

## Systemic Review: Sexual Dysfunction in Women with type 2 Diabetes Mellitus

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### ABSTRACT

Diabetes would not just have a high blood glucose level in the individual body, yet these days diabetes likewise goes with numerous other organic issues like hypertension, feeble the myocardial layer working, sexual broke, and so on. These are some real issue which is these days joined by diabetes to a person's body. Guys are for the most part being determined to have the sexual broke issue, guys, as well as experience a sexual broke issue. As similarly we may see less clinical examinations, including sexual broke issues looked for the sort two diabetic ladies. The primary goal of this article is to illuminate the situation that females proceed with much trouble with regards to the sexual broke Complication that might be physiological or neurotic if there should arise an occurrence of sorting two diabetes in ladies. It chiefly involves the useful extent of females like sexual drive, excitement, vaginal grease, Orgasm and general fulfilment space. Talking about the treatmentaccess of the ailment in the analytic way for it, Diabetes essentially hinders the sexual execution of Diabetic Women. Determinants of sexual ability incorporate age and extent of diabetes.

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## 1. Introduction

Diabetes mellitus is the most frequently occurring chronic disease worldwide and is characterized by hyperglycaemia. It is known to rise speedily with over 550 million to be affected by 2030 (Wild *et al.*, 2004) among all the countries in the world. The prevalence of the disease is also rising with agrowing population, aging, urbanization, physical inactivity and obesity, which will further worsen the situation of disease (Dennerstein *et al.*, 2002). In diabetes mellitus is an outcome of impaired metabolism of fats, lipids, carbohydrates and proteins as well. It is found to be responsible for several organfailurelike renal failure, heart failure, and sexual dysfunction(Pontioli *et al.*, 2013). However, most of the patients with diabetes die due to cardiovascular diseases like stroke. It occurs at a stage when diabetes becomes chronic. Diabetes Mellitusacting an imperative role in the pathogenesis of sexual dysfunction among both females and males. Many studies have been accomplish to study sexual dysfunction in diabetic males, but there are lesser data available in diabetic females due to a number of reasons like a small sample size. According to a study conducted by Pontioli *et al.*, (Enzlin *et al.*, 2003) and Enzlin *et al.*, (Lehman and Jacobs, 2006). The prevalence rate for females lies between 25-71% and

27% respectively. Moreover, large epidemiological studies suggested that the prevalence of sexual dysfunction ranges from 40-60% with higher rates found in postmenopausal women. There are many factors that are responsible for the etiology of sexual dysfunction among females such as neurological, psychological as well as vascular factors (Li *et al.*, 2010; Buvat *et al.*, 1985; Kim and Son, 2006; Skrha, 2003; Orasanu and Plutzky, 2009). Although, the data available for neurological factors areless. Yet some neurological disorders like multiple sclerosis, lumbar radiculopathy etc. Can result in dysfunction of female genital organs (Buvat *et al.*, 1985; Kim and Son, 2006; Skrha, 2003; Orasanu and Plutzky, 2009). The most common and the most useful observation is the Prevalence of diabetes in Asia people mainly it lowers the BMI of the diabetic people.The main reason is that the Asians are recorded as the most prominent race by the IOTF to be prone to the diabetic nature due to the high adiposity content.

### 1.1 Overview for the Sexual Dysfunction

The occurrence of sexual dysfunction can result in symptoms like decreased libido, low accountability, decreased vaginal lubrication, orgasm dysfunction and

dyspareunia. Apart from this, diabetes also has a detrimental impact on the cardiovascular system which leads to diabetic macroangiopathy and diabetic microangiopathy (Doumas *et al.*, 2006; Owiredu *et al.*, 2011). Diabetic macroangiopathy is commonly known to cause the incidence of coronary artery disease and hypertension, whereas diabetic microangiopathy may develop several years after the onset of the disease. In addition to this, hypertension can further aggravate the complications of microangiopathy and macroangiopathy. Thus, there is a great need to control hypertension, which will further lessen the rates of sexual dysfunction (Basson *et al.*, 2000). According to World Health Organization sexual dysfunction refers to a condition in which an individual is not able to participate in sexual intercourse as he/she would wish (American Psychiatric Association, 2013). It is categorized by disorder in the psycho physiological alteration in the sexual cycle of women (Veronelli *et al.*, 2009). Moreover, recently the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) updated a recent definition of sexual dysfunction. It has been grouped into two categories: sexual dysfunction has been put into dyspareunia, vaginismus and female sexual interest or arousal disorder have been put into the "Genito-pelvic pain/penetration disorder" category (Khalilzadeh *et al.*, 2015). In general, female sexual dysfunction can be evaluated based on the score of the Female Sexual Function Index (FSFI). A lower score is associated with sexual impairment in diabetic females. Moreover, at the meta-regression, only BMI was found to be significantly associated with the FSFI score. Increase frequency of sexual dysfunction and lower FSFI score in diabetic women are basically interrelated to her body weight. Many studies have already established that the increased prevalence of dysfunction is commonly linked to obesity (Esposito *et al.*, 2005; Martelli *et al.*, 2012; Enzlin *et al.*, 2002; Mezones-Holguin *et al.*, 2008) and metabolic syndrome (Konuru *et al.*, 2017; Pontiroli *et al.*, 2013).

Type 2 diabetes in relationship with improperly low luteinizing hormone (LH) and follicle-stimulating hormone (FSH) concentrations. Female hormones control about each part of erectile capacity, to the endothelial cells of the corpora cavernosa and from pelvic ganglia to smooth muscle. It likewise balances the planning of the erectile procedure, which happens as a component of sexual want, organizing penile erection with sex. It is as yet hazy level of testosterone is required for good erectile function; in any case, proof from clinical and sub-atomic examinations bolsters the utilization of testosterone supplanting in hypogonadism patients with ED, in spite of the fact that the benefit-chance proportion is indeterminate in cutting edge age. The instruments engaged with testosterone lack in diabetes incorporate low levels of the sex hormone-restricting globulin because of insulin obstruction, expanded aromatase action in instinctive fat tissue leading to an enlarged

change of testosterone in estradiol, leptin opposition causing decreased emission of LH and testosterone, and expanded levels of free testosterone, which may smother the discharge of gonadotropin-releasing hormone and LH. Bellastella *et al.*, 72 proposed a conceivable immune system pathogenesis of hypogonadotropic hypogonadism in type 2 diabetic patients, as showed by the nearness of pituitary antibodies at high titers, as contrasted and age-coordinated controls.

## 2. Risk Factor

There are various established risk factors that are closely linked with the incidence and risk of diabetes mellitus and sexual dysfunction. Various micro vascular and macrovascular complications are caused majorly due to diabetes that greatly affects the sexual functioning by an individual. One of the most commonly occurring risk factor is depression as sexual health is associated with psychological factors. (Newman and Bertelson, 1986; Skrha, 2003) Thereby effecting lifestyle, self image and personal relationships. There is a need to treat depression by taking antidepressants. Besides psychological factors, several behavioural and environmental factors also raise the problem of sexual dysfunction which includes conditions like obesity, overweight, physical inactivity, (Muharam *et al.*, 2016) etc. Obese women are more likely to have more severe and a significant number of sexual problems (Lewis *et al.*, 2010).

Another major reason that potentiates the risk of sexual impairment is social, cultural risk factor which consists of financial issues, limited social relations, employment status and lack of exercise (Peng *et al.*, 2005). Apart from this, there are other factors that contribute to the development of sexual dysfunction such as aging, (Bhasin *et al.*, 2007) cardiovascular diseases, (Maiorino *et al.*, 2014) Hypertension, (Park *et al.*, 2002) genitourinary disease (Feldhaus-Dahir, 2009) and many more chronic diseases (Patil *et al.*, 2017; Kim and Son, 2006). Diabetes mellitus itself is responsible for the high incidence of sexual problems. High glycaemic levels in the blood can result in painful sexual intercourse, commonly known as Dyspareunia (Duby *et al.*, 2014). But, there is limited evidence available to support this. Dyspareunia may be induced when the hydration levels of the vaginal mucous membrane decrease. In addition, atherosclerotic damage and endothelial damage (Brown *et al.*, 2005) may incite the lesser vaginal lubrication and clitoral engorgement. It is evident from several research studies that an imbalance of hormones such as androgens, estrogens and sex hormone binding globulin greatly affects sexual arousal (Feldhaus-Dahir, 2009). However, it can be improved by taking hormone replacement therapy, which is the only best possible treatment currently approved by certain organizations.

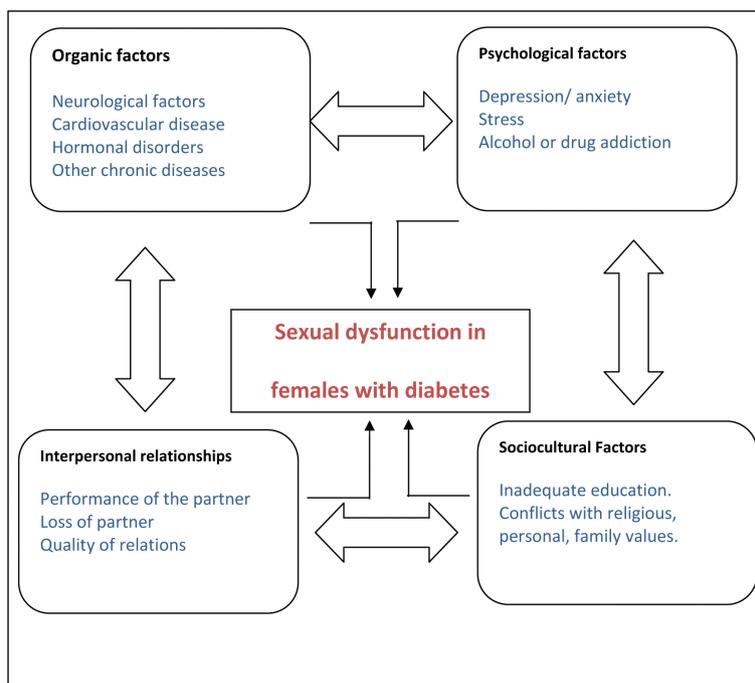
### 3. Pathogenesis

Factors that play a role in the pathogenesis of sexual dysfunction in women includes: organic like hyperglycaemia, neural, vascular, neurovascular factors, psychological and psychosocial derangements.

- **Hyperglycaemia:** It has been already discussed that a decrease in lubrication or hydration of the mucus membrane of vagina lead to dyspareunia and other genitourinary infections. This makes the sexual intercourse, even more difficult to encounter because of the occurrence of arousal disorder.
- **Neural and vascular factors:** It is widely accepted that sexual arousal largely depends on the sympathetic nervous system, noradrenergic/ no cholinergic neurotransmitters (NANC), e.g. Vasoactive intestinal polypeptide (VIP) and nitric oxide (NO). These factors are responsible for the sexual function in diabetic females because these are basically involved in the relaxation of smooth muscles of genital tissues and thus increasing the blood flow, thereby regulating sexual functioning. Diabetes mellitus can lead to various structural as well as functional changes in a female genital organ which impairs the relaxation process of genital tissues (Schram *et al.*, 2009) and ultimately sexual functions get disturbed. Other vascular abnormalities like endothelial cells dysfunction and atherosclerotic damage may reduce the

engorgement of the clitoris and vaginal lubrication which can thereby cause painful sexual intercourse.

- **Diabetic Neuropathy:** Diabetic neuropathy is another important reason that plays a significant role in the pathogenesis of sexual abnormalities. This can impair both normal transduction of sexual stimuli as well as the triggered sexual response (Enzlin *et al.*, 2009; Enzlin *et al.*, 2003; Kumar Patnaik *et al.*, 2017). In this, there is an imbalance in the normal levels of hormones like androgens, estrogens and sex hormone binding globulin (Rockliffe-Fidler and Kiemle, 2003). Furthermore, various endocrinological abnormalities may further aggravate the sexual problems in diabetic women, such as polycystic ovarian syndrome, hypothalamic-pituitary dysfunction and thyroid disorders.
- **Depression:** Nearly half of the women face sexual dysfunction due to depression (Ogbera *et al.*, 2009). Also, depression is strongly associated with diabetes. There can be many reasons other than diabetes that causes depression which may include financial status, employment status, educational background and many more (Fugl-Meyer and Sjogren, 1999). Depression further worsen the complications of diabetes (Basson, 2005) which then affect quality of life, relationship status, confidence, health and a woman's self image which ultimately worsen sexual performance also although the exact mechanism of action of depression in diabetic female is not known.



**Figure 1:** Sexual Dysfunction overlay of pathogenesis in females with Diabetes.

## 4. Diagnosis

In order to observe whether a diabetic woman has sexual dysfunction or not, her sexual and medical history, co-morbid illness, her medication as well as woman's current interpersonal and Psychosocial status, should be evaluated. The various diagnostic approaches include the following:

- The Female Sexual Function Index (FSFI): the FSFI is a brief questionnaire which measures sexual functioning in women. It is used to access domains like sexual arousal, satisfaction and orgasm. The FSFI may also be useful for evaluating the treatment outcome in clinical trials, but this remains to be demonstrated.
- The Brief Index of Sexual Functioning for Women (BISF-W): it refers to short, standardized self report which is used to examine the sexual functioning in women. It provides a comprehensive and reliable

assessment to check the domains of sexual health in a number of women.

- Derogates Interview for Sexual Function (DISF/DISF – SR): it is a brief semi-structured interview, which is designed for the degree estimates the quality of an individual's sexual functioning in quantitative terms. It represents the degree of the phase of the sexual response cycle. It consists of five domains such as sexual arousal, sexual behaviour, sexual cognition, sexual drive and orgasm. It requires 15-20 minutes to access sexual functioning in women and men also.
- The Female Sexual Distress Scale (FSDS): It is used to assess sexually related personal distress among women. It is also useful to check the possibility of depression in women regarding sexual health.

**Table 1:** Comparison of scores in five sexual domains in diabetic and control women.

	Sex drive	Arousal	Lubrication	Orgasm	Satisfaction
Patient	231	228	224	256	242
Control	153	152	152	151	137
P value(0.001)	>0.001	>0.001	>0.001	>0.001	>0.001

**Table 2:** Effect of diabetes on women sexuality

Patient no	Sexual desire	Excitement	Orgasm	Dysparenuia
No.1	No effect	14%Difficulty in vaginal lubrication	Anorgasm in 36%	3% had Dysparenuia
No.2	No effect	Sensibility affected in 27%	Absence of orgasm in 1%	-
No.3	No effect	-	Absence of orgasm in 18%	-
No.4	Decrease in 47%	Sensibility affected in 47%	Anorgasm in 33%	
No.5	Decrease in 20%	In 24 % problem with arousal	No difference	12 % had pain and discomfort
No.6	Decrease in 24%	Reduced vaginal lubrication in 18%	Orgasmic dysfunction in 19%	10% had pain during coitus
No.7	Significantly less desire	Reduced vaginal lubrication in 45%	No difference	
No.8	Decrease in 21%	Problems with lubrication in 18%	Orgasmic dysfunction 15%	21% reported some genital pain

### 4.1 Data Methods

Recovery of studies depended on The MEDLINE, Cochrane Library and EMBASE (until June 2012) utilizing the terms type 1 and type 2 diabetes, insulin-subordinate and non-insulin-dependent diabetes, sexual dysfunction, ladies, restricting this search to human investigations. A manual inquiry was also performed on reference records from s, reviews, publications, and procedures of global congresses.

At the point when consequences of one examination were accounted for in more productions, just the latest and

finish information were considered. Choices on trials to incorporate were taken UN indiscriminately by the three authors. Disagreements were settled by discussion. Excluded trials were related to the purpose behind prohibition. Twenty-six examinations met the incorporation criteria, all distributed as full reports (Table 2).

### 4.2 Extraction of Data

Information concerning Studies, patent characteristics and considering results were disconnected by the three creators and inconsistencies were settled by discourse.

In a few examinations there were more arms, as composite casistics could be part into littler casistics; in such cases, a similar report shows up twice or all the more regularly in figures. Suitable approach as indicated by the favoured revealing things for precise audits and meta-investigations (PRISMA) proclamation was clung to. Since considers were of observational nature, quality criteria for clinical trials were not connected.

### 4.3 Analysis of the Data

Impact measures were (I) the distinction of recurrence of FSD in diabetic and control ladies; and (ii) the distinction of FSFI score in diabetic and in control ladies. Study results (Beck Depression Inventory [BDI] and FSFI) were communicated as SMD, with 95% certainty interims (CIs) evaluated by an arbitrary impacts show as indicated by DerSimonian and Laird . For sexual brokefrequency, study result was communicated as OR, with 95% CI, assessed by irregular impacts demonstrate as indicated by Der Simonian and Laird .Studies were assembled by gatherings of patients (type 1 diabetes, type 2 diabetes, any sort of diabetes), and furthermore as per preselected limits (age, premenopausal or postmenopausal state or either condition, span of diabetes, weight record [BMI], ceaseless diabetic difficulties). Heterogeneity was surveyed through Q and I2 insights for every examination, and potential sources of heterogeneity were talked about where suitable . A P esteem <0.05 was viewed as demonstrative of factually critical heterogeneity. In each figure, vertical line speaks to no distinction in gatherings (0 for SMD, 1 for OR); squares and level lines speak to the point gauges and 95% CI for every examination; precious stones speak to pooled impact measure, with focus speaking to point gauge and width speaking to 95% CI. At long last, a meta-relapse examination was performed in view of consideration incorporated into the meta-investigation, thinking about the accompanying free factors:

age, BMI, size of study, BDI,term of infection, metabolic control (HbA1c); the needy variable was LogOR or LogSMD. Every single factual investigation was performed by STATA 12 (Stata Corporation, College Station, TX, USA).

### 4.4 FSFI(Female Sexual Function Index) Score

The FSFI survey created by Rosen *et al.*, comprises of 19 questions taking into account the multidimensional appraisal of female sexual capacities in connection to the time of the most recent a month. The file has been institutionalized and balanced (in numerous dialect adaptations, including Polish) to separating sexual dysfunctions in ladies matured 18–70 as per the present orders and suggestions of logical affiliations. The survey has archived believability,

affectability, unwavering quality, and inward consistency, and additionally strength and repeatability about perceiving issue of dyspareunia, sexual want, sexual excitement and climax. The inquiries introduced in the survey have been assembled into six spaces sexual desire, lubrication,sexual arousal, sexual satisfaction,orgasm and dyspareunia. The last outcomes are acquired independently for each of the subscales by summing up the basic focuses which are a piece of every one of the areas and contemplating the assigned coefficient; the outcomes are additionally gotten universally (worldwide evaluation). For the evaluation of the specific spaces, the point score which might be gotten ranges from 0 to 6.0 for sexual excitement, grease, dyspareunia and climax; from 1.2 to 6.0 for sexual want.

#### 4.4.1 International index of erectile function (IIEF)

IIEF is an exploration instrument for the examination of male sexual capacities. IIEF is a multidimensional instrument for 5-review self-evaluation of the considerable number of spaces of male sexual capacities in connection to the time of the most recent a month. This list has gotten institutionalization for separating sexual dysfunctions in men (matured 19– 82) as per universal agreement, and it is authoritatively accessible in 32 dialect forms, including Polish. It is described by high validity, dependability, affectability, and repeatability in the discovery of changes, affirmed in more than 50 clinical trial. The utilization of the IIEF in the first or the abbreviated variant (IIEF-5) is a suggested standard in the acknowledgment and appraisal of the erectile broke seriousness review. IIEF poll incorporates 15 things gathered into 5 aggregate spaces (subscales) depicting: I—erection (6 questions); II—climax (2 questions); III—sexual want (2 questions); IV—sex fulfilment (3 inquiries); and V—general sexual fulfilment (2 questions). An extra investigation of the subscale alluding to erection considers separating four conditions of seriousness of erection issue: absence of erection issue (26– 30 focuses); and gentle (17– 25 focuses),moderate(11–16 focuses), and severe(6–10 focuses) erection issue. An esteem equivalent to or lesser than 25 focuses (cut-off point) is consider as the event of clinically critical erectile issue. The Cronbach estimation of IIEF for our outcomes was assessed at the level of 0.930 for type 1 diabetes patients and 0.880 for controls, demonstrating high unwavering quality.

### 4.5 The Beck Depression Inventory (BDI)

The Beck Depression Inventory (BDI) is a 21-point screening tool use for assess the degree of Intensity of mood disorder symptoms (depression). The scale consists of 21 questions evaluated from 0 to 3 points. The results obtained in the BDI fluctuate in the range 0–63. A score below 10 points is considered as normal. Severe depression is suggested by

a score within the range above 24, moderate depression by 16–23, and Mild depression is within the range 10–15. BDI is a questionnaire standardized and validated for Polish conditions which has been numerously applied in studies assessing mood disorders; it possesses a high Cronbach reliability coefficient—0.92–0.93. The Cronbach  $\alpha$  value of BDI for our results was estimated at the level of 0.857 for men and 0.916 for women, showing high reliability.

## 5. Therapeutic Approaches

Currently, there is not any specific treatment available for female sexual dysfunction in diabetes mellitus. The most possible treatment of Female Sexual Dysfunction (FSD) would be related to, optimal diabetic control, psychotherapy and lifestyle changes. Recommendations from various health organizations suggested that adopting a healthy lifestyle and by treating depression can lower the incidence of FSD among females. A study by Giugliano *et al.*, Found a positive correlation between one's adherence to a Mediterranean diet and FSFI score in type 2 diabetic women. Women who were on the Mediterranean diet was found to have the lowest prevalence rate of sexual dysfunction and thereby improving their total FSFI score.

Moreover, maintaining a healthy lifestyle and achieving proper glycemic control may decrease the, endothelial dysfunction, insulin resistance and oxidative stress, resulting in a lower rate of sexual disorders. Furthermore, hormonal replacement therapy (HRT) in postmenopausal women has been approved by FDA to increase the vasodilatation by acting on NO mediated smooth muscle. Also, vaginal lubrication and vulvar engorgement can also be improved by inhibiting PDE5 receptors.

### 5.1 Some Additional Therapeutic Approach

Additionally, sexual function can be improved by using adequate amounts of estrogens in hormone replacement therapy. The mechanism involved in its acts by inducing the proliferation of the superficial layer of the vaginal mucosa, which results in improved vaginal pH, increased vaginal blood flow to enhance the lubrication need for sexual intercourse and elasticity. However, there are also certain studies that have recognized the function of testosterone in female sexual desire, orgasm, arousal and genital sensation. Testosterone seems to improve the sexual function of women, but due to its masculinised side effects, its long term use is not recommended for treating FSD. Psychotherapy is another essential aspect that needs to be treated properly for better sexual functions as depression is found to be the major risk factor in diabetic patients. Cognitive-behavioral psychotherapy is the proposed management for disorders of

desire or vaginismus. Additionally, couple therapy has also been great for partner intimacy. Women with orgasm or arousal disorders can benefit from the FDA approved Eros Clitoral therapy device. The device needs to place over the clitoris, which then produces a gentle vacuum that increases the blood flow to the female genital. This in turn enhances the sensitivity of genital of females. The Inters rim system is a method by which nerve get stimulated and was originally intended for the treatment of urine incontinence. But it is now tested for arousal or orgasm disorders.

## 6. Discussion

An increased prevalence of sexual disorders has been reported in patients with diabetes. The incidence of sexual dysfunction in patients with diabetes related with the duration and age of diabetes (Bağ *et al.*, 2017). Female sexual dysfunction has been known to have many causes which include interpersonal, social, psychological and biological factors. According to recent research studies, there is a significant correlation found between BMI and abdominal circumference of sexual dysfunction. The number of sexual dysfunction is found to be more in obese women with diabetes as compared to normal women.

Theoretically, sexual functioning is also affected by diabetic neuropathy, but clinical studies are quite contradictory. A study by Abu Ali *et al.*, Established a link of sexual dysfunction with that of retinopathy. Another study by B Erol *et al.*, indicates the impairment in the somatic sensory system due to deterioration of genital and extragenital sites in diabetic women. The study included the comparison of protogeometric values of genital sites in diabetic women with sexual impairment or without sexual impairment. Furthermore, the most affecting genital sites in the etiology of diabetes were found to be introits vagina and this site was found to have increased sensory threshold. Other affecting sites include the labiaminora, labia major, clitoris as well as vagina.

Besides this, Tyrer *et al.*, Study on 82 insulin-dependent diabetic women evaluated the effects of diabetes on vaginal lubrication. The results show that inadequate vaginal lubrication is present in 10% of diabetic subjects compared with 2% in the control group. Moreover, Meeking *et al.*, Studied sexual functioning in 161 diabetic subjects with both type 1 and type 2 DM. The study reported reducing sexual desire in nearly 64% of diabetic women. 70% of patients experienced loss of vaginal lubrication and 47% were having lesser sexual pleasure. Also, reduced vaginal sensation was found in 36% of patients. In a later study, it is evident from Schreiner-Engel *et al.*, That diabetes had a negative impact on sexual desire, lubrication sexual satisfaction and orgasmic capacity in both females and males. The results were similar

to most of the researches done so far. One possible drawback of the study was with the patients treated with thyroid disease subclinically hyperthyroid which may affect sexual function. However, if this was influencing the results, then it would show an even greater effect of diabetes on sexual health of both males and females. Doctors and pharmacists dealing with diabetic patients that they should be aware of possible presence of sexual dysfunction in female patients (Elyasi *et al.*, 2015).

## 7. Conclusion

Diabetes mellitus is a leading public health concern across worldwide, which are growing at a faster rate affecting half of the population due to age, urbanization, physical inactivity, obesity, etc. Diabetes also affects the cardiovascular system, psychological and sexual dysfunction to a great extent. The prevalence rate of erectile dysfunction approaches to 50% among males, but the data for females are less conclusive due to a small sample size. There are many risk factors that are responsible for sexual impairment in females out of which psychological issues are considered to be as the main determinant of female sexual dysfunction. Depression plays a major role in the pathogenesis of FSD and interpersonal relationships and may result in poor quality of life. Recent studies indicate that diabetic women are at higher risk for developing sexual dysfunction as compared to women without diabetes. The adoption of a healthy lifestyle and exercise can help in preventing and treating these disorders and also lowering the burden of chronic diseases. However, depression can be treated with some antidepressants. By adopting all of these can help improve sexual activity and well being of an individual.

## Conflict of Interest

The authors declare no potential conflicts of interest.

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