Stallion Journal for Multidisciplinary Associated Research Studies
ISSN (Online): 2583-3340
Volume-3 Issue-3 || June 2024 || PP. 69-73 https://doi.org/10.55544/sjmars.3.3.9

Escherichia col Resistance in Type 2 Diabetes Mellitus with Urinary Tract Infection (UTI)

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www.sjmars.com || Vol. 3 No. 3 (2024): June Issue

Date of Submission: 26-06-2024	**Date of Acceptance:** 29-06-2024	**Date of Publication:** 06-07-2024

ABSTRACT

The Latin and Greek words "diabetes" and "mellitus," respectively, signify sweet and siphon. Diabetes mellitus (DM) is a metabolic disease marked by abnormally elevated blood glucose levels. DM can be divided into two categories: types 1 and 2. T2DM is hypothesized to affect middle-aged and older individuals who have maintained hyperglycemia as a result of bad eating habits and lifestyle choices. 45 urine samples from diabetics with UTIs of different ages were gathered for this study at the National Diabetes Center of Al-Mustansiriyah University in Baghdad Province, Iraq, between October 2023 and February 2024. The samples were handled carefully in the laboratory utilizing the right protocols to avoid any contamination. To categorize bacterial species in the urinary tract, biochemical assays, the standard urine culture (SUC), and other techniques were employed (cultural characteristics, vitek2 system). *E. coli* made up 67% of the bacteria that were identified from the urine of T2DM patients who had UTIs. In this investigation, *E. coli* displayed a high percentage of sensitivity to Nitrofurantoin, Erythromycin, Tetracycline, Oxyacillin, Vancomycin, Teicoplanin, and Imipenem (97%) but resistance to Moxifloxacin, Meropenem, Tigecyclin, Ampicillin, Cefazolin, Ceftriaxone, Ertapenem, Cefoxitin, and Nalidixic acid with rate of 100%.

***Keywords*-** Diabetes type 2 (T2D), Urinary tract infections (UTI), Diabetes Mellitus (DM), multidrug-resistant (MDR).

I. INTRODUCTION

Diabetes type 2 (T2D) affects people all over the world and is a major global health concern. Over 150 million people worldwide suffer from urinary tract infections, or UTIs, which are common bacterial infections [1]. Patients with type 2 diabetes mellitus may have worse results and worsening urinary tract infections. Diabetes patients often get UTIs. The most common causative agent for UTIs is thought to be Gram-negative bacteria in addition to uropathogenic *Escherichia coli* (UPEC), which is linked to a number of unusual but potentially dangerous symptoms, such as phleonephritis, emphysematous cystitis, and fungal infections (especially those caused by Candida species) [1, 2]

High blood sugar levels, which are caused by inadequate insulin secretion or activity, are a hallmark of type 2, the most common kind of diabetes [3] An imbalance between insulin sensitivity and levels leads to the functional deficit of insulin in type 2 diabetes. The two primary causes of insulin resistance are obesity and age, though there are numerous other contributing variables as well [4]. The virulence factor aspartyl proteinase, which boosts metabolic activity and aids in the formation of stress-resistant biofilms in bacteria, is stimulated by insulin to be expressed [5].

Antibiotic-resistant bacteria are common in both the general population and those with diabetes, which is a public health concern. Individuals with diabetes who contract an *Escherichia coli* infection may develop urinary tract infections (UTIs) [6]. *E. coli* is the most frequent cause of UTI in both genders with DM. Clinical risk factors for UTIs in individuals with diabetes mellitus include reduced leukocyte function brought on by hyperglycemia, diabetic microangiopathy,

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recurrent vaginitis, and anomalies of the urinary tract. In individuals with complex UTIs, treatment resistance as well as the existence of a distinct, antibiotic-resistant bacterium are linked to heightened risk [7]. Urine contains liquids, salts, and waste products even if it is uncontaminated by diseases or germs. Urinary tract infections (UTIs) can be caused by bacteria from nearby anus or other sources that enter the urethra. The populations are made up of bacteria, fungi, viruses, and archaea. Though they are more frequently found in the gastrointestinal tract, they can also be found in other exposed tissues such the respiratory, urogenital, and upper cutaneous systems [8]. One example of a bacteria that may cause UTIs is Escherichia coli, which is thought to be a natural part of the intestinal flora [9].

Many bacteria can cause UTIs, but ninety percent of the time, *E. coli* is the main culprit. *E. coli* can cause serious infections if it enters the urinary system, although it can often survive in the human digestive system without harm. In females, the urethra and genital canal are relatively close together. The standard protocol involves the prediction of urinary tract infections using microscopic pyuria. When a fresh, unspun, unstained urine specimen is magnified at a high magnification, the presence of at least five identifiable leukocytes is suggestive of this disease [10]. A dipstick can also be used to detect urinary nitrite. A negative test, on the other hand, may be the consequence of low count bacteriuria or bacterial species (mostly Gram-positive bacteria) that are unable to convert nitrate to nitrite. A positive test indicates the presence of bacteria in the urine[11]. *E. coli* resistance to commonly used antibiotics is a growing concern globally. Resistance mechanisms can vary, and antibiotic options for treatment may be limited in cases of multidrug-resistant *E. coli* infections. Individuals with diabetes who have urinary tract infections must have an accurate diagnosis and treatment. Our study aims to identify the medicines that work best for treating urinary tract infections in diabetics by either preventing the growth of *E.coli* bacteria or by effectively blocking their function.

II. MATERIALS AND METHODS

Study design: This experiment was carried out from October 2023 to February 2024 at the National Diabetes Center of Al-Mustansiriyah University in Baghdad, Iraq. Eighty-eight people, including men and women, between the ages of 10 and 70, were found to have type 2 diabetes. Pregnant and without diabetes individuals were not allowed to participate in the trial.

Sample collection and processing: A sterile tube was used to collect urine samples from patients with type 2 diabetes. Next, using the proper protocols, the samples were processed in the laboratory to avoid contamination. Data and details regarding each participant's clinical symptoms were gathered using a standardized questionnaire.

Bacterial isolates and Cultivation: Using suspended bacteria on Blood and MacConkey agar plates, a microbiological analysis was conducted prior to performing an overnight incubation at 37°C for a loopful of broth. A colony count higher than 105 CFU/mL indicates a severe bacteriuria infection.

Microbiological Analyses: The Vitek 2's automated characterization allowed for the identification of the bacterial isolates and the evaluation of their antibiotic susceptibility. For this objective, isolated colonies from well-known plates were also employed.

III. RESULTS AND DISCUSSION

A total of 45 diabetic patients (41.75±19.26) were recruited; 11 (22.7%) males and 34 (77.3%) women made up this group. Both symptomatic and asymptomatic cases of DM bacteriuria were seen in the total group. Table 1 indicates that 27 (59.1%) of the men and women with high blood pressure do not have it, while 18 (40.9%) do. 37 (81.1%) of the patients did not disclose any such situations, while eight (18.2%) of the patients admitted to having additional medical conditions. Based on our research, all of the patients experienced a UTI, varying in intensity from mild to severe.

Table 1: Demographic characteristic of study

Demographic characteristic (N=45)		N	%
Gender	Female	34	77.3
	Male	11	22.7
	Total	45	100.0
Does the patient suffer from high blood pressure?	No	27	59.1
	Yes	18	40.9
Does he suffer from UTI?	Low	11	25.0
	Middle	18	38.6

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	High	16	36.4
Does the patient suffer from other diseases?	No	37	81.8
	Yes	8	18.2
Age		45	41.75±19 26

In this work, urine sediment samples were examined under a light microscope to determine whether the samples included pus and epithelial cells, which are often linked to bacterial urinary tract infections in either the upper or lower urinary tract. Microscopical examination may indicate colonization as opposed to infection if bacteriuria are present but pyuria are absent [12]. Under such conditions, however, standard urine cultures usually fail to detect any microorganisms[13]. Significant bacteriuria were defined as urine culture plates exhibiting a single bacterial species' CFU/mL of greater than 105. *E. coli* infections, which are common in diabetics, can damage any organ or function in the body [14].

Only 36 of the 45 samples produced growth-positive results, of which 11 (9%) were recognized as isolates from other species and 25 (67%) as isolates from *E. coli*. Moreover, no bacterial growth was observed on any of the study's cultures in 9 (24%) of the samples (figure1).

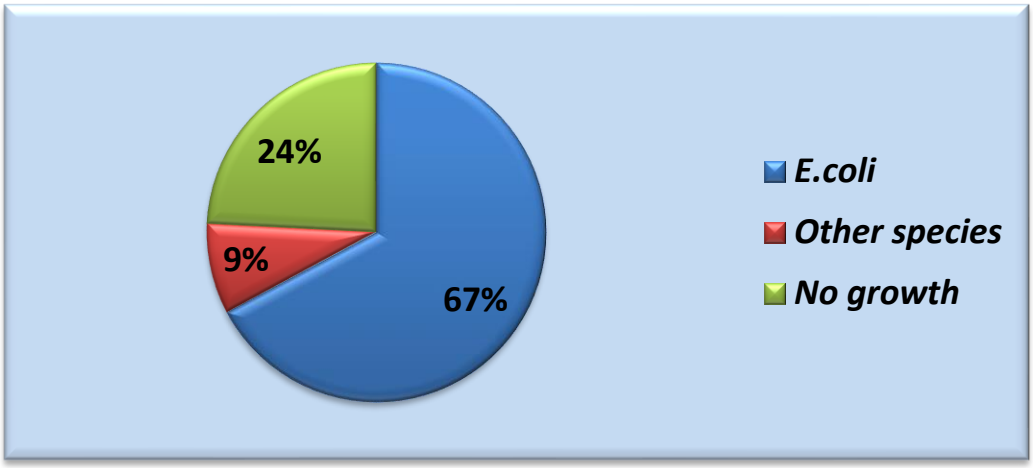

Figure (1): The percentage of isolates from diabetes patients who suffered from UTIs.

Twenty-five gram-negative isolates of *E. coli* were identified using the GN card method for bacteria and the VITEK2 System (bioMérieux) for Enterobacteriaceae. *Coli* bacteria on cultures were confirmed cases of UTIs with both clinical symptoms; the remaining isolates show an extra bacterial growth on one of the study's excloded cultures.

The common isolated bacteria among DM was *E.*coli which constituted 67%. Antimicrobial rsistance was tested to commonly antibiotic drugs including β-lactams (Cefoxitin, Ceftazidime and Imipenem), folic acid inhibitors (Trimethoprim), tetracyclines (Tetracycline), aminoglycosides (Gentamycin, Amikacin), fluoroquinolones (Ciprofloxacin) and quinolones (Naldixic acid). In our study, the *E. coli* bacteria shown 97.7% resistance to Tetracycline, Oxyacillin, Vancomycin, Nitrofurantoin and Imipenem. Najar et al.'s analysis revealed that all *E. coli* isolates to Impienem were antibody-resistant (100%) [15]. The estimated resistance to Oxacillin and Tetracycline in this investigation was 97.7%, compared to 100% in the study by Jaklen Z k et al [16]. According to the research conducted by A.S. Ahmed [17] and colleagues, 73.3% of people were resistant to the antibiotic Tetracycline. However, other studies showed that 100% of the microorganisms were resistant to these medicines [18].

Colistin, Trimethoprim/Sulfamethoxazole, Ciprofloxacin, Piperacilin/Tazobactam, Cefepime, Ticarcillin/Clavulanic Acid, Ticarcillin, Aztreonam, Ceftazidime, and Piperacilin were found to be, respectively, 95.5%, 86.4%, 75%, 66%, 65%, 55%, 52.4%, 50%, 41%, 39%, and 23%. Shafie et al.'s research [19] indicates that were 99.2% and 51.7% less resistant to Colistin and Cefepime, respectively. In accordance with Shafie et al.'s study, the anti-Ciprofloxacin resistance is 77.5%. Eighty-six percent of our research's participants were resistant to Gentamicin, compared to 100 percent in the Hamdan et al., [20] trial and 40 percent in the A.S. Ahmed et al. study [17]. The bacteria had 100% resistance to Moxifloxacin, Meropenem, Tigecyclin, Ampicillin, Cefazolin, Ceftriaxone, Ertapenem, Cefoxitin and Nalidixic acid. This is comparable to the 100% isolation rate of antibody-resistant *E. coli* reported by Najar et al [15]. Because they are involved in both health and disease, as Gore and Ratzke [21] have shown, bladder bacteria may be a very

helpful indicator of pollution. As a result of the bacteria's cell walls being damaged by several antibiotic treatments for urinary tract infections, the organism continued to live in the patients' intestines. Numerous characteristics make up the intricate possible pathogenetic system. It's been demonstrated by Babak P et al. that certain human indigenous flora strains, such as *E. coli* in the digestive system, cling to epithelial cells and produce a variety of potential virulence factors [22]. Furthermore, these bacteria are capable of producing substances that confer resistance. Our results point to the possibility that uropathogenic bacteria, such as *E. coli* or other bacteria, are present in the urinary system due to PH changes caused by urine contents. Antibiotics can be used to treat urine or it can be diluted to lessen the number of harmful germs [23]. The findings of our study indicate that people with T2D had higher amounts of *E. coli* bacteria. This is consistent with earlier research by Shah MA et al. that found *E. coli* bacteria to be linked to recurrent UTI in patients with diabetes mellitus [24]. People with type 2 diabetes have more severe symptoms and have a significantly greater incidence of urinary tract infections (UTIs) than people without the illness [25]. An individual's health may be impacted by these organisms' physiological functions. Unchecked diabetes mellitus has been linked to an increased incidence of urinary tract infections in numerous studies. Women were more likely than men to get the illness [24].

IV. CONCLUSION

Antibiotic resistance is the primary factor contributing to the rise of multidrug-resistant (MDR) UPEC isolates. *E. coli* was found to be the main uropathogen linked to recurrent urinary tract infections (UTIs) in people with type 2 diabetes (T2D). Numerous patterns of treatment resistance were noted, and these were attributed to infections in the final part of the digestive tract. Antibiotic resistance mechanisms in bacteria are diverse. While all Gram-negative organisms in the section demonstrated sensitivity to Nalidixic acid, Loxifloxacin, Cefazolin, Ceftriaxone, Ertapenem, and Tigecyclin, just 23% of Gram-negative bacteria were found to be susceptible to Piperacilin. The management of urinary tract infections is complicated by antibiotic resistance, according to this research. When treating urinary tract infections, antibiotic resistance is a crucial factor to take into account. Reports on urine cultures are required to diagnose urinary tract infections. An empirical analysis on the prevalence of UTIs among Iraqi diabetes patients is made possible by this methodology. Therefore, in order to achieve optimal surveillance and gather precise information regarding the virulence features and antibiotic resistance of various *E. coli* pathotypes, new techniques like high-throughput sequencing are required.

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