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# Prevalence of antibiotic resistance pattern of bacteria isolated from urinary tract infection

**Nirupama Bhimani[a], Riteshkumar Arya[a], Prachi Dave [a], Bhavna Chaudhary[a], Komalben Hirani[b] & Navneet Kumar Singh[c]***

[a]Department of Microbiology, Mehsana Urban Institute of Sciences, Ganpat University, Mehsana, Gujarat, India.

[b]School of Biological Engineering & Life Sciences, Shobhit Institute of Engineering & Technology, Deemed to-Be-University, Modipuram, Meerut, India

[c]Department of Paramedical Sciences, Sumandeep Vidyapeeth Deemed University, Gujarat, India.

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**Abstract-** The present study was aimed to determine the resistance framework of pathogenic bacteria against common antibiotics isolated from the urine samples of patients suffering from an infection of urinary tract. The work was initiated by using 5 urine samples collected from the Pathology Laboratory of JNU Hospital, Jaipur. From those samples, 16 isolates were differentiated based on their morphology and biochemical characteristics. After tentative identification of isolates, an antibiotic sensitivity test was performed on those isolates by using the Kirby Buaer method and susceptibility profiles were identified using the minimum inhibitory concentration (MIC). The male and female both are infected with pathogenic bacteria which cause UTI. Biochemical reactions depicted that patients infected with bacteria were *Escherichia coli, Enterobacter spp., Klebsiella pneumonia, Pseudomonas aeruginosa, Staphylococcus spp., Streptococcus spp.* and *Enterococcus spp*. Based on the antibiotic susceptibility test using eight different antibiotics, three different isolates were found to be resistant to these antibiotics. Trimethoprim (TR-30), Gentamycin (HLG-120), Amoxicillin (AMX-10), Penicillin G (P-1), Ceftazidime (CAZ-30), Ciprofloxacin (CIP-5) and Erythromycin (E-5) were used for this study. This study exhibited the resistance rate of isolates against antibiotics which is a concern of worry for society.

**Key words: UTI (Urinary Tract Infection), Multidrug resistance, antibiotics, pathogenic bacteria.**

## INTRODUCTION

Urinary tract infections are a vital reason for illness in humans.[1] UTI is found to be a normal infection in the human population and it can be defined as an infection in any part of the urinary tract which is caused by bacteria.[2] Approximately 800 million people are infected with UTI every year throughout the world.[2] Liquid waste of the human body is generally called urine which circulates from blood to the kidneys. From the kidney, it transports to the ureters and from the ureters to the urinary bladder where it is stored before exclusion from the body via the urethra. Physiological valves detain the reverse stream of urine from the urinary bladder to the ureters and toward the kidneys. Kidneys are protected by this mechanism from lower urinary tract infection. In contrast, the acidity of normal urine contains some antimicrobial properties. Elimination of urine during urination removes possibly infectious microbes. The urinary system is composed of organs that

*Corresponding author :
Phone : 9898708184
E-mail : navneetspan@gmail.com

remove cellular metabolic waste products and water by regulating the volume of blood and chemical composition. Infection of the urinary tract can be generally classified as Upper UTI: involves the kidney or ureters acute pyelitis-infection of the pelvis of the kidney. Lower UTI: involve infection from the urinary bladder downwards. Infection of the urethra, urinary bladder and prostate respectively called Urethritis, Cystitis, and Prostatitis. The most common UTIs are those of the bladder (cystitis) and the renal pelvis or the kidneys (pyelonephritis).[1]

There are many options available to the treatment of UTI, from them very few are affectabale and use of drugs as a treatment is still conferring prominence. In the current study, we have studied 5 urine samples and isolated 16 isolates to check their antibiotic susceptibility test to find antibiotic resistance patterns of pathogenic bacteria. For that, we have used several antibiotics such as Trimethoprim (TR-30), Gentamicin (HLG-120), Streptomycin (HLS-300), Amoxicillin (AMX-10), Penicillin G (P-1), Ceftazidime (CAZ-30), Ciprofloxacin (CIP-5) and Erythromycin (E-5) (van Belkum, 2006).

**CAUSATIVE AGENT:**

The urinary tract is infected with Gram-positive and Gram-negative both types of bacteria. Among Gram-negative bacteria which can cause UTIs such as *Escherichia coli, Proteus* spp., *Pseudomonas aeruginosa, Acinetobacter spp., Klebsiella* spp., and *Enterobacter* spp. Some Gram-positive bacteria that also cause UTIs such as *Staphylococcus saprophyticus, Enterococcus* spp., *coagulase-negative Staphylococcus spp* and *Staphylococcus aureus.*[3] These are the general causative agents of UTI. Both uncomplicated as well as complicated UTIs, are caused by *E. coli* (75% and 65%), *Klebsiella pneumonia* (6% and 8%), and *Enterococcus* spp. (11 and ~6%), *Proteus mirabilis* and *Pseudomonas aeruginosa* are about 2% and the uncomplicated UTI caused by *S. saprophyticus* is about 6%.[2] Sometimes fungus and viruses are also able to cause UTIs such as *Candida albicans* and *Adenovirus*. In this study, we focus on the bacteria which infect the urinary tract.[4]

**MODE OF BACTERIAL RESISTANCE:**

Multidrug resistance is a major environmental issue nowadays. If a person with UTI was suggested by a doctor for 5 days of infection regarding medication course and who completed 3 days course of medicines after curing of infection, after that some bacteria remain in UT and which increase the chance of re-infection.[5] During division, one of the bacteria undergoes a mutation in its DNA that results in antibiotic resistance, when an antibiotic is added all of the sensitive bacteria are killed, and the antibiotic resistance mutated bacterium which is unaffected by antibiotics and they are continue to divide, forming a population of antibiotic resistance bacteria. In this manner, bacteria sow their resistance against many antibiotics.[6] In another way, bacteria follow resistance such as in the lag phase when bacteria adapt to a new environment, in that condition bacteria can develop tolerance against antibiotic stress and that allows bacteria to remain in high antibiotic concentration which may simplify the sequel development of antibiotic resistance.[1]

## MATERIALS & METHODS

**SAMPLE COLLECTION (n=5):**

Five urine samples were collected from the pathology laboratory of JNU Hospital of Jaipur, India. About 30-100 ml of midstream urine sample was collected aseptically in a sterile screw-cap tube after the initial flow was allowed to escape to avoid skin microflora and immediately processed appropriately.[7]

**ISOLATION OF BACTERIA FROM UTI:**

Urine samples were serially diluted up to $10^{-3}$ in sterile distilled water tubes and 0.1ml of prepared dilution was spread on the plate containing nutrient agar by a sterile L-shaped spreader using the spread plate technique.[8] Overnight 37°C incubation temperature was provided to the plates which were spread with the serially diluted sample. After the overnight incubation period, the distinct colonies were observed on N-agar plates, which were further sub-cultured on N-agar plates for a pure culture of each isolated colony (16) and incubated those plates for 24 hours at 37°C. The next day the plates were checked for colony characteristics (size, shape, margin, elevation, surface, consistency, odor, opacity and pigmentation).[9] After note downs of colony characteristics, Gram's staining was performed of each isolated colony for that on a cleaned glass slide drop of sterile distilled water was placed and then one loop of isolated colony mixed with water drop to prepare a smear and then heat-fixed the smear in medium flame then after a standard procedure of Gram's staining was followed.[10]

**BIOCHEMICAL CHARACTERIZATIONS:**

After the process of gram staining, isolates were checked for their catalase activity, and a catalase test was performed. A sugar fermentation test was performed for whether the isolates ferment sugar or not for that test glucose and lactose sugars were used. The standard microbiological methods for indole production, urea hydrolysis, citrate utilization, methyl red, Voges Proskauer, starch and gelatin hydrolysis were performed for tentative identification of bacteria using Bergey's Manual of Systematic Bacteriology (Volume 2, Parts A-C) following the methods of Rakesh Patel volume 1.[11]

**ANTIBIOTIC SUSCEPTIBILITY TEST:**

Tentatively identified bacteria were checked for their antibiotic susceptibility test for whether they were resistant or susceptible to various antibiotics. Each isolated bacterial suspension was spread on a plate containing Muller Hinton media.[12] Antibiotic disks were placed on the surface of agar on plates and were gently pressed. The antibiotics used were Trimethoprim (TR-30), Gentamicin (HLG-120), Amoxicillin (AMX-10), Penicillin G (P-1), Ceftazidime (CAZ-30), Ciprofloxacin (CIP-5) and Erythromycin (E-5). The plates were overnight incubated at 37°C. The next day overnight culture was observed for a zone of inhibition surrounding antibiotics and measured the zone of inhibition using zone measuring scale.[10] After the completion of the antibiotic susceptibility test, antibiotics were preferred from the panels of the Clinical and Laboratory Standard Institute (CLSI) which was appropriate for particular microorganisms; these were interpreted according to the MIC of particular antibiotics selected from CLSI.[9]

## RESULTS

In the present study, 16 isolates were isolated from 5 urine samples (3 female and 4 male). On sub-culturing of these 16 isolates, most of the bacteria showing similar cultural characteristics (small, round, entire, convex, smooth, translucent, and moist) on the nutrient agar plate. Gram staining shows both Gram-positive as well as Gram-negative bacteria arranged in a single, chain and clusters and gave cocci, large bacilli and small bacilli shapes. Based on biochemical reactions most of the bacteria were negative for urea hydrolysis test, M-R test, V-P test, catalase test and fermented sugar by homofermentative, detailed result expressed in Table 1.

**Table 1- Biochemical Reaction**

| Name of Biochemical test | Result | | | |
|---|---|---|---|---|
| Urea hydrolysis test | - | Sugar fermentation test | | |
| | | Sugars | Acid | Gas |
| M-R test | - | Lactose | + | - |
| V-P test | - | Glucose | + | - |
| Catalase test | - | - = Negative | | |
| Citrate test | - | + = Positive | | |

**Table 2- Antibiotic Susceptibility Test**

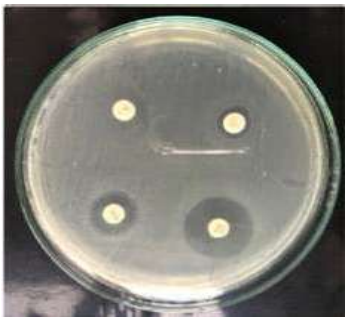
| Isolates | Name of antibiotics(µg/ml) and zone of inhibition (mm) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | TR- 30 | HLG-120 | AMX-10 | P-1 | CAZ-30 | CIP-5 | HLS-300 | E-5 |
| C1,s1 | 10mm/S | 30mm/S | 20mm/S | 12mm/R | 20mm/S | 12mm/R | 33mm/S | 08mm/R |
| C2,s1 | 10mm/R | 29mm/S | 16mm/I | 15mm/S | 11mm/R | 20mm/I | 30mm/S | 06mm/R |
| C3,s1 | 14mm/I | 27mm/S | 06mm/R | 03mm/R | 15mm/I | 10mm/R | 29mm/S | 02mm/R |
| C4,s1 | 17mm/S | 34mm/S | 14mm/I | 14mm/R | 18mm/S | 16mm/I | 32mm/S | 10mm/R |
| C5,s1 | 15mm/I | 31mm/S | 18mm/S | 10mm/R | 13mm/R | 18mm/I | 33mm/S | 06mm/R |
| C1,s2 | 14mm/I | 26mm/S | 11mm/R | 05mm/R | 17mm/I | 07mm/R | 28mm/S | 03mm/R |
| C2,s2 | 06mm/R | 24mm/S | 08mm/R | 02mm/R | 9mm/R | 08mm/R | 25mm/S | 02mm/R |
| C1,s3 | 12mm/I | 30mm/S | 14mm/I | 04mm/R | 12mm/R | 10mm/I | 30mm/S | 04mm/R |
| C2,s3 | 17mm/S | 34mm/S | 18mm/S | 09mm/R | 19mm/S | 16mm/I | 28mm/S | 07mm/R |
| C3,s3 | 14mm/I | 29mm/S | 15mm/I | 07mm/R | 16mm/I | 12mm/I | 27mm/S | 05mm/R |
| C1,s4 | 16mm/S | 33mm/S | 13mm/R | 06mm/R | 10mm/R | 21mm/S | 30mm/S | 06mm/R |
| **C2,s4** | 12mm/I | 27mm/S | 13mm/R | 02mm/R | 18mm/S | 12mm/R | 25mm/S | 04mm/R |
| C3,s4 | 15mm/I | 31mm/S | 18mm/S | 10mm/R | 13mm/R | 18mm/I | 33mm/S | 06mm/R |
| C1,s5 | 14mm/I | 26mm/S | 11mm/R | 05mm/R | 17mm/I | 07mm/R | 28mm/S | 03mm/R |
| C2,s5 | 06mm/R | 24mm/S | 08mm/R | 02mm/R | 9mm/R | 08mm/R | 25mm/S | 02mm/R |
| C3,s5 | 16mm/S | 33mm/S | 13mm/R | 06mm/R | 10mm/R | 21mm/S | 30mm/S | 06mm/R |

Based on the morphological and biochemical characteristics, bacteria were tentatively identified as *E.coli, Enterobacter* spp., *Klebsiella pneumonia, Pseudomonas aeruginosa, Staphylococcus* spp., *Streptococcus* spp. and *Enterococcus* spp. Based on the AST, bacteria showed the following results: all the isolates showed higher sensitivity to HLG-120 and HLS-300 and higher resistance to P-1 and E-5 whereas TR-30, AMX-10, CAZ-3, and CIP-5 were intermediately affected on isolated bacteria and from these drugs, few were highly effective and few were ineffective on used bacteria, a detailed result of AST expressed in Table 2.

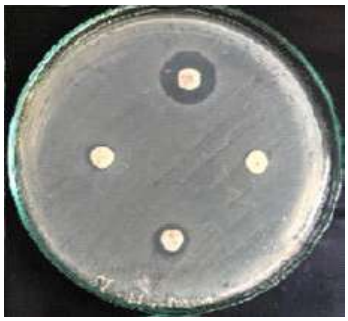
**Table 3- Antibiotic code along with its name, concentration and interpretive criteria**

| Code | Name | Concentration | Zone diameter Interpretive Criteria's | | |
|---|---|---|---|---|---|
| | | | R (= or <) | I | S (= or >) |
| TR | Trimethoprim | 30 mcg/disc | 10 | 11-15 | 16 |
| HLG | Gentamicin | 120 mcg/disc | 12 | 13-14 | 15 |
| AMX | Amoxicillin | 10 mcg/disc | 13 | 14-17 | 18 |
| P | Penicillin G | 1 unit | 14 | - | 15 |
| CAZ | Ceftazidime | 30 mcg/disc | 14 | 15-17 | 18 |
| CIP | Ciprofloxacin | 5 mcg/disc | 15 | 16-20 | 21 |
| HLS | Streptomycin | 300 mcg/disc | 11 | 12-14 | 15 |
| E | Erythromycin | 5 mcg/disc | 13 | 14-22 | 23 |

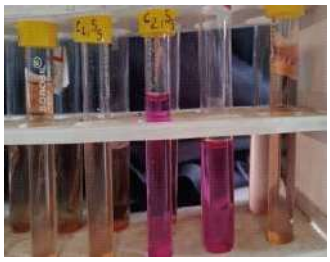
**A. Pure Culture of Isolates**



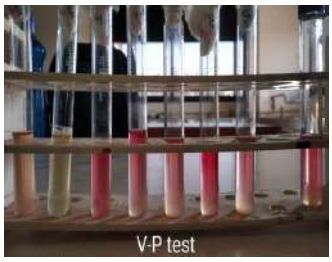
**B. Antibiotic Resistance**



**C. Antibiotic Resistance**



**D. Urea Hydrolysis test**




**E. V-P test.**

**F. Sugar Fermentation test**

**G. Methyl Red**

**Figure 1: phenotypic characterization of *Enterococcus faecium.***

## DISCUSSION

Multiple Drug Resistance (MDR) is a major environmental health issue. Antibiotic resistance increases day by day and microbes that are present in the urinary tract are developing resistance genes. In the current study, we were focused on antibiotic resistance patterns using 8 different antibiotics against bacteria infecting the urinary tract. It was indicated that Gentamicin (120mcg/disc) and Streptomycin (300mcg/disc) were highly affectable on used isolated bacteria. Muhammad and his team member received samples from the indoor (55%), outpatient departments (45%), and medicine departments. Of these samples, 72% were female samples. They collected 3 distinct types of isolates, such as *E. coli, K. pneumoniae* and *P. aeruginosa* from urine samples as uropathogenic. In their study, *E. coli* had shown multidrug resistance and

Amikacin showed maximum (52%) activity against the *E. coli* strain. Amikacin, Nitrofurantoin, and Meropenem showed 57.1% effectiveness in *K. pneumoniae* and that strain was 100% unaffected by Ceftriaxone, Ceftazidime, Ciprofloxacin, and Augmentin antibiotics. *P. aeruginosa* has shown 100% resistance against Ceftazidime and Nitrofurantoin. Christy V. R. and his colleagues also focus on the susceptibility pattern of uropathogenic in the female population. In their study, 63 (45.32) females were UTI positive out of 139 females. They isolated *E. coli and Klebsiella pneumoniae.* Nitrofurantoin, Nalidixic acid, and Co-trimoxazole antibiotics were most effective on *E. coli*. May Sewify and her team members focused on the efficacy of glycemic control on UTI prevalence. In their study, they studied 722 diabetic patients of which 35% were shown uropathogenic positive. Their results focused on glycemic control that reduces UTIs in diabetic patients according to age and gender. Ian Cock and his colleagues 2021 worked on the treatment of UTIs based on plant therapies. They have used about 153 southern African plant species used to treatment of UTIs. Of the 153 plants, 85 plant species were showing activity against bacteria which cause UTI. Zakia Iqbal and his team members also focused on antibiotics for the treatment of UTIs. They isolated about a hundred pathogenic bacterial strains such as *Escherichia* and *Klebsiella* from a pediatric patient with a UTI to check their antibiotic susceptibility. Among those bacterial strains, 80% *E. coli* and 86% *Klebsiella* spp. were extensive drug resistance against antibiotics which were used for their study.

## CONCLUSION

Yet, distinct therapies were used to treat UTI, one of them antibiotics are considered to be major therapy for the treatment of UTI. Multidrug resistance is a major environmental issue nowadays. In this study, we also use antibiotics to check antibiotic resistance patterns of uropathogenic. This study exhibited that the resistance rate of erythromycin-5 and Penicillin G-1 was high. Based on obtained results Gentamicin-120 and Streptomycin-300 may be used for the treatment of urinary tract infections. The limitation of this study is that more urine samples are required for an appropriate conclusion. To create awareness among humans about UTIs more studies will be required. Rather than the usage of drugs other treatments will also be used to cure UTI, such as the use of antimicrobial activity showing probiotics, appropriate plants, nanoparticles of metal ions etc. Increasing the rate of antibiotic resistance of bacteria which cause UTI is a field of scientific research for the treatment of UTI.

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