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Prevalence, Types and Antibiotic Sensitivity Pattern in Urinary Tract Infection (UTI) In Midnapore Town, India

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Abstract

Urinary-tract-infection (UTI) is a major health/hygiene concern in the community with highest morbidity due to the fact of increasing multidrug-resistance in bacterial-uropathogens. Objective: Studies on prevalence of UTI in semi-urban Indian localities. Pattern study of antibiotic-resistance was investigated found in UTI. Aim was also to study the discrepancies in the sensitivity and resistant pattern of different pathogens against particular drug. Material & Methodology: Urine sample were collected (19-males/33-females) from Midnapore scan-center, West Bengal and analyzed. Result: The 40% of the UTI is attributed by *E.coli* followed by *K. oxytocae* (17%), *Staphylococcus aureus* (14%) *(S.aureus*). Female to male infection was 63:37(Figure-1a). The drug susceptibility response suggests that 70-100% of the bacterial isolates from the patients were susceptible to 26% of the drugs in case of *E. coli*, 36.66% in case of *Klebsiella sp*. and *Enterrococci sp*., 50% in case of *Citrobacter sp*. 53.33% of the drugs in case of *S.aureus* and 73.33% in case of *Proteus sp*. Conclusion: *E. coli* is resistant to most of the drugs. Drug-sensitivity pattern of individuals suggests that when a larger number of drugs behave sensitively against *Citrobactor sp*. in more number of patients, a small number of drugs are sensitive to *S. aureus* in in more number of patients.

Keywords: Urinary tract infection; Antibiotic resistance; Drug-sensitivity pattern; India

Abbreviation

MR: Meropenem; CAL: Clavulanic acid; AT: Aztreonam; DO: Doxycycline; OF: Ofloxacin; CA: Ceftazidime; CO: Colistin; PR: Para-aminosalicylic acid; CTX: Cefotaxime; NX: Norfloxacin; CTR: Ceftriaxone; CFM:Cefixime; LE: Levofloxacin; AK: Amikacin; PT: Piperacillin-tazobactam; CPZ: Cefprozil; CXM: Cefuroxime; GM: Gentamicin; NA: Nalidixic Acid; AMC: Amoxycillin; AZM: Azithromycin; COT: Trimethoprim-sulfamethoxazole; GEN: Gentamicin; CAC: Cefaclor; GEM: Gemifloxacin; PRU: Ulifloxacin; NIT: Nitrofurantoin; TB: Tobramycin; CAZ: Ceftazidime.

Introduction

Urinary tract infection (UTI) is a major public health problem and the commonest bacterial infectious disease in the community with a high rate of morbidity. An estimated 150 million people were infected with UTI per annum worldwide which may cost a global economy more than 6 billion US dollars [1]. Clinical studies suggest that the overall prevalence of UTI is higher in women; less complicated UTIs in healthy women have an incidence of 50/1000/year. UTI varies with age and gender, boys between the ages of 1-5 year suffers UTI more frequently and need to be evaluate efficiently [2]. A study conducted to determine the prevalence of community acquired-UTI in rural Odisha showed that prevalence of UTI in females was 45.2% [3]. The lower UTI is defined by the term cystitis and is characterized by symptoms such as dysuria, frequency, urgency, and suprapubic tenderness. The infection usually begins from the lower urinary tract and spreads along upper UTI which is often present in most UTI cases [4]. UTI can be classified into uncomplicated and complicated on the basis of their choice of treatment [5]. UTI is more common in females than in males as female urethra structurally found less effective for preventing the bacterial entry [6], due to the closeness of the genital tract and urethra [7], adherence of urothelial mucosa to the mucopolysaccharide lining [8], menstrual unhygienic practices [9] and using birth control diaphragm [10]. Possibility is that Menstruation and its hygiene management creates abnormally moist conditions in the urogenital that may promote bacterial invasion. The other main factors which make females more prone to UTI are pregnancy and sexual activity [11]. In pregnancy, physiological plasma volume increases and decrease in urine concentration develop glycosuria in up to 70% women which ultimately leads to bacterial growth in urine [12]. Urinary catheter-related infection leads to substantial morbidity and mortality. The incidence of bacteriuria in catheterized patients varies between 3% and 10% per day [13]. A large spectrum of bacteria causes complicated UTI and a number of bacteria cause uncomplicated UTI. However, the most commonly encountered microorganisms are Gram negative bacteria including *Escherichia coli, Citrobacter spp., Enterobacter aerogenes, Enterococci sp., Pseudomonas aeruginosa* and *Proteus sp.* whereas *Klebsiella spp*., *Staphylococcus aureus* and *Salmonella spp*. are found rarely [14]. UTIs are treated with empirical

antimicrobial. Increasing multidrug resistance in bacterial uropathogens is an important and emerging public health problem. Some microorganisms are identified as "ESKAPE pathogens" by the Infectious Disease Society of America (IDSA) which needs new effective therapies. Those microorganisms include *Enterococcus faecium, S. aureus, Klebsiella sp., Acinetobacter spp., Pseudomonas spp.,* and *Enterobacter spp.*

Uropathogenic bacteria are now evolving as multi drug-resistant, showing resistance to more than 2 antibiotics, this is an alarming situation and this leaves the treating physician with few choices of antimicrobial agents to treat UTI. There are more than 15 classes of antibiotics whose targets are involved in essential physiological or metabolic functions of the bacterial cell [15]. Drug resistance genes are one of the causes. The genes for resistance traits can be transferred among bacteria of different taxonomic and ecological groups by means genetic elements such as bacteriophages, plasmids, naked DNA or transposons [15,16]. These genes are generally directed against a single family or type of antibiotic, multiple such genes, each bearing a single drug resistance trait, can accumulate in the same organism. Eventually resistance genes and their hosts spread and propagate to amplify and extend the problem to other hosts and other geographic locations. Low-level to high-level resistance occurs in bacteria through sequential mutations in chromosomes [15,17,18]. *E.coli* and other *Enterobacteriaceae* strains have evolved increasing resistance to fluoroquinolones for mutations in the target enzymes (topoisomerases) and increment of membrane proteins that pump the drugs out of the cell [17,18,19]. Genetic analyses suggest that the long-anticipated transfer of vancomycin resistance to a *methicillin-resistant S. aureus* occurred *in vivo* by interspecies transfer of Tn1546 from a co-isolate of *Enterococcus faecalis* [20]. Biofilms are the predominant phenotype of nearly all the bacteria in their natural habitats, whether they are pathogenic or environmental. Bacterial pathogens form biofilms which protect them from starvation, desiccation and antibiotics. Multidrug resistant strains are efficient biofilm producers, indicating a direct relationship between biofilm formation and antibiotic resistance [21]. *E.coli* pathotypes reside harmlessly in the human intestinal microenvironment but, upon access to sites outside of the intestine, become a major cause of human morbidity and mortality as a consequence of invasive UTI (pyelonephritis, bacteremia, or septicaemia [22]. *E.coli* can form biofilms in the bladder during a urinary tract infection, extracellular matrix (ECM), of *E. coli* is primarily composed of curli a protein polymer and the polysaccharide cellulose promoting adherence to organic and inorganic surfaces and resistance to desiccation, the host immune system, and other antimicrobials [23]. The biofilm formation of urinary *S.aureus* strains was low. The strains showed higher resistance to beta-lactams, in other cases resistance was low [24].

UTI needs a regular monitoring of the antibiotic susceptibility of uropathogens in any particular area because of increasing drug resistance. Factors such as the type of UTI (complicated or uncomplicated), gender, age, and previous history of antibiotic therapy of each UTI patient should also be considered to find out the correct global data on susceptibility and for further appropriate treatments attempts [25]. Antimicrobial susceptibility data of UTI-causing microorganisms changes from time to time and from place to place [26]. Data provided by regional microbiology laboratories on the susceptibility patterns helps to choose the empirical choice of antimicrobials to treat UTI [27,28]. Generally, the antimicrobial treatment is initiated before the laboratories results which may lead to the frequent misuse of antibiotics [29]. The resistance pattern of community acquired uropathogens has not been extensively studied in India [30-32]. Different antimicrobial agents act in different ways. The understanding of these mechanisms as well as the chemical nature of the antimicrobial agents is crucial in the understanding of the ways how resistance against them develops. Broadly, antimicrobial agents may be described as either bacteriostatic or bactericidal. This increased antimicrobial resistance which is the result of irrational and uncontrolled use of the antimicrobials is threat to the public health. The aim of the study is to determine the prevalence of UTI in male and female patients as well as the effect of gender and age on its prevalence. The UTI-causing microorganisms, their distribution among different ages and genders were studied in the current investigation. Other objective was to assess the current antibiotic resistance pattern in the common uropathogens isolated in a tertiary care hospital Midnapore, West Bengal, India.

Materials and Methods

Study area

The study was carried out in Midnapore scan center, Medinipore district, West Bengal.

Sample size

The urine samples of 52 patients comprised of 19 males and 33 females, who had clinical evidence of urinary tract infection as suggested by the physician, were included in this study. The age of the patients included in the study ranged from <1 to 77 years. Patients with hospital acquired infections and patients on antibiotic therapy were excluded from the study.

Sample collection

The study was conducted after the ethical approval which was subjected to the hospital administrations. All patients were carefully instructed on how to collect sample aseptically to avoid external contaminations. In each container boric acid (0.2 mg) was added to prevent the growth of bacteria in urine samples.

Sample processing

Plating, culture and Isolation of the bacterial pathogens were conducted by eligibly experienced and authorized lab technicians in a highly aseptic laboratory condition. All the microscopic examination involving identification of bacterial strains was also performed by authorized lab technicians.

Identification of gram positive and gram negative bacteria

Gram negative and positive bacteria were identified by the standard Gram staining method using Crystal violet, iodine and safranin.

Identification by biochemical characteristics

The bacterial species where structurally identified on the basis of Gram staining including shape, motility, capsule, spore, flagella. Isolated cultures were biochemically identified for catalase, MR, VP, OF (Oxidative/ Fermentative), Indole, Citrate, Urease, nitrate reduction. Then for the third level of identification isolated cultures were subjected to fermentation of Arabinose, DNase, Fructose, Glucose, Inositol, Lactose, Maltose, Sorbitol and sucrose. Isolated cultures were also examined for certain enzymatic reaction such as Acetate utilization, acid phosphatase, alkaline phosphatase, amidase, lysine, ONPG test and phenylalanine deaminase.

Bacteria culture

The isolates were subculture periodically according to the requirement in the following media.

E.coli- Macconkey agar media, *S.aureus*- Mannitol salt agar (MSA) media,
Citrobacter sp.- Eosin methylene blue agar media (EMB*), K.oxytocae*- Nutrient agar media, *Enterrococci sp.*- Bile esculin agar (BEA) media, *Proteus sp*.- Levine EMB agar media

Antibiotic selection and antimicrobial disc susceptibility test

30 antibiotics were selected for the study and antimicrobial disc susceptibility test was performed following the standard kit method (Himedia).

Results

Prevalence rate and frequency distribution of UTI among different age groups

The total prevalence of UTI in female patients was found to be 63% and in males about 37%. These results indicated that the prevalence of UTI was higher in female patients than in males. The highest susceptible age group of UTI patients irrespective of gender was found to be >40 years (48%) followed by ≤ 20 years (31%), and then between 21-40 years (21%).

Some variations were found in age wise susceptibility between males and females. The highest prevalence of UTI in females was found in the age group of >40years (55%); followed by an age group between 21-40 (27%) years and the least susceptible age group was ≤ 20 years (18%), however in males the highest susceptible age group to UTI was ≤ 20 years (53%), followed by age greater than 40 years (37%) and then the least susceptible group was between 21-40 years. Eventually it was found that females are markedly more susceptible to UTI in comparison to males.

Distribution frequency of isolated bacterial uropathogens

Among all the isolated bacterial uropathogens from UTI patients, *Escherichia coli* was found as the dominant bacteria with the prevalence rate of 40%. The second most prevalent isolate was *Klebsiella* oxytocae (17%) followed by *Staphylococcus aureus* (14%), *Citrobacter* sp. (13% *Proteus sp*. (10%) and *Enterococci sp*. (6%).

Gender-wise distribution of uropathogens

The prevalence rate for the occurrence of different uropathogens among males and females were as follows, E. coli infection in females was higher being (43%) than in males (37%). Infection by *Enterrococci sp*. was found only in females comprising 9 of the UTI's conversely being 0 in males. *S. aureus* comprised 21 of the females UTI and 0 of male UTI's. *K. oxytocae* caused 21 of the male UTI's and 15 of female UTI's. *Citrobacter* sp. caused 26% of male UTI's whereas only 6 of the female UTI's. *Proteus sp*. covered 16 of the male UTI's and only 6 of the female UTI.

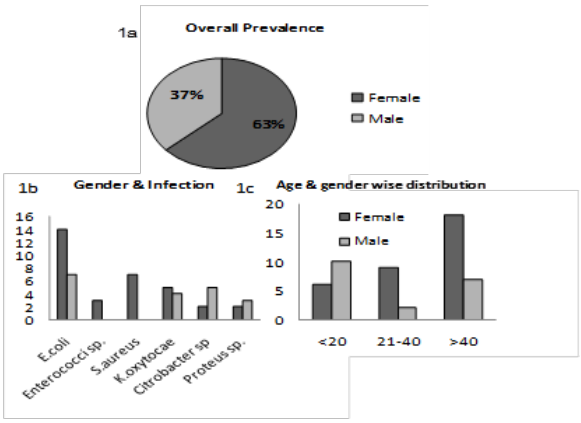

Figure 1: (1a) Overall prevalence of UTI among male and female. (1b) Genderwise infection of different species among male and female. (1c) Age and gender wise distribution of infection among male and female.

Drug resistance

E. coli **against tested antibiotics:** CAL, NF, NIT was found to be sensitive against 100% of the *E. coli* infected individuals followed by MR, AK, G having ≥ 90%sensitivity, following AT, PT and CAC sensitive against ≤ 70% where AT, PT was Intermediate for 30 and CAC for 10 and resistant to the remaining. ≥ 50 of the *E.coli* infected individuals was sensitive to CA, CTX, CTR (40% Intermediate, 10 Resistant), GM, AZM and GEN (20 Intermediate). The least sensitive and highly resistant drugs were DO, OF, CO, AC, CPZ, TB, CAZ, PR (<50 sensitive), CXM, AMC, COT and GEM (10 sensitive).

NA and PRU were resistant to 90% of the *E. coli* infected individuals and intermediate to the remaining 10%.

K. oxytocae **against tested antibiotics:** NF, CPZ, GEN and NET was found to be sensitive for 100% of the *Klebsiella* infected individuals. CAL, AK, PT, CXM was sensitive against >70% of the infected individuals and resistant to the remaining. MR, AT, OF, CA, CTX, NX, LE (15% I), G, AZM (50% I) and COT were sensitive to ≥ 50% of the infected individuals. DO, PR (10% I), CTR (15% I),

CFM (10% I) were sensitive to <50% of the infected individuals and resistant to the remaining. CO, AC, GEM, NA, GM, PO were resistant to 100% of the infected individuals and AMC was resistant to 50% and intermediate for the 50% of the infected individuals.

Enterrococci sp. **against tested antibiotics**: CAL, LZ, VA, PT, AC, CXM, CAC, CTX and NF were sensitive to 100% of the infected individuals. MR (<30% I) and G (30% R) were sensitive to ≥ 70% of the infected individuals. CX (<50% R) and OX (<50% I) were sensitive to ≥ 50% of the infected individuals. L, CFM and AK were sensitive to <50% of the infected individuals and resistant for the remaining. OF was resistant to >60% of the infected individuals and intermediate for the remaining.

AT, DO, SC, LE, GEM, PR, SPX, NX, CS were resistant to 100% of the infected individuals.

S. aureus **against tested antibiotics:** L, LL, VA, CAL, AK, PT, G, LZ, NF, GEN, CXM were sensitive to 100% of the infected individuals.MR (15% R), DO (35% R), CX (15% I & 15% R), CAC (20% R) were sensitive to >60 but <100% of the infected individuals. LE (>30% I, 30% R), AC (15% S, 85% R), PR (20% S, 25% I, 55% R) and GM (70% I) were sensitive to <50% of the individuals. NX was intermediate for 100% of the infected individuals. OF, SPX, MO was resistant to 50% and intermediate to the 50% of the infected individuals.

AT, CTX, CPZ, AMC and AZM were resistant to 100% of the infected individuals.

Citrobacter sp. **against tested antibodies:** PT, TB, MR, CAC, AK, GRN, AZM, NET, LE, CAL, AT were sensitive to 100% of the *Citrobacter* infected individuals. COT, CTR, CFM, CAZ, CTX, PRU, G, CA were sensitive to ≥ 50% of the infected individuals and resistant to less than 50% of the infected individuals.

PR, NX, CXM, CO, PRV, DO were sensitive to <50% infected individuals and resistant to >50% of the individuals. AMC was resistant to 50% and intermediate to the 50% of the infected individuals.

NA, CPZ, GEM, GM were resistant to (bacterial isolation of) 100% of the infected individuals.

Proteus sp. **against tested antibiotics:** MR, CAL, OF, CA, CO, PR, CTX, NX, CTR, CFM, LE, AK, PT, G, CAC, CPZ, COT, TB, CAZ, AMC, GEN and PRV were sensitive to the 100% of the infected individuals.

DO, GM, NF, AZM were resistant to 100% of the infected individuals. AL was intermediate to the 100% of the infected individuals. AC was resistant to >50% and sensitive to <50% of the infected individuals.

Discussion

This study may provide a valuable information on the present scenario of UTI infection and antimicrobial resistance/sensitivity pattern in the district of Midnapore (WB) to improve efficient empirical treatment. Increasing antimicrobial resistance has been documented globally [33-39]. The prevalence of UTI was found to be high including various uropathogens such as *E. coli, Enterrococci sp., S. aureus, Klebsiella sp. citrobacter sp.* and *Proteus sp*. Highest abundance and attribution of *E. coli* (40%) in UTI has been noticed in our studies followed by *K.oxytocae* (17 %), *S.aureus* (14%), *Citrobacter sp.(*13%), *Proteus sp.* (10%) and *Enterrococci* sp.(6%),The proportionate contribution of the first three bacteria's for the infection is like 40%:17%:14% including both male and in the female (**Figure 4a**). This result is consistent with reports from other studies [3,40-45] but differs from the reports in which *P. aeruginosa* [46] and *Klebsiella sp.* [47] were recorded as the predominant bacteria in UTI. however, these results correlates with others in which *Klebsiella spp.* was reported as the second most frequently isolated organism in UTI [48-52]. The studies on UTI in other places of the world also showed that *E. coli* and *Klebsiella spp*. are the commonest uropathogens in UTI [31,32,53-55]. A gender associated difference in the infection was noticed, ratio of the percentage of male to female infection was 63:37 being in accordance with earlier studies **(Figure 1a)** [7,56-61].

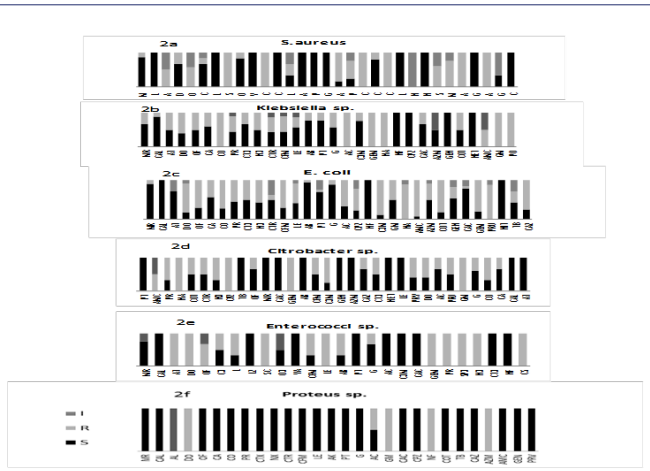

Figure 2: (2a) Susceptibility and resistant pattern of different drugs against *S. aureus* in terms of percentage. (2b) Susceptibility and resistant pattern of different drugs against *Klebsiella sp.* in terms of percentage. (2c) Susceptibility and resistant pattern of different drugs against *E. coli* in terms of percentage. (2d) Susceptibility and resistant pattern of different drugs against *Citrobacter sp.* in terms of percentage. (2e) Susceptibility and resistant pattern of different drugs against *Enterrococci sp.* in terms of percentage. (2f) Suceptibility and resistant pattern of different drugs against *Proteus sp.* in terms of percentage.

E. coli was the predominant in both the genders comprising of 43% in female (**Figure 3 and Figure 4c**) and 37% in males (**Figure 4b**). In females of all age categories, *E. coli* is the most frequently isolated uropathogen which correlates with other studies

[62-64] in contradiction to somewhere *E. coli* causes most male UTIs, followed by other *Enterobacteriaceae and Enterococci* [65,66] second predominant bacteria in males was found to be *Citrobacter sp*. (26%) (**Figure 4b**) whereas only 6% in females (**Figure 4c**), 21% of males **(Figure 4b**) and 15% females were infected by *Klebsiella sp.* (**Figure 4c**), 16% of the males (**Figure 4b**) and 6% of females (**Figure 4c**) were infected by *Proteus sp*., 21% of females (**Figure 4c**) were infected by *S. aureus* and 9% of females **(Figure 4c**) were infected by *Enterrococci sp.* and both had no participation in male infection. It seems like pathogens like *Citrobacter sp.* and *Proteus sp.* are more specific to males whereas *Proteus sp.* are specifically involved in female infection.

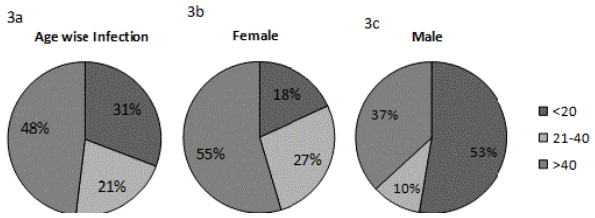

Figure 3: (3a) Age wise infection in both male and female. (3b) Age wise infection in female. (3c) Age wise infection in male.

Selected antimicrobials included in this study possessed both resistance and sensitivity patterns among different uropathogens. Among all the drugs included, NF showed 100% sensitivity against uropathogens like *E.coli, Enterrococci sp., S. aureus, Klebsiella sp.* all the pateints infected with these four bacteria showed response to NF. 100% of the individuals carrying *E.coli* infection responded to NIT, CAL and NF (**Figure 2c**), 100% of the individuals carrying *Enterrococci* infection responded to CAL, AC, LZ, CXM, CAC, NF, CTX, 100% of those carrying *Klebsiella sp* infection responded to NF, CPZ, GEN, NET (**Figure 2b**), 100% of *Citrobacter sp.* infected individuals showed response to PT, TB, MR, CAC, AK, GEN, AZM, CAL, AT (**Figure 2d**). 100% of *Proteus sp*. infected individuals responded positively to MR,CAL. OF, CA, CO, PR, CTX, NX, CTR, CFM, LE, AK, PT, G, CAC, CPZ, COT, TB, CAZ, AMC, GEN, PRV, though *Proteus* infection occurs least **(Figure 2f**). *E.coli* showed 100% resistance to NA, PRU, CXM, AMC (**Figure 2c**), *Enterrococci* sp. was resistant to SPX and NX (**Figure 2e**), *S.aureus* possessed resistance against AMC, SC, CPZ, CFM (**Figure 2a**). *Klebsiella sp*. possessed resistance against CO, GM, PO, AC, GE, NA. Some correlations exist between antibiotic resistance and the biofilm-forming ability of *K.pneumonia* strains [32]. *Citrobacter sp*. were resistant to CPZ, GM, NA, AZM **(Figure 2d**). *Proteus sp.* possessed resistance against DO, GM, NF, AZM (**Figure 2f**).

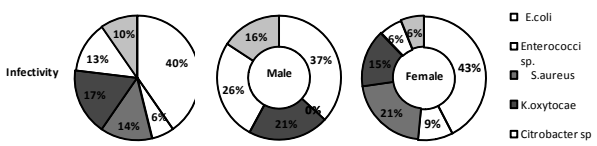

Figure 4: (4a) Pattern of infectivity of different pathogen irrespective of gender. (4b) Pattern of infectivity of different pathogen in male. (4c) Pattern of infectivity of different pathogen in female.

The drug susceptibility response suggests that 70-100% of the bacterial isolates from the patients were susceptible to 26% of the drugs in case of *E. coli*, 36.66% in case of *Klebsiella sp*. and *Enterrococci sp.,* 50% in case of *Citrobacter sp*. 53.33% of the drugs in case of *S. aureus* sp. and 73.33% in case of *Proteus sp*. The greater extent of *E.coli* resistant to most of the drug increases its occurrence and recurrence which is evident from the Pie chart. This is possibly due to the intrinsic and extrinsic support of interactive environmental factors that favors the metabolic and survival benefit to the organism in the natural condition. Since *E.coli* resides harmlessly in the human intestine and tolerates various antibiotics being consumed by humans cause of various diseases, and when this *E. coli* access the urinary tract becomes a major cause of infection with increased resistance due to previous inappropriate use of antimicrobial agents. The 13% patients are found to be infected by each *S. aureus* and *Citrobacter sp.* suggesting their parity in their infectivity and propagation. But, their drug sensitivity pattern in number (%) of individuals suggests that when a larger number of drugs behave sensitively against *Citrobacter sp*. in more number of patients a small number of drugs are sensitive to *S. aureus* in more number of patients. The result shows that *S. aureus* is more resistant than *Citrobacter sp.* against a large number of drugs. Possibly, as explained earlier, the infectivity/ propagation in individuals and the sensitivity/ resistance *in vivo* or *in vitro* may not coincide due to some environmental or intrinsic/ extrinsic factors. Further investigation is necessary to conclude definitive.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interests with respect to the authorship and/or publication of this article.

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