diabetology

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Review

Sexual Dysfunction in Female Patients with Type 2 Diabetes Mellitus—Sneak Peek on an Important Quality of Life Determinant

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Abstract: Type 2 diabetes mellitus (T2DM) is a multisystemic disease with a high global burden and chronic complications. Sexual dysfunction (SD) in patients with T2DM is an often-overlooked complication, despite its high impact on quality of life (QoL). Female sexual disorders can affect women of reproductive age as well as menopausal women. Proposed mechanisms are intertwining a variety of physiological, neurological, vascular, hormonal, and psychological variables. The impairment of sexual function has been linked to hyperglycemia, insulin resistance, chronic low-grade inflammation, endothelial dysfunction, neuropathy, and hormonal abnormalities. There are many different manifestations of female sexual dysfunction, such as insufficient sexual desire, diminished arousal, difficulty in eliciting orgasm, and pain during sexual engagement. Numerous studies have shown that the QoL of patients living with diabetes mellitus (DM) is lower than that of those without DM. SD in women with T2DM leads to deteriorated QoL. Treatment must be individualized based on the diagnosis and the sexual dysfunction as well as underlying medical, psychological, and interpersonal issues. The goal of modern medical care for patients living with diabetes is not to delay death but to improve their health and QoL. The present review article aimed to raise awareness about female sexual dysfunction in patients with T2DM and to provide an overview of its impact on QoL.

Keywords: female sexual dysfunction; type 2 diabetes mellitus; quality of life

Citation: Rogoznica, M.; Perica, D.; Borovac, B.; Belančić, A.; Matovinović, M. Sexual Dysfunction in Female Patients with Type 2 Diabetes Mellitus—Sneak Peek on an Important Quality of Life Determinant. *Diabetology* **2023**, *4*, 527–536. https://doi.org/10.3390/diabetology4040046

Academic Editor: Peter Clifton

Received: 15 September 2023
Revised: 25 October 2023
Accepted: 2 November 2023
Published: 13 November 2023

1. Introduction

Type 2 diabetes mellitus (T2DM) is a multisystemic disease with a high global burden. It is estimated that 500 million individuals are affected by the disease. T2DM has a bigger burden in developed regions (Europe, North America), with approximately equal gender distribution [1]. The pathophysiology of the disease can be explained as non-autoimmune progressive loss of insulin secretion against the background of insulin resistance and metabolic syndrome, which is stated in the American diabetes association guidelines [2]. Chronic complications of T2DM are numerous and they vary with respect to the duration of the disease and the adequate regulation of glycemia [3]. Complications impact the entire bodily system, encompassing the eyes, kidneys, nervous system, vascular system (involving

both micro and macro changes), skin, bones, joints, and susceptibility to infection [4]. These complications have a profound influence on both quality of life (QoL) and overall life expectancy [1,3].

Sexual dysfunction (SD) in patients with T2DM is an often-neglected complication, despite the high impact on QoL [5]. SD is more common in men, with the primary symptom being erectile dysfunction, due to the complex intertwining of microvascular complications, autonomic neuropathy, low testosterone levels, and pelvic vascular disease [3,4]. Compared to male sexuality, the complexity of female sexuality is heavily influenced by psychological and societal variables. The interplay of neurologic, vascular, and hormonal systems is necessary for a normal female sexual response [6]. The prevalence and underlying mechanisms of female sexual dysfunction (FSD), as well as the associated risk factors in women with diabetes, are less clear than in men.

In the past 20 years, there has been a noticeable increase in interest in assessing and improving patients' QoL, particularly in chronic patients. QoL is one of the key indicators for promoting health and well-being in diabetic patients. Numerous studies have shown that the QoL of patients living with diabetes mellitus (DM) is lower than that of those without DM. Furthermore, a higher prevalence of sexual function disorder has been identified in the DM population, which may have a negative effect on QoL [7–11]. FSD frequently goes unrecognized and insufficiently addressed in women with T2DM. Healthcare providers may not routinely initiate discussions about sexual health, and patients may be reluctant to broach the subject, resulting in a deficiency of proper care [5].

This review article aims to heighten awareness regarding the issue of FSD in women with T2DM and to provide an overview of its impact on their QoL.

2. Type 2 Diabetes Mellitus and Chronic Complications

As mentioned earlier, T2DM is a multisystemic disease with a high global burden and an increasing prevalence worldwide. Chronic complications of the disease are a significant public health concern [1]. The rising prevalence of T2DM is associated with various risk factors, including obesity, sedentary lifestyles, unhealthy diets, genetic predisposition, and increasing life expectancy. T2DM has a substantial economic impact on healthcare systems and societies. The direct and indirect costs associated with diabetes management, including medications, hospitalizations, and lost productivity, are significant [1,3]. T2DM affects both men and women, but there are gender-specific aspects to its prevalence, risk factors, and impact on health. For example, postmenopausal women are at a higher risk compared to premenopausal women. This suggests that hormonal changes associated with menopause may play a role in the development of T2DM [1,4,7]. Furthermore, women who have experienced gestational diabetes during pregnancy are at an Increased risk of developing T2DM later in life. Women with polycystic ovary syndrome (PCOS), which is a common endocrine disorder among women, are at an increased risk of insulin resistance and T2DM [1,4,7].

T2DM can lead to a wide range of chronic complications, affecting various organ systems. These complications significantly increase the burden of the disease. T2DM can affect small blood vessels throughout the body, leading to microvascular complications such as retinopathy, nephropathy, and neuropathy [3,4]. T2DM is a major risk factor for cardiovascular diseases, including coronary artery disease, stroke, and peripheral vascular disease. It is a leading cause of heart attacks and strokes globally [1,3,4]. Diabetic nephropathy is a leading cause of end-stage renal disease (ESRD). It results from damage to the small blood vessels in the kidneys and can lead to kidney failure [3,4]. Diabetic neuropathy can affect both the peripheral and autonomic nervous systems. It can lead to sensory loss, pain, and autonomic dysfunction, affecting various body functions. Diabetic retinopathy is a leading cause of blindness in adults; it results from damage to the blood vessels in the retina and can lead to vision impairment or blindness if left untreated [3,4]. Diabetes-related foot problems, including neuropathy and peripheral vascular disease, can lead to foot ulcers and, in severe cases, lower limb amputations [3,4]. The chronic

complications of T2DM can have a profound impact on the QoL for affected individuals. These complications often require ongoing medical care and lifestyle modifications and may lead to disability, reduced mobility, pain, and decreased life expectancy [1,3,4].

3. Definition and Prevalence

Female sexual dysfunction is defined as a persistent or recurring decrease in sexual desire, a persistent or recurring decrease in sexual arousal, dyspareunia, and difficulty or inability in achieving an orgasm [12]. The impairment of sexual function has been linked to hyperglycemia, insulin resistance, low-grade chronic inflammation, endothelial dysfunction, neuropathy, and hormonal abnormalities. These pathways can result in changes in genital blood flow, altered neuronal transmission, and decreased vaginal lubrication, all of which have an influence on sexual response [12,13]. A variety of psychosocial variables, in addition to diabetes-related physiological issues, contribute to sexual dysfunction in women with T2DM. Depression, anxiety, body image difficulties, marital problems, and medication-related adverse effects are among these variables. Furthermore, cultural and societal conventions around sexuality and diabetes may worsen emotions of guilt, stigma, and low self-esteem [12,13].

Female sexual disorders can affect women of reproductive age, which also include perimenopausal women. Menopausal and postmenopausal women are also affected by FSD. The biological and psychosocial components interact intricately to produce the human sexual response. Depending on the situation, these elements can differ between cultures, between people, and even within the same person [14].

FSD is divided into primary and secondary FSD. Primary disorders have symptoms that are not due to a medical or psychiatric condition or a substance, contrary to secondary disorders.

According to the older and more recent literature, the prevalence has not changed over the years. There are between 40–50% of women who suffer from some sexual disorders. In the United States, 12% of adult women (>18 year) report having a problem with their sexual function [15].

In women with T2DM, the prevalence of FSD is about 20–80%, compared to the general female population where it is about 40% [16]. However, a recent study by Derosa et al. showed that the prevalence of FSD is about 87% [17].

There are different tools to detect sexual dysfunction in females, so it is very important which questionnaire is performed; for example, the Arizona Sexual Experience Scale (ASEX) only measures the sexual function over the previous 7 days, whereas the Female Sexual Function Index (FSFI) measures sexual function over the previous 30 days, as well as which population is observed [12,18].

Quality of life is a complex concept defined by the World Health Organization (WHO) as an individual's perspective on life, including their values, aspirations, and standards [19]. It comprises various dimensions of a person's existence, encompassing the cognitive, physical, spiritual, emotional, and social aspects. In modern medical care for individuals living with diabetes, the ultimate objective is not merely to prolong life but to enhance their health and overall QoL [20]. SD in women with T2DM results in a decline in QoL, affecting critical physical, psychological, social, and spiritual aspects of their lives.

When we consider SD and its negative impact on the QoL, it primarily affects the social component and interpersonal relationships. It also affects women's self-confidence and self-awareness. At the same time, depending on the disorder, other domains of QoL are also affected, such as health, spiritual, and psychological components. To evaluate the effects of SD in women, the Sexual Quality of Life-Female (SQoL-F) questionnaire was developed using qualitative data. According to McHorney et al. [21], the 36-item Short-Form Health Survey (SF-36v2) is a widely used and extensively validated instrument designed for Health-Related Quality of Life (HRQoL) assessment. Thus, the most frequently used questionnaires for assessing the latter determinants are SF-36v2 and SqoL-F, both clinical- and science-wise [22,23].

4. Different Domains of Female Sexual Dysfunction

Different diagnostic and classification methods—the DSM (The Diagnostic and Statistical Manual of Mental Disorders) and ICD (International Classification of Diseases)—address organic sexual dysfunction. SDs are broadly classified in ICD-11 and DSM-V based on the stages of sexual activity, from arousal to orgasmic problems. In the following text, we will define four basic groups that belong to sexual disorders [24].

1. Desire disorders include a persistent absence of sex-related physical desire, a lack of sexual engagement, or sexual thoughts or fantasies that cause problems to patients and their partners. There are two main desire disorders: hypoactive sexual desire disorder (HSDD) and sexual aversion disorder (SAD). The questionnaire that can be used for this type of disorder is the Sexual Function Questionnaire (SFQ-V1) [25,26].
2. Arousal disorders are described as a lack of in sexual interest, interest in initiating sexual activity, pleasure, thoughts, and fantasies, including an absence of responsive desire and a lack of subjective arousal of a physical genital response to sexual stimulation: non-genital, genital, or both. The FSFI is the most used questionnaire for female arousal disorders [25,26].
3. Orgasm disorders: Female orgasmic dysfunction is characterized by an orgasm that despite normal levels of subjective arousal, is absent, rare, noticeably lower in intensity, or noticeably delayed in response to stimulation. They can be primary when women have never been able to have an orgasm, and secondary when women are no longer able to experience orgasms, despite once being able to. The female Orgasm Scale is the scale used for diagnosing orgasm disorder in the female population [25,27].
4. Involuntary contraction of the pelvic floor muscles when vaginal entry is attempted or completed, pain that is localized to the vestibule, at other vulvovaginal or pelvic locations, as well as fear or anxiety about penetration attempts are all symptoms of pain disorder. The Multidimensional Vaginal Penetration Disorder Questionnaire is used for determining sexual pain disorders [25,27].

5. The Effect of T2DM on Female Sexual Function

No definite mechanisms of T2DM on SD are yet known so, these are some of the proposed mechanisms (Figure 1).

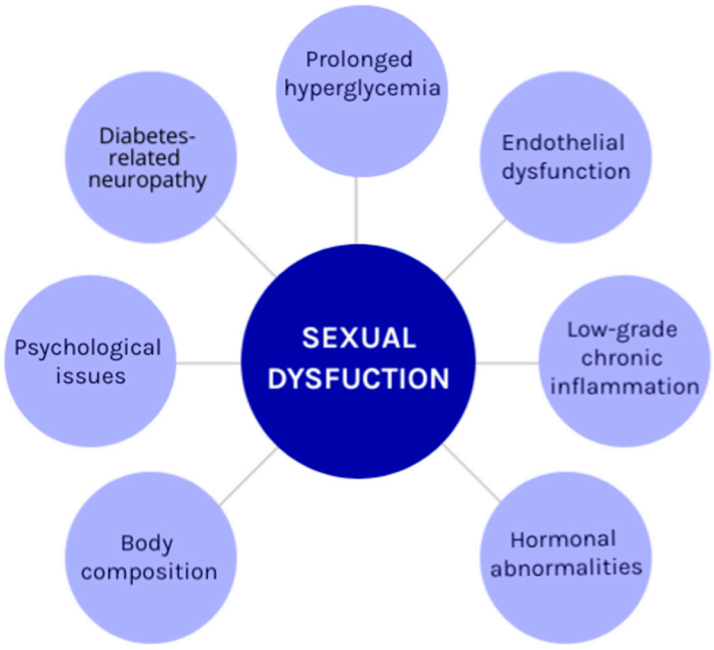

Figure 1. Proposed mechanisms of female sexual dysfunction in patients with type 2 diabetes mellitus.

The main mechanism is prolonged hyperglycemia, which causes cellular damage via a number of mechanisms, including advanced glycation end products (AGEs) and oxidative stress. This cellular damage has an impact on both the vascular and brain tissues involved in sexual response. Endothelial function can be impaired by AGEs, whereas oxidative stress can cause nerve damage, affecting the transmission of sexual inputs and feelings [5]. Hyperglycemia also decreases the hydration of mucous membranes in the vagina and increases the risk of infections, leading to problems with lubrication and dyspareunia [28]. Glycemic variability exacerbates vascular and neural damage, underscoring the importance of stable glycemic control to mitigate sexual dysfunction [29]. There are some studies that correlate better glycemic control with lower incidence of FSD and better outcomes [30].

It is well recognized that low-grade chronic inflammation has drawn attention as a possible mediator of endothelial dysfunction and cardiovascular disease in a number of metabolic diseases, including obesity, metabolic syndrome, and T2DM [3]. Endothelial activation, a pro-inflammatory state, and oxidative stress are caused by hyperglycemia, insulin resistance, hyperlipidemia, and poor dietary habits in both sexes. Through the combined mechanisms that cause damage to the genital area and hormonal abnormalities, diabetes may disrupt all these integrated systems, resulting in sexual dysfunctions [8].

Endothelial dysfunction, a hallmark of diabetes, influences the vascular health of the vaginal tissues. Reduced nitric oxide bioavailability and reduced endothelial signaling hinder normal blood vessel relaxation during sexual excitation, resulting in decreased vaginal blood flow and lubrication [12]. Diabetes-related neuropathy also affects the sensory and autonomic neurons responsible for sexual response, resulting in decreased sensitivity and altered genital reflexes [4,31]. A similar pathophysiological mechanism is observed in female patients with atherosclerosis and cardiovascular diseases. Atherosclerosis involves the buildup of arterial plaques, which can compromise blood flow to various organs, including the genital region, which ultimately leads to endothelial dysfunction and can lead to decreased genital sensitivity, arousal difficulties, and vaginal dryness [32,33]. It is therefore imperative is the early assessment of SD in patients to prevent complications of T2DM and atherosclerosis [16].

T2DM frequently causes hormonal abnormalities, which might contribute to SD. Insulin resistance and hyperinsulinemia affect the hypothalamic–pituitary–ovarian axis, altering sex hormone levels (mainly estrogen) and in the lower part progesterone and testosterone. Women with androgen excess and males with androgen insufficiency had the same cardiometabolic characteristics. The proper balance of estrogens and androgens is critical for maintaining energy metabolism, body composition, and sexual function. These changes can lead to diminished sexual desire, vaginal dryness, and poor genital responsiveness.

The psychosocial side of SD cannot be disregarded. The chronic stress associated with diabetes management, along with the psychological load of the illness, can lead to anxiety, despair, and poor body image. These psychological issues not only aggravate SD but also have an impact on hormone control, brain pathways, and general sexual well-being. The longer duration of T2DM aggravates those changes. Furthermore, SD can strain intimate relationships and disrupt partner communication. Feelings of frustration, guilt, and mutual dissatisfaction may arise, potentially leading to reduced relationship satisfaction. The resulting interpersonal challenges can ripple into other areas of life, affecting social support and overall relationship quality [9,10,13].

6. Sexual Disorders and Menopause

Following menopause, a woman's body and sexual urges may change due to the reduction of estrogen and testosterone levels in the bloodstream. Women who are menopausal or postmenopausal may realize that they are less amenable to being touched and that they are less quickly aroused, so decreased interest in sex may result from this [34].

Symptoms of menopause have a negative impact on QoL. Although women may also suffer changes in sexual function, temperament, and sleep, the most common menopause

symptoms are vasomotor (such as hot flashes and night sweats) and genitourinary (such as vulvovaginal irritation and dryness, dyspareunia, and urine difficulties) [34].

A reduction in the blood supply to the vagina might also be brought on by reduced estrogens levels. That may have a negative impact on vaginal lubrication, making the vagina too dry for pleasurable intercourse. Accordingly, all of the mentioned sexual disorders can affect postmenopausal women: arousal, orgasmic desire, and pelvic pain during intercourse. It is essential to mention that disorders in menopausal women are secondary because of changes in hormonal levels in the bloodstream. Hormonal changes lead to changes in blood vessels and blood supply in internal and external gynecological organs [35].

Menopausal women have a substantially greater prevalence of FSD (63.9%) than women in of reproductive age (41.0%), with a 53.4% overall prevalence among women living with T2DM, as per Esposito et al.'s findings [36].

Women with T2DM can go into early menopause because of microvascular changes in the ovary. Therefore, ovary cells produce fewer hormones, such as estrogen and progesterone, than ovary cells in healthy women. They also have lower vascularization of the external genital organs, so they have vaginal dryness and lower clitoral stimulation [12]. Diabetes significantly alters the vaginal lamina propria vascular network, nitrergic signaling and androgen receptor expression, all of which have an impact on vaginal physiology. The higher risk of FSD development in women with diabetes may be caused by these changes [37].

7. Sexual Dysfunction as Per Gender

Although the distinctions between men's and women's sexuality, as well as their causes and etiologies, are not fully known, it is nevertheless feasible to make assumptions about these disparities. From various viewpoints, including biological, psychological, and biopsychosocial, one might examine sexuality. Although most researchers concur that both biological and sociocultural elements are important, they disagree over how much of an impact each has [28]. The impact of these various elements may differ for various sexual dysfunctions, for different life stages, and under various life circumstances [28].

8. Clinical Studies

The significance of DM in a woman's sexuality was largely ignored until 1970s. Kolodny started to publish on this topic in 1971 [38]. Then, in late nineties, Enzlin and others published a paper of SF in women with DM; since then, interest in the study of FSD in DM women has grown [39]. Results of several studies found the relationship between DM and FSD. A study, conducted by Shi et al., on FSD in Chinese women with T2DM found that diabetic women's overall scores for sexual function (SF) were considerably worse in the study group than in the control group [40]. According to a meta-analysis conducted by Pontiroli et al. that included 26 studies on 3168 diabetic women and 2823 controls, FSD is more common and is linked to a lower FSFI score in diabetic women than in controls [16].

Studying FSD in diabetic women has proven to be difficult because of the constant definitional changes, the exclusion of distress from studies of women's sexual dysfunction, and the high incidence of FSD in the general population as a result [4]. The lack of consistency in study designs among published clinical trials evaluating the impact of DM on women's sexuality makes it challenging to directly compare studies and draw conclusive findings.

FSD is relatively high in population without T2DM; therefore, study samples in patients with T2DM should be large to demonstrate this difference. Many studies have made no distinction between DM type 1 and type 2 [8]. The ability to account for the impact of the menopausal state and its treatment on sexuality is limited since authors usually combine pre- and postmenopausal women. The treatment of DM has changed in recent decades; consequently, women suffer less from SD. These variables may partially account for the variance in findings across research conducted at various times, and they

raise the possibility that it may never be possible to compare studies conducted in different time periods.

In order to better understand the connection between DM and FSD, larger, more inclusive studies that include both women with DM and appropriate control groups are required. These studies should also use updated definitions of FSD.

Studies of women with diabetes have generally found weak or nonexistent correlations between sexual problems and age, duration of diabetes, body mass index (BMI), diabetic complications, medication, glycemic control, hormonal treatment, and menopausal status [31,39,41], in contrast to what has been found in studies on men with diabetes. However, in a study by Abu on 613 diabetic women and 524 healthy women, it was found that worse SF was significantly connected with longer diabetes duration, older age, higher BMI, the existence of cardiovascular problems, and the presence of diabetic sequelae [42]. Espasito found that metabolic syndrome and atherogenic dyslipidemia were independent predictors of FSD in 595 women with T2DM; nevertheless, depression and marital status were the two biggest independent predictors of FSD [36]. In contrast to male sexuality, female sexuality is much more complex and is greatly impacted by psychological and sociological factors, which was found in a review study conducted by Siddiqu et al.; it was discovered that psychological factors have a pathological predominance in sexual function issues in diabetic patients [43].

In the past two decades, there has been a rise in the attention given to QoL especially in chronic patients, which has prompted researchers to focus their efforts on identifying the elements that are most likely to improve it. In some studies, the association between SF and QoL in women at fertility age has been reported. Kiadaliri et al. observed that the QoL of diabetic patients was lower than that of their healthy peers in a systematic review study on diabetes in Iran [44]. Soltan et al., in their study, found no correlation between the SD and QoL in women with T2DM [45]. The current study set out to explore the relationship between sexual function and QoL in diabetic women seeking medical attention, taking into account the sparse and contentious existing studies in this area, as well as the cultural variations that have an impact on QoL and sexual function in various countries [8,9].

9. Interventions and Management

SD may indirectly impact diabetes management. Emotional distress and reduced self-esteem can lead to poor adherence to diabetes management strategies, including medication and lifestyle modifications. The resulting suboptimal glycemic control further reinforces the cycle of sexual dysfunction and decreased QoL [9]. Achieving and maintaining optimal glycemic control is essential for minimizing the impact of T2DM on sexual function. Effective management strategies should encompass lifestyle modifications, antidiabetic medications, insulin therapy, and continuous glucose monitoring to achieve stable glycemic control. By addressing hyperglycemia, one can positively impact vascular health, hormonal regulation, and neural pathways related to sexual function. Patient-centered care should prioritize open communication, individualized treatment plans, and sensitivity to the emotional impact of sexual dysfunction. Encouraging women to voice their concerns and providing tailored interventions can help mitigate the negative effects on QoL. These interventions are essential to improving the QoL of women with T2DM experiencing sexual dysfunction.

Other approaches have been integrated into the management of FSD, including medical and lifestyle modifications. Medical treatment options encompass hormone therapy, particularly in cases where hormonal imbalances contribute to FSD, leading to the prescription of hormone replacement therapy (HRT), such as estrogen [9–11]. Another option involves phosphodiesterase type 5 (PDE-5) inhibitors, commonly used to address arousal and orgasm difficulties in women due to their ability to enhance vaginal blood flow [9–11]. For women facing vaginal dryness or discomfort, topical estrogen treatments such as creams or rings can effectively improve vaginal health [9–11].

Lifestyle modifications are also crucial and include factors such as exercise, diet, stress reduction, smoking cessation, and moderating alcohol intake, all of which can have a positive impact on one's overall well-being and health. Over-the-counter products such as vaginal lubricants and moisturizers are available to alleviate vaginal dryness and discomfort.

Lastly, sexual aids such as vibrators or other similar devices can be beneficial for some women in enhancing sexual pleasure [9–11]. Psychological interventions play a vital role in the treatment of SD in women with T2DM. These interventions can address the emotional and psychological factors contributing to sexual dysfunction, help women cope with the challenges of T2DM, and improve their overall well-being. Interventions include cognitive-behavioral therapy, sex therapy, mindfulness and relaxation techniques, psychoeducation, and couple's counseling [9]. Addressing physical, psychological, relational, and societal dimensions is crucial. Multidisciplinary approaches involving healthcare providers, psychologists, sex therapists, and partners can provide comprehensive support. Foremost, raising awareness about the relationship between T2DM, sexual dysfunction, and QoL is vital [11].

10. Conclusions

SD in women with T2DM is a multidimensional issue that has significant effects on their general well-being and QoL. A thorough understanding of the underlying mechanisms, together with patient-centered therapies, is required in order to improve sexual well-being in this group. Healthcare practitioners may provide holistic treatment that enhances the overall quality of life for women with T2DM by addressing the complex interplay between diabetes, hormonal changes, physiological changes, psychological variables, and cultural effects. All of this will bring better compliance of the patients, better glycemic control, and above all, fewer complications of the disease. Most importantly, raising awareness about the relationship between T2DM, SD, and QoL in women is vital.

Raising awareness of SD, especially among female patients with T2DM, should lead to their seeking professional help and support as early as possible to improve their sexual well-being and overall QoL.

Author Contributions: Conceptualization, M.R., D.P., B.B., A.B. and M.M.; writing—original draft preparation, M.R., D.P. and B.B.; writing—review and editing, A.B., M.M., M.R., D.P. and B.B.; supervision, A.B. and M.M. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest.

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