WOMEN'S SEXUAL HEALTH

Sexual Dysfunction in Women Treated for Type 1 Diabetes and the Impact of Coexisting Thyroid Disease

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ABSTRACT

Introduction: More sexual problems are reported among people treated for diabetes; however, this situation is less explored in women than in men.

Aim: To analyze the presence and causal links of female sexual dysfunction (FSD) among Czech women treated for type 1 diabetes.

Methods: 40 women completed a national version of the Female Sexual Function Index (FSFI), Female Sexual Distress Scale-revised (FSDS-R), and Beck's Depression Inventory—II (BDI-II). A metabolic and endocrine analysis was done using blood samples. Data were statistically analyzed using SPSS v.24 and the R environment.

Main Outcome Measures: Patient details (personal information, diabetes-related data, and sex history), sexual performance (the FSFI and FSDS-R scores), and level of depression (the BDI-II score) were measured.

Results: FSD was present in 58% of the participants (based on the FSFI score), and 38% women declared significant sexual distress (according to their FSDS-R score). Even though only 4 women fulfilled the criteria for depression, we observed a strong association between BDI-II and FSFI (for total FSFI score $P = .012$, $\rho = -0.394$) resp. FSDS-R scores ($P < .001$, $\rho = 0.552$). Although we were not able to establish a clear direct connection between FSD and metabolic control, BDI-II scores were closely correlated with glycosylated hemoglobin ($P = .009$, $\rho = 0.407$). The duration of diabetes (based on FSDS-R: $P = .046$) but neither age nor the presence of chronic diabetic microvascular complications was associated with a higher FSD occurrence. We also observed an association between FSD and the presence of autoimmune hypothyroidism, even when successfully treated (FSDS-R: $P = .009$; FSFI: $P = .067$).

Conclusion: FSD is more common in women with type 1 diabetes than in healthy women, and coexisting thyroid autoimmune disease seems to exacerbate FSD. Women suffering from type 1 diabetes, and particularly those with additional endocrinopathies, should be actively screened for FSD. **Stechova K, Mastikova L, Urbaniec K, et al. Sexual Dysfunction in Women Treated for Type 1 Diabetes and the Impact of Coexisting Thyroid Disease. Sex Med 2019;7:217—226.**

Key Words: Autoimmune Thyroid Disease; BDI-II; Diabetes; Female Sexual Dysfunction; FSFI; FSDS-R; Insulin; Insulin Pump; Life Quality; Sexarche

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INTRODUCTION

Sexuality is an important part of human life and is influenced by the interaction of many factors.[1] It is a cornerstone of partner relationships, and it impacts both the physical and mental health of a person.[2,3]

Sexual dysfunction is defined in different ways, but all definitions share a common thread: either a person's sexual life fails to meet their expectations or a disturbance in their normal sexual response cycle leads to lower or no sexual satisfaction. In women, the situation is much less clear than in men, because female sexual dysfunction (FSD) is the multidimensional disorder with the lack of universally accepted diagnostic procedures and with no direct negative impact on childbearing potential. According to the Diagnostic and Statistical Manual of Mental Disorders, 5th edition, there are 3 main categories of FSD: female sexual interest/arousal disorder, female orgasmic disorder, and genito-pelvic pain/penetration disorder.[4–8] Any serious illness, including diabetes, can potentially, whether directly or indirectly, contribute to sexual dysfunction development.

Diabetes mellitus (DM) is a chronic disease caused by an absolute or relative lack of insulin and subsequently elevated blood glucose levels. The resulting hyperglycemia, if not corrected, leads to malfunctions of different organs because of the development of chronic microvascular and macrovascular complications. There are 2 main types of DM. Type 1 diabetes (DM1; representing the second-most common form of diabetes) is an autoimmune disease characterized by T cell–mediated destruction of insulin-producing pancreatic beta cells. DM1 usually (but not exclusively) develops during childhood or young adulthood. In people suffering from DM1, other autoimmune diseases are present more frequently than in the non-DM1 population; the most frequent coexisting autoimmune disease is autoimmune thyroiditis. Type 2 DM (DM2), which is the most common type of diabetes, is characterized primarily by high insulin resistance (ie, a relative lack of insulin) with subsequent lowering of insulin production.[9]

The worldwide prevalence of DM in the adult population in 2014 was 8.5% (422 million people). In the Czech Republic, with ≈10 million citizens, almost 1 million people are treated for diabetes, mostly DM2. 56,000 patients are reported to have DM1, 28,000 of whom are women.[10–12]

The connection between diabetes and male sexual dysfunction, in the form of diabetes-induced erectile dysfunction, is well established.[13] However, there are fewer studies focusing on FSD among diabetic women, with even fewer successfully identifying factors that contribute to FSD.[3,14] According to more recent studies, it seems evident that the life prevalence of at least 1 type of sexual dysfunction is higher among diabetic women than that of the general population. However, these studies differ widely in the FSD prevalence data, which vary from 18–71% for DM1 women and even more for DM2 women (12–88%). It was calculated, in the only meta-analysis on this topic, that the odds ratio is 2.27 for FSD in DM1 patients and slightly higher (2.49) for DM2 women.[14,15] Regarding factors potentially contributing to FSD in diabetic women, the first to be logically listed are chronic diabetic microvascular changes that lead also to neuropathy, either peripheral or autonomic, which can affect an adequate response of female genitalia to sexual stimuli. The studies that represent follow-up of Diabetes Control and Complications Trial (DCCT), such as the Epidemiology of Interventions and Complications (EDIC) and urologic assessment of this study, have first provided clear evidence that there is a direct link between sexual dysfunction and autonomic neuropathy (particularly cardiovascular autonomic neuropathy) in women treated for DM1.[16] However, less-obvious factors can contribute to the development of FSD in diabetic patients as well, such as psychiatric problems related to a chronic, lifelong disease.[15]

The purpose of our study was to map FSD among Czech women suffering from DM1. We tried to determine the causes, risk factors, and conditions that were related to sexual dysfunction in these diabetic women who were treated with insulin and had a diabetes diagnosis that often predated their sexarche.

MATERIAL AND METHODS

Study Population

We assessed women suffering from DM1 who were being treated in the Diabetes Center of the Department of Internal Medicine at the University Hospital Motol, Prague, the Czech Republic. This study was approved by the University Hospital Motol Ethics Committee, and all data were analyzed anonymously. Participants were asked to give written consent before participation. Inclusion criteria were DM1 and an active sexual life. The exclusion criterium was the presence of an active/untreated psychiatric disease. 40 women with DM1 met the inclusion criteria and fully participated in the study; all women were treated using an intensified insulin regimen. Insulin administration via continuous subcutaneous insulin infusion (CSII, insulin pump) was used by 25 of 40 women, whereas 15 of 40 patients were treated using multiple daily insulin injections. The mean duration of diabetes within the study cohort was 14 years. Table 1 provides a complete characterization of the study participants.

Study Design

Participants were interviewed, answered 4 different questionnaires, and gave blood samples. The first questionnaire (which was prepared specifically for this research) covered personal information and was subdivided into 4 parts: (i) general information (including diabetes-related data), (ii) education and family status, (iii) obstetric/gynecologic history, and (iv) sexual activity anamnesis. Details regarding questions in this questionnaire are presented in Supplementary Table 1.

Table 1A. Study group characteristics: Numeric variables

Normal (laboratory) values (range)	Median	IQR	Min	Max
Age (y)	32	24–41	19	52
DM duration (y)	14	9–17	1	32
HbA1c (20–42 mmol/L)	68.5	57.3–79	37.0	112.0
HbA1c (4–6% DCCT)	8.4	7.4–9.4	5.5	12.4
BMI (20–25)	24.4	21.4–27.4	18.0	33.5
TSH (0.35–4.8 mIU/L)	2.1	1.2–3.1	0.37	4.5
fT4 (11.5–22.7 pmol/L)	14.3	13.2–15.3	11.8	19.3

BMI = body mass index; DCCT = Diabetes Control and Complication Trial; DM = diabetes mellitus; HbA1c = glycosylated hemoglobin; IQR = interquartile range; Max = maximum; Min = minimum; TSH = thyroid gland–stimulating hormone; fT4 = free thyroxine.
FSFI total score = 24.7; FSFI median for each Subdomain: Desire = 3.6; Arousal = 4.1; Lubrication = 4.8; Orgasmus = 4.2; Satisfaction = 3.6; Pain = 4.8; FSDS = 7.5.

The second questionnaire assessed the level of depression. We used the Czech version of the Beck's Depression Inventory–II (BDI-II) scale.[17–21] This questionnaire consisted of 21 questions that covered symptoms of depression, with each symptom being graded for severity. The minimal score was 0, and the maximum was 63. The cutoff for depression, on the BDI-II, varies among countries; we used a value of 17 (ie, scores <17 were considered to show no depression), which showed the best sensitivity and specificity for the Czech population.[19–21]

Table 1B. Study group characteristics: Categorical (nominal) variables

Chronic diabetic microvascular complications	
Diabetic retinopathy	20% (n = 8)
Diabetic sensory motor neuropathy	25% (n = 10)
Diabetic autonomic neuropathy	39% (n = 11)
Diabetic nephropathy	15% (n = 6)
Hypertension	25% (n = 10)
Education	
Elementary school	2.5% (n = 1)
Secondary school	70% (n = 28)
University	27.5% (n = 11)
Employment and disability pension	
Full time	67.5% (n = 27)
Unemployed and no disability pension	20% (n = 8)
At least partial disability pension	12.5% (n = 5)
Marital status	
Single	62.5% (n = 25)
Married	20% (n = 8)
Divorced	15% (n = 6)
Widow	2.5% (n = 1)
Living status	
Alone	28% (n = 11)
In household with a partner	48% (n = 19)
In household with parent(s)	24% (n = 10)
Smoking	
Never	75% (n = 30)
Smoker	20% (n = 8)
Ex-smoker	5% (n = 2)

The third and fourth questionnaires evaluated sexual function. We used the Czech version of 2 internationally validated questionnaires: (i) the Female Sexual Distress Scale-Revised (FSDS-R), and (ii) the Female Sexual Function Index (FSFI).[22–24] The original FSDS scale was created to calculate distress, which is one of the most important symptoms of FSD.[23] We used the revised version (FSDS-R), which consisted of 13 questions, where the seriousness of distress is measured as a frequency. The minimum score was 0, the maximum was 52, and the cutoff score was ≥11.[25,26] The FSFI had 19 questions, which assessed 6 features of the female sexual response: desire, arousal, lubrication, orgasm, satisfaction, and pain. The answers were assessed according to how often each feature occurred. The minimal score was 2, the maximum was 36, and the cutoff was ≤26.5.[22,27,28]

Each blood sample was analyzed in a biochemistry laboratory according to standard laboratory protocols. We analyzed the level of glycosylated hemoglobin (HbA1c; measured by using capillary electrophoresis), thyroid gland–stimulating hormone (TSH), and free fraction of thyroxine (fT4; both parameters measured by chemiluminescence immunoassay).

Finally, we compared the information given by women with their previous hospital records (ie, with a patient's latest results from regular screenings for chronic microvascular diabetic complications, eg, tests for cardiac autonomic neuropathy, podiatric examinations, ophthalmologic examinations, and microalbuminuria). Briefly, for cardiac autonomic neuropathy diagnosis, a complete Ewing's test battery was used.[29] Podiatric examination was done according to the standardized protocol and included examination of vibration, tactile, and thermic sensation, as well as photoplethysmography and measurement of ankle and toe blood pressure to express ankle/brachial and toe/brachial indexes.[30] Ophthalmologic examination included examination of the posterior segment conducted by an ophthalmologist specializing in retina, with the posterior pole being examined by slit lamp biomicroscopy and the peripheral retina being examined by indirect ophthalmoscopy. During each visit color photographs of the fundus were taken, and optical coherence tomography was provided.[31] Microalbuminuria was measured in the first morning urine sample.[32] In some cases, additional information was available, such as echocardiography and Doppler ultrasound scans of carotid arteries (ie, assessment of macrovascular complications).

Data Analysis

We compiled all the above-mentioned data in 1 data file represented by 1 data table. Data were processed by using SPSS software v.24 (SPSS Inc, Chicago, IL, USA) and by using the R environment.[33] The first step in the statistical analysis was checking the data for normality. The significance threshold was set at $P = .05$. Data indicating interesting trends are also

displayed in the article. Our study did not contain a control group because data from a recent nationwide study (focusing on, among other things, the sexual life of healthy Czech women of comparable age) were available.[34]

The main aim of our study was to map FSD by using the FSFI and FSDS-R score. For FSFI we searched for differences in the total score as well as in FSFI subcategory scores.

Several parameters were used as grouping variables (details of the grouping variables are presented in Supplementary Table 2). We tested differences between the FSFI and FSDS-R score of patients in defined subgroups. Additionally, we tested whether score distribution differed between the 2 questionnaires. For comparison of the 2 groups, the Mann-Whitney U test was used.

The second part of the analysis was carried out on the same patient subgroups. However, this time we checked whether the ratios of patients who fell into the cutoff category differed between subgroups. This testing was carried out using the 1-sided χ^2 proportion test.

The third part analyzed the correlation between several pairs of variables. This testing was carried out using the 1-sided Spearman's correlation test.

RESULTS

Diabetes-Related and General Clinical Descriptive Data

Blood levels of HbA1c (a parameter reflecting diabetes compensation) varied from 37−112 mmol/mol, mean 69.9 mmol/mol (DCCT 5.5−12.4%, mean = 8.5%). According to national standards,[28] adult DM1 patients should have HbA1c values <45 mmol/mol (6.3% DCCT), and <60 mmol/mol (7.6% DCCT) if additional comorbidities exist. The stricter criterion was met by only 7.5% of the study population (3 women). One-quarter of the study participants (n = 10; 25%) met the more moderate (<60 mmol/mol) HbA1c criterion.

The presence of chronic diabetic complications was as follows: without chronic microvascular diabetic complications, 21 of 40; 1 diabetic complication, 8 of 40; and multiple chronic microvascular diabetic complications, 11 of 40 (ie, ≥2 complications). Macrovascular complications were not reported. 10 patients had therapy-controlled arterial hypertension, and 8 of 40 were on dyslipidemia therapy. Details are presented in Table 1.

Gynecologic-Obstetric Anamnesis

Most women (n = 36) visited their gynecologist regularly (at least once per year). Gynecologic anamneses revealed that 12 women had irregular menstrual cycles, 13 women reported higher glycemia during menstruation, and 3 women were postmenopausal. Recurrent gynecologic infections were reported by 16 of 40 women with a mean of 4 infections per year, whereas 8 women suffered from recurrent lower urinary tract infections with a mean of 2 infections per year.

Less than one-half of the women had delivered ≥1 child (19 women were mothers). 4 women reported spontaneous abortion(s), and 8 women had undergone ≥1 artificial (induced) abortion. In our cohort, 29 women (72.5%) reported that they always use some type of contraception. These women had, unsurprisingly, significantly fewer artificial abortions than women who admitted occasional sexual intercourse with no contraception, but there were no further specific characteristics. 50% of the women who had sexual intercourse with their partner regularly use hormonal contraception (All women reported having male partners, so this issue was relevant).

Data Related To Sexual Function—General Description

31 women had a permanent sexual partner. 27 women (67.5%) reported that they had sexual intercourse only occasionally (less than monthly). The rest of the women reported that they had sexual intercourse at least twice a week. The mean number of sexual partners, to date, was 6, median 4 partners (range 1−40 partners). 10 women (25%) reported that they had never masturbated.

Among CSII users (n = 25), only 3 women reported never detaching their insulin pump during sexual intercourse. An insulin pump was considered by 22 of 25 CSII users to be intrusive and disruptive during sexual intercourse, especially with respect to the partner. Only 8 women (20%) reported that they had had the opportunity to discuss their sexual life and associated problems with their diabetologist. Sexual function was assessed using both the FSDS-R and FSFI questionnaires (Table 1).

The mean FSFI total score was 21.3. and the decrease was almost equally distributed across all studied domains. The prevalence of FSD in the study group, according to this scale, was 58% (23 of 40 women). The FSDS-R mean score was 10.9, and, based on the FSDS-R score, the presence of a significant sexual distress was 38% (15 of 40 women). Scores on both questionnaires were significantly correlated ($\rho = -0.524$, $P = .001$; Table 2).

Factors Associated With Sexual Function Data

First, we wanted to know whether there was any difference between women who suffered from diabetes before they started their sexual life (26 of 40) and those who had had their first sexual intercourse prior to developing diabetes (14 of 40). We did not find any difference between these groups either in the FSDS-R ($P = .941$) or in the FSFI scales ($P = .294$).

Second, we looked at chronic diabetic complications and the possible impact on FSD. We failed to establish any connection between FSD and the presence of diabetic complications ($P > .1$).

Third, we investigated glycemic control; we used HbA1c as the parameter. An initial threshold level for HbA1c of 60 mmol/mol (DCCT = 7.6%) was set as a reference point. 13 women had

Table 2. FSDS-R and FSFI scores—both scoring systems correlations

	FSDS-R score	FSD presence (based on FSDS-R score)
FSFI total score		
Correlation coefficient	−0.524	−0.427
Sig. (2-tailed)	0.001	0.006
N	40	40
FSD presence (based on FSFI total score)		
Correlation Coefficient	0.652	0.666
Sig. (2-tailed)	0.000	0.000
N	40	40

CI = confidence interval; FSFI = Female Sexual Function Index; FSDS-R = Female Sexual Distress Scale Revised; Sig. = significance.

HbA1c $\leq$ 60 mmol/mol (DCCT $\leq$ 7.6%). At this level, there was no significant difference in the number of women with FSD. Then we applied 70 mmol/mol and 80 mmol/mol as discriminating thresholds (DCCT = 8.6 and 9.5%, respectively). At 70 mmol/mol, there was no significant difference in the number of women with FSD (nor was any trend present). There were 9 women with a HbA1c value > 80 mmol/mol. These women had worse scores on both the FSFI ($P = .093$) and FSDS-R ($P = .107$) questionnaires than those with better metabolic control. However, this finding was not statistically significant, except for the subdomain of "lubrication" on the FSFI ($P = .05$).

Fourth, we looked at the connection between FSD and the duration of diabetes. The initial threshold value was set at 10 years (13 of 40 women had diabetes for $\leq$10 years). No statistically significant results were found in this group. When the threshold was changed to 15 years, 25 of 40 women had diabetes for $\leq$15 years; women (15/40) suffering from DM >15 years had a significantly higher presence of FSD based on the FSDS-R ($P = .046$). However, this was not confirmed by results based on FSFI scores ($P = .233$).

To check whether the duration of diabetes was confounded by age, we tested the association between FSD and age. Only the subdomain of "desire" on FSFI scores showed a dependency between scores and higher age (FSFI: $P < .001$, $\rho = -0.530$). These findings show that the influence of diabetes duration on FSD was an independent factor.

The mean BDI-II scale score was 9 points, and only 4 of 40 women fulfilled the criteria for depression. Despite this fact we observed a strong association between BDI-II scores and FSFI (for the total FSFI score $P = .012$, $\rho = -0.394$), as well as FSDS-R scores ($P < .001$, $\rho = 0.552$), Figure 1. The strongest negative impact was observed in the subdomain of "arousal" ($P = .006$, $\rho = -0.429$). In the FSFI subdomains, only the "pain" subdomain showed no significant correlation. The BDI-II score was also closely correlated with HbA1c levels ($P = .009$, $\rho = 0.407$; Supplementary Figure 1).

11 women reported that diabetes has a significant negative impact on their sexual life. These women had no additional special characteristics (ie, significant correlations with other studied factors).

Finally, we focused on the presence of other autoimmune diseases. 22 of 40 women were treated for hypothyroidism (due to autoimmune thyroiditis). There were more women with FSD among the women with thyropathy, based on the FSFI ($P = .067$) and FSDS-R ($P = .009$) (Figure 2). Regarding FSFI subdomains, "desire" and "satisfaction" were significantly affected in women treated for hypothyroidism ($P = .004$ and $P = .045$, respectively). There was also a strong correlation between the intensity of sexual distress, based on the FSDS-R score and the presence of treated hypothyroidism ($P = .008$ and

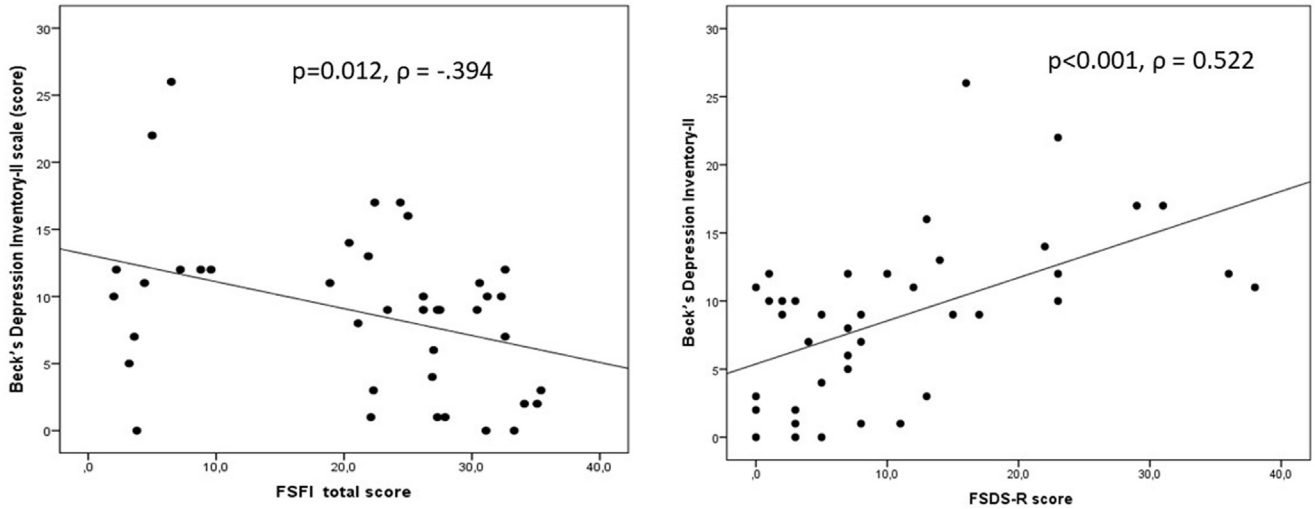

Figure 1. The association between BDI-II scores and FSFI as well as FSDS-R scores (lower BDI-II depression score is connected to higher FSFI total score and to lower FSDS-R score). BDI-II = Beck's Depression Inventory-II scale; FSFI = Female Sexual Function Index; FSDS-R = Female Sexual Distress Scale Revised.

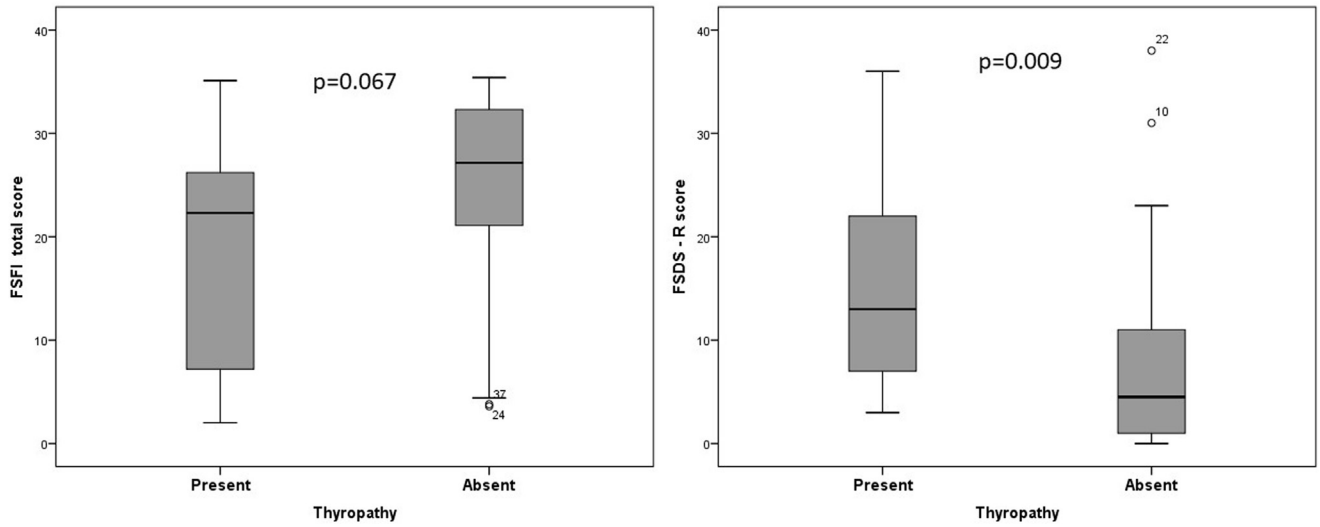

Figure 2. Thyropathy and FSD (women with thyropathy had lower FSFI total score and higher FSDS-R score than women without this comorbidity). FSD = female sexual dysfunction; FSFI = Female Sexual Function Index; FSDS-R = Female Sexual Distress Scale Revised.

$\rho = -0.419$, respectively), but no associations with fT4 or TSH values were observed.

DISCUSSION

In this study, we focused on FSD in DM1 patients. We found that 58% of women had FSFI scores lower than its cutoff, and, according to FSDS-R scores, 38% of study participants presented significant sexual distress. Data from the last nationwide survey conducted in 2011 described, among healthy Czech women, an FSD prevalence of 20% and incidence of 10.5% (ie, problems reported at the time of investigation).[35] Our data clearly indicate that the situation regarding sexual problems is much worse in women with DM1 than among the population of healthy Czech women. As has been already stated in the Introduction, other studies of DM1 women of similar age reported a prevalence of FSD in the wide range of 18–71%.[15,36–39] The total FSFI score in our study was lower than in the majority of other studies with diabetic women of similar age.[37,40,41] It is difficult to explain this discrepancy, because we had no access to concrete data from other studies, but we do not consider our study group to be unique. Our data also showed that impairment of sexual function was present in all FSFI domains studied, with the most pronounced negative effect in the subdomains of arousal, orgasm, and satisfaction. The pathophysiology of FSD in diabetic women is certainly very complex, with the contribution of biologic, as well as psychological, factors. There are many theories supported by animal model observations, but there is a less evidence from human studies.[42] The various stages of the sex cycle are modulated by neural pathways and hormones. For normal sexual function, intact central nerve pathways (in cortex, hypothalamus, and reticular formation), peripheral nerves (involving autonomic, as well as somatic, nerves), and intact vascular systems are required.[42] The first offering explanation for higher FSD occurrence among women treated for DM, as has already been mentioned, seems to be the impact of chronic diabetic complications (neuropathy in particular). Many authors have focused on this relationship, but less evidence was presented.[16,38,41] We also found little evidence for this causal relationship. There are 2 possible explanations. First, neither neuropathies of peripheral somatic nerves nor autonomic neuropathy are homogeneous entities. Second, there are different degrees of neuropathy severity. For example, the manifestation of cardiac autonomic neuropathy, the most common autonomic neuropathy, has 3 degrees of severity.[16,38,41] Finding a clear relationship between neuropathy and FSD requires a large group of neurologically well classified patients. Therefore, it is not surprising that the EDIC study of 580 DM1 women found a link between FSD and cardiac neuropathy.[16] Moreover, nowadays central diabetic neuropathy is increasingly being discussed,[43] which further complicates understanding the impact of diabetic neuropathy on the FSD pathophysiology. On the other hand, in recent years DM1 treatment has dramatically changed (introduction of insulin analogues, the expansion of insulin pump therapy, and continuous glucose monitoring). Patients can thus achieve better diabetes control with less negative impact to their general health status. Thus, newly diagnosed patients cannot be compared with patients diagnosed for many years ago (eg, patients in EDIC study). Even though these patients are now stabilized properly, their metabolic memory was negatively influenced during first years of diabetes therapy, when modern therapeutic modalities have not been available yet. This claim is supported by our evaluation of the effect of diabetes duration on FSDS-R and FSFI scores. We showed that, in women who had had diabetes $\geq$15 years, there was a significantly higher presence of FSD, mainly based on sexual distress, which could not be fully explained by their age.

Regarding modern treatment modalities, it is necessary to stress that insulin pumps, which represent the most modern and the most flexible way of implementing an intensified insulin

regimen, were perceived rather negatively in relation to sexual activities among women, and further research needs to be done to determine what effect pump disconnection (ie, the length and frequency of insulin infusion interruption) during sex has on metabolic compensation.

Another probable risk factor for FSD development seems to be increasing age, but none could prove it as an independent negative predictive factor of FSD. On the other hand, a trend can be found in which lower sexual function scores in study groups are usually associated with increasing age of the study participants.[14] We confirmed this observation, but only in the FSFI subdomain of "desire." This is not surprising, because hormonal changes are connected to increasing age.

In our group, most women developed diabetes before they started their sexual life. We observed that women who developed diabetes after sexarche seemed to have similar levels of sexual distress. Our hypothesis, which was that the presence of diabetes may be a barrier to establishing intimate relationships, was not confirmed; however, there are no studies to compare with it.

The influence of depression (mental health status) on FSD is a controversial topic that needs further study.[41,44] Some authors have reported increased FSD in diabetic women suffering from depression.[36,38,44] The presence of depression in our group was surprisingly low, even lower than the depression rate in the general Czech population,[34] but a strong association between the BDI-II scale score and FSD, according to both questionnaires, was observed. Some researchers have suggested that depression is a major determinant of FSD in diabetic women,[37,40] and, according to our results, this may even be true for subclinical depression. An important finding may be the strong association between HbA1c and BDI-II scale scores. We found a partial connection between poor diabetes compensation and FSD (the worse score was in the "lubrication" subdomain in women with HbA1c >80 mmol/mol). The same observation was made in other studies as well.[40,45] It is logical that metabolic control would be closely related to well-being and could influence performance status, the incidence of urinary and other infections, as well as the beginning and course of diabetic complications. However, the size of our study group makes establishing discriminating HbA1c threshold values for each tested subdomain problematic.

It is well known that patients with 1 autoimmune disease are at greater risk for development of other autoimmune disease(s). The most common other autoimmune disease in diabetes patients is autoimmune thyroiditis, leading to thyropathy. There are several studies examining fertility in women with hypothyroidism (ie, the impact of hypothyroidism on ovarian and menstruation cycles); however, there are few studies looking at sexual dysfunction in these women.[46] In our study, we showed that women who suffered from diabetes and autoimmune thyroiditis (leading specifically to hypothyroidism) had a significantly higher occurrence of FSD with respect to sexual distress compared with diabetic women without thyropathy. Furthermore, we analyzed each FSD domain, and, based on the FSFI, associations between sexual desire, satisfaction, and distress were confirmed. This relationship needs further exploration. Some authors measured TSH and fT4 levels.[47] Veronelli et al[45] in 2009 studied FSD in diabetic, obese, and hypothyroid women in comparison to control subjects. Their results agree with our findings that, in women suffering from thyroid disease, lower arousal and desire was observed. It is necessary to stress that all women in our study had normal free thyroxine and TSH levels at the time of their FSD assessment. This suggests that thyroid hormone substitution was effective, and the women were clinically euthyroid. In an interesting study of sexual function and depressive symptoms in women with thyroid autoimmunity and subclinical hypothyroidism, it was found that both conditions (particularly if they occur together) may negatively affect female sexual function and psychological well-being. Authors suggested that it is possible that patients with autoimmune Hashimoto's thyroiditis are more prone to the development of atherosclerosis, leading to subsequent tissue impairment.[48] Moreover, diabetes itself leads to accelerated atherosclerosis and subclinical inflammation. So, it seems likely that, in the presence of both diseases, the atherosclerotic process may be more potentiated.

First of the weaknesses of our study is the size of the study group, but it is necessary to keep in mind that such research is very sensitive. Furthermore, Czech women are generally unwilling to describe their intimate life, even anonymously. Another weakness of our study is that the FSD presence was not objectivized. There are objective validation methods for FSD (for instance clitoral color-flow Doppler ultrasound scanning, with assessment of the pulsatility index),[49] but the doctors, who are the most in contact with these patients, are diabetologists, and these methods are not applicable in their praxis. For screening purposes, validated questionnaires are well suited, even if all the questionnaires must be viewed as being potentially subjective.

We also did not study the impact of other psychological problems that are more frequent among DM1 patients (such as anxiety or subclinical forms of eating disorders), and it would be necessary to concentrate on them in future studies. It has been proposed that FSD is related to certain types of personality and coping strategies.[50,51] Thus, it would be interesting to study this relationship in women treated for DM1 as well. We plan to follow up patients from this study in the future and to monitor their cardiovascular health. In men it was well established that erectile dysfunction is an independent risk factor and an important predictor for the development of major cardiovascular diseases,[52] but the relation between sexual and cardiovascular health in women is not as well defined as in men.[49] Generally, we suppose that sexual health can serve as a marker of general health status, even in patients treated for a lifelong disease such as DM1.

CONCLUSIONS

We found several disturbing outcomes in our study. The first was that the DM1 women had much higher rates of FSD than healthy women of comparable age. Coexisting thyroid

autoimmune disease seems to exacerbate FSD. Women treated for DM1, particularly those with additional endocrinopathies, should be actively screened for FSD by their diabetologists, who should pay more attention to this topic. In case of suspicion of FSD presence, they should refer a patient to a specialist on FSD. Women suffering from diabetes (all types of diabetes), based on the nature of the disease, have a quality of life (QoL) that is often lower than the QoL of healthy persons,[53] so it is important to look at all the ways in which their QoL can be improved, and diabetologists can play an important role in this regard.

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REFERENCES

1. World Health Organization. Sexual and reproductive health, working definitions; Available at: http://www.who.int/reproductivehealth/topics/sexual_health/sh_definitions/en/. Accessed June 13, 2018.
2. Morokqff PJ, Gillilland R. Stress, sexual functioning, and marital satisfaction. **J Sex Res 1993;30:43-53.**
3. Monga M, Alexandrescu B, Katz SE, et al. Impact of infertility on quality of life, marital adjustment, and sexual function. **Urology 2004;63:126-130.**
4. Chen CH, Lin YC, Chiu LH, et al. Female sexual dysfunction: Definition, classification, and debates. **Taiwan J Obstet Gynecol 2013;52:3-7.**
5. Rosen RC, Barsky JL. Normal sexual response in women. **Obstet Gynecol Clin N Am 2006;33:515-526.**
6. Basson R, Berman J, Burnette A, et al. Report of the international consensus development conference on female sexual dysfunction: Definitions and classifications. **J Urology 2000;163:888-893.**
7. World Health Organization. The ICD-10 classification of mental and behavioral disorders. Available at: http://apps.who.int/classifications/icd10/browse/2016/en#/F52.0. Accessed July 17, 2018.
8. IsHak WW, Tobia G. DSM-5 changes in diagnostic criteria of sexual dysfunctions. Reprod Sys Sexual Disorder, https://doi.org/10.4172/2161-038X.1000122.
9. Holt RIG, Cockram C, Flyvbjerg A, et al. Textbook of diabetes. 5th ed. Hoboken, NJ: Wiley-Blackwell; 2017.
10. American Diabetes Association. Diagnosis and Classification of Diabetes Mellitus. **Diabetes Care 2004;27(Suppl. 1):S5-S10.**
11. World Health Organization. Diabetes, fact sheet; Available at: http://www.who.int/mediacentre/factsheets/fs312/en/. Accessed June 13, 2018.
12. Institute of health information and statistics of the Czech Republic. Care of diabetics; Available at: http://www.uzis.cz/en/catalogue/care-diabetics. Accessed July 17, 2018.
13. Malavige LS, Levy JC. Erectile dysfunction in diabetes mellitus. **J Sex Med 2009;6:1232-1247.**
14. Pontiroli AE, Cortelazzi D, Morabito A. Female sexual dysfunction and diabetes: A systematic review and meta-analysis. **J Sex Med 2013;10:1044-1051.**
15. Maseroli E, Scavello I, Vignozzi L. Cardiometabolic risk and female sexuality-Part I. Risk factors and potential pathophysiological underpinnings for female vasculogenic sexual dysfunction syndromes. **Sex Med Rev 2018;6:508-524.**
16. Hotaling JM, Sarma AV, Patel DP, et al. Cardiovascular autonomic neuropathy, sexual dysfunction, and urinary incontinence in women with type 1 diabetes. **Diabetes Care 2016;39:1587-1593.**
17. Beck AT, Ward CH, Mendelson M, et al. An inventory for measuring depression. **Arch Gen Psychiatr 1961;4:561-571.**
18. Beck AT, Steer RA, Ball R, et al. Comparison of Beck Depression Inventories —IA and — II in psychiatric outpatients. **J Pers Assess 1996;67:588-597.**
19. Preiss M, Vacir K. BDI-II. Beckova sebeposuzovaci skala pro dospele. Brno: Psychodiagnostika; 1999 [in Czech].
20. Ptacek R, Raboch J, Vnukova M, et al. Beckova skala deprese BDI II—standardizace a vyuziti v praxi. **Ces a Slov Psychiatr 2016;112:270-274 [in Czech].**

21. Ociskova M, Prasko J, Kupka M, et al. Psychometric evaluation of the Czech Beck Depression Inventory-II in a sample of depressed patients and healthy controls. **Neuroendrocrinol Lett 2017;38:98-106.**
22. Rosen R, Brown C, Heiman J, et al. The Female Sexual Function Index (FSFI): A multidimensional self-report instrument for the assessment of female sexual function. **J Sex Marital Ther 2000;26:191-208.**
23. Derogatis LR, Rosen R, Leiblum S, et al. The Female Sexual Distress Scale (FSDS): Initial validation of a standardized scale for assessment of sexually related personal distress in women. **J Sex Marital Ther 2002;28:317-330.**
24. ter Kuile MM, Brauer M, Laan E. The Female Sexual Function Index (FSFI) and the Female Sexual Distress Scale (FSDS): Psychometric properties within a Dutch population. **J Sex Marital Ther 2006;32:289-304.**
25. Derogatis LR, Clayton A, Lewis-D'Agostino D, et al. Validation of the Female Sexual Distress Scale-Revised for assessing distress in women with hypoactive sexual desire disorder. **J Sex Med 2008;5:357-364.**
26. Aydin S, Onarak OI, Topalan K, et al. Development and validation of Turkish version of the Female Sexual Distress Scale-Revised. **Sex Med-UK 2016;4:e43-e50.**
27. Wiegel M, Meston C, Rosen R. The Female Sexual Function Index (FSFI): Cross-validation and development of clinical cutoff scores. **J Sex Marital Ther 2005;31:1-20.**
28. Meston CM. Validation of the Female Sexual Function Index (FSFI) in women with female orgasmic disorder and in women with hypoactive sexual desire disorder. **J Sex Marital Ther 2003;29:39-46.**
29. Ewing DJ, Martyn CN, Young RJ, et al. The value of cardiovascular autonomic function tests: 10 Years' experience in diabetes. **Diabetes Care 1985;8:491-498.**
30. Czech Diabetological Society. Recommended procedure for prevention, diagnosis and therapy of the diabetic food syndrome. Available at: http://www.diab.cz/dokumenty/standard_diab_noha.pdf [in Czech]. Accessed January 2019.
31. Czech Diabetological Society. Recommendation for management of the diabetic retinopathy; Available at: http://www.diab.cz/dokumenty/standard_retinopatie.pdf [in Czech]. Accessed January 2019.
32. Czech Diabetological Society. Recommended procedures for diabetic kidney disorder. Available at: http://www.diab.cz/dokumenty/standard_dmev_ledviny.pdf [in Czech]. Accessed January 2019.
33. R Development Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing. Available at: http://www.R-project.org; Accessed June 2018.
34. Holla K, Jezek S, Weiss P, et al. The prevalence and risk factors of sexual dysfunction amongst Czech women. **Int J Sex Health 2012;24:218-225.**
35. Skrha J, Sumnik Z, Pelikanova T, et al. Recommendation for management of the type 1 diabetes mellitus. **Diabetes Metab Endocrinol Nutr 2016;19:156-159 [in Czech].**
36. Dimitropoulos K, Bargiota A, Mouzas O, et al. Sexual functioning and distress among premenopausal women with uncomplicated type 1 diabetes. **J Sex Med 2012:1374-1381.**
37. Nowosielski K, Drosdzol A, Sipinski A, et al. Diabetes mellitus and sexuality—Does it really matter? **J Sex Med 2010;7:723-735.**
38. Enzlin P, Mathieu C, Van Der Bruel A, et al. Prevalence and predictors of sexual dysfunction in patients with type 1 diabetes mellitus. **Diabetes Care 2003;26:409-414.**
39. Enzlin P, Rosen R, Wiegel M, et al. Sexual dysfunction in women with type 1 diabetes: Long-term findings from the DCCT/EDIC study cohort. **Diabetes Care 2009;32:780-785.**
40. Salonia A, Munarriz RM, Naspro R, et al. Women's sexual dysfunction: A pathophysiological review. **BJU Int 2004; 93:1156-1164.**
41. Tagliabue M, Gottero C, Zuffranieri M, et al. Sexual function in women with type 1 diabetes matched with a control group: Depressive and psychosocial aspects. **J Sex Med 2011; 8:1694-1700.**
42. Marson L, Giamberardino MA, Costantini R, et al. Animal models for the study of female sexual dysfunction. **Sex Med Rev 2013;1:108-122.**
43. Malone JI. Diabetic central neuropathy: CNS damage related to hyperglycemia. **Diabetes 2016;65:355-357.**
44. Leedom L, Feldman M, Warner P, et al. Symptoms of sexual dysfunction and depression in diabetic women. **J Diabetes Complicat 1991;5:38-41.**
45. Veronelli A, Mauri C, Zecchini B, et al. Sexual dysfunction is frequent in premenopausal women with diabetes, obesity, and hypothyroidism, and correlates with markers of increased cardiovascular risk. A preliminary report. **J Sex Med 2009; 6:1561-1568.**
46. Bhasin S, Enzlin P, Coviello A, et al. Sexual dysfunction in men and women with endocrine disorders. **Lancet 2007; 369:597-611.**
47. Cortelazzi D, Marconi A, Guazzi M, et al. Sexual dysfunction in pre-menopausal diabetic women: clinical, metabolic, psychological, cardiovascular, and neurophysiologic correlates. **Acta Diabetol 2013;50:911-917.**
48. Krysiak R, Drosdzol-Cop A, Skrzypulec-Plinta V, et al. Sexual function and depressive symptoms in young women with thyroid autoimmunity and subclinical hypothyroidism. **Clin Endocrinol (Oxf) 2016;84:925-931.**
49. Maseroli E, Fanni E, Cipriani S, et al. Cardiometabolic risk and female sexuality: Focus on clitoral vascular resistance. **J Sex Med 2016;13:1651-1661.**
50. Ciocca G, Carosa E, Stornelli M, et al. Post-traumatic stress disorder, coping strategies and type 2 diabetes: psychometric assessment after L'Aquila earthquake. **Acta Diabetol 2015; 52:513-521.**
51. Crisp CC, Vaccaro CM, Pancholy A, et al. Is female sexual dysfunction related to personality and coping? An exploratory study. **Sex Med 2013;1:69-75.**

52. Jannini EA. SM = SM: The interface of systems medicine and sexual medicine for facing non-communicable diseases in a gender-dependent manner. **Sex Med Rev 2017;5:349-364.**

53. Jacobson AM, Braffett BH, Cleary PA, et al. The long-term effects of type 1 diabetes treatment and complications on health-related quality of life: A 23-year follow-up of the Diabetes Control and Complications/Epidemiology of Diabetes Interventions and Complications cohort. **Diabetes Care 2013; 36:3131-3138.**

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.esxm.2019.03.001.