ANALYSIS OF UROPATHOGENS AND ANTIBIOTIC SENSITIVITY PATTERNS IN DIABETES MELLITUS PATIENTS AT A TERTIARY CARE HOSPITAL: AN OBSERVATIONAL STUDY.

Kumar Durgeshwar[a,*] , Sanjeev Kumar[b], Naween Kumar[c], U. C. Jha[d]

[a] Senior Resident, Department of Medicine (EmergencyMedicine), DMCH, Laheriasarai, Darbhanga, Bihar, India
[b] Specialist Medical Officer, Department of Medicine, SDH, Banmankhi, Purnia, Bihar, India
[c] Assistant Professor, Department of Medicine, DMCH, Laheriasarai, Darbhanga, Bihar, India
[d] Professor and Head of the Department, Department of Medicine, DMCH, Laheriasarai, Darbhanga, Bihar, India

Abstract.

Background:

Diabetes Mellitus (DM), affects various systems within the body. Patients with untreated diabetes are at risk of developing a range of complications that contribute to increased morbidity and mortality rates. Diabetes Mellitus exerts various persistent impacts on the Urogenital system. UTIs have been widely acknowledged as a substantial concern among individuals diagnosed with DM.

Methods:

A potential observational research was conducted consisting of individuals with diabetes mellitus exhibiting positive indications of urinary tract infection. Exclusion criteria encompassed gestational diabetes, patients with compromised immune systems, and individuals presenting with congenital kidney malformations.

Results:

The study encompassed a total of 110 incidents of UTIs. Among them were a total of 35 males, and 75 females. The age group predominantly comprised between the ages of 55 and 70 years. Escherichia coli was identified as the prevailing microorganism isolated in the sample. Gram-positive organisms proved a sensitivity rate of 100% to Linezolid and Vancomycin. Gram-negative microbes demonstrated a sensitivity rate of 100% to Polymyxin B.

Conclusion:

Urogenital tract infection is a commonly observed difficulty in individuals with diabetes mellitus. The identification of the most prevalent causative organisms and their corresponding antibiotic sensitivity patterns is imperative within a tertiary care hospital setting to establish an enhanced antibiotic policy.

Recommendation:

It is strongly recommended that further studies be conducted with a larger sample size to provide additional support for the findings obtained in this study.

Keywords: Diabetes Mellitus, Urinary tract infection, Antibiotic sensitivity, Submitted: 2023-09-26, Accepted: 2023-09-29

*Corresponding author.
Email address: drkdyadav@gmail.com (Kumar   Durgeshwar)

1. INTRODUCTION.

The risk of infection is elevated in individuals with diabetes, and such infections can lead to various complications. Patients with DM exhibit weakened tolerance to infections. The reciprocal relationship between infections and diabetic control is characterized by adverse impacts on one another. The individual with diabetes exhibits a modified reaction to infection due to their inherent vulnerability to infection, as well as their capacity to initiate a typical inflammatory response [1].

The complement system is a pivotal component in the orchestration of humoral immunity. The composition comprises a combination of serum and surface proteins, which primarily serve to facilitate the phagocytosis and opsonization of microbes by neutrophils and macrophages, as well as to initiate the breakdown of said microbes. Furthermore, it is noteworthy that the activation products of complement play a crucial role in providing the secondary signal required for the stimulation of B-lymphocytes and subsequent production of antibodies [2].

People diagnosed with DM exhibit reduced secretion of IL-1 and IL-6 by mononuclear cells and monocytes upon stimulation with lipopolysaccharides. The observed phenomenon of diminished interleukin production is believed to be a direct result of an inherent cellular abnormality present in individuals diagnosed with DM [3]. However, it has been reported in other studies that the augmented process of glycation may exert inhibitory effects on the synthesis of IL-10 by myeloid cells. Additionally, it can also lead to a decrease in the expression of MHC class I on the outermost layers of myeloid cells, thereby compromising cellular immunity [4].

During episodes of hyperglycemia, it is possible to observe a reduction in the mobilization of polymorphonuclear leukocytes, as well as a decline in chemotaxis and phagocytic activity. The presence of hyperglycemia in the biological atmosphere additionally hinders the antimicrobial efficacy through the inhibition of glucose-6-phosphate dehydrogenase (G6PD), thereby aug-menting the process of programmed cell death in polymorphonuclear leukocytes, and diminishing the ability of polymorphonuclear leukocytes to traverse across the endothelial layer [5].

Immunoglobulin glycation has been observed to manifest in individuals diagnosed with diabetes, exhibiting a direct correlation with elevated levels of HbA1c. This phenomenon has the potential to adversely impact the physiological efficacy of antibodies. A notable decrease in chemotaxis has been observed in polymorphonuclear leukocytes (PMNs) among patients diagnosed with diabetes, including both type 1 and type 2, when compared to individuals in the control group [6]. The findings of various studies have demonstrated the presence of compromised chemotaxis and phagocytosis in the monocytes of individuals diagnosed with diabetes [7].

The primary purposes and objectives of the present research were to carefully observe and analyze the clinical manifestations and laboratory findings associated with genitourinary tract infections in individuals diagnosed with diabetes. The objective of this study is to analyze the urine sample culture yield, discharge culture yield, and microscopic investigation findings in individuals with urinary tract infections (UTIs) who have diabetes. Additionally, this study aims to identify the most frequently isolated causative organisms in culture and determine their antibiotic sensitivity patterns.

2. MATERIAL AND METHODS.

2.1. Study Design and Population.

The current investigation was conducted in the Department of Medicine, in collaboration with the Department of Microbiology at DMCH, Lehariasarai, for two years.

2.2. Inclusion and exclusion criteria.

This study included individuals diagnosed with DM who exhibited symptoms of urogenital tract infection and were admitted to the medical ward. Only patients whose urine sample culture yielded optimistic results for micro-organisms were involved in the study. The patient was diagnosed

with diabetes mellitus by the established diagnostic criteria. The individuals with diabetes who were not included in the study encompass those with congenital renal anatomical abnormalities, gestational diabetes mellitus, HIV patients, individuals on steroid therapy, those with malignancies, and transplant recipients.

2.3. Data Analysis.

The patients underwent initial screening for urogenital tract infection through urine samples and discharge culture. Each patient with positive results underwent an inquiry regarding their age, sex, period of symptoms, presenting complaints, treatment history for urinary tract infection, glycemic control, similar episodes history, and any urinary tract instrumentation history. A comprehensive examination of the patients was conducted. A thorough evaluation including both general and systemic examinations was performed. The patient's medical history and physical examination findings were duly documented in the standardized proforma.

All the standard laboratory tests including hemoglobin level, differential count, total leukocyte count, fasting blood sugar, blood urea, glycosylated hemoglobin (HbA1c), and serum creatinine were performed. Ultrasonography was performed. A radiographic examination of the abdominal region utilizing a direct X-ray technique, as well as a computed tomography (CT) scan of the abdominal region, was performed in specific instances. A comprehensive evaluation was conducted, encompassing both routine and microscopic examinations of urine and discharge samples. Additionally, culture and antibiotic sensitivity testing were performed on the urine and discharge specimens.

Isolation of Microorganisms from Urine samples: A mid-stream urine sample was obtained and subsequently forwarded to the Department of Microbiology for analysis. The sample was expeditiously cultured within a time frame of two hours. The urine specimen was subjected to thorough mixing before its inoculation onto culture plates. The inoculation procedure involved the aseptic introduction of urine samples onto the

nutrient agar plates, specifically MacConkey and blood agar. This was achieved using a sterile platinum loop that had been calibrated to dispense either 0.01 or 0.001 ml of the urine specimen. Subsequently, the plates were subjected to incubation at a temperature of 37 ºC for 24 hours under aerobic conditions. The enumeration of colonies was performed on individual plates. The quantity of CFU is amplified by a factor of 1000 when a 0.001 ml loop is employed, or by a factor of 100 when a 0.01 ml loop is employed, to ascertain the concentration of microorganisms per ml in the initial specimen.

Bacteriuria of clinical significance was defined as the presence of bacterial colonies with a count equal to or exceeding 105 per milliliter in the culture. The identification of organisms was accomplished through the assessment of their colonial characteristics and the application of various biochemical methodologies. The antibiotic sensitivity pattern was assessed through the implementation of the disc diffusion method, utilizing a multidisciplinary approach.

3. RESULTS.

In the current investigation, researchers incorporated a total of 110 instances of culture-positive urinary tract infections (UTIs) observed in diabetic patients aged 14 years and older. At the initial stage, 200 patients were examined for eligibility, however, 90 patients were excluded from this study due to not being eligible. The data collection period spanned two years, and the study was conducted at the esteemed DMCH, Lehari-asarai. Among a cohort of 110 individuals diagnosed with diabetes, it was observed that 35 of them were of the male gender, while the remaining 75 individuals were of the female gender. The age group with the highest patient population is 55-70 years, closely followed by the age group of 44-56 years. The age set of 25-36 years exhibited the lowest patient volume.

The present study observed a predominance of patients diagnosed with type 2 diabetes mellitus. The predominant presenting symptoms identified in the current study were dysuria, rose occurrence

of micturition, and high temperature. The urine samples obtained from diabetic patients were subjected to microbiological analysis, resulting in the isolation of various microorganisms. Among these, *Escherichia coli* was found to be the most prevalent, accounting for 48 isolates (43.6%). Following *Escherichia coli, Klebsiella* was the second most commonly isolated microorganism with 21 isolates (19.1%). *Pseudomonas* species were also identified in 13 isolates (11.8%), while *Staphylococcus* species and *Streptococcus* were found in 11 isolates (10%) and 9 isolates (8.1%) respectively. *Candida* species were identified in six cases, accounting for 5.4% of the total isolates. Additionally, mixed growth was observed in two cases, representing 1.8% of the isolates. The antimicrobial susceptibility testing revealed that both *Staphylococcus* and *Streptococcus* isolates exhibited a 100% susceptibility rate to Vancomycin and linezolid. Furthermore, it is notable to mention that *Streptococcus* exhibited a remarkable sensitivity rate of 100% towards Nitrofurantoin.

The susceptibility of all gram-negative organisms to Polymyxin B was observed to be 100%. *Escherichia coli* exhibited the lowest sensitivity towards Norfloxacin. *Klebsiella* exhibited the lowest susceptibility to cefotaxime and cotrimoxazole. *Pseudomonas* exhibited the lowest susceptibility to Norfloxacin. The cumulative antibiotic sensitivity demonstrated the greatest efficacy with nitrofurantoin, subsequently succeeded by amikacin. The concentrations of cefotaxime and norfloxacin were determined to be significantly lower.

4. DISCUSSION.

The current investigation comprised a cohort of 110 individuals diagnosed with Diabetes Mellitus and urinary tract infection (UTI) who were admitted to the general medicine ward. Of the total sample size, 35 individuals were identified as male patients, while 75 individuals were identified as female patients. This study demonstrates a strong correlation with the findings of Janifer *et al.*, which similarly reported a substantially greater incidence of urinary tract infections

(UTIs) among women compared to men [8].

In the study of Aswani *et al.* [9] the authors identified dysuria as the predominant showing signs of UTIs, with a prevalence of 75.3%. This was trailed by an amplified occurrence of urination, reported by 66% of the participants. Fever was also observed as a common presenting symptom, with a prevalence of 61%. The researchers have identified that fever was the predominant presenting symptom, accounting for 57.4% of cases. This was followed by dysuria, which was reported in 41.4% of cases, and an increased frequency of micturition, observed in 27.3% of cases.

Among a total of 110 cases, gram-positive organisms were identified in 20 cases, Gram-negative bacteria were identified in 90 cases, *Candida* sps. were identified in 6 cases, and a combination of multiple species was observed in 2 cases upon culture analysis. Janifer *et al.* [8] conducted a study in which they observed a predominance of cases involving Gram-negative organisms, trailed by Gram-positive bacteria and *Candida* sps, sequentially.

The bacterial composition of the sample revealed that *E. coli* accounted for 43.6% of the total population, followed by *Klebsiella* species at 19.1%, *Pseudomonas* at 11.8%, *Staphylococcus* at 10%, and *Streptococcus* at 8.1%. Additionally, *Candida* species were present, representing 5.4% of the overall microbial community. This study is in concordance with the findings of Shill *et al.*, [10] wherein it was determined that *Escherichia coli* was the predominant microorganism that was isolated.

Gram-positive bacteria demonstrated 100% susceptibility to both Linezolid and Vancomycin while exhibiting the lowest susceptibility to Norfloxacin. Gram-negative bacteria demonstrated 100% susceptibility to Polymyxin B while exhibiting the lowest susceptibility to Norfloxacin. The antibiotic susceptibility pattern of the identified organisms revealed that Nitrofurantoin and Amikacin exhibited the most significant cumulative antibiotic sensitivity rates, with percentages of 73.4% and 66.3% respectively. Cefotaxime was determined to exhibit the lowest level of sensitivity among the tested antibiotics. In a study

Table 1: **Microorganisms isolated from individuals with diabetes and urogenital tract infections in the research.**

Isolated Micro-organisms	Number of positive cases	Percentage (%)
E. coli	48	43.6
Klebsiella	21	19.1
Pseudomonas	13	11.8
Staphylococcus	11	10
Streptococcus	9	8.1
Candida	6	5.4
Mixed	2	1.8

conducted by Aswani *et al.*, [9] it was observed that the isolated strains of *Escherichia coli* exhibited heightened susceptibility to carbapenems in both individuals having diabetes (93.8%) and without diabetes (95.1%) individuals. Conversely, these strains displayed reduced susceptibility to ampicillin, with a prevalence of 16.7% in diabetics compared to 17% in non-diabetics. In a work conducted by Shill *et al.*, [10] it was determined that meropenem exhibited the highest efficacy among antibiotics, with amikacin ranking second in terms of effectiveness.

5. CONCLUSION.

The frequency of urogenital infection is greater in female individuals having diabetes compared to their male counterparts. The prevailing manner of appearance was characterized by dysuria, heightened occurrence of urination, and pyrexia. The primary etiological factor contributing to the heightened incidence of UTI in persons with diabetes mellitus is likely elevated blood glucose levels. Therefore, it is imperative to implement stringent glycemic management strategies to mitigate the occurrence of UTIs in diabetic patients. The sensitivity to antibiotics exhibits variability between gram-positive and negative bacteria. The antibiotic susceptibility profile of Gram-positive bacteria demonstrated a higher degree of sensitivity towards Vancomycin, Linezolid, Nitrofurantoin, Amikacin, and Ampicillin, in descending order. In contrast, Gram-negative bacteria exhibited greater susceptibility to Polymyxin B, with subsequent sensitivity observed towards Nitrofu-

rantoin, Gentamycin, and Ampicillin. The implementation of a comprehensive antibiotic policy within tertiary care hospitals is imperative to ensure optimal therapeutic outcomes and mitigate the inappropriate utilization of antimicrobial agents.

6. LIMITATIONS.

The limitations of this study include a small sample population who were included in this study. The findings of this study cannot be generalized for a larger sample population. Furthermore, the lack of a comparison group also poses a limitation for this study's findings.

7. RECOMMENDATION.

It is strongly recommended that further studies be conducted with a larger sample size to provide additional support for the findings obtained in this study.

8. ACKNOWLEDGEMENT.

9. LIST OF ABBREVIATIONS.

DM- Diabetes Mellitus
UTI- urinary tract infection

IL- Interleukin
MHC- major histocompatibility complex
G6PD- glucose-6-phosphate dehydrogenase
HbA1c- glycated hemoglobin
PMN- polymorphonuclear leukocyte
HIV- Human Immunodeficiency Virus
CT- computed tomography
CFU- colony forming unit

10. SOURCE OF FUNDING.

11. CONFLICT OF INTEREST.

The authors report no conflicts of interest in this work.

12. PUBLISHER DETAILS.

13. REFERENCES.

1. Bagdade JD, Root RK, Bulger RJ. Impaired leukocyte function in patients with poorly controlled diabetes. Diabetes. 1974 Jan 1;23(1):9-15.

2. Geerlings SE, Hoepelman AI. Immune dysfunction in patients with diabetes mellitus (DM). Pathogens and Disease. 1999 Dec 1;26(3-4):259-65.

3. Peleg AY, Weerarathna T, McCarthy JS, Davis TM. Common infections in diabetes: pathogenesis, management and relationship to glycaemic control. Diabetes/metabolism research and reviews. 2007 Jan 1;23(1):3-13.

4. Price CL, Al Hassi HO, English NR, Blakemore AI, Stagg AJ, Knight SC. Methylglyoxal modulates immune responses: relevance to diabetes. Journal of cellular and molecular medicine. 2010 Jun 1;14(6b):1806-15.

5. Vardakas KZ, Siempos II, Falagas ME. Diabetes mellitus as a risk factor for nosocomial pneumonia and associated mortality. Diabetic Medicine. 2007 Oct 1;24(10):1168-71.

6. Mowat AG, Baum J. Chemotaxis of polymorphonuclear leukocytes from patients with diabetes mellitus. New England journal of medicine. 1971 Mar 25;284(12):621-7.

7. Schaeffer AJ, Jones JM, Dunn JK. Association of in vitro Escherichia coli adherence to vaginal and buccal epithelial cells with susceptibility of women to recurrent urinary-tract infections. New England Journal of Medicine. 1981 Apr 30;304(18):1062-6.

8. Janifer J, Geethalakshmi S, Satyavani K, Viswanathan V. Prevalence of lower urinary tract infection in South Indian type 2 diabetic subjects. Indian Journal of nephrology. 2009 Jul;19(3):107.

9. Aswani SM, Chandrashekar UK, Shivashankara KN, Pruthvi BC. Clinical profile of urinary tract infections in diabetics and non-diabetics. The Australasian medical journal. 2014;7(1):29.

10. Shill MC, Huda NH, Moain FB, Karmakar UK. Prevalence of uropathogens in diabetic patients and their corresponding resistance pattern: results of a survey conducted at diagnostic centers in Dhaka, Bangladesh. Oman medical journal. 2010 Oct;25(4):282.