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The Incidence of Bacterial Urinary Tract Infections and Associated Risk Factors among Patients of Controlled and Uncontrolled Diabetes Mellitus in Sana'a City- Yemen

In UTIs researches:

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Abstract:

The high prevalence of UTIs among DM patients, which is attributed to various impairments in the immune system (low urinary concentration of interleukin -8 and interleukin -6, lower urinary leucocyte cell count). In addition, poor metabolic control and incomplete bladder emptying due to autonomic neuropathy may all contribute to the enhanced risk of UTIs in these patients. DM is associated with UTIs through its effect on the host immune system. Therefore, we detect the incidence of bacterial UTIs in controlled and uncontrolled DM patients in Sana'a City- Yemen, Determine the suitable antibiotic susceptibility against bacterial UTIs in controlled and uncontrolled DM patients, Explore the relationship between bacterial UTIs and the main risk factors in controlled and uncontrolled DM patients. In this cross-sectional study, urine samples were collected from 225 participants from Prof. Mohammed Bamashmous Internal Medicine, Republican Authorized Teaching, Al-Olaqi Specialized Laboratories and Baghdad Laboratories. The sample was processed by physical, chemical and microscopic examination and cultured in CLED agar, MacConkey agar and blood agar, after incubation the sample in 37°C aerobically was proceeded by Gram stain and biochemical test. Among the 225 analyzed samples, 49 (21.8%) were showing sterile urine samples, while 9 (4.0%) showed mixed growth of bacteria possibly due to improper collection of the sample. The remaining 122 (54.2%) samples were positive (significant) with colony count 10^5 CFU/ml, 34 (15.1%) were positive (suspected) with colony count 10^3 - 10^4 CFU/ml, 11 (4.9%) were non-significant with colony count less than 10^2 . The number of subjects with UTI was clearly higher in the uncontrolled glycemic group ($n = 158$, 89.8%) in comparison to the controlled glycemic group ($n = 18$, 10.2%). Our results showed that T2DM was more prevalent (145, 78.7%) than T1DM (39, 17.3%) and GDM (9, 4%) in uncontrolled DM than controlled DM. The women's show high spread of UTIs than men especially in uncontrolled DM than controlled DM this was significant < 0.05 . The prevalence and the distribution of Gram-negative more than Gram-positive bacteria isolated from the clinical samples for both controlled and uncontrolled glycemia groups. *E. coli* (77, 49.4%) was the dominant and significant in UTIs < 0.01 . The high prevalence of UTI confirms that uncontrolled DM is significantly associated with more UTI and regulation of glucose helped to reducing the complications and urinary tract infection. Diabetic patients especially uncontrolled women, are recommended to submit mid-stream urine specimens at regular intervals for culture and routine investigations even the absence of any urinary tract symptoms.

1 Introduction:

Diabetes Mellitus (DM) is a chronic metabolic disease associated with serious complications in various organs including the kidney (Giannakopoulos *et al*, 2019, Al-Areqi *et al*, 2022, Salari *et al*, 2022). In 2017, it was estimated that there were 425 million people with diabetes aged 20-79 years, which is predicted to rise to 642 million in 2040. The worldwide prevalence of DM has risen dramatically over the past two decades (Dave *et al*, 2018, International Diabetes Federation, 2018). Bacterial UTIs are the second virulence factors, which play as a subsidiary part in the anatomical function abnormalities in the kidney, bladder. The obstruction of collecting systems for normal urine flow include renal, ureteric, bladder calculi and benign prostatic hypertrophy, cystic renal disease. In addition, UTIs caused in specific diseases like DM due to the abnormalities in host defense mechanisms and these infections follow surgery or procedures that which done in urinary tract (Al-Ofairi *et al*, 2018, Aydin *et al*, 2020). UTI results from bacteria particularly that exist in the intestinal tract, vagina, nearby the urethra and the ascension of the fecal derived organism from peri-urethral tissues to the bladder and kidneys. These adhere to the bladder receptors sites and if they possess the virulence factors for pyelonephritis they ascend the ureter in the continuous film of urine that reach the ureter to the kidneys (Edrees and Anbar, 2020, Nwafie *et al*, 2021). In women, there are high incidence of UTIs during childbearing age due to sex intercourse or the use of contraception (e.g. diaphragm and spermicides). Especially, in elderly women, patients lose of estrogen causes a change in the vaginal flora, loss of lactobacilli in the vaginal flora, decreased bladder capacity and increased urine production, decreased lower urinary tract sensory and decreased voided volume that resulted in bacterial UTI colonization (Shah *et al*, 2019). Women patients had a higher risk of urinary tract infection than male patients. The cause of higher prevalence of UTI among women is thought to be due to anatomical predisposition compared with male. Women have a short and wide urethra with close proximity to the anus, allowing intestinal organisms easier access to the urethra. Another possible cause may be due to changes in physiological environment of the vagina among diabetic women, such as decreases in normal flora and a less acidic pH of the vaginal surface, this may be exacerbated among women with poor hygiene (Strome *et al*, 2019, Edrees and Anbar, 2020, Cela-Lopez *et al*, 2021, Moradi *et al*, 2021, Jain *et al*, 2022).

The high prevalence of UTIs among DM patients, which attribute to various impairments in the immune system (low urinary concentration of interleukin-8 and interleukin-6, lower urinary leucocyte cell count). In addition, poor metabolic control and incomplete bladder emptying due to autonomic neuropathy may all contribute to the enhanced risk of UTI in these patients (Shah *et al*, 2019, Al-Shammakh *et al*, 2019). The different bacterial species have been colonizing in the urinary tract of diabetic patients due to glycosuria that created a suitable environment for bacterial growth. Also, bladder dysfunction and depletion of local urinary cytokine secretion, depressed T-cell-mediated immune response, decreased production of prostaglandin E, thromboxane B₂ and leukotriene B₄ and depressed antioxidant systems. DM is associated with UTI through its effect on the host immune system especially in type 1 that is considered an autoimmune disease (Shah *et al*, 2019, Jagadeesan *et al*, 2022). In our country "Yemen", there is no published data about the association between UTIs and controlled and uncontrolled DM, therefore the present study has been conducted to explore the incidence of bacterial UTIs and associated risk factors among patients of controlled and uncontrolled DM in Sana'a City- Yemen. The present study has designed to: Detect the incidence of bacterial UTIs in controlled and uncontrolled DM patients in Sana'a City- Yemen, Determine the suitable antibiotic susceptibility against bacterial UTI in controlled and uncontrolled DM patients, Explore the relationship between bacterial UTIs and the main risk factors in controlled and uncontrolled DM patients.

2 Material and Methods:

Study Population: Urine samples were collected from 225 participants from Prof. Mohammed Bamashmouh Internal Medicine, Republican Authorized Teaching, Al-Olaqi Specialized Laboratories and Baghdad Laboratories in Sana'a City, Yemen during the period between June 2022 to June 2023. A questionnaire was conducted for all participants and detailed information on demographic characteristics and other data related to UTIs and DM, was taken for each participant; it is ethically approved.

Urine and blood Collection and Processing: Taken 1.5 ml of blood was collected in EDTA tubes from all participants for determination of glycosylated hemoglobin.

(HbA1c) and 3.5 ml of blood was collected in to serum tubes from the most participants for determination of RBS, FBS, PPBS, Creatinine and Urea. Participants were instructed on How to collect clean catch midstream urine samples in to labeled sterile containers and immediately taken to the laboratory for urine analysis and urine culture. The urine culture carried out within 30 minutes from specimens collection to avoid contamination. The sample was processed by physical, chemical and microscopic examination and cultured in CLED agar, MacConky agar and blood agar, after incubation the sample in 37°C aerobically was proceeded by Gram stain and biochemical test. Finally spread part from suspension colony in Muller Hinton agar to determine susceptibility test.

identification of Isolated Microorganism: Count the approximate number of colonies estimate the number of bacteria, i.e. colony-forming units (CFU) per ml of urine. Colonies were counted on CLED and multiplied by the loop volume. A bacterial count of (100.000) 10^5 per ml was considered significant for UTI. Counts between (100- 10.000) 10^2 - 10^4 per ml was considered as suspected /doubtful bacteriuria. While counts less than (100) 10^2 per ml was considered no significant bacterial growth (contaminated) (Cheesbrough, 2006). UTIs isolate were identified following growth characteristics and biochemical test. Results were not considered for more two clinical isolate obtained from the same patients and the sample considered contamination. No-growth plates were considered as sterile. Biochemical tests were done for both Gram-positive and Gram negative.

Susceptibility Test:

Antibiotic performed susceptibility testing on urine with bacteriuria, particularly from patients with a history of recurring UTI. Antibiotic Susceptibility test was performed by the disc diffusion (Kirby-Bauer) method using Mueller-Hinton Agar.

agar for bacterial isolates. The sensitivity plates were incubated aerobically at 37°C for 24hrs, and the zone of inhibition were recorded. A zone of inhibition greater than 15mm was considered as sensitive, a zone between 13 and 15 as intermediate, and a zone less than 13mm as resistant (Cheesbrough, 2006).

Statistical Analysis: The data were analyzed using a statistical package of social science program (SPSS, version 21) and the results was presented as percentages, mean, standard deviation, median and range. Chi-square X² test was used for categorical variables and to determine significance in variable and UTIs.

3 Results:

Demographic characteristics : Our study showed that the higher older ages of DM patients were higher than other groups with the mean range of age group was (37.86±15.84), also an uncontrolled DM patients were higher than controlled DM ones with significant differences ($P < 0.01$), as showing in Table 4.1 and 4.2 and Figures 4.1. Our data showed that DM is highly incidence in women than men, especially in uncontrolled DM than controlled DM ones with significant differences ($P < 0.01$), as showing in Tables 4.1 and 4.2 and Figures 4.1. The results showed that DM is highly incidence in long duration, especially in an uncontrolled DM than controlled DM ones with significant differences ($P < 0.01$). Our results showed that T2DM was more prevalent than T1DM and GDM, with significant differences ($P < 0.01$). Our results body mass index (BMI) showed that were higher in the case of an uncontrolled DM patients than in controlled DM ones, as showing in Tables 4.1 and 4.2 and Figures 4.1. The results also showed that infections are more prevalent in Sana'a City where it was more prevalence in the cases of uncontrolled DM patients than those who were controlled, then followed by the cities of Taiz and Hadramout, Radaa, all of them showing significant in Figure 4.1.

Table 3.1 Demographic Characteristics in Controlled and Uncontrolled DM Patients

characteristics	controlled	uncontrolled	P-value
Age:	N(%)	N(%)	
13-19	7(14.2%)	10(5.6%)	$P < 0.01$
20-29	0(0%)	15(8.8%)	
30-59	28(57%)	94(53.3%)	
>60	14(28.8%)	57(32.3%)	
Total	49(21.7%)	176(78.3%)	
Gender:	N(%)	N(%)	
Female	28(57.2%)	102(60%)	$P < 0.01$
Male	21(42.8%)	74(40%)	
Total	49(21.7%)	176(78.3%)	
Duration of DM:	N(%)	N(%)	
One year	13(26.5%)	33(18.8%)	$P < 0.01$
1-5 years	10(20.4%)	42(23.8%)	
5-10 years	11(22.5%)	33(20.4%)	
>10 years	15(30.6%)	68(37%)	
Total	49(21.7%)	176(78.3%)	
Type of DM:	N(%)	N(%)	
Type 1	11(22.4%)	28(15.9%)	$P < 0.01$
Type 2	35(71.6%)	142(80.7%)	
GDM	3(6%)	6(3.4%)	
Total	49(21.7%)	176(78.3%)	
BMI:	N(%)	N(%)	
30-50	15(30.6%)	24(13.6%)	$P < 0.01$
50-80	27(55%)	74(42%)	
80-100	7(14.4%)	75(42.7%)	
100-120	0(0%)	3(1.7%)	
Total	49(21.7%)	176(78.3%)	

Residency for DM :

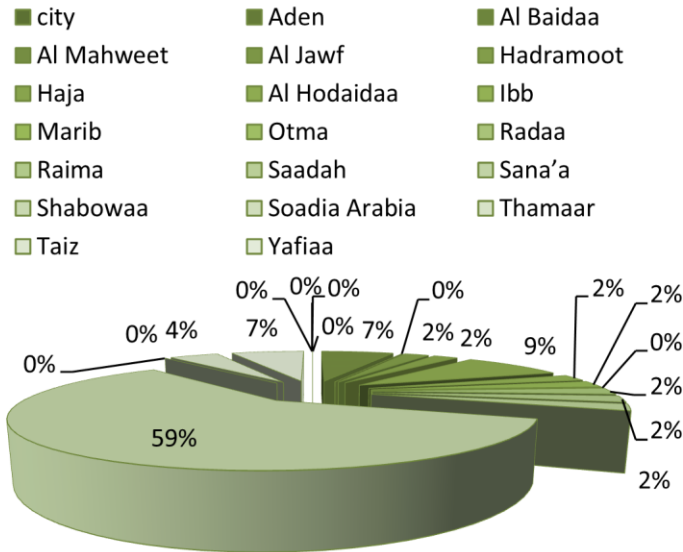


Figure3.1TheResidencyforControlledandUncontrolled DM Patients

Symptoms and ASB in DM Patients : The symptoms waremorespread in uncontrolled DM thancontrolled DM and the ASB (108,48%),urgency (88,39.1%) Burning (77,34.2%) frequency (72,32.0%) dysuria (60,26.7%)Supra-pubic pain (49,21.8%)itching(60,26.7%)incontinous(38,16.9%)flank pain(56,24.9%) fever(22,9.8%) hematuria(5,2.2%)discharge (11,4.9%)vomiting(11,4.9%)chills(2,0.9%)intable3.2.

Complication in DM Patients : The study also showed higher prevalence in complication of DM in uncontrolled DM comparedwithcontrolledDM andtheperipheralneuropathyis themoreprevalence(186,82.7%),retinopathy(125,55.6%) obesity(99,44%)incompletebladder(88,39.1%)cholesterol (67,29.8%)nephropathy(24.0%)cardiovascular(51,22.7%) hypertension(81,36%)prostatesyndrome(18,8.0%)

Risk Factors: The results showed the risk factors and the more effect is the diet, insurance statusphysical activity , showing qhat ,tobacco consumption these were higher in uncontrolledDMcomparedincontrolledDMalsoeducation andtherapy haverelationship withuncontrolledDMall of the factors in respectably were significant **in table 3.4**

Table3.2prevalenceofsymptomsofUTIincontrolledand uncontrolled DM patients

Symptoms	Controlled	Uncontrolled	P. value
ASB	N(%)	N(%)	
YES	23(47%)	85(48%)	P<0.01
NO	26(53%)	91(52%)	
Total	49(21.7%)	176(78.3%)	
Symptoms:			
Dysuria:	N(%)	N(%)	
Yes	10(20.4%)	50(28.4%)	
No	39(79.6%)	126(71.6%)	
Total	49(21.7%)	176(78.3%)	
Urgency:	N(%)	N(%)	
Yes	17(34.6%)	71(40%)	P<0.01
No	32(65.4%)	105(60%)	
Total	49	176	
Frequency:	N(%)	N(%)	
Yes	10(20.4%)	62(36.4%)	P<0.01
No	39(79.6%)	114(63.6%)	
Total	49(21.7%)	176(78.3%)	
Burning:	N(%)	N(%)	
Yes	13(26.6%)	64(36%)	P<0.05
No	36(73.4%)	112(64%)	
Total	49	176	
Hematuria:	N(%)	N(%)	
Yes	2(4%)	3(1.7%)	
No	47(96%)	173(98.3%)	
Total	49(21.7%)	176(78.3%)	
Suprapubicpain:	N(%)	N(%)	
Yes	5(10.2%)	44(25%)	
No	44(89.8%)	132(75%)	
Total	49(21.7%)	176(87.3%)	
Vomiting:	N(%)	N(%)	
Yes	0(0%)	11(4.%)	P<0.05
No	49(100%)	165(93.7%)	
Total	49(21.7%)	176(78.3%)	
Fever	N(%)	N(%)	
Yes	0(0%)	22(12.5%)	P<0.01
No	49(100%)	154(87.5%)	
Total	49	176	
Discharge:	N(%)	N(%)	
Yes	1(2%)	10(5.7%)	P<0.01
No	48(98%)	166(94.3%)	
Total	49(21.7%)	176(78.3%)	
Incontinous:	N(%)	N(%)	
Yes	6(12.2%)	32(18.1%)	P<0.05
No	43(87.8%)	144(81.9%)	
Total	49	176	
Itching:	N(%)	N(%)	
Yes	9(18.3%)	51(28.9%)	
No	40(81.7%)	125(71.1%)	
Total	49(21.7%)	176(78.3%)	
Flank pain:	N(%)	N(%)	
Yes	11(22.4%)	55(31.2%)	P<0.05
No	38(77.6%)	121(68.8%)	
Total	49(21.7%)	176(78.3%)	
Chills:	N(%)	N(%)	
Yes	0(0%)	2(1.1%)	
No	49(100%)	174(98.9%)	
Total	49(21.7%)	176(78.3%)	

Table 3.3 prevalence of complications in controlled and uncontrolled DM patients

Complication	Controlled N(%)	Uncontrolled N(%)	P.value
Incomplete bladder:			
Yes	14(28.5%)	74(42%)	P<0.01
No	35(71.5%)	102(58%)	
Total	49(21.7%)	176(78.3%)	
Prostate syndrome:			
Yes	6(12.2%)	12(6.8%)	P0.01
No	43(87.8%)	164(93.2%)	
Total	49(21.7%)	176(78.3%)	
Hypertension:			
Yes	14(28.5%)	67(38%)	P<0.01
No	35(71.5%)	109(62%)	
Total	49(21.7%)	176(78.3%)	
Obesity:			
Yes	12(24.4%)	87(49.4%)	P<0.01
No	37(75.6%)	89(50.6%)	
Total	49(21.7%)	176(78.3%)	
Cardiovascular:			
Yes	7(14.2%)	44(25%)	P<0.01
No	42(85.8%)	132(75%)	
Total	49(21.7%)	176(78.3%)	
Nephropathy:			
Yes	6(12.2%)	48(27.2%)	P<0.01
No	43(87.8%)	128(72.8%)	
Total	49(21.7%)	176(78.3%)	
Neuropathy:			
Yes	14(28.5%)	65(36.9%)	P<0.01
No	35(71.5%)	111(63.1%)	
Total	49(21.7%)	176(78.3%)	
Cholesterol:			
Yes	9(18.3%)	58(33%)	P<0.01
No	40(81.7%)	118(67%)	
Total	49(21.7%)	176(78.3%)	
Peripheral:			
Yes	31(63.2%)	155(88%)	P<0.01
No	18(36.8%)	21(12%)	
Total	49(21.7%)	176(78.3%)	
Retinopathy:			
Yes	22(45%)	103(58.5%)	P<0.01
No	27(55%)	73(41.5%)	
Total	49(21.7%)	176(78.3%)	

Check of DM : HbA1c, FBS, RBS, PPBS, Creatinine, and Urea were more higher in uncontrolled DM than controlled DM and no appear any significant relationship with UTIs the mean was for all in **table 3.5**.

Table 3.4 Risk Factor Affected in Controlled and Uncontrolled DM Patients

Risk factors	Controlled N(%)	Uncontrolled N(%)	P. value
Diet:			
Yes	29(59%)	13(7.3%)	P0.01
No	20(41%)	163(92.7%)	
Total	49(21.7%)	176(78.3%)	
physical activity:			
Yes	40(82%)	62(46%)	P<0.01
No	9(18%)	114(64%)	
Total	49(21.7%)	176(78.3%)	
qhatchowing:			
Yes	10(20.4%)	123(69.8%)	P<0.01
No	39(79.6%)	53(30.2%)	
Total	49(21.7%)	176(78.3%)	
tobacco consumption:			
Yes	6(12.2%)	61(34.6%)	P<0.01
No	43(87.8%)	115(65.4%)	
Total	49(21.7%)	176(78.3%)	
Insurance status:			
Yes	9(18.3%)	10(5.6%)	P<0.01
No	40(81.7%)	166(94.4%)	
Total	49(21.7%)	176(78.3%)	
Material status:			
Married	30(61.2%)	121(68.7%)	P<0.01
Unmarried	10(20.4%)	18(10.2%)	
Widow	9(18.4%)	37(21.1%)	
Total	49(21.7%)	176(78.3%)	
Education:			
Above	0(0%)	3(1.7%)	P<0.01
Graduate	9(18.3%)	13(7.3%)	
High secondary	3(6.3%)	7(3.9%)	
Secondary	10(20.4%)	33(18.7%)	P<0.01
Primary	14(28.5%)	50(28.4%)	
Illiterate	13(26.5%)	70(40%)	
Total	49(21.7%)	176(78.3%)	
Thereby:			
Insulin	13(26.5%)	35(20%)	P<0.01
Insulin plus oral	7(14.2%)	27(15.3%)	
antidiabetes Oral	27(55.3%)	95(54%)	
antidiabetes	2(4%)	19(10.7%)	P0.01
Without	49(21.7%)	176(78.3%)	
Total			

Chemical Examination and UTIs: The result also showed that in the case of the chemical test, the presence of nitrite, protein, blood and leucocyte indicates the presence of infections, and also the presence of glucose was an indicator of the case of high and the appearance of sugar in the urine in the chemical test. Likewise, the protein was the same thing that affected in uncontrolled DM patients, while its appearance was less and was almost negligible in the case of diabetes patients in **table 3.7**.

Table3.5CheckforDM Patients

character	N	Mean_+SD	P Value	95%confidence interval	
HbA1c:	225	8.8+4.1	<0.01	Lower bound 0.000	Upper bound 0.21
FBS:	156	190+89	0.7	0.923	0.979
RBS:	47	205.49+136.6...and the median .140	0.9	0.965	0.999
PPBS:	144	297.7+124.5	0.5	0.482	0.612
Ceratinine:	141	0.9055+0.873.....and the median .08	0.7	0.719	0.828
Urea:	140	28.50+11.5	0.2	0.230	0.348

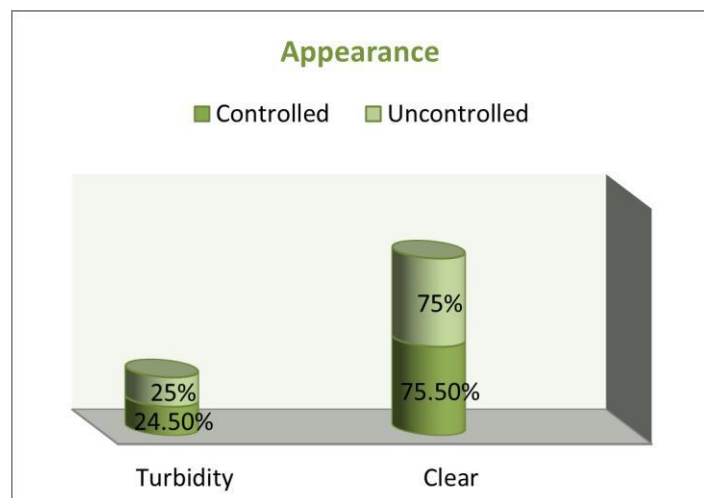


Figure3.6ThePhysicalExaminationinControlledand Uncontrolled DM Patients

Microscopic Examination and UTIs: The results also showed that the microscopic test indicates the presence of urinary infections, especially WBC, RBC, Epithelial Cell, Mucus, Bacteria and Yeast, where all of these were more in the case of uncontrolled DM patients than the controlled DM and since the increase in the most of them, bacterial growth was found after culturing the samples that including more than one of them and a strong relationship was found in all of the above while there was no relationship in the rest such as cast, *Schistosoma* in table.3.8 .

Table3.7ChemicalExaminationinDMPatients

Chemical examination	DM	Pvalue
PH:	N(%)	P0.3
Acidic alkaline	205(91.1%) 20(8.9%)	
Specific gravity: Mean+SD	2.38+11.8	P0.8
Blood:Mean+SD	2.71+0.75	P0.06
Nitrite: Mean+SD	2.56+0.66	P0.2
Protein: Mean+SD	2.81+0.84	P0.1
Glucose: Mean+SD	3.59+0.71	P0.3
Ketone:Mean+SD	2.86+0.82	P0.07
Bilirubin: Mean+SD	3.0+0.89	P0.3
Urobilinogen: Mean+SD	2.83+0.57	P0.05

Table3.8.MicroscopicExaminationinDMPatients

Microscopic examination	DM Mean+SD	Pvalue
WBC:	7.50+5.59	P<0.01
RBC:	2.22+2.39	P0.01
Epithelial Cell:	2.14+0.76	P<0.01
Crystals:	3.14+1.04	
Mucus:	2.09+7.6	P<0.01
Cast:	N(%)	
Seen	7(3.1%)	
No	218(96.9%)	
Bacteria:	N(%)	P<0.05
Seen	20(8.9%)	
No	205(91.1%)	
Amorphous:	3.14+1.04	
Yeast:	N(%)	P<0.05
Seen	9(4%)	
No	216(96%)	
Parasite ova:	N(%)	
<i>S.haematubium</i>	3(1.3%)	
<i>E.vermicularius</i>	1(0.4%)	

Study Population: This study was conducted on urine samples from 225 diabetic patients during the period between July 2022 and December 2022. Among the 225 analyzed samples, 49 (21.8%) were showing sterile urine samples, while 9 (4.0%) showed mixed growth of bacteria possibly due to improper collection of the sample. The remaining 122 (54.2%) samples were positive (significant) with colony count 10^5 CFU/ml, 34 (15.1%) were positive (suspected) with colony count 10^3 - 10^4 CFU/ml, 11 (4.9%) were non-significant with colony count less than 10^2 for uropathogens in table 3.8. The studied population was classified according to the glycemic status; patients with controlled glycemia ($HbA1c < 6.5$) and patients with uncontrolled glycemia ($HbA1c \geq 6.5$). The number of subjects with UTI was clearly higher in the uncontrolled glycemic group ($n = 158$, 89.8%) in comparison to the controlled glycemic group ($n = 18$, 10.2%).

In the addition the UTI was higher in T2 than other T1 and GDM in uncontrolled DM than controlled DM. The women's show high spread of UTIs than men especially in uncontrolled DM 106 than controlled DM 25 this was significant 0.013 but the man's show low UTIs in status uncontrolled DM 74 and in controlled DM was just 21 and this was significant < 0.05 in Figure 3.9

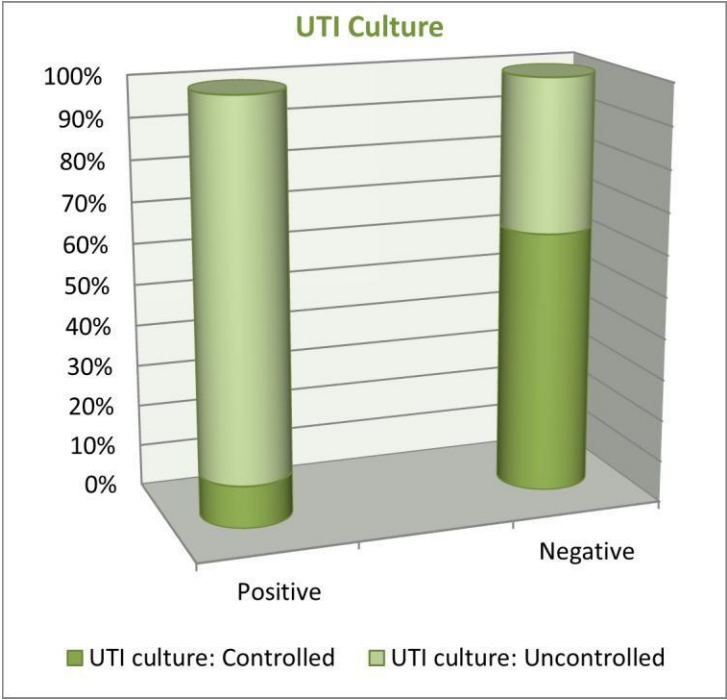


Figure 3.4 UTI in DM Patients

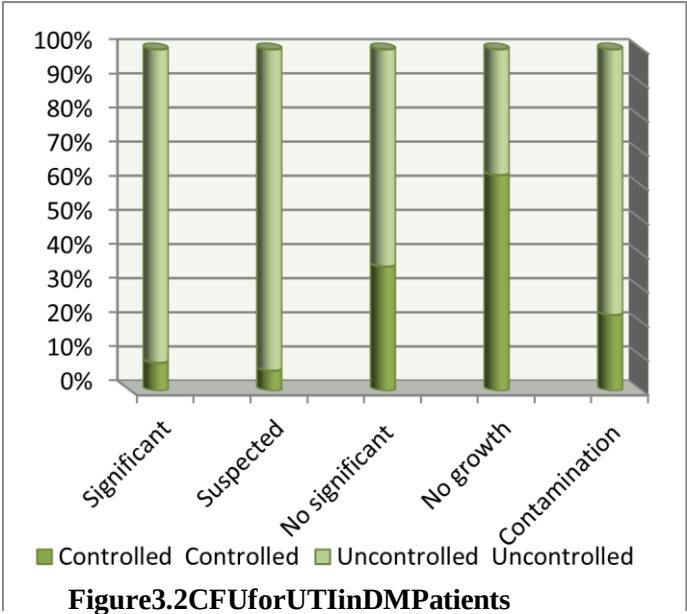


Figure 3.2 CFU for UTI in DM Patients

The prevalence and the distribution of Gram-negative more than Gram-positive bacteria isolated from the clinical samples for both controlled and uncontrolled glycemia groups. These isolates from both females and males represented clinically significant pathogens. *E.coli* (77,49.4%) was the dominant and significant in UTIs $P < 0.01$ after that was *K.pneumoniae* (17,10.8%) *S.aureus* (13,8.8%), *P.aeruginosa* (10,6.4%) *P.mairabilis* (8,5.1%) *Citrobacter* (5,3.2%) *St.agalactiae* (5,3.2%) *S.saprophyticus* (4,2.5%) *P.valgarius* (3,1.9%) *K.other Sp* (3,1.9%) *St.other pneumoniae* (1,0.6%) *St.pyogens* (1,0.6%) all these show any significant

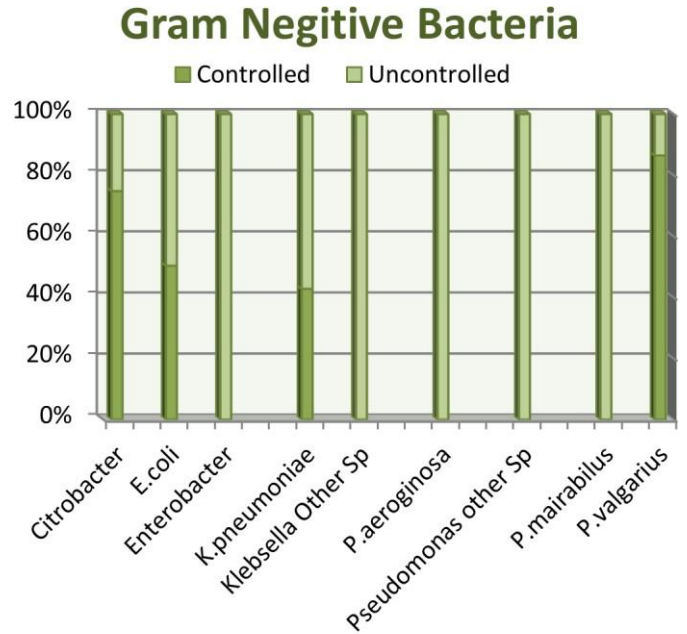
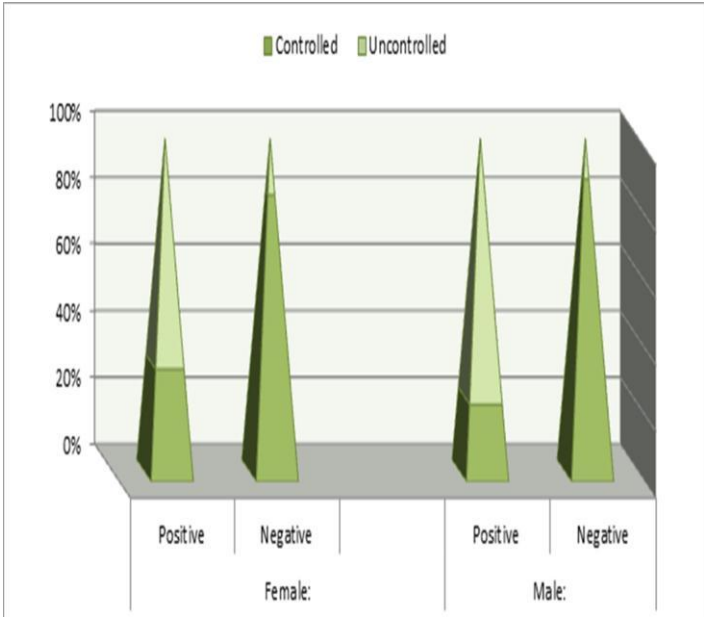
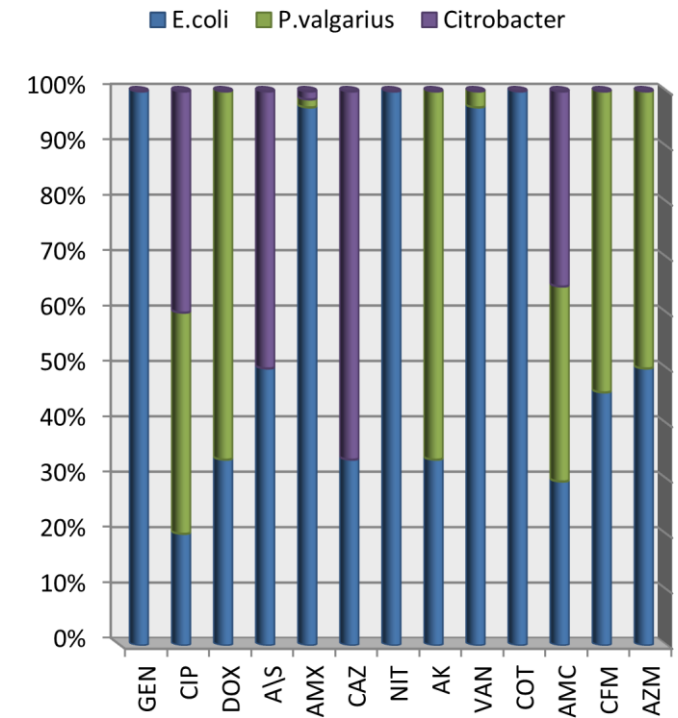
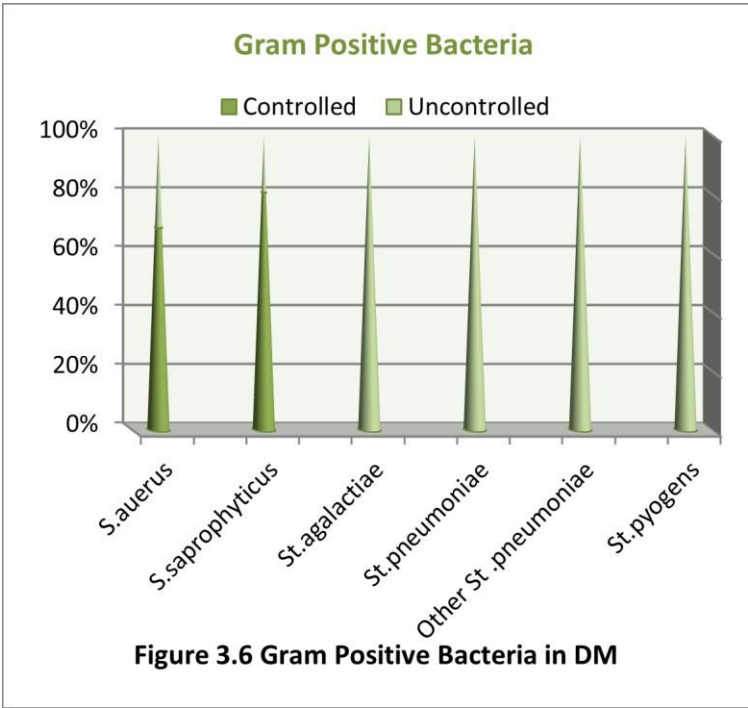
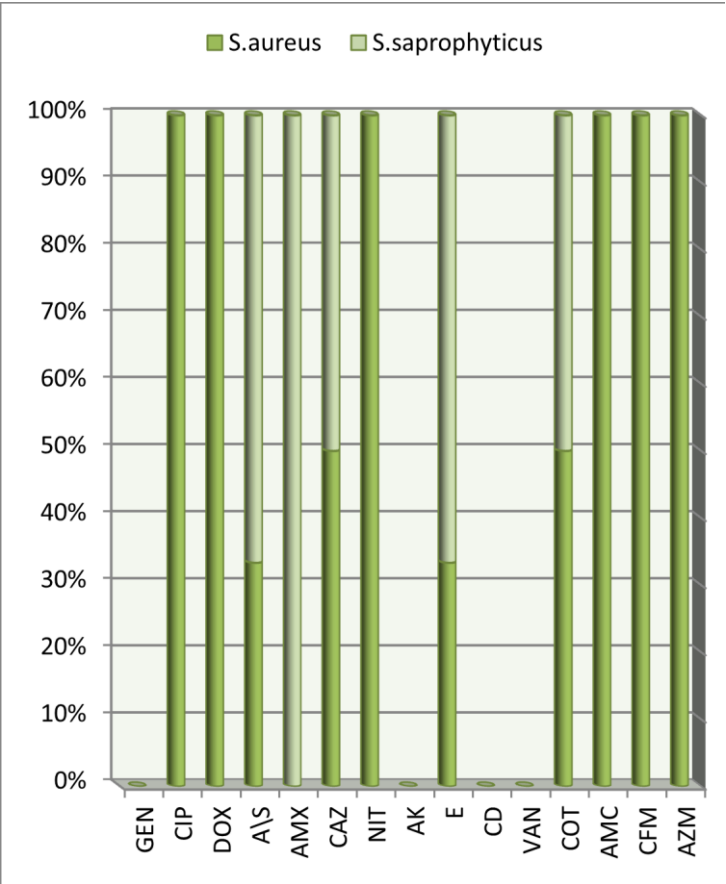


Figure 3.5 Gram Negative Bacteria in DM



Antibiotics for UTI in DM Patients UTIs:

The results also showed more resistant to antibiotics in all uncontrolled and controlled DM patients: GEN (52.4%), AK (41.3%), NIT (40.9%), DOX (29.8%), CIP (29.3%), COT (27.6%), VAN (24.9%), CD (24.9%), CAZ (18.2%), AMC (17.3%), E (16.0%), AMX (14.2%), AS (12.9%), AZM (11.1%), CFM (4.2%).



4. Discussion:

The study showing higher of UTI in older age and the mean range of age was (37.86+15.84) also its higher in uncontrolled DM than controlled DM this was significant 0.0001 this agree with (Muthulakshmi and Gopalakrishnan, 2017, Al-Ofairy *etal*,2018)and dis agree with (Swify *et al*, 2016,Ahmed *et al*, 2020, Edrees and Anbar,2020).Also the duration of DM especially in duration higher than 10 years showedHigh spread of UTIs in status uncontrolled DM and few in controlled DM 74 (32%) this is was significant 0.0001this agree with(Swify *et al*, 2016, Al-Ofairy *et al*, 2018, Dave*et al*,2018,)butthiswasdisagreewith). (Ebidor *et al*,2015,Dave *et al*,2018,Ahmed*et al*, 2020). because the susceptibility of DM patients could be explained by diminished neutrophil response, lower urinary cytokines, and leukocyte concentration which might facilities the adhesion of microorganisms to uroepthelial cellOur results showed that T2DM was more prevalent than T1DM and GDM. observed the UTI more and significant in Type 2 and GDM(0.0001,0.003) respectably (Shah and Paracha, 2016, Al-Ofairy *et al*, 2018 Shah *et al*, 2019,Desouky *et al*, 2020). These results were similar with other reports which illustrated that DM is the comments' metabolic diabetes constituting nearly 90% of the diabetes population.Our results also showedthat highweight from50-80 andfrom80-100 was significant on UTIsaffects the regulation of sugar and was higher in the case of uncontrolled DM than in controlled DM, while this agree with(Desouky *et al*, 2020) and dis agreewith(Swify *et al*, 2016)Whoshowed no relationship between weight and UTI. The results also showed that infections are more prevalent in the city of Sana'a ,Where it was more prevalent in the cases uncontrolled than those who were controlled , then followed by the cities of Taiz and Dhamar and all these cities showed a significant relationship 0.001,0.02,0.01 respectivelythis maybe because the study was in Sana'a City and the most of patients from Sana'a City. The symptoms ware more spread in uncontrolled DM than controlled DM , urgency ,Burning ,frequency, dysuria , Supra-pubic pain , itching , incontinous . this agree with (Muthulakshmi and Gopalakrishnan , 2017,Anejo- Okopi *etal*, 2017 ,Dave *et al*, 2018, Shah *et al*, 2019). but this dis agreewith (Al-Ofairy *et al* 2018, Gomez- Ochoa and Vega-Vera, 2019,Al-Baghdadi *et al*, 2021) Who wereshowed that the asymptomatic (ASB) bacteriuria were the most common infection in diabetic patients.

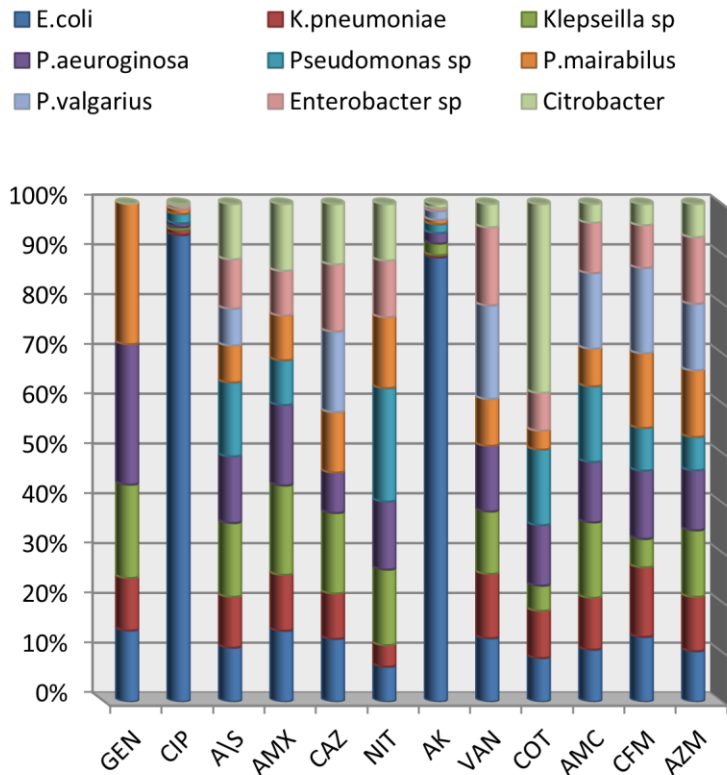


Figure3.10AntibioticsResistantinGramPositivein Uncontrolled DM Patients

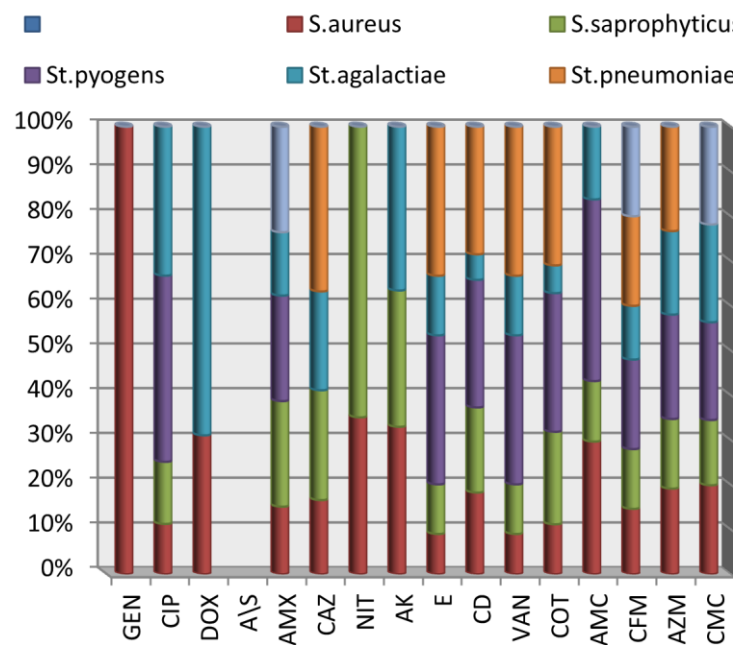


Figure3.11AntibioticsResistantinGramPositivein UncontrolledDMPatients

All these were higher than other types of symptoms of UTI may be because bladder is a store house for urine. Uropathogens can enter and colonize in bladder much easier than other part of urinary tract system flank pain, fever, hematuria, discharge, vomiting, chills this may be symptoms when the uropathogen reach in to kidney. Our study also showed higher prevalence in complications of DM in uncontrolled DM compared with controlled DM and the peripheral neuropathy is the more prevalence (186, 82.7%), then retinopathy (125, 55.6%) obesity (99, 44%) (Sweify *et al*, 2016, Dave *et al*, 2018, Al-Shammakh *et al*, 2019). Obesity might be considered as a cofounder in the correlation between glycemic control and UTI as obesity rates are about (99, 44%) in our study this agree with (Sewify *et al*, 2016). Nephropathy (54, 24.0%) cardiovascular (51, 22.7%) hypertension (81, 36%) prostate syndrome (18, 8.0%) incomplete bladder (88, 39.1%) cholesterol (67, 29.8%). Also the study showed the risk factors effect in controlled DM and have related with UTIs is the diet (18.3%) was significant 0.0001, physical activity (45.3%) was significant 0.0001 and showing qhat (59.1%) was significant 0.01, tobacco consumption (29.8%) was significant 0.002, insurance status (8.4%) was significant 0.004, material status was significant, these were higher in uncontrolled DM compared in controlled DM and were all of them significant. This agree with (Anejo-Okopi *et al*, 2017, Saghire *et al*, 2019). Our results showed that in the case of treatment in patients with diabetes, oral antidiabetes, oral antidiabetes are more used than others, followed by insulin. A strong relationship was also found in the case of education, as the percentage of illiterate persons reached 70 in the case of non-member, while those who joined were 13, and the total percentage was 36.9% followed by primary with a percentage of 64 (28.4%) this agree with (Sweify *et al*, 2016, Dave *et al*, 2018). Predisposing conditions to urinary tract infection were renal calculi, older age female gender, high glucose in blood and the main factors increasing the susceptibility of UTIs in Yemen comparing with developed countries were that large of patients with DM and self-monitoring and follow up for check and adjust treatment in Patients is low or absent. In addition, there were high occurrence of possible co-existent factors that increase the susceptibility to contract UTI among patients of those, personal hygiene, sexual practices and water intake (Anejo-Okopi *et al*, 2017, Dave *et al*, 2018, Giannakopoulos *et al*, 2019, Storme *et al*, 2019, Jagadeesan *et al*, 2022). FBS, RBS, PPBS, Creatinine, and Urea and the mean and standard deviation for all of them were (190+89, 205.4+136.6, 297+124, 0.9+0.8, 28.5+11.5) they were more higher in uncontrolled DM than controlled DM and no appear any significant or relationship with UTIs the

mean was for all this agree to (Shah and Paracha, 2016, Al-Ofairy *et al*, 2018) and disagree with (Desouky *et al*, 2020). HbA1c (8.8+4.1) was significant 0.004 to UTI this agree to (Shah *et al*, 2019, Desouky *et al*, 2020, Ahmed *et al*, 2020). Also the study show the physical examination for urine analysis the yellow, orange (0.0001, 0.0001) respectably and more spread in patients with DM in all uncontrolled and controlled DM this agree with (Parida *et al*, 2018) may be the normal color ranges from yellow to orange and this result of the pigment called urochrome, however disease states can cause the color of urine to change from normal color extremes. Our result also showed that in the case of the chemical test, the presence of nitrite, that observed markedly in the samples from which Gram -negative bacterial like *E. coli*, *K. pneumoniae* and *proteus* spp are able to reduce nitrate present in urine to nitrite this agree with (Parida *et al*, 2018), protein, blood, leukocyte in state of exist of pus or WBC in urine that indicate to inflammation may be bacterial or other inflammation, and also the presence of glucose was an indicator of the case of high and the appearance of sugar in the urine and in this status we observed yeast in microscopic examination (Parida *et al*, 2018). That affected in uncontrolled DM patients, while its appearance was less and was almost negligible in the case of controlled patients in (Gomez - Ochoa and Vega - Vera, 2020, Shah and Paracha, 2016). Glucoseuria was also found to be associated with UTI this agree with (Swaify *et al*, 2016, Alsamarai *et al*, 2016, Al-Ofairy *et al*, 2018). Diabetic patients may be appeared to be at a higher risk for colonization with the virulent make suitable environment for adhesion of uropathogens and genital infection in uroepithelial cell and promote colonization and invasion. The microscopic examination of urine showed that the white blood cell (WBC), red blood cell (RBC), epithelial cell, mucus, bacteria, yeast, was significant in all of them (<0.0001, 0.01, 0.0001, 0.0001, crystals, 0.004, 0.004) respectively crystals, *Schistosma*

haematobium, *Entrobium vermicularis* increased in uncontrolled DM than controlled DM and they found a heavy and appreciable bacterial growth in patients with bacteriuria this agree to (Shah and Paracha, 2016, Al-Ofairy *et al*, 2018, Parida *et al*, 2018, Al-Shammakh *et al*, 2019, Awosolu *et al*, 2020, Taghipour *et al*, 2020). Generally, urine is considered sterile and germ free different studies found that most uropathogens responsible for UTIs colonize the colon and perianal region.

Faucal pathogen that ascend with the opening of urethra, stick to the wall of urethra, multiply and move up towards bladder and causing signs and symptoms. Pathogenesis can be ascending or haematogenous route this agrees with (Shah *et al*, 2019). DM is a metabolic disorder resulting from a defect in insulin secretion or insulin action or both leads to chronic hyperglycemia (Al Ofairy *et al*, 2018). In the present study, we investigated the possible impact of the glycemic control on the UTI prevalence, antimicrobial drugs susceptibility in diabetic patients and complications and risk factors in patients in controlled and uncontrolled DM. Our main findings are the following there is much higher prevalence of UTI in diabetic patients with uncontrolled glycemia, the glycemic control does affect the distribution of UTI according to age. This finding agrees with (Coronel *et al*, 2015, Sewify *et al*, 2016, Ahmed *et al*, 2020, Dave *et al*, 2018, Shah *et al*, 2019). DM attributes various impairment in the immune system (low urinary concentration of interleukin-8 and interleukin-6, lower urinary leucocyte cell count and granulocyte dysfunction possibly because of abnormal intracellular calcium of immune cell) poor metabolic control and incomplete bladder emptying due to autonomic neuropathy may all contribute to the enhanced risk of UTI in DM. UTI are documented as an inflammatory response of the uro-epithelium by bacterial invasion that are usually associated with bacteriuria and pyuria (Nitan *et al*, 2015, Shah *et al*, 2019, Mamo *et al*, 2019, Jagadeesan *et al*, 2022). Our results show that UTIs in female (61.9%) more than in male (38.1%) and this was significant 0.004 this agrees with (Shah and Paracha, 2016, Obeagu *et al*, 2016, John *et al*, 2016, Al-Ofairy *et al*, 2018, Parida *et al*, 2018, Shah *et al*, 2019) and disagree with (Ahmed *et al*, 2020) who showed that men are more prone to UTIs than women. In terms of gender, females are more prone to UTI than males. Women are vulnerable to UTI due to their anatomy and reproductive physiology, short urethra, urethra closer to perirectal area where pathogen colonies easier, absence of bacteriostatic prostatic secretion and sexual intercourse. Gram negative bacteria are more commonly causing UTI than gram positive bacteria. *E. coli* remains the most common etiological agent of UTIs. *E. coli* is bacterium of the digestive tract. It can spread, especially, in women for anatomical reasons: down to the anus and then back in the urinary tract by multiplying and causing UTIs. This agrees with many studies (Sewify *et al*, 2016, Al Ofairy *et al*, 2018, Dave *et al*, 2018, Shah *et al*, 2019, Ahmed *et al*, 2020).

This disagrees with (Patnaik *et al*, 2017). Who reported that the most frequent bacterial infection is caused by *K. pneumoniae* and (Sewify *et al*, 2016) that who report that

the *Candida albicans* this differentiate because we don't culture fungi in our study. Gram-negative strains including *E. coli* predominant because the bacterial factors comprise the type 1 fimbriae which are present in all *E. coli* strains and probably have a role in promoting initial colonization and other bacterial factors contribute to the pathogenicity in diabetes mellitus this may be due to the majority of diabetic patients in this investigation take anti-diabetic drugs regularly which may reduce their susceptibility and second was *K. pneumoniae* were agreement with previous reported studies (Alsamara *et al*, 2016, Ahmed *et al*, 2020, Shah *et al*, 2019). The study also showed more resistant to antibiotics in all uncontrolled and controlled DM patients GEN (52.4%) AK (41.3%) NIT (40.9%) DOX (29.8%) CIP (29.3%) COT (27.6%) VAN (24.9%) CD (24.9%) CAZ (18.2%) AMC (17.3%) E (16.0%) AMX (14.2%) AS (12.9%) AZM (11.1%) CFM (4.2%) CMC (1%) Indeed, high resistance to this first-line antibiotic is of big concern to clinicians in Yemen and other alternatives should be developed antibiotics resistance among bacteria in our study is may be due to several reasons including the wide use of antibiotics by patients themselves (self-treatment), the blind treatment (prescribe antibiotics by physicians without antibiotics sensitivity test) (Swify *et al*, 2016, Angoti *et al*, 2016, Mazzariol *et al*, 2017, Ahmed *et al*, 2020). Enterococci exhibit intrinsic and acquired resistance to various antibiotics such as *Beta*-lactams, aminoglycosides, macrolides, lincosamides, cotrimoxazole, glycopeptides, associated with mobile genetic elements or chromosomal exchange and mutation (Gianakopoulos *et al*, 2019, Miguel *et al*, 2020).

5. Consolation and Recommendation : These findings add further evidence to the importance of tighter glycemic control in reducing the occurrence of UTI and most probably improving the clinical outcome. UTI are more frequent and are likely to have a more complicated course in DM patients. The high prevalence of UTI confirms that uncontrolled DM is significantly associated with more UTI.

The prevalence among female was higher than males in uncontrolled DM than controlled DM. Regulation of glucose helped to reducing the complications and urinary tract infection. Common conditions predisposing to UTI in DM were diet, physical activity, what chowing, tobacco consumption, insurance status were significantly that leading to increasing the glucose in the blood as UTI. Symptoms more frequent than Asymptomatic. The symptoms were more spread in uncontrolled DM than

controlled DM. The prevalence and the distribution of Gram-negative more than Gram-positive bacteria isolated from the clinical samples for both controlled and uncontrolled glycemia groups. *E.coli* remains the most common etiological agent of UTIs. *E.coli* is bacterium of the digestive tract. The study also showed higher prevalence in complication of DM in uncontrolled DM compared with controlled DM and the peripheral neuropathy is the more prevalence. More resistant to antibiotics in all uncontrolled and controlled DM patients and the cause maybe is randomly used to antibiotics. Diabetic patients especially uncontrolled women, are recommended to submit mid-stream urine specimens at regular intervals for culture and routine investigations even the absence of any urinary tract symptoms. Screening of urine samples for antimicrobial sensitivity while initiating the course of treatment among all UTI cases to check for and prevent resistance. Glucose control with regular check and therapy dose have impact on the episode of UTI.

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