-Oke *et al* 2019³¹ unveils that in Nigeria *Klebsiella* isolates shows 70% resistance against Augmentin, Chloramphenicol amoxycillin and gentamycin. The findings of³² indicates that in Pakistan *Klebsiella* isolates was showing resistance against Fosfomycin (22%).

4 | CONCLUSION

In the current study it was concluded that in UTI patients *Klebsiella* is present as a uropathogen, whose frequency is found to be higher in females and in elderly patients. It is also investigated that after biochemical identification *Klebsiella* is the most frequently infectious species in UTIs. Furthermore, the antibiotic susceptibility of *Klebsiella* isolates discloses that it is Multidrug Resistant (MDR), showing highest resistance against mostly prescribed antibiotics like Ampicillin imipenem doxycycline gentamycin cefepime. Nitrofurantoin and Fosfomycin are the two antibacterial drugs showing good results against uropathogenic *Klebsiella* isolates It is recommended that the lavish use of antibacterial should be prohibited and prior to any medication infection should be diagnosed properly, so that problem of increasing resistance to antibiotics will be eliminated.

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