DOI: 10.5455/msm.2021.33.240-243
Received: Nov 12 2021; Accepted: Dec 24, 2021

ORIGINAL PAPER Mater Sociomed. 2021 Dec; 33(4): 240-243

Correlation Between Inflammatory and Biochemical Parameters in Patients with Diabetes and Urinary Tract Infection

Azra Burekovic[1,2], Edhem Haskovic[3], Faruk Ceric[3], Dzenana Halilovic[1]

[1]Clinical Center University of Sarajevo[1]

[2]Faculty of Medicine, University of Sarajevo[2]

[3]Faculty of science and mathemathics, [4]Department of biology, University in Sarajevo[3]

Corresponding author:
Azra Burekovic, Associate Professor. Clinical Center University of Sarajevo, Bolnička 25, Faculty of Medicine, University of Sarajevo. Phone: 061-228-928, azraburekovic@hotmail.com, ORCID ID: https://orcid.org/0000-0002-1158-510X.

ABSTRACT

Background: Hyperglycemia, polyuria, and glycosuria are all risk factors for the frequency of urinary tract infections in patients with diabetes. **Objective:** The aim of this study is to establish correlation between inflammatory and biochemical parameters in patients with diabetes and urinary tract infection. **Methods:** Total number 116 patients were monitored, at the ages between 18-95 years, with diabetes and urinary tract infection, of which 59.49% women and 40.51% men. Patients were with a duration of diabetes from 0 to over 20 years, with an average fasting glycemia of 9.54 mmol/l, and postprandial glycemia 13.94 mmol/l, HbA1C 9.92%, which have been poorly regulated in the last 3-4 months. Inflammatory parameters SE, CRP, leukocytes were correlated with inflammatory parameters of urine sediment and positive urine cultures. **Results:** Average values of urea, creatinine, and proteinuria were positively correlated with the duration of diabetes. Escherichia coli, Enterococcus feecalis, and Candida albicans were the most common pathogens isolated in urine culture, 51 patients had reinfection once, 39 patients had two reinfections, and 26 patients had three reinfections during the 6-month follow-up. **Conclusion:** Duration of diabetes, long-term poor glycoregulation lead to microangiopathic changes in the kidneys in the form of diabetic nephropathy with retention of nitrogenous substances of urea, creatinine with proteinuria, and acute hyperglycemia, polyuria and glycosuria, further leading to frequent urinary tract infections.

Keywords: Diabetes mellitus, urinary tract infection, hyperglycemia.

1. BACKGROUND

Urinary tract infections are among the most common infections in the human population, especially in women. Risk factors for their occurrence in the hospital environment are placement of a urinary catheter, initiation of urological instruments, surgical interventions, abuse or frequent use of antibiotics, chronic kidney disease, diabetes mellitus and kidney transplantation. Urinary tract infections are usually caused by bacteria, which is the most common Escherichia coli. In addition, common pathogens are Klebsiella spp, Proteus mirabilis and Pseudomonas aeruginosa. The virulence of the microorganism and the sensibility of the urinary tract to infection are equally important for the development of a urinary tract infection (1). Due to high blood sugar levels, patients with diabetes have polyuria and glycosuria, which is a suitable environment for the development of urinary tract infections. Recurrent urinary tract infections are defined as infections that have recurred at least three times during the previous year or two infections in the previous six months. They present a special problem, because about 20% to 35% of women have a re-infection after the first urinary tract infection, and 10% of women have three to five infections a year. Antibiotics such as trimethoprim sulfomethaxazole, cephalosporins and penicillins are therapeutics used to treat urinary tract infections (2). Diabetes mellitus is basically a deficient disease that occurs due to absolute or relative lack of insulin. The main subtypes of diabetes are type 1 and type 2. Type 1 diabetes is present in children and adolescents, and type

2 is present in adults. The classic symptoms of diabetes are: polyuria, polydipsia and polyphagia. The disease is manifested by metabolic disorders and chronic complications, macrovascular (changes in blood vessels of the brain, large blood vessels of the lower extremities) and microvascular (changes in the retina, renal arterioles, lower extremity arterioles and nerve vessels) (4-7).

2. OBJECTIVE

The aims of the study were to a) Correlate the glycoregulation of diabetes depending on HbA1c levels and the frequency of urinary tract infections in patients with diabetes; b) Determine the frequency of recurrent urinary tract infection during 6 months in patients with diabetes; c) Compare inflammatory parameters (SE, CRP, Leucocytes) with urine sediment and urine culture; d) Compare the duration of diabetes with the functional status of the kidneys by monitoring the levels of nitrogenous substances (urea, creatinine, proteinuria).

3. PATIENTS AND METHODS

Participants

The study was conducted as a retrospective-prospective, comparative and descriptive study, spanning from July 2019 to July 2021, with patients from the Counselling Canter for Diabetes of the Health Centre at the Canton Sarajevo. The study included patients of both sexes with a diagnosis of diabetes mellitus and urinary tract infection, at the ages between 18 to 95 years, with the total 116 of patients. During the research, the following parameters were monitored: fasting glucose, glucose level 2 hours after a meal, HbA1C values, urea, creatinine values, SE values, CRP, leukocytes, urine sediment findings, proteinuria and urine culture.

Procedure

Biochemical parameters were monitored from medical records in 116 patients diagnosed with diabetes mellitus and urinary tract infections. Analyzes were performed on automatic analyzers Dimension RXL Max and Radiometer-ABL 800.

Research methods

The following biochemical parameters were monitored: fasting glucose, glucose levels 2h after meals, HbA1C, urea, creatinine, inflammatory parameters: SE, CRP, leukocytes, as well as urine sediment: proteins, leukocytes, erythrocytes, urine cultures for the 116 patients with a diagnosis of Diabetes mellitus and urinary tract infection.

Statistical analysis

The obtained research results were processed using descriptive and analytical statistics; the analysis and data processing were done through Excel 2010. Mathematical–statistical indicators used in data analysis are: arithmetic mean, standard deviation, coefficient of variation, minimum value, maximum value and t-test.

4. RESULTS

The study included patients of both sexes with a diagnosis of diabetes mellitus and urinary tract infection, at the ages between 18 to 95 years, with the total 116 of patients. 47 participants were men (40.51%) and 69 participants were women (59.49%). Most of the participants were over 65 years old, in both sexes. Of the total number of patients who had diabetes and urinary tract infection, 32 participants had diabetes for up to 5 years, 30 participants between 6 to 10 years, 36 of them between 11–20 years, and 18 participants had diabetes for over 20 years. During the monitoring of glycoregulation parameters, the average value of fasting glucose was 9.54 mmol/l, with average glucose value 2 h after meals 13.94 mmol/l, and an average HbA1C value of 9.92% were found. Maximum value of fasting glucose levels was 20,80 mmol/l, glucose value 2h after meals 27 mmol/l, with maximum value of HbA1C of 15.40%. Minimum value of fasting glucose levels was 4 mmol/l, glucose value 2h after meals was 5.60 mmol/l, with minimum value of HbA1C of 5.10% (Table 1). During the monitoring of inflammatory parameters in patients with diabetes and urinary tract infection, the average value of CRP that was found was 45.84 mg/dl, average value of leukocytes was 10.15x10^9/l and sedimentation rate was 36 mm/h. The maximum CRP value was 328 mg/dl, maximum leucocytes value was 30.10x10^9/l, with the maximum sedimentation rate of 160 mm/h. The minimum CRP value was 0.20 mg/dl, minimum leucocytes value was 3.65x10^9/l, with the minimum sedimentation rate of 2 mm/h (Table 2). The values of nitrogenous substances were monitored (urea, creatinine, proteinuria) in patients with diabetes and urinary tract infection, where the average values of urea were 10.71 mmol/l, average values of creatinine were 112 µmol/l, with average proteinuria values of 0.67 g/dl were found. The maximum values of urea were 66.10 mmol/l, the maximum values of creatinine were 510 µmol/l, with maximum proteinuria values of 4.20 g/dl. The minimum values of urea were 2.70 mmol/l, the minimum values of creatinine were 15 µmol/l, with minimum proteinuria values of 0.03 g/dl (Table 3). In the urine cultures of the participants who were divided by sex, the following bacteria and fungi were isolated: Escherichia coli in a total of 35 patients, with a higher prevalence in women (67.56%) than in men (32.43%); Pseudomonas aeruginosa in a total of 7 patients, with a higher prevalence in women (85.71%); Proteus mirabilis in 4 patients in the same incidence ratio; Candida albicans in 21 patients with a higher prevalence in women (52.38%); Enterococcus faecalis in 22 patients with a higher prevalence in women (54.54%); Klebisella pneumoniae in 16 patients with a higher prevalence in women (56.25%); Staphylococcus epidermidis in 4 patients with a higher prevalence in women (75%); Streptococcus agalacticae in 2 patients in the same incidence ratio; Enterobacter cloacae in 2 patients in the same incidence ratio; Streptococcus sp. isolated in 1 woman (100%). The value of inflammatory parameters (CRP, leukocytes and sedimentation rate) increased in patients with diabetes and urinary tract infection. CRP values in patients with diabetes mellitus and urinary tract infections range from 0.2 mg/l up to 328 mg/l. Leukocyte values are in the range of 3.65 x10^9/l up to 30.10x10^9/l. Sedimentation values in these participants range from 2 mm/h to 160 mm/h. The functional status of the kidneys was monitored on the basis of nitrogen parameters (urea, creatinine, proteinuria). There is a negative correlation between nitrogen parameters (urea, creatinine and proteinuria) with the duration of diabetes (Graph 1). The inflammatory parameter CRP was increased in patients who

	Fasting glucose (mmol/l)	HbA1C (%)	Glucose levels 2h after meals (mmol/l)
Average value	9.54	9.92	13.94
Standard deviation	2.97	2.48	3.91
Variance	8.80	6.17	15.32
Kurtosis	1.54	-0.57	0.64
Skewness	0.94	0.40	0.56
Maximum value	20.80	15.40	27
Minimum value	4	5.10	5.60

Table 1. Valuation of glycemic control parameters in patients with diabetes and urinary tract infections

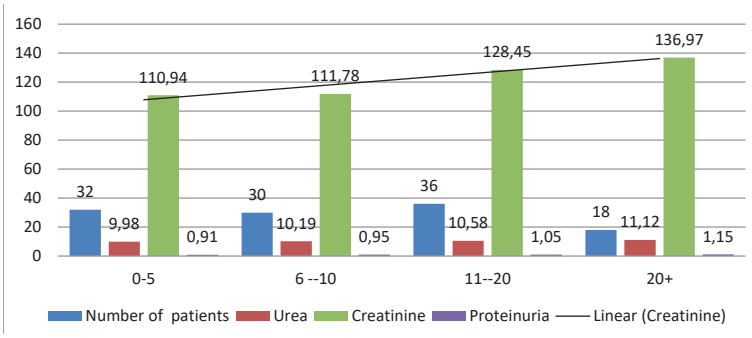
	CRP (mg/dl)	Leucocytes (10^9/l)	Sedimentation (mm/h)
Average value	45.84	10.15	36
Standard deviation	7177	4.80	32.97
Variance	5151.21	23.00	1086.98
Kurtosis	3.87	4.33	2.47
Skewness	2.08	1.88	1.61
Maximum value	328	30.10	160
Minimum value	0.20	3.65	2

Table 2. Values of inflammatory parameters in patients with diabetes and urinary tract infections

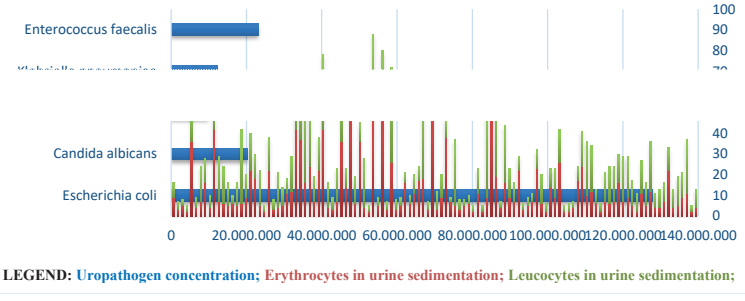
had increased values of leukocyte sedimentation rate and erythrocyte sedimentation rate, while urine culture in such patients was positive for 1 to 3 types of bacteria. Patients who have had a urinary tract infection three times are more likely to have a recurrence of a urinary tract infection. Escherichia coli is the most isolated bacteria with a urine concentration of 128,001,000 CFU/ml. Other types of bacteria are significantly less represented than Escherichia coli (Graph 2). There is a slight increase in HbA1C values with an increase in the concentration of bacteria in the urine of patients with diabetes mellitus and urinary tract infections.

	Urea (mmol/l)	Creatinine (μmol/l)	Proteinuria (g/dl)
Average value	10.71	112	0.67
Standard deviation	9.11	74.80	0.79
Variance	83.07	5595.03	0.63
Kurtosis	11.87	8.77	5.48
Skewness	2.86	2.64	2.19
Maximum value	66.10	510	4.20
Minimum value	2.70	15	0.03

Table 3. Values of nitrogen parameters in patients with diabetes and urinary tract infections



Graph 1. Correlation between the duration of diabetes with the functional status of the kidneys, following the level of nitrogenous substances (urea, creatinine, proteinuria)



Graph 2. Comparison of the frequency of individually isolated pathogenic bacteria in urine culture with the results of urine sediment in patients with diabetes and urinary tract infections

5. DISCUSSION

Urinary tract infections are much more common in patients with diabetes, and the incidence increases with age. In patients with diabetes, urinary tract infections can be a significant problem (8). The main risk factors for urinary tract infections in patients with diabetes are the following: inadequate glycemic control, duration of diabetes, diabetic nephropathy, and anatomical and functional abnormalities of the urinary tract (9). In the studies conducted in the United States based on the data from the databases of health facilities, where 70,000 patients with type 2 diabetes participated, it was found that 8.2% were diagnosed with urinary tract infections within one year (12.9% of women and 3.9% of men, with an increase in incidence with age). 100 patients older than 60 years with type 2 diabetes participated in a prospective study conducted in India. Bacteriuria was found in 43% of patients, more common among female patients (43%), the duration of diabetes was over 15 years, and the urine cultures showed that Escherichia coli (69.8%) was the most common cause (10). A study conducted in Pisa involved 10,221 patients older than 50 years. In patients who had asymptomatic bacteriuria, 346 of them (229 females and 117 males) were diagnosed with Diabetes mellitus (90% type 2), and 975 of them (679 females and 296 males) were not diabetics. The average value of the HbA1C in diabetics was 7.8% ± 1.6 SD. Escherichia coli is the uropathogen that was most frequently isolated and was the cause in 32.5% of urinary tract infections in patients with diabetes as well as in 31.4% of male patients who were not diagnosed with diabetes. Escherichia coli was more frequent in women (54.1% in diabetics and 58.2% in non-diabetics) (11). 3,652 patients with Type 2 diabetes were included in a study in China, where 409 patients were diagnosed with urinary

tract infections. The incidence of urinary tract infections was higher in female patients (24.13%). HbA1C values were 9.54 ± 0.13%. Escherichia coli is the most commonly isolated microorganism in patients with urinary tract infections. Analysis of pathogenic microorganisms for infections revealed that Escherichia coli infections were more common in females than in males, while infections caused by Klebsiella pneumoniae, Entrococcus, and Staphylococcus occurred much more frequently in male than female patients (12). A prospective study conducted in the United States in which 223 patients (202 females and 21 males) participated, of which 14 patients had diabetes mellitus. The mean leukocyte count was 16,960 ± 5869 / mm3. The mean CRP was 15.65 ± 8.56 mg/dl (13). In a study conducted in Turkey, 123 patients with type 2 diabetes mellitus participated. In the study, asymptomatic bacteriuria was found in 22 of 173 (17%) patients with type 2 diabetes mellitus. Leukocyte counts were 36.97 ± 169 mm3 (14). A prospective study conducted by Kumar S. et al. Involved 105 patients diagnosed with type 2 diabetes mellitus and pyelonephritis. Pyelonephritis was much more common in males (62:43) than in females (15). The study, conducted by Ming-Cheng W. and colleagues, involved 271 patients, of whom 80 were non-diabetic and 190 were diabetic. HbA1C values were 8.0 ± 2.1% (16). In our study, HbA1C values were 9.92 ± 2.48%. According to our study and the study conducted by Ming-Cheng W. HbA1C values differ by 1.92 ± 0.38%. From the obtained research results we can conclude that the values are almost identical.

6. CONCLUSION

According to the data, it can be concluded that urinary tract infections are more common in female patients with diabetes mellitus than in male patients. In 26 patients, urinary tract infection was registered three times, in 32 patients twice, and 51 patients had a urinary tract infection once in six months, while all patients were monitored. In patients with urinary tract infection and diabetes after correlation of glycoregulation parameters (glucose on an empty stomach, glucose 2h after a meal and HbA1C) with the bacterial concentration in urine, a negative correlation of all parameters of glycoregulation with bacterial concentration was observed. Comparison of inflammatory parameters (SE, CRP and leukocytes) with urine sediment and urine culture showed that the values of sedimentation, CRP and leukocytes increased together with urine sediment values, and such patients had a positive urine culture on 1 of 3 types of isolated bacteria. By correlating the duration of diabetes with the functional status of the kidneys, elevated values of nitrogen parameters were observed (urea, creatinine, proteinuria) in patients who had a longer duration of diabetes. By comparing the frequency of individual pathogenic bacteria in urine culture with urine sediment, it was noticed that Escherichia coli is the most common uropathogen that causes urinary tract infection. In addition, Enterococcus faecalis, Klebsiella pneumoniae, Candida albicans, and Pseudomonas aeruginosa have also been found.

- **Patient Consent Form:** All participants were informed about subject of the study.
- **Author's Contribution:** A.B. and F.C. gave substantial contributions to the conception or design of the work in acquisition, analysis, or interpretation of data for the work. Dz.H. had a part in article preparing for drafting or revising it critically for important intellectual content. E.H. gave final approval of the original research and made substantial contribution in monitoring of the data compilation and evaluation of results.
- **Conflicts of interest:** There are no conflicts of interest.
- **Financial support and sponsorship:** None.

REFERENCES

1. Pavić S, Andrić A, Antić M, Jovanović M, Novković A, Pavić A. Etilogija, epidemiološki i kinički parametri infekcija urinarnog trakta kod bolesnika sa Diabetes mellitusom. Medicinski glasnik Specijalne bolnice za bolesti štitaste žlezde i bolesti metabolizma. 2019 Jan; 24(74): 135-140. doi:10.5937/medgla1972135P.
2. Đukanovć Lj. Rekurentne infekcije mokraćnih puteva:antimikrobna i imunoaktivna profilaksa. Biomedicinska Istraživanja. Jan 2016; 6(2): 146-156. doi: 10.7251/BII1502146DJ.
3. Flores-Mireles AL, Walker JN, Caparon M, Hultgren SJ. Urinary tract infections: epidemiology, mechanisms of infections and treatment options. Nauret Revievs Microbiology. 2015 May; 13: 269–284. doi: https://doi.org/10.1038/nrmicro3432
4. Fajgelj A, Grujić M, Macanović M, Mikeš A, Numić N, Pašić I. Interna medicina II. Sarajevo: Svjetlost; 1989.
5. Heljić B. Dijabetologija. Sarajevo: Medicinski fakultet Univerziteta u Sarajevu; 2011.
6. Aganović I, Metelko Z. Šećerna bolest. Interna medicina. Zagreb: Naklada Ljevak; 2008.
7. Ašimi V Z, Bureković A. et all. Smjernice za tretman diabetes mellitusa. Sarajevo: Perfecta; 2017.
8. Sharma S, Govind B, Naidu KS, Kinjarapu S, Rasool M. Clinical and Laboratory Profile of Urinary Tract Infections in Type 2 Diabetics Aged over 60 years. Journal of Clinical and Diagnostic Research. 2017 Apr; 11(4): OC25–OC28. doi: 10.7860/JCDR/2017/25019.9662.
9. Ronald A, Ludwig E. Urinary tract infections in adults with diabetes. International Journal of Antimicrobial Agents. 2001 Apr; 17(4): 287-292. doi: https://doi.org/10.1016/S0924-8579(00)00356-3.
10. Nitzan O, Elias M, Chazan B, Saliba W. Urinary tract infections in patients with diabetes mellitus: review of prevalence, diagnosis and management. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy. 2015 Feb; 8: 129-136. doi: 10.2147/DMSO.S51792.
11. Bonadio M, Costarelli S, Morelli G, Tartaglia T. The influence of diabetes mellitus on spectrum of uropathogens and the antimicrobial resistance in elderly adult patients with urinary tract infections. BMC Infectious Disease. 2006 Mar; 6(1): 54. doi: https://doi.org/10.1186/1471-2334-6-54.
12. He K, Hu Y, Shi CJ, Zhu QY, Mao MX. Prevalence, risk factors and microorganism of urinary tract infections in patients with type 2 diabetes mellitus: a retrospective study in China. Therapeutics and Clinical Risk Management. 2018 Feb; 14: 403-408. doi: 10.2147/TCRM.S147078.
13. Rollino C, Beltrame G, Ferro M, Quattrocchio G, Sandrone M, Quarello F. Acute pyelonephritis in adults: a case series of 223 patients. Nephrology Dialysis Transplantation. 2012 Feb; 27(9): 3488-3493. doi: 10.1093/ndt/gfr810.
14. Turan H, Serefhanoglu K, Torun N A, Kulaksizoglu S, Kulaksizoglu M, Pamuk B, Arslan H. Frequency, risk factors, and responsible pathogenic microorganisms of asymptomatic bacteriuria in patients with type 2 diabetes mellitus. Japanese Journal of Infectious Diseases. 2008 May; 61(3): 236-238.
15. Kumar S, Ramachandran R, Mete U, Mittal T, Dutta P, Kumar V, Rathi M, Jha V, Gupta L K, Sakhuja V, Kohli SH. Acute pyelonephritis in diabetes mellitus: Single center experience. Indian Journal of Nephrology. 2014 Dec; 24(6): 367-371. doi: 10.4103/0971-4065.135347.
16. Wang CM, Tseng CC, Wu BA, Lin HW, Teng HC, Yan JJ, Wu JJ. Bacterial characteristics and glycemic control in diabetic patients with Escherichia coli urinary tract infection. Journal of Microbiology, Immunology and Infection. 2013 Feb; 46(1): 24-29. doi: https://doi.org/10.1016/j.jmii.2011.12.024.