

Evaluation of Diabetic Women in Terms of Lower Urinary Tract Symptoms, Overactive Bladder and Urinary Incontinence

Diyabetik Kadın Hastaların Alt Üriner Sistem Semptomları, Aşırı Aktif Mesane ve İdrar Kaçırma Açısından Değerlendirilmesi

İ Fatih Bıçaklıoğlu¹, İ Murat Yavuz Koparal², İ Ender Cem Bulut³, İ İrfan Şafak Barlas⁴, İ Bora Küpeli⁴, İ İlker Şen⁴

¹İzmit Seka State Hospital, Clinic of Urology, Kocaeli, Türkiye

²Recep Tayyip Erdoğan University Training and Research Hospital, Clinic of Urology, Rize, Türkiye

³Van Training and Research Hospital, Clinic of Urology, Van, Türkiye

⁴Gazi University Faculty of Medicine, Department of Urology, Ankara, Türkiye

What's known on the subject? and What does the study add?

Diabetic bladder dysfunction is known to be associated with lower urinary tract symptoms, overactive bladder and urinary incontinence. We have demonstrated in this study that randomized controlled studies should be performed to obtain more significant results.

Abstract

Objective: In this study, we aimed to evaluate the association of lower urinary tract symptoms (LUTS), overactive bladder (OAB) and urinary incontinence (UI) with age, diabetic complications and glycaemic control in diabetic women.

Materials and Methods: A total of 81 women diagnosed with Diabetes Mellitus were included in the study. Demographic characteristics including age, height and weight of patients, full medical history, urine culture, serum creatinine levels and glycaemic control parameters including serum fasting blood glucose levels, serum satiety blood glucose levels and serum HbA1c levels. Turkish version of the OAB-V8, urinary distress inventory-6 (UDI-6), incontinence impact questionnaire (IIQ-7) and the International Prostate Symptom Score (IPSS) were applied.

Results: The mean age was 58.6±11.8 years. Thirty-five (43.2%) of the patients had diabetes-related complications. There was no statistically significant relationship between OAB-V8, UDI-6, IPSS, IIQ-7 questionnaire scores and glycaemic control parameters, age, and presence of diabetic complications.

Conclusion: To better understand the etiopathogenesis of diabetic bladder dysfunction and related complications including LUTS, OAB and UI, we need randomized controlled studies with a greater number of patients.

Keywords: Overactive bladder, Urinary incontinence, Diabetes

Öz

Amaç: Bu çalışmada, diyabetik kadınlarda alt üriner sistem semptomları (AÜSS), aşırı aktif mesane (AAM) ve üriner inkontinans (Üİ) ile yaş, diyabetik komplikasyonlar ve glisemik kontrol arasındaki ilişkiyi değerlendirmeyi amaçladık.

Gereç ve Yöntem: Çalışmaya Diabetes Mellitus tanısı konan toplam 81 kadın hasta dahil edildi. Hastaların yaş, boy ve kilosunu içeren demografik verileri, tam tıbbi öyküsü, idrar kültürü, serum kreatinin ile serum açlık kan şekeri, serum tokluk kan şekeri ve serum HbA1c seviyelerini içeren glisemik kontrol parametreleri kaydedildi. Hastalara AAM-V8, üriner distress envanteri-6 (ÜDE-6), inkontinans etkisi anketi (İEA-7) ve Uluslararası Prostat Semptom Skoru (UPSS) sorgulama formlarının valide edilmiş Türkçe versiyonları uygulandı.

Bulgular: Yaş ortalaması 58,6±11,8 yıl idi. Hastaların 37'sinde (%43,2) diyabetle ilişkili komplikasyonlar vardı. AAM-V8, ÜDE-6, UPSS, İEA-7 anket puanları ile glisemik kontrol parametreleri, yaş ve diyabetik komplikasyonların varlığı arasında istatistiksel olarak anlamlı bir ilişki bulunamadı.

Sonuç: Diyabetik mesane disfonksiyonu etyopatogenezi ile AÜSS, AAM ve Üİ gibi ilgili komplikasyonları daha iyi anlamak için, daha fazla sayıda hasta ile yapılacak randomize kontrollü çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Aşırı aktif mesane, Üriner inkontinans, Diyabet

Correspondence: Murat Yavuz Koparal MD, Recep Tayyip Erdoğan University Training and Research Hospital, Clinic of Urology, Rize, Türkiye

Phone: +90 533 612 51 45 **E-mail:** drkoparal@yahoo.com **ORCID-ID:** orcid.org/0000-0002-8347-5727

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Introduction

Diabetes Mellitus (DM) is characterized by an absolute or relative insufficiency of insulin secretion or by structural abnormalities in the insulin molecule, which are heterogeneous with the aetiology, genetic and clinical pattern (1). Chronic complications including neuropathy, retinopathy and nephropathy are common and well-known. Diabetic bladder dysfunction (DBD) / diabetic cystopathy with lower urinary tract symptoms (LUTS) is also common; however, it is not given as much attention as other complications. For many years, LUTS in DM has been thought to be due to the paralysis of the detrusor (2,3). Recent studies have shown that DBD is characterized by poor bladder emptying and overflow urinary incontinence (UI), as well as storage symptoms that point to overactive bladder (OAB) in these patients (3). Although DBD is now well-described in the literature, it is not clear how OAB and UI develop in diabetic patients. Therefore, we aimed to evaluate the association of LUTS, OAB and UI with age, diabetic complications and glycaemic control parameters in diabetic women, since symptoms associated with benign prostatic hyperplasia (BPH) in male patients may lead to confusion.

Materials and Methods

Study Design

A total of 81 women diagnosed with DM before 18 years of age, no history of pregnancy and no history of urinary tract infection, who applied to the Gazi University Faculty of Medicine, Department of Urology and Endocrinology from January 2014 to July 2014 were included in the study. The study was approved by the Gazi University of local ethics committee (date: 23.12.2013, no.: 257).

Recording Clinical Data

Demographic characteristics including age, height and weight of patients, full medical history, urine culture, serum creatinine levels and glycaemic control parameters including serum fasting blood glucose (FBG) levels, serum satiety blood glucose (SBG) levels and serum HbA1c levels. Turkish version of the OAB-V8, urinary distress inventory-6 (UDI-6), incontinence impact questionnaire-7 (IIQ-7) (4,5) and the International Prostate Symptom Score (IPSS), which was also used for women in various studies, were applied (6,7). The IIQ-7 questionnaire was not applied to patients with no evidence of incontinence.

Target glycaemic control values were determined as <6.5%, 6.5% - 9%, >9% for serum HbA1c, as <120 g/dL and ≥120 g/dL for serum FBG, and as <140 g/dL and ≥140 g/dL for serum

SBG according to the Turkish Association of Endocrinology and Metabolism DM Working Group (8).

Statistical Analysis

The normal distribution of continuous variables was evaluated by visual (histogram and probability plots) and analytical (Kolmogorov-Smirnov and Shapiro-Wilk tests) methods. Independent Sample t-test and one-way analysis of variation was used as parametric tests in two independent groups and more than two independent groups, respectively. Mann-Whitney U test was used as non-parametric test if the data did not fit normal distribution. The results were evaluated in a confidence interval (CI) of 95% and a significance level of $p < 0.05$. SPSS Statistics 15.0 was used for statistical analysis of research data.

Results

Of the 81 diabetic women participating in the study, 33 (40.7%) were from the endocrinology department and 48 (59.3%) were from the urology department. The mean age of the patients was 58.6 ± 11.8 years. In diabetic patients, passed time following the diagnosis of DM was mean 10.96 ± 7.99 years. In urological symptom questionnaire, 35 patients (43.2%) reported frequent urination in daytime; these patients had a mean urination of 8.8 ± 1.15 times. Sixty-seven (82.7%) of the patients had nocturia and got up to urinate 2.7 ± 1.9 times per night. Urgency was found in 52 (64.2%) patients. Forty-eight (59.3%) of the patients were found to have UI. Eight (9.9%) of these patients had stress UI, 22 (27.2%) had urge UI and 20 (24.7%) had mixed UI.

Thirty-five (43.2%) of the patients had diabetes-related complications. Three of patients (8.3%) had diabetic nephropathy, 14 (38.9%) had peripheral neuropathy, 13 (36.1%) had diabetic retinopathy, 1 (2.8%) had diabetic foot, 2 (5.6%) had diabetic retinopathy and nephropathy and 3 (8%) had peripheral neuropathy and diabetic retinopathy.

Serum HbA1c level of the patients was mean 8.14 ± 2.25 %. Patients were sorted into three groups as <6.5%, 6.5% - 9%, >9% according to the serum HbA1c levels. The relationships among these groups according to the OAB-V8, UDI-6, IPSS and IIQ-7 questionnaire scores are shown in Table 1. There was no statistically significant difference among these groups.

Serum FBG level of the patients was mean 141.48 ± 44.55 g/dL. Patients were divided into two groups as <120 g/dL and ≥120 g/dL according to serum FBG levels. The relationship between these groups according to the OAB-V8, UDI-6, IPSS and IIQ-7 questionnaire scores are shown in Table 2. There was no statistically significant difference between these groups.

Serum SBG level of the patients was mean 213.84 ± 69.09 g/dL. Patients were divided into two groups as <140 g/dL and ≥140

g/dL according to serum SBG levels. The relationship between these groups according to the OAB-V8, UDI-6, IPSS and IIQ-7 questionnaire scores are shown in Table 3. There was no statistically significant difference between these groups.

Patients were divided into two groups according to presence of diabetic complications. The relationship between these groups according to the OAB-V8, UDI-6, IPSS and IIQ-7 questionnaire scores are shown in Table 4. There was no statistically significant difference between these groups.

Patients were divided into two groups as <60 years and ≥60 years according to age. The relationship between OAB-V8, UDI-6, IPSS

and IIQ-7 questionnaire scores is shown in Table 5. There was no statistically significant relationship between these groups.

Patients were divided into two groups according to presence of OAB. The relationship between the groups according to the

Table 1. Evaluation of total score of questionnaire forms in terms of HbA1c level

	HbA1c (%)	Patients (n)	Score (mean ± SD)	p
OAB-V8	Group 1 (<6.5)	22	16.50±8.623	0.368
	Group 2 (6.5-9)	37	13.32±9.165	
	Group 3 (>9)	22	15.32±7.473	
	Total	81	14.73±8.594	
UDI-6	Group 1 (<6.5)	22	5.59±3.568	0.941
	Group 2 (6.5-9)	37	5.24±4.179	
	Group 3 (>9)	22	5.45±3.334	
	Total	81	5.40±3.761	
IPSS	Group 1 (<6.5)	22	9.91±6.761	0.768
	Group 2 (6.5-9)	37	8.89±7.109	
	Group 3 (>9)	22	10.00±5.219	
	Total	81	9.47±6.494	
IIQ-7	Group 1 (<6.5)	12	11.17±6.576	0.590
	Group 2 (6.5-9)	20	10.10±4.811	
	Group 3 (>9)	16	8.88±6.490	
	Total	48	9.96±5.805	

SD: Standard deviation, HbA1c: Hemoglobin A1c, OAB-V8: Overactive bladder-V8, UDI-6: Urinary distress inventory-6, IPSS: International Prostate Symptom Score, IIQ-7: Incontinence impact questionnaire-7

Table 2. Evaluation of total score of questionnaire forms in terms of fasting blood glucose level

	FBG (g/dL)	Patients (n)	Score (mean ± SD)	p
OAB-V8	Group 1 (<120)	30	15.67±8.73	0.455
	Group 2 (≥120)	51	14.18±8.55	
UDI-6	Group 1 (<120)	30	5.77±4.13	0.499
	Group 2 (≥120)	51	5.18±3.54	
IPSS	Group 1 (<120)	30	9.53±7.03	0.946
	Group 2 (≥120)	51	9.43±6.22	
IIQ-7	Group 1 (<120)	18	10.17±5.99	0.850
	Group 2 (≥120)	30	9.83±5.79	

FBG: Fasting blood glucose, OAB-V8: Overactive bladder-V8, UDI-6: Urinary distress inventory-6, IPSS: International Prostate Symptom Score, IIQ-7: Incontinence impact questionnaire-7, SD: Standard deviation

Table 3. Evaluation of total score of questionnaire forms in terms of satiety blood glucose level

	SBG groups (g/dL)	Patients (n)	Score (mean ± SD)	p
OAB-V8	Group 1 (<140)	15	17.53±7.33	0.163
	Group 2 (≥140)	66	14.09±8.77	
UDI-6	Group 1 (<140)	15	6.40±3.35	0.254
	Group 2 (≥140)	66	5.17±3.83	
IPSS	Group 1 (<140)	15	10.87±6.41	0.359
	Group 2 (≥140)	66	9.15±6.51	
IIQ-7	Group 1 (<140)	9	9.67±6.36	0.869
	Group 2 (≥140)	39	10.03±5.75	

SBG: Satiety blood glucose, OAB-V8: Overactive bladder-V8, UDI-6: Urinary distress inventory-6, IPSS: International Prostate Symptom Score, IIQ-7: Incontinence impact questionnaire-7, SD: Standard deviation

Table 4. Evaluation of total score of questionnaire forms in terms of diabetic complications

	Diabetic complications	Patients (n)	Score (mean ± SD)	p
OAB-V8	Group1 (no)	46	14.54±8.17	0.826
	Group 2 (yes)	35	14.97±9.23	
UDI-6	Group1 (no)	46	5.35±3.56	0.898
	Group 2 (yes)	35	5.46±4.05	
IPSS	Group1 (no)	46	10.09±6.99	0.329
	Group 2 (yes)	35	8.66±5.77	
IIQ-7	Group1 (no)	24	10.96±5.99	0.237
	Group 2 (yes)	24	8.96±5.55	

SD: Standard deviation, OAB-V8: Overactive Bladder-V8, UDI-6: Urinary Distress Inventory-6, IPSS: International Prostate Symptom Score, IIQ-7: Incontinence Impact Questionnaire-7

Table 5. Evaluation of total score of questionnaire forms in terms of age

	Age (years)	Patients (n)	Score (mean ± SD)	p
OAB-V8	Group 1 (<60)	40	14.45±9.17	0.775
	Group 2 (≥60)	41	15.00±8.08	
UDI-6	Group 1 (<60)	40	5.20±3.83	0.648
	Group 2 (≥60)	41	5.59±3.72	
IPSS	Group 1 (<60)	40	8.60±6.34	0.237
	Group 2 (≥60)	41	10.32±6.60	
IIQ-7	Group 1 (<60)	25	11.24±5.47	0.112
	Group 2 (≥60)	23	8.57±5.95	

SD: Standard deviation, OAB-V8: Overactive Bladder-V8, UDI-6: Urinary Distress Inventory-6, IPSS: International Prostate Symptom Score, IIQ-7: Incontinence Impact Questionnaire-7

Table 6. Evaluation of groups with and without overactive bladder in terms of FBG, satiety blood glucose and HbA1c

	OAB groups	Patients (n)	Level (mean ± SD)	p
FBG (g/dL)	Group 1 (with OAB)	52	148.23±48.37	0.068
	Group 2 (without OAB)	29	129.38±34.23	
SBG (g/dL)	Group 1 (with OAB)	52	220.94±78.07	0.339
	Group 2 (without OAB)	29	201.10±47.67	
HbA1c (%)	Group 1 (with OAB)	52	8.37±2.61	0.601
	Group 2 (without OAB)	29	7.72±1.31	

FBG: Fasting blood glucose, SBG: Satiety blood glucose, HbA1c: Hemoglobin A1c, SD: Standard deviation, OAB: Overactive bladder

serum HbA1c, FBG and SBG levels is shown in Table 6. There was no statistically significant difference between these groups.

Discussion

DM is an increasingly prevalent chronic metabolic disease in which the organism cannot utilize carbohydrates, fats and proteins. DM has various complications and requires continuous medical care. Relatively minor complications, such as DBD, have been ignored for many years. However, patients with DM have been shown to have LUTS rate of up to 80% (9). In this study, we aimed to evaluate the bladder functions of DM patients using various questionnaires to demonstrate the importance of DBD. We did not include male patients because BPH associated symptoms in male patients are believed to mask or increase LUTS associated with DM.

One of the well-known methods for assessing LUTS is the use of the IPSS questionnaire, which has been used in BPH for many years. However, the use of the IPSS questionnaire alone is not sufficient for the evaluation of bladder dysfunction in diabetic patients. Several questionnaires including the OAB-8 questionnaire which is used for OAB, the UDI-6 questionnaire which is used to assess LUTS and incontinence, and the IIQ-7 questionnaire which is used to evaluate incontinence, have been shown to be useful in evaluating LUTS (10,11,12).

DM patients with LUTS have been shown to have more storage symptoms, such as urgency and urge UI (3). Therefore, we applied the OAB-V8, UDI-6, IPSS and IIQ-7 questionnaires to determine patients' symptoms. Although the IPSS questionnaire was originally designed to assess LUTS associated with BPH in men, it has been shown that it can also be used in the evaluation of LUTS in women (6,7).

Many studies show the association between diabetic complications and glycaemic control (13). Glycaemic control is the most important parameter affecting complications in diabetic patients. Although its clinical indicator is mainly shown by serum HbA1c level, serum FBG and serum SBG levels was

suggested to be used as glycaemic control targets by the Turkish Association of Endocrinology and Metabolism DM Working Group (8).

Chiu et al. (14) divided patients [279 diabetic (133 females, 146 males)] and (578 non-diabetic (266 female, 292 male)) into three groups in their study according to serum HbA1c levels [<7 (65 patients), 7-8.9 (65 patients), and >9 (79 patients)] and the OAB Symptom Score questionnaire was applied to all patients. They found serum HbA1c level and age as independent predictors in terms of OAB/urgency, urge UI and nocturia. In the study of Fayyad et al. (15), the clinical data of 148 diabetic women were recorded and questionnaires were applied to evaluate LUTS. The results of this study indicated that there was no statistically significance relationship between LUTS and HbA1c level, age, duration of diabetes, neuropathy and insulin usage. In the study of Liu et al. (16), the clinical data of 1.359 (707 male, 652 female) type 2 diabetic patients were recorded and the OAB symptom score test was applied for the evaluation of LUTS. Patients were divided into two groups as with OAB and without OAB, it was found that there was no significant difference between the groups in terms of serum HbA1c level, renal function and body mass index. In multivariate analyses, age and gender were found to be independent risk factors in terms of OAB.

In our study, patients were divided into three groups according to serum HbA1c target levels as <6.5% (22 patients), 6.5-9% (37 patients), and >9% (22 patients) which were determined by the Turkish Association of Endocrinology and Metabolism DM Study Group (8). No statistically significant difference was found among these three groups' questionnaire form scores (OAB-V8, UDI-6, IPSS and IIQ-7). Patients were also divided into two groups according to serum FBG (<120 g/dL, 30 patients and ≥120 g/dL, 51 patients) and serum SBG (<140 g/dL, 15 patients and ≥140 g/dL, 66 patients) which are the other glycaemic control parameters except serum HbA1c. The mean scores of the questionnaires showed no statistically significant difference between the two groups.

Different results from studies in the literature suggested us that insufficient standardization of patients and variability of the questioning forms result in different interpretations. Furthermore, the subjectivity of the questioning forms and the symptoms that are increasing with age regardless of diabetes, may be other factors in obtaining different outcomes. Nevertheless, it is generally observed that the results of these studies support our results.

Liu et al. (16), in their study in which patients were divided into two groups as with OAB and without OAB, they found no significant difference between groups in terms of serum HbA1c, renal function, and body mass index. In our study, we divided our patients into two groups (with OAB and without

OAB) and we found an increase in the OAB group in terms of serum HbA1c, serum FBG and serum SBG. However, it was not statistically significant. Especially in terms of serum FBG level, the p value was 0.068. This statistic suggests that, if the number of patients participating in the study were increased, statistically significant results could be obtained. Furthermore, all our patients in the OAB group may not have had DBD and, in some of the patients who had achieved glycaemic control targets for DM, OAB disease might be seen depending on other etiologic factors, especially in relation to age.

Other factors lead to LUTS in diabetic women is the age of the patient and the passed time following the diagnosis of DM. Deterioration of detrusor functions with aging has been shown to lead to LUTS (17). Sarici et al. (18) showed that age was a risk factor for OAB and UI. In the study of Wen et al. (19) including 9.805 patients (3.129 men and 6.676 women), they showed an increase in OAB prevalence with age in both men and women. However, in DM patients, an increase in years may accelerate impairment of the detrusor function.

Chiu et al. (14) and Liu et al. (16) have shown that age is an independent risk factor in multivariate analyses. In our study, there was no effect of patient age on the symptoms due to DBD. In our study the mean age was 58.6 ± 11.8 (20-89) years and similar to their studies. Since we could not perform the multivariate analysis due to the small sample size, we could not find any statistically significant difference between age groups in terms of the questionnaire scores. This result, which is different from other studies, may be due to the fact that the patients in the current the study were not selected from certain age groups. For example, 41 of the patients in our study were between 55 and 65 years of age, 2 patients were 20-30 years of age, 3 patients were 30-40 years of age and 3 patients were 80-90 years of age. In the study of Palleschi et al. (20), the results of OAB questionnaire in diabetic patients were shown to increase with age and disease duration.

A significant relationship between development of diabetic complications and the development of DBD was established in many studies (21,22). In the study of Tai et al. (21) which was evaluating the presence of metabolic syndrome in the development of OAB in diabetic women, diabetic neuropathy and nephropathy were shown to be independent risk factors in women with type 2 DM. In the study of Karoli et al. (22) which was evaluating diabetic women in terms of chronic complications of diabetes, the prevalence of OAB was 53%. Additionally, there was a significant relationship between the presence of chronic complications including diabetic neuropathy, nephropathy and metabolic syndrome, and LUTS and OAB. Diabetic complications also appear to be significant predictors of bladder dysfunction. In our study, we did not find any statistically significant difference between the two groups

(with diabetic complications: 46 patients; without diabetic complications: 35 patients) in terms of the questionnaire scores. We think that the lack of a meaningful relationship between these complications in our study may be due to the small sample size or the underdevelopment of more insidious complications such as peripheral neuropathy.

Conclusion

To better understand the etiopathogenesis of DBD and related complications including LUTS, OAB and UI, we need randomized controlled studies with a greater number of patients. There is also need for physicians to question how DBD seriously impairs the quality of life. DBD should be considered as a significant problem related to DM and investigate for diabetic patients.

Ethics

Ethics Committee Approval: The study were approved by the Gazi University of local ethics committee (date: 23.12.2013, no.: 257).

Informed Consent: Consent form was filled out by all participants.

Peer-review: Internally peer-reviewed.

Authorship Contributions

Concept: B.K., İ.Ş., Design: B.K., İ.Ş., Data Collection or Processing: F.B., E.C.B., İ.Ş.B., Analysis or Interpretation: F.B., M.Y.K., Literature Search: F.B., M.Y.K., E.C.B., İ.Ş.B., B.K., İ.Ş., Writing: M.Y.K.

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