# To determine the antimicrobial susceptibility patterns of microorganisms isolated from the urinary tract in diabetic patients in and around Indore region

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**Abstract:**
**Background**: Null hypothesis is there is no difference in the clinical and microbiological profile of UTI between diabetic patients and non-diabetic controls.**Aim and Objective:** The present study is to determine the antimicrobial susceptibility patterns of microorganisms isolated from the urinary tract.**Materials & Methods:** Adults (18 years and older) of both sexes were included in the study. The study population was divided into two groups: diabetic patients, who had diabetes mellitus, and non-diabetic controls, who appeared healthy and had no history of diabetes or any underlying illness. Diabetic patients were enrolled in the study during routine check-ups at hospital diabetic units. **Results:** Two hundred twenty people took part in the study, and samples of their blood and midstream pee were taken (130 diabetic patients and 120 non-diabetic individuals). Out of 130 diabetic patients, only 59 individuals (42 %) had asymptomatic bacteriuria (ASB). An elevated risk of ASB was seen in people with a history of either frequent UTI (OR = 8.889, 95% CI: 2.876-30.924) or recurrent UTIs (OR = 5.478, 1.946-4.8.675). Staphylococci were the most common type of bacteria found in the urinary tract. Diabetic patients had a higher rate of Candida spp isolation compared to controls ($P < 0.001$). Urinary tract isolates showed similar levels of resistance to commonly used antibiotics such as erythromycin, cotrimoxazole, and flucytosine, according to the results of antimicrobial susceptibility tests. **Conclusion:** It was also found that diabetic persons may be more prone to bacteriuria as a result of gender, menopause, repeated UTIs, and a lack of formal education. These factors all play a role in this susceptibility. It's also possible that having bacteriuria is linked to not having completed formal schooling, which can be particularly problematic for people who have diabetes.

## Introduction:

The bad effects of high blood sugar cause some parts of the body that have nothing to do with the immune system may also make them more likely to get sick. Poor local circulation, which can be caused by both macrovascular disease and microvascular dysfunction, can make it take longer to respond to infections and for wounds to heal [1]. When a person has sensory neuropathy in their legs, they may not feel it when they are hurt. This can cause them to not take care of small wounds properly, which can make them more likely to get an infection [2]. Autonomic neuropathy can cause the bladder to not empty all the way, which can make it easier for bacteria to take hold of the urinary tract [3]. Also, there is evidence that a high amount of glucose in the urine can make some bacteria and yeasts grow faster [4]. People with diabetes have been known to get infections in their bladder, kidneys, vagina, gums, feet, and skin [5].

Patients with diabetes often get Urinary Tract Infections (UTIs), which is the sixth major effect of diabetes [6]. Several studies have shown that diabetes and UTIs, which usually happen in the urinary system, are linked [7]. Klebsiella pneumonia, Escherichia coli, Streptococcus agalactiae, Enterococcus faecalis, and coagulase-negative UTIs are often caused by Staphylococcus, Streptococcus pyogenes, and Candida albicans [8]. Both cystitis and bacteriuria are infections of the lower urinary tract, but they are usually mild and can be treated with antibiotics. Infections of the kidneys or ureters can sometimes start in the lower urinary system and move up. Diabetes patients are more likely to get upper urinary tract infections, pyelonephritis, and renal or perinephric abscesses [9]. Emphysematous infections are infections that get worse when bacteria break down food and release gas. The link between UTIs and diabetes is still up for debate, but there is some evidence that lower urinary tract infections can

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move to the upper urinary tract and cause more serious problems, especially in people who already have diabetes [10].
The null hypothesis is there is no difference in the clinical and microbiological profile of UTI between diabetic patients and non-diabetic controls. Therefore, the objective of the present study is to determine the antimicrobial susceptibility patterns of microorganisms isolated from the urinary tract.

**Materials & Methods:**
Adults (18 years and older) of both sexes were included in the study. The study population was divided into two groups: diabetic patients, who had diabetes mellitus, and non-diabetic controls, who appeared healthy and had no history of diabetes or any underlying illness. Diabetic patients were enrolled in the study during routine check-ups at hospital diabetic units. During free diabetes/hypertension screening exercise, non-diabetic controls were recruited from the general community. Clustered sampling was used because participants were sampled at specific locations, specifically diabetic outpatient departments. Purposive sampling was used because the study targeted adults (aged 18 and over), and clustered sampling was used because participants were sampled at specific locations. Participant inclusion criteria include all males and non-pregnant females > 18 years of age., subjects who consented or assented to participate in the study, people not suffering from any known underlying sickness as stated in the questionnaire, people who had not taken antibiotics or steroids for one week preceding the sample analyses. Participant exclusion criteria include people <18 years of age, all pregnant women, people suffering from any chronic disease such as hypertension, hepatitis, rheumatoid arthritis, cancer, HIV/AIDS, heart disease, and kidney disease, and people who had received antibiotics or steroids for one week before sample collection.
Statistical analysis:

To analyze all of the data, the Chi-square test was performed, and after that, the statistical program for the social sciences was used to compute the odds ratio for each variable to identify factors that increase the likelihood of ASB (SPSS). To conduct a more in-depth examination of the variables that were substantially connected, it was necessary to take into consideration immutable aspects such as age and gender. A multivariate logistic regression study was carried out to ascertain which demographic, medical, and laboratory parameters best predict ASB in diabetic people.

**Results:**
The hierarchical cluster for the antimicrobial resistance pattern of Gram-positive bacteria revealed 4 distinct clusters namely: Vanco-E-Cfx; E-Cfx-Aug; Genta-Doxy; Cotrim-Ox. The Genta-Doxy cluster was the most active against Gram-positive bacteria while Cotrim-Ox was the least active. A total of 71 isolates of GPC were tested for their susceptibility to 8 different antibiotics (Table 1). Gram-positive bacteria exhibited high resistance to oxacillin (63; 88 %), cotrimoxazole (48; 67 %), and augmentin (35; 52 %). All isolates of S. aureus were resistant to 3 of the antibiotics (Augmentin, vancomycin, and oxacillin). Similarly, all NGS strains were resistant to vancomycin but no resistance was demonstrated against gentamicin. All Gram-positive bacteria except Coagulase negative Staphylococci (CNS) did not show any resistance to gentamicin. A comparison of the antibiotic resistance with the site of isolation revealed that Gram-positive isolates from the urinary tract were generally more resistant than those from the oral cavity. However, this difference was not statistically significant ($P = 0.127$).

Generally, regardless of diabetic status, participants aged 50 years and above presented more than 42 (48.8 %) with ASB while those less than 40 years presented least (44; 51.2 %) with ASB (Table 2). However, there was no significant difference in the distribution of ASB concerning age in both diabetic patients ($P = 0.856$) and non-diabetic controls ($P = 0.571$). On the other hand, a highly significant difference was noticed in the distribution of ASB concerning sex in both diabetic patients and non-diabetic controls ($P < 0.001$).
86 (35%) of the 250 subjects had substantial bacteriuria (Table 3). It was also discovered that more diabetic patients (59; 42%) than non-diabetic controls (31; 28.3%) had significant ASB, and the difference in prevalence between diabetic patients and non-diabetic controls was significant ($P = 0.019$).
Two hundred and fifty midstream urine samples yielded 102 isolates (Figure 1). Candida, Klebsiella, Serratia, Staphylococcus, Streptococcus, Escherichia, Pantoea, Proteus, Citrobacter, and Enterobacter were among the many microbes identified. Staphylococcus (31; 30%), Klebsiella (17; 17%), Candida (16; 16%), Escherichia coli and Serratia (11; 11%), and other gram-negative bacteria were the most frequently isolated taxa.

| Antibiotics | GBS (n = 3) | CNS (n = 58) | *S. aureus* (n = 5) | NGS (n = 5) | Total (n =71) |
|---|---|---|---|---|---|
| Augmentin | 1 (50.0) | 26 (45.8) | 4 (100) | 4 (66) | 35(52) |
| Cefuroxime | 0 (0.0) | 20 (33.9) | 0 (0.0) | 0 (0.0) | 20 (28) |
| Doxycycline | 0 (0.0) | 10 (18) | 0 (0.0) | 0 (0.0) | 10 (14) |
| Cotrimoxazole | 2 (100) | 38 (67.8) | 2 (50.0) | 6 (83) | 48 (67) |
| Vancomycin | 1 (50.0) | 13 (22.2) | 4 (100) | 6 (100) | 24 (33) |
| Oxacillin | 2 (100) | 54 (86.4) | 4 (100) | 4 (66) | 63 (88) |
| Gentamicin | 0 (0.0) | 6 (10.9) | 0 (0.0) | 0 (0.0) | 6 (8) |
| Erythromycin | 1 (50.0) | 17 (28.8) | 4 (100) | 4 (66) | 26 (36) |

**Table 1:** Antimicrobial susceptibility patterns of Gram-positive bacteria

| Age | Diabetics with ASB (n = 55) | Non-diabetics with ASB (n = 31) | Total Number with ASB (n = 86) |
|---|---|---|---|
| 18-30yrs | 5 (8 %) | 5 (15 %) | 10 (12%) |
| 31-40yrs | 5 (8 %) | 4 (12 %) | 9 (11 %) |
| 41-50yrs | 18 (32 %) | 7 (24 %) | 25 (29 %) |
| 51 and above | 27 (52 %) | 15 (49 %) | 42 (49 %) |
| **χ2-test: χ2 = 6.783; P = 0.856** | | **χ2-test: χ2 = 4.931; P = 0.571** | |
| **Gender** | | | |
| Male | 6 (10 %) | 4 (12.9 %) | 10 (11 %) |
| Female | 49 (90 %) | 27 (87.01 %) | 76 (88 %) |
| **χ2-test: χ2 = 18.325; P < 0.001** | | **χ2-test: χ2 = 21.482;P < 0.001** | |

**Table 2: Distribution of asymptomatic bacteriuria with respect to age and gender in diabetic patients and non-diabetic control**

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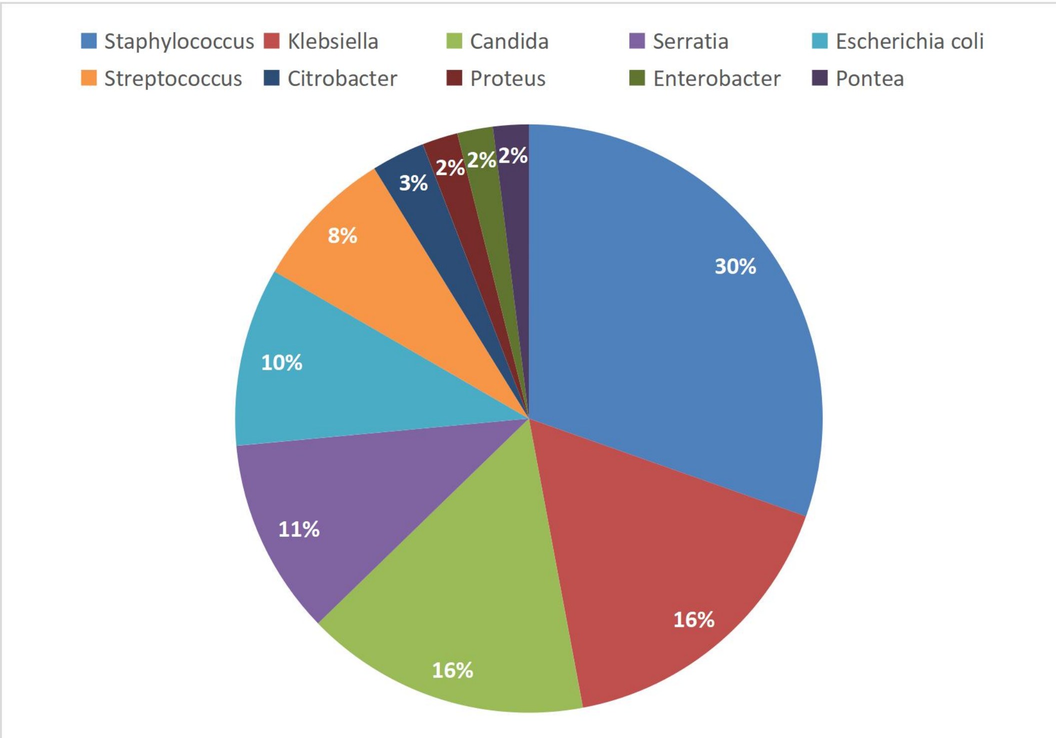
| Participant type | Prevalence of Bacteriuria n (%) | 95%CI LB – UP | Total |
|---|---|---|---|
| Diabetic patients | 55 (42 %) | 34- 66.8 | 130 |
| Non-diabetic controls | 31 (28.3%) | ,18.6 – 35 | 120 |
| **Total** | **86 (35 %)** | **29 – 42** | **250** |

χ2-test: χ2 = 9.523; df = 1; P = 0.019

**Table 3: Prevalence of asymptomatic bacteriuria among diabetic patients and non-diabetic controls**

**Figure 1: Details of urinary isolates in study participants**



**Discussion**

Diabetes Mellitus is extremely common in India. Diabetes is associated with a variety of life-threatening effects, and research has found a link between diabetes and infectious illnesses [11]. Urinary tract infections (UTIs) can have devastating repercussions, particularly in diabetes patients [12]. There is a paucity of information regarding the incidence of urinary tract infections (UTIs) in diabetic patients, despite the significant complications associated with infectious diseases in diabetes. This research was conducted to define the microbiological profile of UTIs that occur in diabetic patients and determine the influence that these infections have on the clinical presentation of diabetes in patients from the Indore region. This study was a case-control study with a total of 250 participants, 130 of whom had diabetes mellitus and 120 of whom did not. Participants from the general population who did not have diabetes made up the subjects in the control group. All of the people that took part in the study were at least 18 years old.

According to the findings of this experiment, asymptomatic bacteriuria was present in 52% of diabetic patients and 48% of non-diabetic controls. Earlier studies indicated a prevalence of 5.3% to 26.0% in diabetic patients [13], whereas more recent studies found 3.5% to 15% in non-diabetic subjects [14]. These findings are more conclusive than those of the previous studies. According to the findings of earlier studies [15], the prevalence of ASB was found to be 36.1% among diabetes patients in Nigeria [16], 47.2% among diabetes patients in Cameroon, and 18.5% among non-diabetic individuals in Italy. It suggests that estimates of the prevalence of ASB are inconsistent. It reported a high frequency of 36.1% in T2DM [17], but other studies found a prevalence of 17.8% and higher in diabetic patients. In a different study, the prevalence of ASB among diabetic patients was found to be 40%, in comparison to the group that served as the control [18]. Variations in the prevalence of bacteriuria have been attributed to variations in sample size, geographical location, culture, and screening method [19].

Coagulase-negative Staphylococcus was found to be the most common type of bacteria in this study (31; 30%), followed by Klebsiella (17; 16%), Candida (16; 16%), and E. coli (10; 10%). Gram-negative bacteria were the species that were isolated from the urinary tracts of the research participants the most frequently. This runs counter to the findings of previous studies [20] that indicated E. coli to be the causative agent of the disease. E. coli was the most common type of bacterium that was found. Other types of bacteria are much more common than E. In addition to this, the prevalence of E. coli in the urinary system has also been documented [21]. Except for Candida sp. The frequency of isolating uropathogens was comparable between diabetic patients and non-diabetic patients, except for Serratia sp., which was isolated from diabetic patients more frequently than they were from non-diabetic controls. Other than those two exceptions, the isolation frequency of uropathogens was the same. People who have diabetes tend to have higher glucose levels, and it has been hypothesized that this may foster the growth of Candida species. In this study, Klebsiella sp was not isolated from diabetic patients but rather from non-diabetic controls (10, or 34%). However, the mechanism that underlies the differential in bacterial colonization between diabetics and non-diabetics is unknown at this time. It was a noteworthy discovery that coagulase-negative Staphylococci and Candida species both played a role in bacteriuria and their clinical importance. In addition, it appears from the findings of this research that diabetes may play an important part in the colonization of bacteria in the urinary tract.

Candida species exhibited high levels of resistance to flucytosine (71; 92.7%), moderate levels of resistance to fluconazole (39; 50.6%), and low levels of resistance to miconazole (26; 33.3%). (Figure 8). Because resistance to flucytosine is so widespread, this antifungal medication is most often administered in conjunction with an azole [22]. These findings provided further evidence that the development of resistance to azole antifungal drugs has already been seen by other studies. In a recent study [23], it was found that the azole MIC values of non-albicans Candida isolates were much higher than those of C. Albicans isolates. The usage of these antifungal drugs for therapeutic and preventative purposes may have contributed to an alarmingly high number of cases of resistance. There was no evidence of resistance to nystatin that could be found. In general, it has been found that polyene antifungal drugs are met with modest levels of resistance.

The majority of the bacterial isolates tested in this study exhibited a high level of resistance to the antibiotics oxacillin, cotrimoxazole, erythromycin, and clindamycin. According to the findings of this research, the Gram-positive bacteria with the highest level of resistance were CNS. There have been reports that these bacteria exhibit a high level of resistance to a variety of antibiotics. The fact that 15% of CNS are resistant to gentamicin and a similar 22.5% are resistant to vancomycin may be a clue that gentamicin-vancomycin-resistant strains are circulating in the population. Infections caused by these types are notoriously challenging to cure, and if left untreated, could result in death. Vancomycin, a glycopeptide antibiotic that is frequently used to treat severe infections caused by multi-resistant Gram-positive bacteria, was ineffective against all of the S. aureus isolates, which is an interesting finding. Vancomycin resistance in S. aureus has been linked to the production of VanA proteins [24], indicating that this resistance is becoming more widespread.

The level of resistance shown by Gram-negative bacteria to gentamicin was the highest, while their resistance to ciprofloxacin was the lowest. Additionally, a resistance ranging from moderate to high was seen both to cephalosporins of the second and the third generation. These findings are consistent with those found in earlier reports in the area under investigation [, as well as those found in other developing nations that documented 18.8% resistance to ceftriaxone. It was determined that the formation of extended-spectrum beta-lactamase (ESBL) was the cause of ceftriaxone resistance. High rates of resistance have also been documented [25] among uropathogens in Cameroon, and the findings of that country's study are comparable to those of the present investigation. In one of these types of research, it was shown that amoxicillin resistance to all Gram-negative isolates was 87%, piperacillin resistance was 74%, and cotrimoxazole resistance was 73%. The generation of beta-lactamases is typically connected with the development of resistance to penicillins. The high level of resistance to cotrimoxazole in the research area may be the result of its regular usage in the treatment of UTIs and other infectious disorders. Resistance to nitrofurantoin is typically quite rare; the moderate level of resistance that was identified in this investigation may be attributed to the evolution of cross-resistance. Additionally, it was discovered that the E. coli strains used in this research were resistant to multiple antibiotics, particularly gentamicin, nalidixic acid, doxycycline, cefuroxime, and erythromycin. According to the findings of other scientists [26], the presence of multi-drug resistance in E. coli is a widespread phenomenon.

In the current investigation, gentamicin resistance was found to differ between Gram-negative bacteria (39, or 73.3%) and Gram-positive bacteria (6, or 8.5%). This distinction might be because Gram-negative bacteria have an unusually high number of efflux pumps in their cells [27]. When comparing the patterns of antimicrobial resistance seen in oral and urine isolates, researchers found no significant difference between the two. In addition, when comparing the resistance patterns of diabetic patients and non-diabetic controls, there was not a significant difference ($P > 0.05$). This provides evidence that microorganisms from both of these sources are subjected to the same levels of antimicrobial agent exposure.

In a nutshell, the findings of the current investigation demonstrated that urinary tract isolates had a rate of antimicrobial resistance that was somewhere between moderately high and moderately high. This could be a result of the widespread and careless use of antibiotics like these, which are available to a large number of people at a reasonable cost.

**Conclusion**

Two things are known about the diabetic patients in the present study, first, ASB is quite common among them, and second, there may be a shift in the normal development of the disease. Another notable discovery was that coagulase-negative Staphylococci and Candida species both have significant clinical significance in bacteriuria. This was an extremely significant finding. It was also found that diabetic persons may be more prone to bacteriuria as a result of gender, menopause, repeated UTIs, and a lack of formal education. These factors all play a role in this susceptibility. It's also possible that having bacteriuria is linked to not having completed formal schooling, which can be particularly problematic for people who have diabetes.

**Conflict of interest:**

The present study authors do not have any conflict of interest among themselves

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