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Original Article

The impact of Diabetes Mellitus on Lower urinary tract symptoms (LUTS) in both male and female patients

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ABSTRACT

Introduction: Contemporary studies examine the connection of Diabetes Mellitus (DM) with Lower urinary tract symptoms (LUTS), alone or associated with other factors of the metabolic syndrome. However, little research has occurred concerning patients with diabetes of both genders and sexes without other diseases of the lower urinary tract. The aim of this study is to examine the relationship between DM and LUTS.
Methods: The study enrolled 110 patients with DM and 134 healthy individuals. The IPSS questionnaire was used for the evaluation of symptoms from lower urinary tract. Data was analyzed with univariate and multivariate logistic regression using SPSS v.24.
Results: Analysis with moderate/severe LUTS as dependent variable and plausible confounding factors (age group, BMI, hypertension, dyslipidemia, years with DM and reported HbA1c) as covariates revealed that only HbA1c levels correlated independently with the presence of moderate/severe LUTS ($p = 0,024$, OR:2,729, CI:1,144–6,509) in diabetic women, while there was no statistically significant difference between male groups. HbA1c levels' correlation with IPSS-voiding and IPSS- storage score was not statistically significant. Quality of life is also affected in women with diabetes mellitus (p: 0,02).
Conclusion: Only an increase in HbA1c was independently connected with a deterioration of LUTS in the female group.

1. Introduction

Diabetes Mellitus is a metabolic disorder that affects the secretion and function of insulin. It is divided into 4 different categories: type I, type II, gestational diabetes and other non-specific types of diabetes mellitus based on the pathophysiological mechanisms. In 2015 the prevalence of diabetes in Greece was 608.800 patients [1]. In particular, the incidence of DMI in Greece reached 9,7 patients per 100.000 residents [2], while Diabetes Mellitus type II (DMII) affects 80–90% of patients, especially those suffering from obesity [3].

The presence of LUTS in patients with DM has been investigated in few studies suggesting the connection between autonomous neuropathy, caused by DM, and bladder function [4]. Moreover, both the detrusor muscle and urothelium are affected in diabetic patients [5,6,7,8]. Other studies suggest the connection between BPH, which is a major factor of LUTS, with DM. They claim that hypoxia, increased autonomous neural activity and insulin itself, as a growth factor, are contributors to prostate hyperplasia [9]. Chronic inflammation is, also, suspected for the pathogenesis of BPH [10].

More than half of male and female diabetic patients suffer from bladder dysfunction [11]. Diabetic cystopathy is a rare condition characterized by decreased sensitivity of the bladder, difficulty initiating micturition, urine flow disturbance and post voiding residual. Overactive bladder and fullness sensation were other common symptoms in bother sexes in 39–61% of patients. Particularly in women, DM was associated with 30–100% of patients with urge [12] and to fewer extent with stress incontinence especially in

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those that were insulin-treated [13]. In men, symptoms are traditionally connected to bladder outlet obstruction (BOO) due to BPH. More than that DM is a causative factor for BPH and LUTS [14,15,16].

With respect to the incidence of DM in Greek population and its negative impact on the quality of life further investigation on the type of symptoms in each sex is necessary. The aim of this study is to investigate whether patients, both male and female, with DM have statistically significant difference in the presence of LUTS compared to general population. Furthermore, the type of symptoms, obstructive and voiding, were studied in association with other modifiable factors. The identification of symptomatology and risk factors for LUTS is important for improving preventive care strategies in general practice.

2. Material and methods

We conducted a cross-sectional comparative study with a case-control design. The study included patients with diabetes that visited the outpatient clinics in 424 GMHE from December 2016 until March 2017 and also people from general population. The work has been approved by the appropriate ethical committees related to the institution. Data acquisition concerning LUTS was using IPSS. Participants were initially informed about the aim of the research and reassured about their anonymity and their participation was also voluntary. Participants enrolled in the study after their verbal informed consent. In total 282 questionnaires were answered. However, 38 participants were not included on account of fulfilling the exclusion criteria. The inclusion criteria referred to patients from 20 to 79 years old, both male and female, with diabetes mellitus type I, type II, subclinical and gestational. In the study were not included those with a personal history of benign prostate hyperplasia, prostate cancer, those who underwent prostate operation and patients suffering from neurogenic bladder, urinary tract infection or psychiatric disease. More than that, all participants consuming 5-a reductase inhibitors, a-blockers, antimuscarinic drugs, antidepressants, diuretics and antihistaminic drugs were ruled out.

The participants completed a comprehensive questionnaire consisting of two parts. The first part consists of 7 questions about age, sex, anthropometric measures like weight (in kilograms) and height (in meters) used for BMI calculation (kg/m^2), educational level and number of parity. Medical history data was extracted as well. Respondents were questioned about the type of diabetes, HbA1c (%), personal control of diabetes, years of disease and diabetic complications (retinopathy, nephropathy, neuropathy). The type of treatment (insulin, diet or antidiabetic pills) and the presence of other comorbidities such as hypertension (blood pressure > 130/85 mmHg or the use of antihypertensive drugs), dyslipidemia (HDL< 40 mg/dL, triglycerides >150 mg/dL or the use or antilipidemic drugs) were asked too. The second part of the questionnaire included IPSS questionnaire which is a translated and validated tool for assessing LUTS in Greek population. The presence of LUTS was categorized as asymptomatic (IPSS score 0–7), moderate [8–19] and severe (20–35). Score equal or above 8 reflected the presence of clinically significant LUTS. Furthermore, IPSS-voiding and IPSS-storage scores were estimated. Presence of voiding symptoms was defined as the sum of IPSS questions on intermittency (Q3), weak stream (Q5), and straining (Q6). Storage symptoms were defined as a sum of questions on frequency (Q2), urgency (Q4), and nocturia (Q7). BMI was also calculated.

SPSS version 24.0 was used for statistical analysis. Except for descriptives (mean ± SD, %), normality test was used for selecting parametric and non-parametric variables and their respective analysis. Binary logistic regression analysis was performed with the presence of moderate-severe LUTS as dependent variable and DM and other confounding variables of interest as covariates to identify independent determinants of LUTS. Analysis was performed for diabetics and non-diabetic group and each sex separately. IPSS-

Table 1
General characteristics of the study population.

		Number (N)	%
Sex	Male	137	56,1
	Female	107	43,9
Age	20–39	23	9,4
	40–59	123	50,4
	>=60	98	40,2
Nationality	Greek	240	98,4
	Other	4	1,6
hypertension	yes	94	38,5
	no	150	61,5
dyslipidemia	yes	86	35,24
	no	158	64,75
Vit D deficiency		1	0,4
		Median	Interquartile Range
Number of children		2	1
BMI		27,19	6,68
Diabetic Patients			
		Number (N)	%
Type of diabetes	Type I	10	9,09
	Type II	96	87,27
	Gestational Diabetes	4	3,63
Treatment	diet	10	9,1
	1 oral antidiabetic drug	36	32,7
	2 oral antidiabetic drugs	36	32,7
	insulin	28	25,5
		Median	Interquartile Range
HbA1c (%)		6,9	1,35
Years with diabetes		8,5	11

Table 2
Prevalence of moderate/severe luts by presence of DM.

	P value	Odds ratio	95% C.I.
male	0,405	1,511	0,572–3,993
female	0,028	3,061	1,131–8,286

voiding and IPSS-storage symptoms' correlation with certain variables was further examined in particular subgroups. Statistical significance was set at 0.05 with a confidence interval (CI) of 95%. The reliability of the scale was estimated through calculation of Cronbach's alpha: 0.594. However, further analysis revealed that Q2, Q4, Q7 and Q3, Q5, Q6 have good internal consistency.

3. Results

The final sample included 244 respondents assigned into 2 groups, 110 patients with diabetes (45%) and 134 healthy individuals (55%). The demographics of the respondents are shown in Table 1. The prevalence of moderate/severe LUTS by gender was calculated. Moderate/severe LUTS were significantly more prevalent in women with diabetes with an odds ratio of 3,061 (95% confidence Interval = 1.131–8.286; Table 2) compared to women without diabetes, while there was no statistically significant difference between male groups. Binary logistic regression subgroup analysis with moderate/severe LUTS as dependent and plausible confounding factors (age group, BMI, hypertension, dyslipidemia, years with DM and reported HbA1c) as covariates revealed that only HbA1c levels correlated independently with the presence of moderate/severe LUTS (p = 0,024, OR:2,729, CI:1,144–6,509) in women with diabetes (Table 3). The aforementioned relation was further explored; Spearman's rank Order Correlation between HbA1c levels and IPSS-voiding and IPSS-storage score was obtained. There was small, positive correlation between HbA1c and IPSS-storage (r:0,176, p:0,22, n:50) and IPSS-voiding score (r: 0,109, p:0,45, n:50) neither statistically significant. Quality of life is also affected in women with diabetes mellitus (p: 0,02) compared with non-diabetic women especially in those with type II diabetes, whereas there was no difference in score between the male groups (p: 0,336).

4. Discussion

The prominent finding of our study is that diabetes mellitus is an independent risk factor for moderate/severe LUTS and QoL in women. In our study women with diabetes had a 3-fold increased risk for moderate/severe LUTS compared with women without diabetes. Moreover, in the same group, each increase per unit in HbA1c causes a 2,5-fold increased risk for moderate/severe LUTS. However, there was no discrimination in the impact of DM on voiding and storage symptoms.

Several factors associated with LUTS in previous studies, were taken into account as covariates in our analysis. Years with DM, dyslipidemia, hypertension, BMI as constituents of MetS and age group as a risk factor for LUTS (due to BPH in men) were not significantly associated with moderate/severe symptoms in multivariable analysis. This fact could be explained by the small sample size in our study. Additionally, the fact that DM was a risk factor for LUTS only in women could be explained by prostate hyperplasia that occurs in older men covering the effects of DM. Furthermore, years with diabetes were not a prevalent causative factor for LUTS, possible because of the presence of HbA1c as a measure of DM regulation.

Our results concerning female patients are in accordance with a recent review of Capon G et al. (2016) were LUTS were more common in the population with diabetes with an estimated prevalence between 37 and 70%, and are probably underestimated in routine practice. In the same study, symptoms were heterogeneous, both storage and voiding, and were frequently associated with other diabetic complications [17]. On the contrary a systematic review from K. S. Coyne et al. (2013) reports mixed results from studies evaluating the association between UUI and diabetes in women. Another review from James R. and Hijaz A. (2014) supports that aging and obesity are significantly associated with worsened LUTS in women with diabetes [18]. Regarding MetS and overactive bladder, Amarenco G et al. (2014) in their review supported the idea that storage symptoms are deteriorated by MetS components (dyslipidemia, hypertension, central obesity and DM), in contrast to our study results where there was no specific association [19]. Concerning male patients, several studies, particularly in Asian populations, did not find an association between male LUTS and MetS [3,20,21]. Other studies associate strongly the components of the MetS with moderate and severe LUTS [22] especially in older men [23].

Our study tries to investigate the effect of DM on LUTS in Greek population of both genders. Moreover, storage and voiding symptoms are analyzed in each subgroup. The different results between genders could be explained by structural differences in the lower urinary tract (presence of prostate, different length of urethra). However apart from peripheral neuropathy and diabetic cystopathy, DM has also been implicated in BPH in men [5,7,8]. The molecular effect DM on bladder is yet blur and further studies are necessary.

There are some limitations regarding study design, which should be taken into consideration. First of all, the sample size could be bigger and stratified including more patients and controls in each group. Recall bias is also plausible, since patients are asked to answer about their medical history and HbA1c values without further tests, especially prostate volume and uroflow. Additionally, a cross-sectional study design is not able to draw causal conclusions. Nevertheless, the present findings constitute the rationale for further research on the importance of diabetes' role in LUTS. Last

Table 3
Independent determinants of moderate/severe luts subgroup analysis (p values).

	male		female	
	Absence of DM	Presence of DM	Absence of DM	Presence of DM
Age group 20-39	0,824	0,117	0,558	0,549
Age group 40-59	0,918	0,078	0,498	0,709
Age group >60	0,717	0,039	0,975	0,459
bmi	0,185	0,937	0,112	0,090
Hypertension	0,179	0,451	0,639	0,150
Dyslipidemia	0,399	0,416	0,421	0,758
Years with DM	–	0,308	–	0,309
Reported HbA1c	–	0,312	–	,024

but not least, the wide range of LUTS includes symptoms that are not evaluated by IPSS questionnaire such as the type of UI, post-micturition symptoms and symptoms caused by other factors.

In our study, diabetes mellitus was associated with moderate/severe LUTS in women but not in men. In particular, increase in HbA1c levels, increase significantly the risk of moderate/severe LUTS in women with diabetes. However, there was no clarification about differences between storage and voiding symptoms. Thus, further investigation on the mechanisms of this association is essential.

Declaration of interest

The research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2018.11.009.

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