Comparative Study: The Incidence of Urinary Tract Infection in diabetic Patients in the Eastern Region of Libya and their Antibiotics Sensitivity Pattern

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Abstract:

Urinary tract infections (UTIs) are one of the most common infections in both outpatient and inpatient settings. The term *urinary tract infection* applies to a heterogeneous group of clinical syndromes. Clinical entities in "UTI" include asymptomatic bacteriuria, acute uncomplicated cystitis, recurrent cystitis, complicated UTI, catheter-associated asymptomatic bacteriuria, catheter-associated UTI (CAUTI), prostatitis, and pyelonephritis. Appropriate classification of UTI syndrome is crucial for optimal diagnosis and management. The various categories of UTI are distinguished by the presence or absence of symptoms referable to the urinary tract; the patient's sex and comorbid conditions.UTI is a common infection observed in diabetic patients due to high level of sugar in the urine and often incomplete empting bladder from damage to bladder nerve . There is usually burning pain when passing urine , a need to pass urine frequently or sometimes discomfort in lower abdomen or blood in the urine (hematuria). Most simple urinary infections respond well to three to five days of oral antibiotic. Generally a fever ,back or flank pain suggest kidney infections which will usually need intravenous antibiotic . comparative study collected from 200 UTI diabetic patients between our data research of master degree in Benghazi during one year from Jan 2014 to Dec 2014. Compare with 110 samples UTI diabetic patients in Tobruk Medical Center during six months from Jan 2018 to Jun 2018.

In the present study the most common uropathogens *E.coli* followed by *Candida spp* , *Klebsiella* , *Staphylococcus aureus* , *Coagulase negative staphylococci*, *Pseudomonas spp*, *Proteus*, and *Enterococcus spp*. The result found highly resistance in diabetic patients to antimicrobial especially *Pseudomonas spp*. The effective antibiotics are Nitrofurantoin , Ciprofloxacin, Ceftriaxone and Vancomycin. in our study we found that the incidence of UTIs was higher among diabetic patients (women and men) age between 41 to 50 (70.5%) as compared to age group of 31-40 years i.e 67% with a difference of about 38% less percentage of UTI was found in age group of 20-30 i.e (20%) and the results agree with those demonstrated by Nicolle *et al.*, 1996 (7) who found that both men and women with diabetes have an increased risk of acute infection requiring hospital admission and which may increase the probability of 20 to 30 fold under the age of 44 and three to five fold over the age of 44.diabetic patient with UTI in both gram positive and negative bacteria showed significant level of resistance to most antimicrobial agents tested. Multidrug resistance to two or more drugs was observed in bacterial isolates. Also *candida spp* most common in diabetic patients.

Aims And Objectives

- To study the prevalence of pathogenic organisms from urine samples in patient in the Eastern Region of Libya by routine culture.
- To see the preliminary antibiotic sensitivity and resistance pattern of pathogenic bacteria in such urine samples which can help to devise antibiotic policies later.
- To give awareness about prevention and control of UTIs in diabetic patients.

1. Introduction

Urinary tract infections (UTIs) are one of the most common infections in both outpatient and inpatient settings. The term *urinary tract infection* applies to a heterogeneous group of clinical syndromes. Clinical entities in "UTI" include asymptomatic bacteriuria, acute uncomplicated cystitis, recurrent cystitis, complicated UTI, catheter-associated asymptomatic bacteriuria, catheter-associated UTI (CAUTI), prostatitis, and pyelonephritis. Appropriate classification of UTI syndrome is crucial for optimal diagnosis and management. The various categories of UTI are distinguished by the presence or absence of symptoms referable to the urinary tract; the patient's sex and comorbid conditions (1). UTI is a common infection observed in diabetic patients due to high level of sugar in the urine and often incomplete empting bladder from damage to bladder nerve . There is usually burning pain when passing urine, a need to pass urine frequently or sometimes discomfort in lower abdomen or blood in the urine (hematuria). Most simple urinary infections respond well to three to five days of oral antibiotic. Generally a fever back or flank pain suggest kidney infections which will usually need intravenous antibiotic. Bacteria in the urine without any symptoms of infection (asymptomatic bacteriuria) are three times more common in people with diabetes . This does not predispose to infection and does not require antibiotic (2). Diabetic patients are at a higher risk of developing acute pyelonephritis, renal abscess, abnormalities of bladder scarring and pyelitis . The most important predisposing factor in diabetic patients with urinary tract infection is bladder dysfunction as a result of diabetic neuropathy and cytopathic. vaginitis and generalized vascular disease. High level of urinary glucose has also been shown to impair phagocytic function of the leucocytes. People with diabetes have dysfunctional bladders which contract poorly. The presence of diabetic predisposes to much more severe infections, especially in patients with poor diabetic control, acute ketoacidosis, or diabetic complications such as nephropathy, vasculopathy and neuropathy. This Asymptomatic infection can lead to severe kidney damage and causes renal failure (3). UTIs are caused by uropathogens which multiply at the notch of the urethra and migrate towards the bladder. UTI is a result of various factors which may trigger Infection. Recurrent UTI is a nasty infection in sexually active young women and patients with DM. DM is also a leading cause of overactive bladder or neurogenic bladder. It is a serious clinical problem for people with DM. Hospitalization for pyleonephritis occurs 15 times more frequently in diabetic patients. Diabetes may increase the risk for certain urinary tract disorders, including asymptomatic bacteriuria, perirenal abscess, and emphysematous pyelonephritis (4). Asymptomatic bacteriuria is common in diabetic women. In a prospective study of non-pregnant women with diabetes mellitus, 26% had significant bacteriuria ($> 10^5$ cfu/mL) compared with 6% of controls.

Women with type I diabetes were particularly at risk if they had had diabetes for a long time or complications had developed, particularly peripheral neuropathy and proteinuria. Risk factors in patients with type II diabetes were old age, proteinuria, a low body mass index and a past history of recurrent UTIs.

Glucosuria and the increased formation of advanced glycosylation end products may play a role in the development of diabetic complications and may also contribute to the development of UTI, because these factors can lead to disturbances in monocyte migration and cytokine production (5). Yeast cells may be contaminants or represent a true yeast infection. They are often difficult to distinguish from red cells and amorphous crystals, but are distinguished by their tendency to bud. Most often they are *candida,* which may colonize bladder, urethra, or vagina. The pathogenic yeasts of candidiasis in probable descending order of virulence for humans are: *C. albicans*, *C. tropicalis*, *C. stellatoidea*, *C. glabrata*, *C. krusei*, *C. parapsilosis*, *C. guilliermondii*, *C. viswanathii*, *C. lusitaniae*, and *Rhodotorula mucilaginosa*. *Candida glabrata* is the second most common *Candida* pathogen after *C. albicans*, causing infections of the urogenital tract (6).In all suspected cases, a urine culture would ideally be obtained for susceptibility testing before starting therapy so the initial empirical therapy can be tailored appropriately. The decision points in managing acute pyelonephritis include ruling out complicated infection (pregnancy, nephrolithiasis, obstruction) and then determining whether the patient can take oral antibiotics as an outpatient. If oral therapy is feasible, oral ciprofloxacin in a 7-day regimen is the preferred regimen if local resistance rates to the fluoroquinolones do not exceed 10%. The extended-release formulation of ciprofloxacin for 7 days or a once daily dose of levofloxacin for 5 days can also be used, albeit the evidence is not as robust. TMP-SMX is also effective if the pathogen is susceptible, but in the absence of evidence to support short-course therapy a 14-day course is the official recommendation. If susceptibility of the uropathogen is not known, an initial single IV dose of ceftriaxone or a long-acting aminoglycoside is recommended before outpatient oral therapy. In a study comparing ciprofloxacin to TMPSMX, an initial dose of IV ceftriaxone resulted in improved outcomes in women receiving TMP-SMX who had a resistant uropathogen. Oral beta-lactam agents are not recommended for treatment of pyelonephritis given inferior efficacy rates. In women being admitted for IV therapy, a broad-spectrum agent should be given until the susceptibilities of the organism are known. This can be achieved with a carbapenem agent, an aminoglycoside with or without ampicillin, or extended spectrum betalactam with or without an aminoglycoside, or another regimen chosen on the basis of local resistance patterns. Broader spectrum empirical therapy with agents to which resistance is least common and longer treatment durations are measures intended to blunt the negative effects of host compromise on treatment outcomes. Combinations of a beta-lactam and a beta-lactamase inhibitor (e.g., ampicillin-sulbactam, ticarcillinclavulanate, and piperacillin -tazobactam) could also be considered. The IDSA has issued evidence-based guidelines on the diagnosis, prevention, and treatment of CAUTI .

The goal of limiting exposure to antimicrobial therapy and thus limiting selection pressure for resistant organisms is balanced by the awareness that microbial eradication requires a longer duration of therapy in patients with a urinary catheter.

Seven days is the recommended duration of anti -microbial treatment for patients whose symptoms resolve promptly, and 10 to 14 days is recommended for patients with a delayed response. For those with CAUTI who are not severely ill, a 5-day regimen of levofloxacin may be considered.(7).

2. Material And Methods

2.1 Collection of urine samples and transport :-

Urine samples were collected by sampling the mid-stream flow by the clean–catch technique**.** Once collected , a specimens of urine was transported to the laboratory without delay , as urine being excellent culture medium so that bacteria can reach apparently significant numbers in a short time . So the multiplication of bacteria in the urine should be prevented by storage in a refrigerator at 4°C (8).

2.2 Sample processing :-

The specimens were collected from the diabetic patients admitted from different wards of hospital. These were processed for bacterial species identification by standard microbiological procedures and antibiotics sensitivity testing. Specimens were taken from urine were inoculated on routine culture media like Blood agar, Cysteine lactose electrolyte deficient (CLED) agar , MacConkey agar and Sabouraud agar.

2.3 Antibiogram for Uropathogens

Isolates were tested for antimicrobial susceptibility by the Kirby-Bauer disk diffusion technique on nutrient agar plates. The tops of 4 to 5 well-isolated uniform colonies were touched with an inoculating loop and used to inoculate 4 to 5 ml of normal saline solution. The swab was used to streak the surface of the nutrient agar plate in the three directions. The antimicrobial disks were stored at -20°C when not in use; the disks were allowed to reach room temperature before being opened. The disks were placed into the surface of the incubated agar plate no later than 15 minutes after inoculation. A maximum of 7 disks were used. The plates were incubated at 37°C for 18 to 24 hours. After this time, the zone of the inhibition was measured to the nearest millimeter and the results were interpreted following the appropriate guidelines as stated by manufacturer (9).

3. **Results**

In the present study the comparative was done in two places as the follow firstly a total of two hundred (200) diabetic cases with suspected UTI(figure1) were included from various diabetic clinics in Benghazi for prevalence of UTI during a period of one year ranging from Jan 2014 to Dec 2014. Breakup of patients studied with diabetes was 200 (F=128, M=72) with age group ranging from 20 to 70 years in both sexes. The distribution pathogenic organisms as (figure 2). Antibiotics sensitivity test result as (figures 3 - 4).

Comparative with 110 diabetic cases with UTI (F=77, M=33) were collected from various clinic wards of Tobruk Medical Center during a period of six months ranging from Jan 2018 to Jun 2018. When do culture to urine samples the result 30(27.2%) positive culture whereas 80 (72.7%) negative culture. The same results when compare with Benghazi diabetic clinic except   we found Enterococci spp more common in Tobruk diabetic population , also in effect of some antibiotics like Nitrofurantoin, Amoxicillin-clavulanate and ciprofloxacin in Gram negative bacteria.

The notice more antibiotics resistance in diabetic patients in both places result from low immunity and use the drug for a long period. Because of the massive- and miss- use of these antimicrobials, besides they are purchased directly from the pharmacies without doctors' prescription as self- medication is a common practice and the initial use of antimicrobial before the laboratories results of antimicrobial susceptibility, the restrictions should be put on antibiotic prescribing (10).
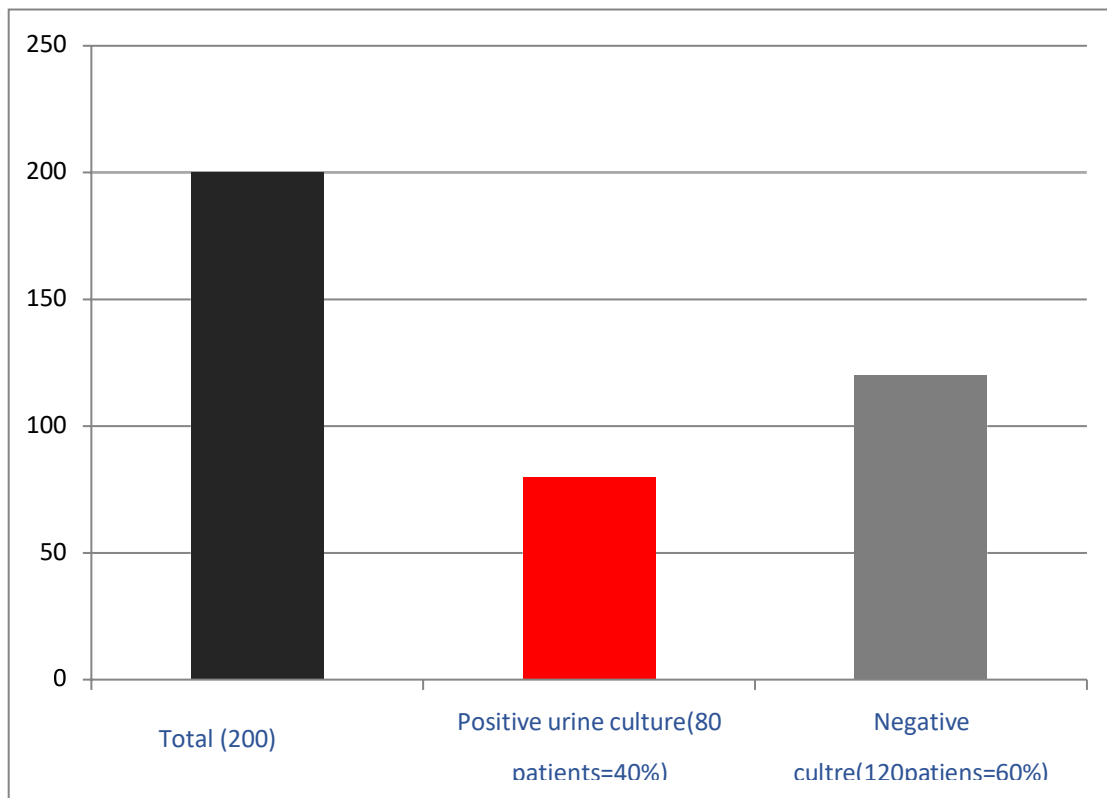
Figure 1: Percentage of positivity of cultures in diabetic patients.
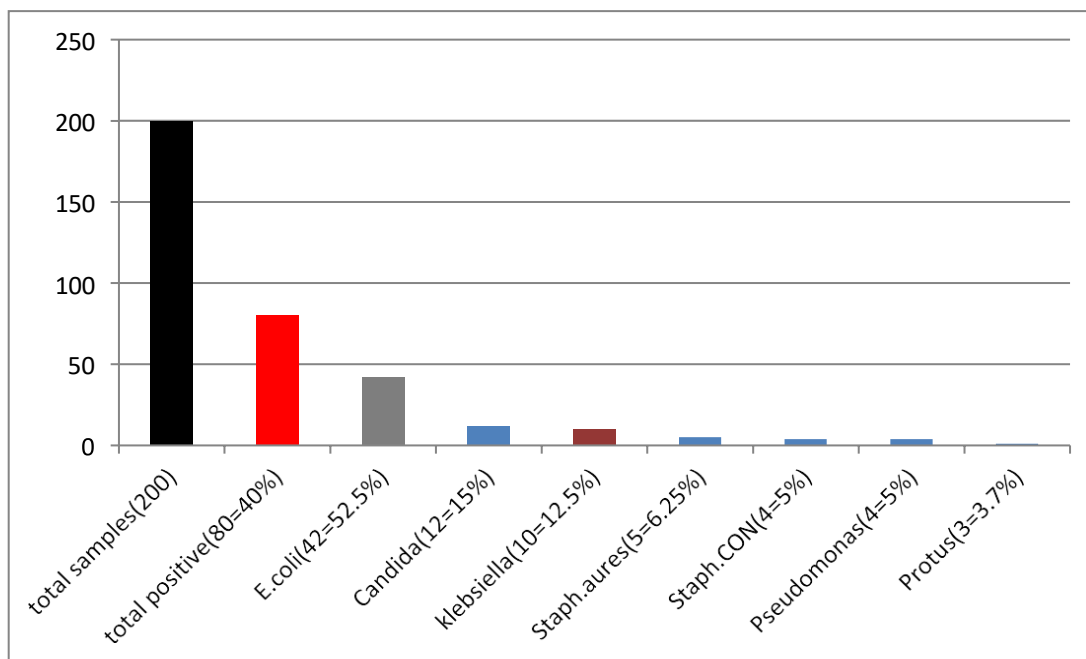

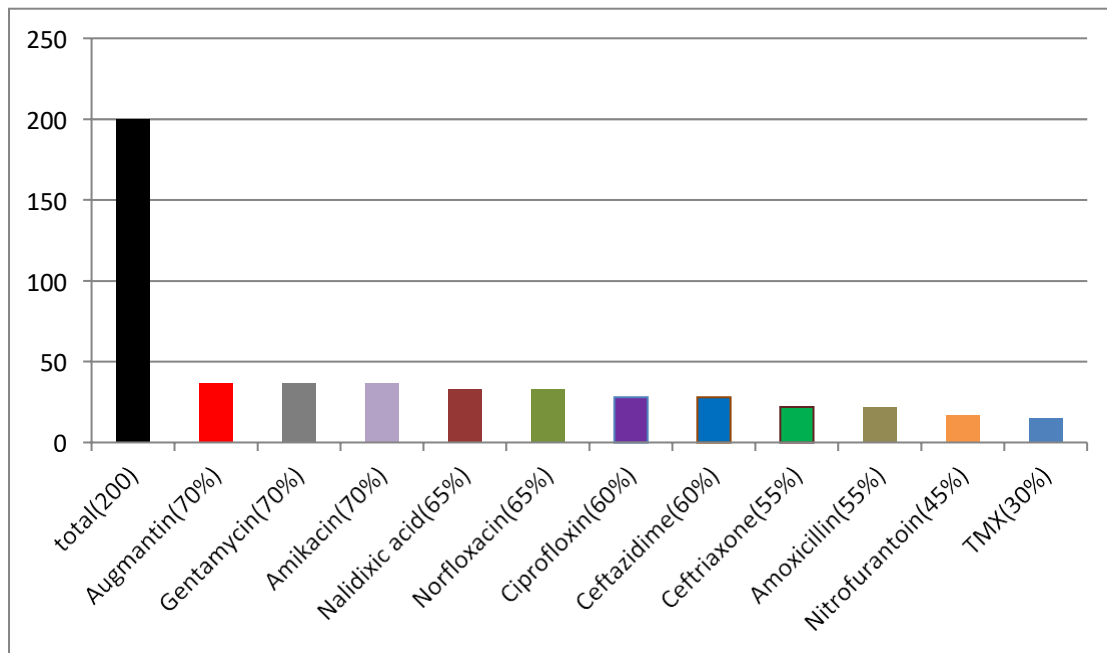Figure 2: Organisms positivity distribution in diabetics out of total positives.

Figure 3 : Preliminary antibiotics sensitivity pattern of Gram-negative bacteria.
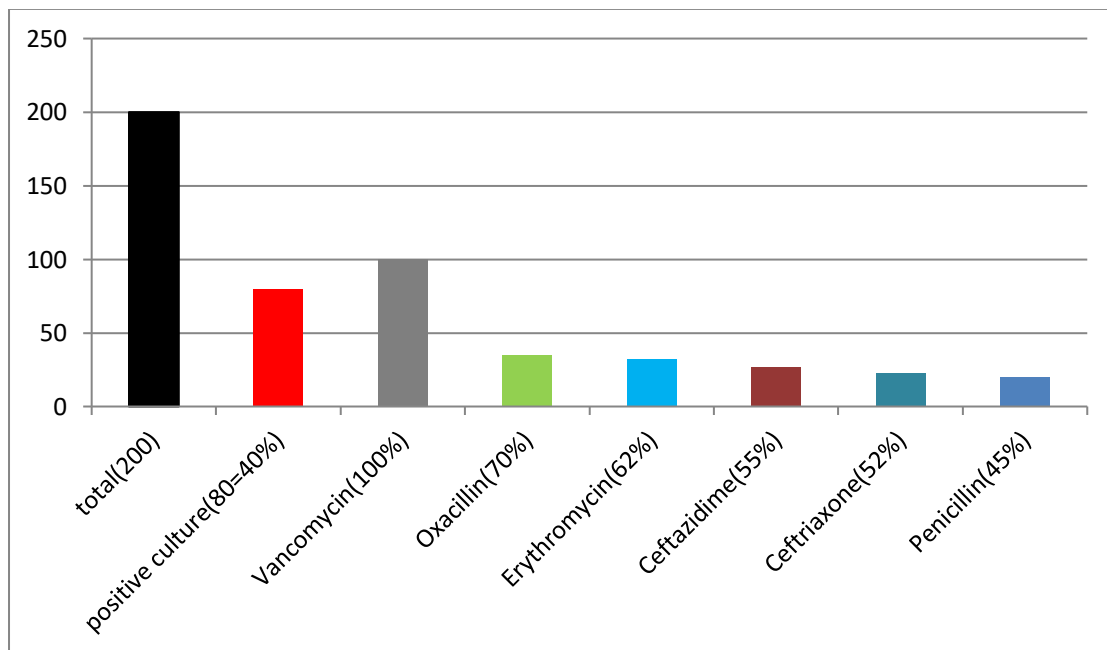

Figure 4: Preliminary antibiotics sensitivity pattern of Gram-positive bacteria.
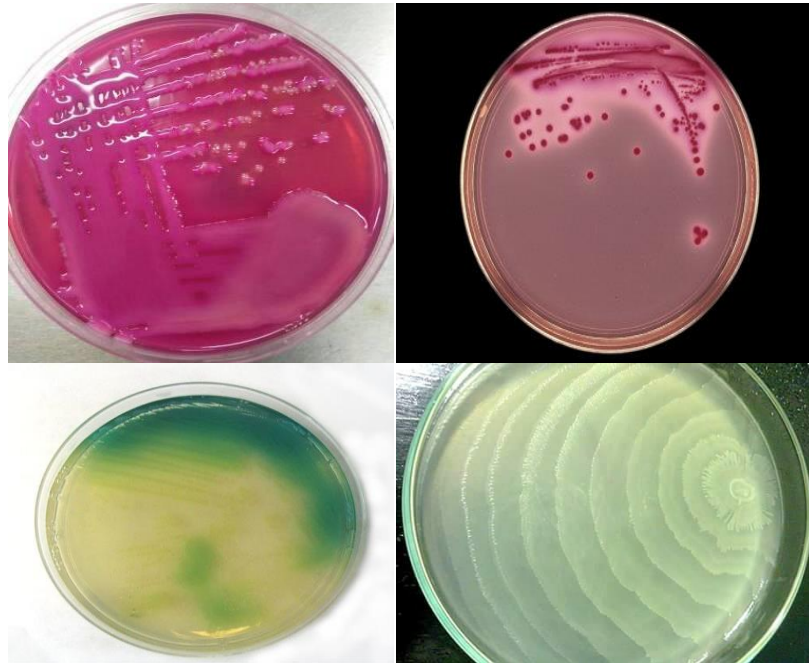
Figure 5: Showing Gram negative bacteria growing on the different media.

Figure 6: antibiotic sensitivity –Kirby Bauer method.

4. Discussion

Urinary tract infections are very commonly seen in diabetes worldwide as pointed out by a number of studies. Keeping in view lot number of such cases in Libya in general whereas both Benghazi and Tobruk in particular. When we comparing our study with other researchers across the globe, we found that most of the studies had similar results.

In our study we found that the incidence of UTIs was higher among diabetic patients(women and men) age between 41 to 50 (70.5%) as compared to age group of 31-40 years i.e 67% with a difference of about 38% less percentage of UTI was found in age group of 20-30 i.e (20%) and the results agree with those demonstrated by Nicolle *et al*., 1996 (11) who found that both men and women with diabetes have an increased risk of acute infection requiring hospital admission and which may increase the probability of 20 to 30 fold under the age of 44 and three to five fold over the age of 44.

Also another study which gave similar results as ours was done in 1966 by Renko M *et al*(12) in which they showed in 121 of 2702(4.5%) of controls which showed bacteriuria as in our cases as 6%.

In a study by Goswami *et al* .,2001(13) on bacterial urinary tract infections (UTI) and renal scarring in 155 diabetic individuals and 128 healthy controls shown that the prevalence of UTI in diabetes mellitus was higher , when compared to that in controls. *Escherichia coli* was the most commonly grown organism (64.3%), followed by *Staphylococcus aureus* (21.4%) and *Klebsiella pneumonia* (14.3%). prevalence of renal scarred was higher in patients with diabetes (28/155 or 18.0%), when compared to that of controls (7/128 or 5.4%). Fifty percent of patients with diabetes and UTI had renal scarring.

When we compared our antibiotics sensitivity profile with those of other studies in the past we could not find resistance a bit more now as compared as before Trimethoprime-sulfamethoxazole (TMP/SMX) was thought to be standard therapy for uncomplicated cystitis but Fluoroquinolones are more effective now than Trimethoprime-sulfamethoxazole in treating diabetic patients, the antimicrobial therapy of diabetic patients with complicated urinary tract infection is similar to that of non-diabetic patients because the pathogens are usually *Enterobacteriaceae* (14).

E. coli isolated from hospitalized patients were resistant to Amoxicillin , Amoxycillin-clavulanate , Trimethoprim and Ciprofloxacin with higher rate than those from outpatients.

The drug resistance of the various urinary tract infection (UTI) pathogens from patients of different gender and age group of Pakistanis was studied and *E.coli* was found to be the most frequent causative agent of UTI (66%) followed by *candida* spp. *pseudomonas* spp (7.3%).

Klebsiella spp (5.5%) and *Proteus* were found in less than 1% of the cases .in their study *E.coli* showed variable antimicrobial resistance to different antibiotic 92%, 86%, 80%, 62%, 47%, 20% and 4% of the isolate were found to be resistant to Ampicillin, Cotrimoxazole, Ciprofloxacin, Gentamicin, Nitrofurantoin and Amikacin , respectively. The most effective in vitro agents were found to be amikacin followed by gentamicin and ciprofloxacin among the orally administrated ones (15).

In our study, Vancomycin was found to be 100% effective in *Staph.aures* infection followed by Oxacillin 70% , Erythromycin at 62% , Ampicillin and Penicillin at 50% and 45% respectively and is in agreement with a lot of such studies.

1. Conclusion

In conclusion, our study comparative between two regions explored the most prevalent UTIs causing pathogens among tested patients. Numbers of different bacterial species, with *E.coli* followed by *Candida spp , Klebsiella , Staphylococcus aureus , Coagulase negative staphylococci, Pseudomonas spp, Proteus, and Enterococcus spp..* showed more resistance to most of tested antimicrobials. This study found that Nitrofurantoin, Amoxicillin-clavulanate and Ciprofloxacin are the most effective used antibiotics. However, due to high resistant rate to the commonly used antibiotics, we highly recommend performing antibiotic susceptibility in all UTIs patients.

Acknowledgements

Conflict of Interest:
I (author) have no conflict of interest.

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