Comparative Analysis of Uropathogens and Their Drug Resistance Patterns Relating to Urinary Tract Infections (UTI)

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Abstract*:* Urinary tract infection (UTI) is a group of diseases that arise from bacterial colonization of the genitourinary tract, which spans from the kidney's renal cortex to the urethral meatus. A total of 90 individuals with UTI were noticed in the current investigation. There were 45 diabetes individuals and 45 non-diabetic people among them. In this present study, the diabetes group included 26 females and 19 males, whereas the non-diabetic group possessed 29 females and 16 men. There was an important variation in the subjects' urine sugar levels. Rising blood sugar levels were elevated in 45.55% of patients, while postprandial blood sugar levels were elevated in 31.11% of cases. To analyze the study's major observations, several laboratory testing and resistance to medication tests were done. SPSS was employed to verify the study's findings. E Coli was the most often identified pathogen in both diabetes and non-diabetic individuals (46.7% and 53.3%, respectively). Klebsiella spp. came in second for both those with diabetes and non-diabetics, contributing to 61.5% and 38.5% of cases, respectively. The comparison of the number of medications resistant in diabetes and non-diabetic groups was shown to be significant, with the diabetic group having a higher total number of drug obstruction.

Keywords: *Antibacterial, Bacterial strains, Diabetic group, Drug resistance, E. coli, UTI, Uropathogens.*

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INTRODUCTION

UTI is a group of diseases caused by microbe invasion of the tract of the genitals, which spans from the kidney's renal cortex to the urethral meatus. Anatomical anomalies of the urinary tract, decreased local defensive systems, decreasing immunological function, and cognitive impairment, as well as concomitant illnesses such as diabetes, cancer, steroid usage, and chronic debility, can all be sources of risk for UTI[1]. Due to their urinary system structure and reproductive physiology, women are more prone to UTI. The female compared to male UTI ratio within geriatrics as well as the younger population varies greatly, 50:1 and 2:1, respectively [1,2]. Gram-positive and gram-negative bacteria have both been linked to UTI. E. coli was the single most prevalent cause of UTIs among diabetic and non-diabetic people. Other organisms reported include Citrobacter species, Candida albicans, Enterococcus species, Enterobacter, streptococci, Proteus, staphylococci, Klebsiella and also Pseudomonas species [3-5].

Antimicrobial usage in elderly persons with UTI is widespread. Furthermore, past research has shown that 40-75% of antimicrobial usage is improper, and that these antimicrobial drugs inevitably result in the emergence of antibiotic resistance. The advent of strains of bacteria that are resistant continues to provide a problem in treating and controlling the global dissemination of such diseases [6]. As a result, antibiotic resistance has grown into a major public health issue especially diabetic UTI [7]. As a result, there is little known about the pathogenic bacteria that arise from UTI in diabetes individuals and their antibiotic susceptibility profiles. As a result, the goal of this work was to isolate pathogenic bacteria and their susceptibility to antimicrobial patterns. The current study also intends to learn about the microbiology characteristics of UTI in diabetics and non-diabetics in medical center facilities.

LITERATURE REVIEW

According to Maharjan et al., [8] UTIs are among the most prevalent bacterial illnesses, impacting 150 million individuals globally each year. UTIs are a major source of morbidity in elderly men and women of all ages. Regular instances of recur a condition called with septicemia, renal damage, and problems resulting by regular antimicrobial usage, which include high-level resistance to antibiotics and Clostridium difficile colitis, are all serious consequences. Recurrent UTI episodes are often marked by dysuria and urine frequency or hesitation. Additional investigation is warranted if evidence either the history as well as physical examination reveals a complex infections or a different health condition. To establish the diagnosis along with guide therapy, at least single clinical episode has to be confirmed by urine culture [9]. According to recent research, indwelling catheters are responsible for 70-80% of complex UTIs, accounting for a considerable number of cases each year [10]. Included are those affecting the connective tissue (pyelonephritis or prostatitis), which commonly develop in the context of obstructive urinary tract disease or after instrumentation. Chronic UTI is more common among diabetics [11].

Bacteria in urine in levels of 105CFU/ml or greater in two successive samples of urine in women or one urine specimen in males, with no urinary tract-specific symptom.

MATERALS AND METHODS

A. UTsI:

Recurrent UTIs: These occur often in women, especially healthy women without normal genitourinary anatomy. A minimum of three UTIs during 12 months, or a multiple recurrence within six months, is considered recurrent UTI. Recurrences are usually caused by the same organism that caused prior illnesses. Antibiotic resistance is a typical method by the way bacteria can avoid the harmful effects of antimicrobial drugs that is defined based on in vitro quantitative assessment of bacterial sensitivity to antibacterial agents.

B. Methodology

A microscopic examination of a new specimen of urine collected using acceptable procedures can establish pathogenic investigations. A considerable number of bacteria isolated from urine culture can be used for verifying the diagnosis. Aside from microbiological tests, radiographic techniques and other procedures can be used to discover the specific etiology, predisposing factors, the existence of abnormalities, and repercussions.

Informed consent:

Patients who met the eligibility criteria received information on the nature of the investigation and were allowed to participate in the trial after providing written and informed permission. During the 18-month trial period, a total of 90 individuals diagnosed with UTI regardless of type 2 diabetes were invited to participate.

C. Sample collection

Non-invasive methods:

• Clean capture "mid-stream urine sample" (MSU): This is the easiest and most common sample to collect. Clean collect mid-stream urine was collected in a 30 ml wide mouthed, sterile, and leak resistant plastic container [4,11]. The patient is instructed to thoroughly cleanse the perineum and genitalia with water and a mild soapy substance. Antiseptics during washing or cleaning are not advised[9].

• Condom catheters: They are especially useful in obtaining samples from older men who are not suffering from urinary retention issues but do have a severe functional or as mental disorder, which includes dementia. It has a reduced infection risk with catheters that are embedded.

Invasive methods:

• Indwelling Urinary Catheter: Residents with indwelling catheters can be sampled, but only if the catheter is 14 days old. If a catheter has been in place for more than 14 days, the medical instrument should be changed and the sample should be taken from the freshly placed catheter.

• In and Out Urinary Catheterization: It produces the same quality sample as suprapubic aspirate instead runs the risk of introducing germs into the bladder. It is only used when a clean discharged sample has not been obtained as well as suprapubic extraction is not possible.

• Suprapubic Aspiration: This is the gold standard for diagnosis. Any number of species is deemed noteworthy.

• Dip-slide method: The urine is gathered in a dip sliding container with a tiny tray of various media planted on it. Extra urine is emptied before incubating charged dipping slides.

• Gram's stain: A low-cost approach for detecting bacteriuria. For identifying colonies with a count of 105 CFU/ml, confirming the existence of even one microorganism per immersion into an oil field in uncentrifuged urinate has a precision of 94% and a preciseness of 90%. It may detect gram-positive or gram-negative bacteria on a wet film quickly before culture results arrive, allowing an empirical therapy to be initiated. Culture Culture of numbers Urinary pathogens thrive successfully on both simple and selective medium when incubated overnight at 37°C. The most often used media are blood agar, MacConkey agar, especially "Cystine lactose electrolyte deficiency (CLED) agar. MacConkey and CLED agars offer the extra benefit of distinguishing fermenters made from lactose from non-lactose fermenters. They also prevent Proteus spp. from swarming, while CLED agar inhibits Staphylococcus saprophyticus less. Blood agar is suggested for economically precise microorganisms.

Filter paper method: A standard L-shaped filter paper strip (12 x 6 mm) disinfected about 160^{0}C over one hour is employed. Angulated end subsequently foot are submerged in the well-mixed, uncentrifuged urine the specimen, pressed on chosen medium, and incubated. Although eight to ten samples may be analyzed in tandem on a single plate, this approach is both quick and cost effective.

D. Investigations

1. Urine culture and sensitivity
2. Blood sugar levels (Fasting, Postprandial, Random)
3. Urine routine microscopy
4. Glycosylated haemoglobin (HbA1c)

- Urine culture - With the aid of competent laboratory personnel, clean emptied midstream specimens of urine were collected using sterile special urine collecting containers. Each patient was given a pamphlet and instructions on how to obtain a proper midstream pee sample to minimize contaminants prior to sample collection. All of the samples were inoculated with 10 L of urine using a calibrated inoculation needle, and each sample was inoculated on three different media: blood agar, MacConkey agar plates, and CLED agar (Oxoid, Basingstoke, UK). For noticeable growth, all plates have been incubated at 37°C for 24-48 hours.

- The urine routine and microscopy analysis were performed using Dx Urine DS 11 strips of reagent for urine analysis utilizing a very early morning, mid-stream, clean capture urine sample from a sterile container.

- All isolates were tested for antibacterial sensitivity on diagnosing sensitivity test plates using the Kirby-Bauer technique as defined by the "Committee of Clinical Laboratory International Standards" (CLIS, 2014). To make bacterial inoculums, freshly produced bacteria were suspended in 5 mL of sterile saline. "Mueller Hinton plates" of agar were streaked using a sterilized cotton swab. "Becton and Dickinson Company (Franklin Lakes, NJ)" supplied filter paper disks with a specific percentage of antimicrobial medicines.

- To estimate blood HbA1c levels, arterial specimens of blood were obtained in an EDTA vacutainer (2ml) under aseptic conditions and analyzed using a latex immunoturbidimetric analysis (automatically) on an EM360 Transasia machine. It represents blood sugar levels throughout the previous eight to twelve-week span.

E. Statistical analysis:

For statistical analysis, IBM Inc.'s "Statistical Package for Social Sciences (SPSS)" trial version 23 was employed. The data from the research proforma sheet was imported into statistical software over additional analysis. Frequency and percentage were used to express qualitative data. The mean +/standard deviation along with median were used to depict data that is quantitative. For frequency analysis, the data was organized into tables and graphs. The "Chi square test" and the "student's 't' test" were utilized, and a 'p' value of 0.05 was considered statistically significant.

RESULTS

There were 55 girls and 35 men among the 90 cases. In our study, the female:male ratio was 1.57:1. Females were substantially more impacted than males (p=0.035). The majority between the patients were among the ages of 51 and 60, with 33 cases, followed by those 41 to 50 years with 23 cases, 61 to 70 years alongside 17 cases, less than 40 years with 9 cases, and 71 to 80 years with 8 cases (Figure 1). Age groups 41 to 50 and 51 to 60 were substantially more impacted in comparison to other age groups (p<0.001).

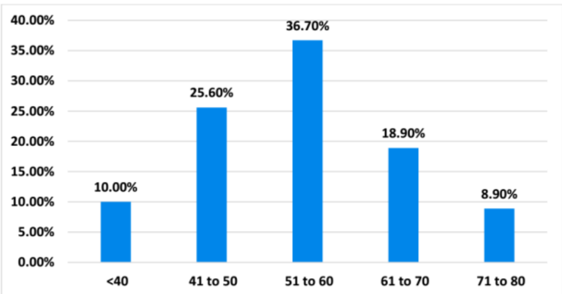

Fig. 1. Distribution of age groups

We had total 45 cases who were diabetic (50%) & 45 cases were non diabetic. Fasting blood sugar level was raised in 41 cases and post prandial blood sugar was raised in 28 cases.

Significant difference was seen in the random blood sugar levels of the patients (p < 0.001). Majority of the patients had 5-7 WBCs (Table 2) on routine urine examination, 28 (31.1%) followed by (27.8%) cases with no WBCs, (23.3%) cases with 8 - 10 cells and (17.8%) cases had more than 10 WBCs.

TABLE II. URINE WBC

Urine WBC	**Frequency**	**%**
Nil	25	28
5-7 cells	28	31
8-10 cells	21	23
>10 cells	16	18
Total	90	100

There was no any significant difference in urine WBC counts. ($p = 0.31$).Out of 90 cases, 29 had no urine sugar (32.22%). In those with urine sugar, 30 had +1 (33.3%) followed by, 12 cases with 3+ (13.3%), 10 cases had 4+ (11.1%) and 9 cases had 2+ (10%) urine sugar. Substantial dissimilarity was realized between the urine sugar values (see Table 3) of the participants. ($p < 0.001$).

TABLE III. EVALUATION OF URINE SUGAR LEVELS

Urine Sugar	**Frequency**	**%**
0	29	32
1+	30	33
2+	9	10
3+	12	13
4+	10	11
Total	90	100
$X^2 = 25$, DF:3, $p< 0.001$ (Significant)		

The most common organism isolated was E Coli in 60 cases and Klebsiella spp.in 13 cases.

TABLE IV. ORGANISMS ISOLATED

Organism Isolated	**Frequency**	**%**
E. Coli	60	67
Klebsiella spp.	13	14
Enterobacter Spp,	6	7
Coagulase Positive Staphylococcus	6	7
Pseudomonas aerogenosa.	5	6
Total	90	100
$X^2 = 124.78$, DF:3,'p' < 0.001, Significant		

According to Table 5, a total of 70 cases remained resilient to Trimethoprim + Sulfamethoxazole, whereas 20 instances were sensitive. There was a substantial difference in Trimethoprim + Sulfamethoxazole resistant among diabetics and non-diabetics (p=0.011).

TABLE V. "TRIMETHOPRIM + SULFAMETHOXAZOLE SENSITIVITY & RESISTANCE IN DIABETICS AND NON-DIABETICS"

Test		**Diabetic**		**Total**
		No	***Yes***	
Trimethoprim + Sulfamethoxazole	Resistant	30	40	70
	Sensitive	15	5	20
Total	45	45	90	

There was a substantial difference in Ampicillin resistance between diabetics along with non-diabetics (Table VI), particularly individuals with diabetes displaying higher resistance (p=0.001).

TABLE VI. "AMPICILLIN SENSITIVITY & RESISTANCE IN DIABETICS AND NON-DIABETICS"

Test			**Diabetic**	**Total**
		No	***Yes***	
Ampicillin	Resistant	21	36	57
	Sensitive	24	9	33
Total		45	45	90

There had been a substantial difference within Amoxicillin resistance as shown in table VII between diabetics and non-diabetics, particularly diabetic patients displaying greater resistance (p=0.006).

TABLE VII. "AMOXICILLIN SENSITIVITY & RESISTANCE IN DIABETICS AND NON-DIABETICS"

Test		**Diabetic**		**Total**
		No	***Yes***	
Amoxicillin	Resistant	25	37	62
	Sensitive	20	8	28
Total		45	45	90

The results showed significant variation in 1st generation Cephalosporin resistance between diabetics and nondiabetics (Figure 2), having diabetic patients displaying higher resistance ($p<0.001$).

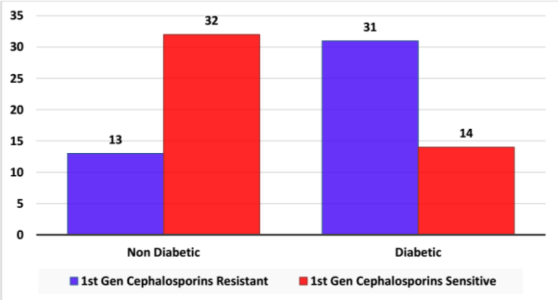

Fig. 2. 1st generation Cephalosporins sensitivity & resistance in Diabetics

Three of the 16 individuals that had been sensitive to all of the medicines were diabetic, whereas the remaining 13 were not. A single medication resistance was observed in seven individuals, four of whom were diabetic and three of whom were not. When we looked at all 90 patients, there was no correlation across the microorganisms and the amount of medications they were resistant as shown in Figure 3, 4 and 5.

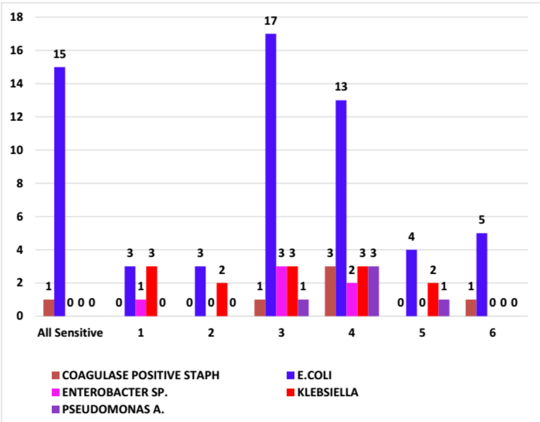

Fig. 3.Organisms and number of drugs resistant

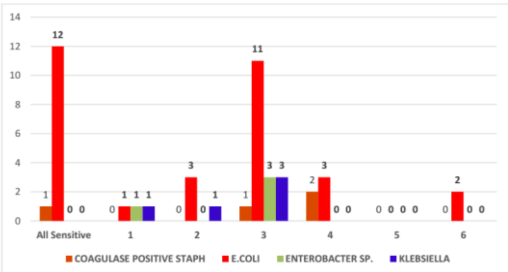

Fig. 4. Organisms and number of drugs resistant in non-diabetics

II. DISCUSSION

UTI is a serious issue in both diabetics and nondiabetics. Because antimicrobial drugs are widely used, drug-resistant microbes arise. Kumar et al. [12] studied 256 diabetic individuals with a female:male proportion of 1.28:1, with 112 men and 144 females. In the non-diabetic group, women (n = 156) outnumbered males (n = 94; 37), which was comparable to the current research. The majority of research indicated that female UTIs outnumber male UTIs. The main cause may be anatomical predilection in females, which allows bacteria accessibility to the bladder [8-13].

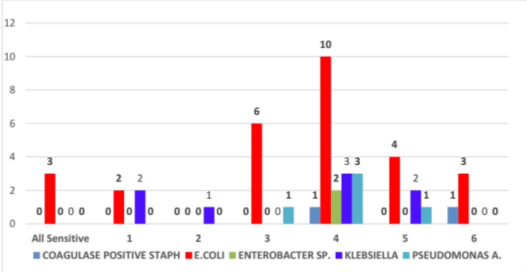

Fig. 5. Organisms and number of drugs resistant in Diabetics

According to a research conducted by Mageto et al. [14], 54.2% of UTI infections had higher fasting blood sugar levels. Furthermore, Maharjan et al. [8] discovered 96% of patients with raised fasting sugar levels, a number greater than the current research.

Karam et al. [9] found that the most common organisms identified were E Coli in 21 cases, Klebsiella spp. in 6 instances, and so on, which is comparable to the current study. According to Zubair et al. [15], E. coli was the most prevalent Gram negative strain (77 of total isolates), next to Klebsiella spp. in 8 along with Proteus mirabilis 2 [16].

There was a substantial difference in Ampicillin resistance comparing diabetics along with nondiabetics, having diabetic patients displaying higher resistance.

TABLE VIII. COMPARISON OF VARIOUS STUDIES

Author and Year	**Sample size and Study design**	**Results**	**Conclusions**
Kumar et al [11]	n= 506. Prospective comparative study	“Observed frequency of organisms isolated: E Coli (60%), Klebsiella spp. (17.1%), Enterobacter spp. (8.6%), Coagulase Positive Staphylococcus [COPS] (5.7%), Pseudomonas aerogenosa (14.3%)”	E Coli was most commonly identified micro-organism in both diabetic and non-diabetic groups. Pseudomonas aerogenosa was identified in 14% diabetic cases.
Zubair et al [15]	n = 199. Observational study	“Observed frequency of organisms isolated in diabetic patients: E Coli (71%), Klebsiella pneumoniae (7.48%), Staphylococcus aureus (9.35%)”	E Coli is the most frequent uropathogen responsible for urinary tract infection in diabetics followed by Staphylococcus aureus sensitive to Nitrofurantoin, Cefixime and Norfloxacin.
Woldemariam et al [10]	n = 248. Cross sectional study	“Observed frequency of isolated uropathogens: E Coli (23.2%), Coagulase Negative Staphylococcus [CONS] (12.5%), Enterococcus spp. (10.7%), Candida albicans (17.9%)”	E coli was the predominant bacterial isolate in diabetics. Large number of these isolates had shown resistance to Ampicillin and penicillin.
Valluri et al [16]	n = 100. Prospective cross-sectional study	“Observed frequency of organisms isolated in diabetics: E Coli (44.45%), Klebsiella spp. (22.23%), Enterococcus (11.12%). Pseudomonas (11.12%)”	Patients with deranged blood sugar levels had higher frequency of bacteruria. E Coli was the most common isolate found responding to cephalosporins and aminoglycosides
Ramrakhia et al [5]	n = 1074. Cross sectional study	“Isolation rates of uropathogens in diabetics: E Coli (60%), Klebsiella (23.3%), Enterococcus (3.3%), Pseudomonas (3.3%), Coagulase Positive Staphylococcus (3.3%). Isolation rates of uropathogens in non diabetics : E Coli (72%), Klebsiella (11.1%), Pseudomonas (11.1%)”.	E. coli was the most common organism in both the diabetic and nondiabetic groups (60% vs 72%; P=0.73). Frequency of Klebsiella was considerably higher in the participants of diabetes but it was not significant (23.3% vs 11.1%; P=0.29)
Present Study	n = 90. Cross sectional and Observational study	“Organisms isolated were E Coli in 60 cases (66.7%) followed by Klebsiella spp.in 13 cases (14.4%), Enterobacter Spp. in 6 cases (6.7%), Coagulase Positive Staphylococcus in 6 cases (6.7%) and Pseudomonas aerogenosa in 5 cases (5.6%)”.	E Coli is the most common organism found in both diabetic and non-diabetic group. Nitrofurantoin, Fluoroquinolones and Cephalosporins showed higher sensitivity in both the groups.

\CONCLUSION

Diabetes mellitus makes people more vulnerable to UTI. In the current study, females were more likely than males to have a UTI throughout both categories (diabetics along with non-diabetics). For both diabetes and non-diabetic groups, the most common isolated were E.coli and Klepsiella spp. The majority of the isolates tested positive for intermediate to low levels of resistance against one or more antimicrobials. When compared to non-diabetic patients, diabetic subjects shown resistance to numerous antimicrobial treatments. According to the findings of this study, Fluoroquinolones, first-generation Cephalosporins (Cephalexin and Cefadroxil) and Nitrofurantoin should be administered empirically until culture and sensitivity data are received.

REFERENCES

[1] James SL, Abate D, Abate KH, Abay SM, Abbafati C, Abbasi N, Abbastabar H, Abd-Allah F, Abdela J, Abdelalim A, Abdollahpour I. "Global, regional, and national incidence, prevalence, and years lived with disability for 354 diseases and injuries for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017". The Lancet. 2018 Nov 10;392(10159):1789-858.

[2] Ahmed SS, Shariq A, Alsalloom AA, Babikir IH, Alhomoud BN. "Uropathogens and their antimicrobial resistance patterns: Relationship with urinary tract infections". International Journal of Health Sciences. 2019 Mar;13(2):48.

[3] Venkatesh RK, Prabhu MM, Nandakumar K, Sreedhara K, Pai R. "Urinary tract infection treatment pattern of elderly patients in a tertiary hospital setup in south India: a prospective study". J Young Pharm 2016;8(2):108-113.

[4] Seo YB, Lee J, Kim YK, Lee SS, Lee JA, Kim HY et al. "Randomized controlled trial of piperacillin tazobactam, cefepime and ertapenem for the treatment of urinary tract infection caused by extended-spectrum beta lactamase-producing Escherichia coli". BMC Infect Dis 2017;17(1):404.

[5] Ramrakhia S, Raja K, Dev K, Kumar A, Kumar V, Kumar B. "Comparison of incidence of urinary tract infection in diabetic vs non-diabetic and associated pathogens". Cureus. 2020 Sep 17;12(9).

[6] Belete MA, Saravanan M. "A systematic review on drug resistant urinary tract infection among pregnant women in developing countries in Africa and Asia; 2005–2016". Infection and drug resistance. 2020 May 18:1465-77.

[7] Czajkowski K, Broś-Konopielko M, Teliga-Czajkowska J. "Urinary tract infection in women. Menopause Review/Przegląd Menopauzalny". 2021 Apr 21;20(1):40-7.

[8] Maharjan, Narayani& Thapa, Niresh & Maharjan, Muna & Sharma, Vijay & Maharjan, Nabina & Paudyal, Rabin. "Pattern of bacteria causing urinary tract infection and their antibiotic susceptibility profile in diabetic and non-diabetic patients in lalitpur, nepal-a hospital based study". 2018;7: 1248-5348.

[9] Karam MR, Habibi M, Bouzari S. "Urinary tract infection: Pathogenicity, antibiotic resistance and development of effective vaccines against Uropathogenic Escherichia coli. Molecular immunology". 2019 Apr 1; 108:56-67.

[10] Murray CJ, Callender CS, Kulikoff XR, Srinivasan V, Abate D, Abate KH, Abay SM, Abbasi N, Abbastabar H, Abdela J, Abdelalim A. "Population and fertility by age and sex for 195 countries and territories, 1950–2017: a systematic analysis for the global burden of disease study 2017". The Lancet. 2018 Nov 10; 392(10159):1995-2051.

[11] Nigussie D, Amsalu A. "Prevalence of uropathogen and their antibiotic resistance pattern among diabetic patients". Turkish Journal of Urology. 2017 Mar; 43(1):85.

[12] Kumar R, Kumar R, Perswani P, Taimur M, Shah A, Shaukat F. "Clinical and microbiological profile of urinary tract infections in diabetic versus non-diabetic individuals". Cureus. 2019 Aug 22; 11 (8).

[13] Woldemariam HK, Geleta DA, Tulu KD, Aber NA, Legese MH, Fenta GM, Ali I. "Common uropathogens and their antibiotic susceptibility pattern among diabetic patients". BMC infectious diseases. 2019 Dec; 19:1-10.

[14] Mageto VM, Gatwiri MS, Njoroge W. "Uropathogens antibiotic resistance patterns among type 2 diabetic patients in Kisii Teaching and Referral Hospital, Kenya". The Pan African Medical Journal. 2018;30.

[15] Zubair KU, Shah AH, Fawwad A, Sabir R, Butt A. "Frequency of urinary tract infection and antibiotic sensitivity of uropathogens in patients with diabetes". Pakistan Journal of Medical Sciences. 2019 Nov;35(6):1664.

[16] Valluri Soma Sekhar, Ramadhenu Rajendra Prasad, M. Rajyalakshmi. "A clinical and microbiological profile of urinary tract infection in diabetes mellitus patients, a South India perceptive". International Journal of Contemporary Medicine Surgery and Radiology. 2020; 5(1):A143-A147.