



# Sexual functioning and depressive symptoms in women with various types of prediabetes — a pilot study

Funkcjonowanie seksualne i objawy depresyjne u kobiet z różnymi typami stanu przedcukrzycowego — badanie pilotażowe

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## Abstract

**Introduction:** No previous study has investigated sexual functioning in prediabetic women. This study was aimed at investigating sexual function in young women with various types of prediabetes.

**Material and methods:** The study included four groups of women: women with isolated impaired fasting glucose (Group A; n = 19), isolated impaired glucose tolerance (Group B; n = 18), presence of both impaired fasting glucose and impaired glucose tolerance (Group C; n = 18), as well as matched healthy controls (Group D; n = 19). All participants completed questionnaires evaluating sexual function (Female Sexual Function Index — FSFI) and the presence and severity of depressive symptoms (Beck Depression Inventory-Second Edition — BDI-II).

**Results:** The total FSFI and BDI-II scores were lower in Group C than in the remaining groups of women, while the total FSFI score was lower in Groups A and B than in Group D. Patients with both impaired fasting glucose and impaired glucose tolerance had lower scores in all domains (sexual desire, arousal, lubrication, orgasm, sexual satisfaction, and dyspareunia). Compared to Group D, Group A was characterised by lower domain scores for sexual desire and sexual satisfaction, and Group B by lower domain scores for desire, arousal, and orgasm. In all groups of prediabetic women, the overall FSFI score correlated negatively with the degree of insulin resistance and weakly with the total BDI-II score.

**Conclusions:** Impaired fasting glucose and impaired glucose tolerance may disturb sexual functioning and induce depressive symptoms. (*Endokrynol Pol* 2018; 69 (2): 175–181)

**Key words:** depressive symptoms, impaired fasting glucose, impaired glucose tolerance, sexual functioning

## Streszczenie

**Wstęp:** W poprzednich badaniach nie oceniano funkcjonowania seksualnego kobiet ze stanem przedcukrzycowym.

Badanie miało na celu ocenę funkcji seksualnych u młodych kobiet z różnymi typami stanu przedcukrzycowego.

**Materiał i metody:** Badanie objęło cztery grupy kobiet: kobiety z izolowaną nieprawidłową glikemią na czczo (grupa A, n = 19), izolowaną upośledzoną tolerancją glukozy (grupa B, n = 18), występowaniem zarówno nieprawidłowej glikemii na czczo i upośledzonej tolerancji glukozy (grupa C, n = 18) oraz zdrowe kobiety (grupa D, n = 19). Wszystkie uczestniczki badania wypełniły kwestionariusze oceniające funkcje seksualne (Indeks Funkcji Seksualnych Kobiet — FSFI) oraz obecność i nasilenie objawów depresyjnych (*Beck Depression Inventory-Second Edition* — BDI-II).

**Wyniki:** Całkowite wartości skali FSFI i BDI-II były niższe w grupie C niż w pozostałych grupach kobiet, podczas gdy całkowita punktacja FSFI była niższa w grupach A i B niż w grupie D. Pacjentki z nieprawidłową glikemią na czczo i zaburzeniami tolerancji glukozy miały niższe wyniki we wszystkich podskalach (pożądanie seksualne, pobudzenie seksualne, lubrykacja, orgazm, satysfakcja seksualna i dyspareunia). W porównaniu z grupą D, grupa A charakteryzowała się niższymi wynikami w domenach dla pożądania seksualnego i satysfakcji seksualnej, podczas gdy grupa B miała niższe wyniki w domenach dla pożądania, pobudzenia seksualnego i orgazmu. We wszystkich grupach kobiet ze stanem przedcukrzycowym ogólny wynik FSFI korelował negatywnie ze stopniem insulinooporności i słabo z całkowitym wynikiem skali BDI-II.

**Wnioski:** Nieprawidłowa glikemia na czczo i upośledzona tolerancja glukozy mogą zaburzać funkcjonowanie seksualne i wywołać objawy depresyjne. (*Endokrynol Pol* 2018; 69 (2): 175–181)

**Słowa kluczowe:** objawy depresyjne, nieprawidłowa glikemia na czczo, upośledzenie tolerancji glukozy, funkcjonowanie seksualne

## Introduction

From a pathophysiological and prognostic point of view, impaired fasting glucose (IFG) and impaired glucose tolerance (IGT), although classified together as

prediabetes, are metabolically distinct disorders, with only a limited overlap [1–4]. Subjects with IGT have marked muscle insulin resistance with less pronounced hepatic insulin resistance, while subjects with IFG have severe hepatic insulin resistance with normal or



near-normal muscle insulin sensitivity [3]. Both IFG and IGT are characterised by a reduction in early-phase insulin secretion, while subjects with IGT also have impaired late-phase insulin secretion [3]. After adjusting for hypertension and dyslipidaemia, only IGT remains an independent risk factor of cardiovascular events or death [1]. Moreover, the association between IGT and diabetes development is better demonstrated than for IFG. In an analysis of six prospective studies, the risk of developing diabetes was found to be approximately 3.6% to 8.7% per year in patients with IGT [5]. A study of 1245 Italian telephone company employees carried out for 11.5 years found that, unlike baseline IGT, baseline IFG did not predict progression to diabetes mellitus [6].

It seems that the presence of glucose homeostasis disorders may impair female sexual functioning. Sexual dysfunction was observed in most studies including women with type 2 diabetes [7–10], in whom the relative risk of sexual dysfunction is estimated at 2.29 [11]. Moreover, most [12–14], but not all [15], studies revealed that the prevalence of sexual dysfunction was higher in women with metabolic syndrome than age-matched healthy controls. However, these studies have serious limitations. Some of them included postmenopausal women [12, 15] and they did not investigate a relationship between the type of glucose metabolism impairment and female sexual function. Therefore, the aim of the present study was to compare sexual function and depressive symptoms between patients with various types of prediabetes.

## Materials and methods

### Study population

The study population consisted of 55 women (aged 25–45 years) with recently diagnosed and previously untreated prediabetes, who were recruited among subjects with a familial history of type 2 diabetes, body mass index above 25 kg/m<sup>2</sup>, or previous gestational diabetes. On the basis of fasting and 2-h postchallenge plasma glucose, prediabetic patients were allocated into one of the three groups: women with isolated IFG (Group A; n = 19) (fasting plasma glucose at least 100 mg/dL but less than 126 mg/dL, and plasma glucose concentration two hours after a 75-g oral glucose load less than 140 mg/dL); women with isolated IGT (fasting plasma glucose less than 100 mg/dL, and a 2-h postchallenge glucose level at least 140 mg/dL but less than 200 mg/dL) (Group B; n = 18); and women with concomitant IFG and IGT (IFG + IGT) (fasting plasma glucose at least 100 mg/dL but less than 126 mg/dL, and a 75-g oral glucose load between 140 and 200 mg/dL) (Group C; n = 18). Prediabetic patients were compared with 19 age- and weight-matched control subjects with normal glucose tolerance (fasting plasma glucose level

less than 100 mg/dL and a 2-h postchallenge glucose level less than 140 mg/dL) (Group D; n = 19). Subjects were excluded if they met at least one of the following criteria: diabetes, hyperprolactinaemia, hypogonadism, thyroid disorders, polycystic ovary syndrome, impaired renal or hepatic function, psychiatric problems, postpartum complications, and developmental or acquired anomalies of the female reproductive system. We also excluded women with a history of urogynaecological operations that could affect sexual function, pregnant or breastfeeding women, sexually inactive women, as well as women receiving any treatment. All participants were informed of the study aims and provided written consent before entering the study, which was further approved by the local Ethics Committee.

### Methods

Venous blood samples were collected from the antecubital vein at 8 a.m. after an overnight 12-h fasting. Plasma glucose, plasma lipids (total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides) and serum insulin were assayed by routine laboratory techniques using commercially available kits (Roche Diagnostics, Basel, Switzerland; DRG Instruments GmbH, Marburg, Germany). LDL-cholesterol levels were measured directly. Moreover, glucose levels were measured 2 h after oral ingestion of 75 g of glucose. The homeostasis model 1 for insulin resistance index (HOMA1-IR) was calculated as [fasting plasma glucose (mg/dL) × fasting plasma insulin (μU/mL)]/405].

Immediately after blood collection, all women considered for enrolment were asked to complete a questionnaire assessing their demographic characteristics, smoking, physical activity, education, occupation, stress exposure, general health, number and duration of marriages, number of sexual partners, deliveries, and abortions. Moreover, the participants completed questionnaires evaluating their sexual functioning and depressive symptoms. At the time of filling in the questionnaires, neither the subjects nor the investigators were aware of the biochemical results. Although all potential participants completed the questionnaires, only data of women with IFG and/or IGT and data of control women were included in the final analyses.

The female sexual function index (FSFI), used in our study, evaluates all phases of the female sexual cycle, sexual satisfaction, and dyspareunia in the last four weeks [16–18]. This 19-item questionnaire includes six domains: sexual desire (items 1 and 2), sexual arousal (items 3–6), lubrication (items 7–10), orgasm (items 11–13), satisfaction (items 14–16), and pain (items 17–19). FSFI items are scored on a 0–5 or 1–5 scale, with 0 indicating no sexual activity. Scores for each of the six domains were calculated by adding individual

domain question scores and multiplying by the domain factor (0.6 for desire, 0.3 for arousal and lubrication, and 0.4 for orgasm, satisfaction, and pain). The total FSFI score, which is the sum of the scores for all individual domains, may range from 2.0 to 36.0. Higher scores indicate better sexual function, and a total FSFI score less than 26.55 is suggestive of sexual dysfunction [16–18].

The presence and severity of depressive symptoms were measured with the Beck Depression Inventory Second Edition (BDI-II), consisting of 21 items and being a valid and reliable measure of depressive state [19]. These items are adjusted to measure depressive symptoms corresponding with the diagnostic criteria for depressive disorders outlined in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition [20]. Each item is rated on a four-point Likert scale from 0 (not present) to 3 (severe). The total score, being a sum of the item scores, may range from 0 to 63. The BDI-II score of 0–13 was categorised ‘minimal’, 14–19 ‘mild’, 20–28 ‘moderate severe’, and 29–63 ‘severe’ depression [19].

### Statistical analysis

Kolmogorov-Smirnov test was used to assess the distribution of variables. Quantitative data without a normal distribution were natural log-transformed to normalise their distributions prior to statistical analysis. Study groups were compared using analysis of covariance followed by Bonferroni post hoc tests after consideration of age, smoking, body mass index, waist circumference, marital status, education, occupational activity, type of work, profession, physical activity, stress exposure, and blood pressure as potential confounders. The  $\chi^2$  test was used for all qualitative variables. Correlations were calculated using Pearson’s *r*-tests. Differences were described as statistically significant if *p* values were less than 0.05.

## Results

### General characteristics of the study groups

There were no differences between the groups in terms of age, body mass index, eating disorders, smoking (number of cigarettes and duration of smoking), physical activity, education, occupational activity, type of work performed, stress exposure, number of sexual partners, number and duration of marriages, number of deliveries, as well as in systolic and diastolic blood pressure (Table I). Expectedly, fasting plasma glucose levels were higher in Groups A and C than in Groups B and D, while 2-h postchallenge plasma glucose levels were higher in Groups B and C than in Groups A and D. All groups of women with prediabetes had higher levels of triglycerides, higher HOMA1-IR and lower levels of HDL cholesterol than women with normal glucose tolerance (Table I).

### Assessment of sexual function

The mean total FSFI score was lower in women with IFG + IGT than in the remaining groups of women, as well as lower in Groups A and B than in Group D. Sexual dysfunction was diagnosed in five women (26%) from Group A, five women (28%) from Group B, eight women (44%) from Group C, as well as in two women (11%) from Group D (Table II). Compared to Group D, Group A was characterised by lower domain scores for sexual desire and sexual satisfaction, Group B by lower domain scores for sexual desire, arousal, and orgasm, while Group C by lower scores for all domains. The mean domain score for desire was higher in group C than in Group A and Group B, while the mean score for satisfaction was higher in Group C than in Group B (Table II).

### Assessment of depressive symptoms

The total BDI-II score, as well as the percentage of women with total and mild depressive symptoms, differed between women with IFG + IGT and the remaining groups of participants (Table III). Moreover, the BDI-II score was insignificantly higher in women with isolated IFG (*p* = 0.062) and isolated IGT (*p* = 0.057) than in control subjects (Table III).

In all studied groups, the mean total FSFI score negatively correlated with the total BDI-II score (Group A: *r* = -0.40 [*p* < 0.001]; Group B: *r* = -0.38 [*p* < 0.001]; Group C: *r* = -0.43 [*p* < 0.001]; Group D: *r* = -0.34 [*p* < 0.01]) and with HOMA1-IR (Group A: *r* = -0.35 [*p* < 0.01]; Group B: *r* = -0.37 [*p* < 0.01]; Group C: *r* = -0.41 [*p* < 0.001]; Group D: *r* = -0.29 [*p* < 0.05]). In all groups of patients, the BDI-II score correlated with body mass index (Group A: *r* = 0.42 [*p* < 0.001]; Group B: *r* = 0.47 [*p* < 0.001]; Group C: *r* = 0.44 [*p* < 0.001]; Group D: *r* = 0.51 [*p* < 0.001]). In women with isolated IFG, there were negative correlations between HOMA1-IR and sexual desire (*r* = -0.48 [*p* < 0.001]), and between HOMA1-IR and sexual satisfaction (*r* = -0.35 [*p* < 0.01]). Women with isolated IGT showed a negative correlation between HOMA1-IR and sexual desire (*r* = -0.52 [*p* < 0.001]), sexual arousal (*r* = -0.29 [*p* < 0.05]), and orgasm (*r* = -0.32 [*p* < 0.01]). In IFG + IGT patients, HOMA1-IR negatively correlated with all domain scores (*r* values between -0.30 [*p* < 0.05] for dyspareunia and -0.49 [*p* < 0.001] for desire). No other correlations were significant.

## Discussion

The present study shows, for the first time, that disturbances in female sexual functioning may occur in women with even mild abnormalities of glucose homeostasis, which is accompanied by depressive symptoms. Moreover, individual dimensions of sexual functioning

**Table I. Sociodemographic characteristics, plasma lipids, and glucose homeostasis markers in the study population****Tabela I. Charakterystyka socjodemograficzna, lipidów osocza i markery homeostazy glukozy w populacji badanej**

	Group A <sup>1</sup>	Group B <sup>2</sup>	Group C <sup>3</sup>	Group D <sup>4</sup>
Number of patients	19	18	18	19
Age [years; mean (SD)]	35 (5)	36 (5)	37 (5)	35 (6)
Body mass index [kg/m <sup>2</sup> ; mean (SD)]	29.5 (3.2)	29.8 (3.5)	30.2 (4.0)	28.9 (4.2)
Smokers (%)/Number of cigarettes a day [n; mean (SD)]/ Duration of smoking [months, mean (SD)]	37/12 (5)/115 (55)	39/11 (6)/120 (52)	44/14(7)/123 (48)	42/12 (6)/110 (47)
Physical activity: total/once a week/several times a week/ /once a month (%)	58/21/16/21	56/22/11/22	50/22/6/22	53/21/11/21
Primary or vocational/secondary/university education (%)	21/32/47	22/39/39	28/28/44	26/32/42
Occupational activity/Blue-collar/white-collar/pink-collar workers (%)	74/21/21/32	72/17/17/39	72/22/11/39	68/21/16/32
Number of sexual partners [n; mean (SD)]	2.1 (0.6)	1.9 (0.8)	2.3 (0.8)	1.7 (0.8)
Number of marriages [n; mean (SD)]/ duration of marriages [months; mean (SD)]	1.2 (0.6)/71 (25)	1.1 (0.6)/53(28)	1.0 (0.5)/83 (29)	0.9 (0.5)/80 (28)
Number of deliveries [n; mean (SD)]/ Number of abortions [n; mean (SD)]	1.9 (0.8)/0.4 (0.4)	1.8 (0.6)/0.4 (0.4)	1.6 (0.7)/0.4 (0.3)	1.7 (0.6)/0.2 (0.3)
Stress exposure (%)	84	78	83	79
Systolic blood pressure [mmHg; mean (SD)]	132 (14)	135 (12)	136 (11)	131 (15)
Diastolic blood pressure [mmHg; mean (SD)]	84 (8)	85 (8)	86 (7)	83 (8)
Fasting glucose [mg/dL; mean (SD)]	112 (6) <sup>d, f</sup>	89 (5)	115 (5) <sup>d, f</sup>	86 (8)
2-h post-glucose load plasma glucose [mg/dL; mean (SD)]	124 (10)	168 (15) <sup>b, f</sup>	175 (12) <sup>b, f</sup>	118 (10)
HOMA1-IR [mean (SD)]	4.4 (1.6) <sup>f</sup>	4.6 (1.4) <sup>f</sup>	6.0 (1.7) <sup>a, c, f</sup>	2.0 (0.6)
Total cholesterol [mg/dL; mean (SD)]	230 (24)	239 (28)	245 (32)	240 (30)
LDL cholesterol [mg/dL; mean (SD)]	132 (15)	138 (14)	143 (18)	137 (11)
HDL cholesterol [mg/dL; mean (SD)]	45 (10) <sup>e</sup>	43 (10) <sup>e</sup>	42 (11) <sup>e</sup>	55 (11)
Triglycerides [mg/dL; mean (SD)]	235 (40) <sup>e</sup>	243 (46) <sup>e</sup>	256 (50) <sup>e</sup>	204 (46)

SD — standard deviation

<sup>1</sup>women with isolated impaired fasting glucose; <sup>2</sup>women with isolated impaired glucose tolerance; <sup>3</sup>women with both impaired fasting glucose and impaired glucose tolerance; <sup>4</sup>control women with normal glucose tolerance<sup>a</sup>*p* < 0.05, <sup>b</sup>*p* < 0.001 vs. Group A; <sup>c</sup>*p* < 0.05, <sup>d</sup>*p* < 0.001 vs. Group B; <sup>e</sup>*p* < 0.05, <sup>f</sup>*p* < 0.001 vs. Group D**Table II. Sexual functioning in women with prediabetes****Tabela II. Funkcjonowanie seksualne kobiet ze stanem przedcukrzycowym**

Variable	Group A <sup>1</sup>	Group B <sup>2</sup>	Group C <sup>3</sup>	Group D <sup>4</sup>
FSFI score [mean (SD)]	29.73 (2.80) <sup>d</sup>	29.63 (2.65) <sup>d</sup>	26.80 (2.86) <sup>a, c, f</sup>	32.97 (3.05)
FSFI score ≤ 26.55 (%)	26 <sup>d</sup>	28 <sup>d</sup>	44 <sup>a, c, e</sup>	11
Sexual desire [mean (SD)]	4.86 (0.60) <sup>e</sup>	4.70 (0.59) <sup>e</sup>	4.07 (0.65) <sup>b, c, f</sup>	5.67 (0.61)
Sexual arousal [mean (SD)]	5.02 (0.69)	4.75 (0.64) <sup>e</sup>	4.45 (0.72) <sup>f</sup>	5.56 (0.63)
Lubrication [mean (SD)]	5.12 (0.73)	5.40 (0.54)	4.64 (0.79) <sup>d</sup>	5.45 (0.58)
Orgasm [mean (SD)]	4.88 (0.83)	4.57 (0.65) <sup>e</sup>	4.36 (0.49) <sup>f</sup>	5.44 (0.66)
Sexual satisfaction [mean (SD)]	4.76 (0.55) <sup>e</sup>	5.17 (0.62)	4.31 (0.76) <sup>c, e</sup>	5.38 (0.45)
Dyspareunia [mean (SD)]	5.09 (0.46)	5.04 (0.37)	4.97 (0.35) <sup>d</sup>	5.47 (0.49)

SD — standard deviation

<sup>1</sup>women with isolated impaired fasting glucose; <sup>2</sup>women with isolated impaired glucose tolerance; <sup>3</sup>women with both impaired fasting glucose and impaired glucose tolerance; <sup>4</sup>control women with normal glucose tolerance<sup>a</sup>*p* < 0.05, <sup>b</sup>*p* < 0.01 vs. Group A; <sup>c</sup>*p* < 0.05 vs. Group B; <sup>d</sup>*p* < 0.05, <sup>e</sup>*p* < 0.01, <sup>f</sup>*p* < 0.001 vs. Group D



Table III. Depressive symptoms in premenopausal women with prediabetes

Tabela III. Objawy depresyjne u kobiet ze stanem przedcukrzycowym przed menopauzą

Variable	Group A <sup>1</sup>	Group B <sup>2</sup>	Group C <sup>3</sup>	Group D <sup>4</sup>
BDI-II score [mean (SD)]	10.4 (3.7)	10.7 (3.5)	14.2 (2.5) <sup>a, b, d</sup>	7.8 (3.4)
depressive symptoms [n (%)]	4 (21)	5 (28)	10 (56) <sup>a, b, c</sup>	2 (11)
mild symptoms [n (%)]	4 (21)	4 (22)	9 (50) <sup>a, b, c</sup>	2 (11)
moderate symptoms [n (%)]	0 (0)	1 (6)	1 (6)	0 (0)
severe symptoms [n (%)]	0 (0)	0 (0)	0 (0)	0 (0)

SD — standard deviation

<sup>1</sup>women with isolated impaired fasting glucose; <sup>2</sup>women with isolated impaired glucose tolerance; <sup>3</sup>women with both impaired fasting glucose and impaired glucose tolerance; <sup>4</sup>control women with normal glucose tolerance<sup>a</sup>p < 0.05 vs. Group A; <sup>b</sup>p < 0.05 vs. Group B; <sup>c</sup>p < 0.01, <sup>d</sup>p < 0.001 vs. Group D

are affected in a prediabetes type-dependent manner. The decrease in FSFI was most pronounced in women with the concomitant presence of IFG and IGT, less expressed in women with isolated IGT, and mildest in isolated IFG. On the basis of the obtained results, it seems that concomitant presence of both IFG and IGT is associated with a greater risk of sexual dysfunction and of depressive symptoms, making subjects with this type of prediabetes particularly prone to the earlier development and faster progression of impaired sexual functioning and depressive symptoms. Prediabetic states usually remain asymptomatic and are diagnosed either incidentally or, as in the case of our study, by screening of patients at high diabetes risk. In the light of our research, it seems reasonable to assume that premenopausal women with sexual dysfunction, which is not a consequence of another disorder or treatment, should be evaluated for the presence of fasting or postprandial hyperglycaemia.

The obtained results suggest that sexual dysfunction in all groups of our patients was in part a consequence of insulin resistance. The severity of sexual dysfunction correlated with HOMA1-IR and — also to a lesser extent — with plasma triglycerides and HDL cholesterol, abnormal levels of which are characteristic for atherogenic dyslipidaemia, which is commonly found in subjects with impaired insulin sensitivity [21]. However, the fact that these correlations were at most moderate and there was no relationship between body mass index and sexual function suggests that other mechanisms, not investigated by our research group, are also responsible for the observed changes. In our previous studies, IFG or IGT increased secretion of proinflammatory cytokines from human monocytes and lymphocytes, and induced low-grade systemic inflammation and a procoagulant state [22–25]. Taking into account the complex proatherogenic action of all these cytokines [26, 27], an important role of monocytes and T lymphocytes [28, 29], low-grade inflammation [30], as well as enhanced coagulation and

diminished fibrinolysis at various stages of atherogenesis [31], all these changes may contribute to an increased risk of the development and progression of atherosclerosis in prediabetic subjects. Interestingly, in line with this hypothesis, patients with the concomitant presence of both IFG or IGT were characterised by higher monocyte release of tumour necrosis factor- $\alpha$ , interleukin-1 $\beta$ , interleukin-6, and monocyte chemoattractant protein-1, as well as by higher plasma levels of high-sensitivity C-reactive protein than subjects with the presence of IFG alone or IGT alone [23]. Moreover, compared to lymphocytes from IFG subjects, phytohemagglutinin-activated T cells from IFG patients produced larger amounts of interleukin-2, interferon- $\gamma$ , and tumour necrosis factor- $\alpha$  [22], which may explain why impairment in orgasm was observed in women with IGT, but not in women with IFG.

Another possible explanation for sexual dysfunction in women with IFG and/or IGT is an association between adverse glucose metabolism and neuropathy. Hyperglycaemia, dyslipidaemia and the metabolic syndrome, found in the participants of our study, as well as microvascular disease, not determined in our study but observed relatively commonly in prediabetic patients [32], are regarded as causative factors of peripheral and/autonomic neuropathy. Although generally milder in comparison to diabetes, neuropathy occurs more frequently in prediabetic patients than in the general population and mainly affects small fibres mediating sensory function. Finally, impaired sexual function may result from abnormal production of hormones, playing a role in the regulation of sexual cycle, sexual satisfaction, and pain. These hormones include testosterone, dehydroepiandrosterone and prolactin because disorders associated with their increased production are often accompanied by glucose metabolism disorders, while metformin, known to reduce glucose levels and to inhibit progression of IGT to diabetes [33], decreased circulating levels of these hormones [34–38].

Among all domains of FSFI, particular attention should be given to sexual desire. Impaired desire was the only sexual dysfunction observed in all groups of women with prediabetes. There were statistically significant differences in desire between women with both IFG and IGT and women with IFG alone or IGT alone. Moreover, correlations between HOMA1-IR and desire were stronger than correlations between insulin resistance and arousal, lubrication, orgasm, satisfaction, and pain. Interestingly, in our recent study, only sexual desire was disturbed in young women with macroprolactinaemia, which contrasted with multidimensional impairment of sexual function in women with elevated monomeric prolactin, probably because the amount of monomeric prolactin released locally from macroprolactin complexes is lower than that found in patients with monomeric hyperprolactinaemia [39]. Furthermore, apart from arousal, only desire was disturbed among all groups of women with thyroid disease: women with euthyroid Hashimoto's thyroiditis, non-autoimmune hypothyroidism, and autoimmune thyroid hypofunction [40]. All these findings taken together suggest that desire may be particularly susceptible to even small changes in metabolism or hormone balance.

Contrary to sexual dysfunction, depressive symptoms were observed exclusively in women with both IFG and IGT, and this finding was in disagreement with the presence of correlations between the total FSFI and BDI-II scores in all study groups. This means that, apart from impaired sexual functioning, worsened mood is also related to other conditions. One of these includes eating disorders, particularly obesity or overweight, found in many participants of our study because the BDI-II score correlated with body mass index. This association probably results from body dissatisfaction and low self-esteem associated with obesity or being overweight, and/or from a negative perception of eating disorders by society. Alternatively, depressive symptoms may be associated with a proinflammatory state. In agreement with this explanation, monocyte release of tumour necrosis factor- $\alpha$ , interleukin-1 $\beta$ , interleukin-6, and monocyte chemoattractant protein-1, which are postulated to play a role in the development of depression [41], was higher in IGF + IGT patients than in patients with either IFG or IGT alone [23]. The study protocol does not allow us to conclude whether, in the studied subpopulations of subjects with prediabetes, depressive symptoms are a consequence or a causative factor for sexual dysfunction.

Our study has several limitations that should be considered. Although well-validated, the utility of FSFI and BDI-II questionnaires is limited by their subjectivity. All groups of patients included a small number of patients, and therefore it cannot be excluded that

larger groups would ensure significant differences in other domains. Because current pharmacotherapy belonged to the exclusion criteria, sexual functioning may differ in subjects receiving hypoglycaemic and/or hypolipidaemic agents. Finally, although oral glucose tolerance test has poor repeat-test reproducibility, we measured fasting and 2-h postchallenge plasma glucose only once [42]. This strategy allowed us to minimise the possibility that the participants were aware of their clinical state but decreased the precision of assessment of glucose homeostasis.

## Conclusions

To sum up, the results of our study demonstrate that prediabetic women are characterised by disturbances in sexual functioning, the extent of which depends on the type of glucose metabolism abnormality. Sexual dysfunction is particularly pronounced in women with the concomitant presence of IGF and IGT and may be causatively linked to depressive symptoms.

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