

Erectile dysfunction: the factors of erectile dysfunction among men diabetic mellitus type 2

Özlem Ceyhan*, Teame Russom Hadgu, Pınar Tekinsoy Kartın

Department of Internal Diseases Nursing, Erciyes University, Faculty of Health Sciences, Kayseri, Turkey

ABSTRACT

Erectile dysfunction (ED) as sexual dissatisfaction in diabetic mellitus type 2 (DM T2) in men has many psychological, social, and functional problems. However, it is often overlooked by health professionals and around half of male DM patients never discuss or share their problems with their caregivers. In addition, findings in regard to the significance of DM T2 in ED development are varying. Therefore, the objective of this review was to determine the associations between ED and DM T2 in men and to discriminate the determining factors of ED in DM T2 men. The current review used a solid body of research findings that indicate poorly controlled blood sugar, advancing age, duration from the diagnosis of DM, lipid panel irregularity, high body mass index (BMI), and unhealthy lifestyles as the major determining factors of ED in DM T2 in men. Therefore, health-care providers are expected to consider ED as a medical condition that requires regular screening of all DM T2 male patients, as it is routinely applying for other common complications of diabetes in medical practices, for early diagnosis, effective management, and complication prevention.

Key words: Diabetes mellitus T2, erectile dysfunction, factors of erectile dysfunction, men

INTRODUCTION

Diabetes mellitus (DM) is a lifelong disease that develops due to the failure of pancreatic islet cells to produce enough insulin or because of the body cells' insensitiveness to insulin hormone. Wild *et al.* estimated the prevalence of diabetes to be 2.8% of the population in 2000 or at least 171 million people worldwide suffers from diabetes, and it is estimated 366 million incidences by the year of 2030 globally.^[1] The marked increase in blood sugar level associated with diabetes gives rise to serious microvascular and macrovascular complications such as erectile dysfunction (ED) that prevents successful sexual performance, causes loss of vision resulted from retinopathy, nephropathy that leads to kidney failure, peripheral neuropathy that causes foot ulcers and amputations, and autonomic neuropathy that affects genitourinary, gastrointestinal, and cardiovascular system.^[2]

ED is a medical condition characterized by recurrent or persistent failure to achieve and/or maintain a penile erection sufficient for satisfactory sexual experience.^[3] ED can disturb normal life of diabetic patients in many ways; emotional distress, mental strain, poor interpersonal relationship, and interference with sexual life.^[4] The pathological process of ED in DM type 2 (DM T2) patients is multifactorial. These factors include tissue damage due to high accumulation of advanced glycation end-products (AGEs) and oxygen free radicals; neuropathy due to impaired nitric oxide (NO) synthesis, decreased and impaired cyclic guanosine monophosphate (cGMP) activity, and NO-dependent selective nitrergic nerve deterioration; and vasoconstriction due to increased endothelin receptor A binding sites and upregulated RhoA/Rho-kinase pathway.^[5]

ED is a common complication of DM; however, it is the most neglected medical condition by health professionals. Several studies^[6-8] demonstrated that the prevalence of ED in diabetic men fluctuates from 35% to 90% versus in an overall population (26%). Unfortunately, half of diabetic men never discuss or share their problems with their caregivers.^[9] Results from several reports in regard to ED and DM correlation provided inconsistent figures; some demonstrated diabetic men were 3 times at increased risk to have ED as compared with non-diabetic men,^[10,11] and others demonstrated nearly half of diabetic men were afflicted with some sort of sexual discomfort.^[9] In contrast, a national population-based findings showed no difference in ED prevalence among diabetic and non-diabetic patients.^[7,12] The role of glycemic level as a strong marker of reduced erectile function in DM T2 men is still debated. Few investigations indicated increased risk of ED in DM T2 patients with poorly controlled glycemic level^[13,14] while others reported no association between ED and glycemic control.^[8]

ED in general and in DM men specifically has many psychological and social problems. Several articles pointed out ED has negative implications over emotional status of an individual^[15,16] and the associated increase in antidepressant drugs usage.^[16] ED in the presence of normal sexual desire results in unwanted outcomes such as mental strain, poor interpersonal relationship, and interference with sexual activities.^[4] Therefore, the objective of this review is to determine the associations between ED and the determining factors in DM T2 in men.

Address for correspondence:

Dr. Özlem Ceyhan, Department of Internal Diseases Nursing, Erciyes University, Faculty of Health Sciences, Kayseri, Turkey. Phone: +90-352-207 66 66-28566. Fax: +90-352-437 92 81. E-mail: ozlemceyhan06@gmail.com

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FACTORS OF ED IN DIABETIC II MEN

The underlying cause of ED is multifactorial but generally classified into organic and psychogenic. Successful penile tumescence depends on exact balance between psychological, hormonal, neuronal, vascular, and cavernosal factors. Therefore, an alteration in any one or combination of these factors may account for the development of ED. It has been known that ED secondary to DM is typically psychogenic in origin. However, other organic factors that amplify the problem in DM T2 patients are also described. Recent studies clearly explained that poorly controlled blood sugar (hyperglycemia),^[13,14] advanced age,^[7,17-22] longer duration of the disease,^[7,20,21] lipid panel abnormalities,^[23,24] high body mass index (BMI),^[15,25,26] and unhealthy lifestyle^[17,18,27] are the independent elements that are apparent to impart ED.

HYPERGLYCEMIA

Hyperglycemia causes microangiopathy and macroangiopathy in DM patients through the production of AGEs. The AGEs, which are products of non-enzymatic reactions between glucose, lipids, proteins, or nucleic acids, have been mentioned as initiators of the mechanism of vascular damage.^[28] The combination of AGEs with vascular collagen leads to vascular alternations such as thickening, loss of elasticity, and endothelial dysfunction.^[29] It is also underscored that AGEs contribute ED by generating oxygen free radicals which are responsible for oxidative cell damage and reduced secretion of NO, resulting in decreased cGMP, and impaired cavernosal smooth muscle relaxation. Moreover, AGEs cause potassium channels modification permitting intracellular calcium release that ultimately result in smooth muscle relaxation.^[28,30] Anwar *et al.* and Kendrick *et al.* described the importance of increased blood sugar in ED development.^[15,16] In addition, Weinberg *et al.* and Aviva studied out a linear association between ED and worse erectile function score in patients with high-level hemoglobin A1c (HbA1c). However, few findings^[8] did not show any correlation between HbA1c and ED in diabetic T2 men. Previously conducted study aimed at assessing the relationship between uncontrolled hyperglycemia and ED found adverse erectile function score as the HbA1c level rises.^[31] Further study identified elevated level in random blood sugar, fasting blood sugar, and postprandial blood sugar are common findings in patients impacted with ED compared to these without ED, reflecting the association of worse HbA1c levels and ED.^[15] Romeo *et al.*^[31] underscored tight blood sugar control maintains satisfactory erectile performance. Consistent to Romeo *et al.* findings, studies conducted in developed countries^[20,32] reported low prevalence as compared to those done in developing world due to the fact that in developed countries DM may be early detected and blood sugar may be well controlled, and therefore, ED is prevented.

Age

The prevalence and severity of ED increase with advancing age.^[12,33-35] The factors that underlie ED in older patients are numerous and no single etiology is at the forefront. Some organic conditions such as DM are often blamed as a primary factors of ED by altering normal male sexual interest and function in older patients.^[35-38] Another crucial factor that involves in the development of age-related ED is decreased endocrine function in the production of androgen hormone.^[39,40] Moreover, elder patients are more prone to psychological problems such as

depression that ultimately expose them to ED.^[12,41,42] It has been long known that age in DM T2 is an independent predictor of ED.^[8,43,44] However, it is worth to note that though ED is generally common in older people, it befalls in any age between 20 and 98 years.^[17-19] Several articles^[12] described that ED is prevalent among older diabetic men. Other investigations identified an increment in prevalence and severity of ED as the patient age progresses^[6,7,12,15,21] and discovered that the increment was striking between the ages of 41 and 80 years. A study conducted by Mutagaywa *et al.*^[6] showed age was correlated significantly with ED, particularly in these 60 and above years old that had nearly 15 times higher risk for ED.

Duration and Course of the Disease

As far as the duration of DM is concerned, patients with DM for longer period of time are at high risk to suffer from ED. ED occurred with increasing prevalence from 56% in men with diabetes mellitus for <5 years to 72% in those with DM for more than 20 years.^[7,12,21] Moreover, longer duration of the disease and presence of other complications such as retinopathy and neuropathy increase the risk of ED in diabetic patients.^[7,12,21]

Dyslipidemia

Abnormal blood cholesterol, particularly elevation in low-density lipoprotein (LDL) and reduction in high-density lipoprotein (HDL) levels, is linked to high risk of ED. Oxidized LDL is believed to compromise sexual function through modifying the endothelial and smooth muscle cells of the penis.^[45] A wide body of study also showed high LDL correlated to decreased NO and reduced bioavailability in penile and vascular tissue.^[46] A comparison study among DM patients with and without ED found a significant higher values of serum LDL, very LDL (VLDL), and triglycerides in patients with ED.^[15] Furthermore, evidence demonstrated the relationship between atherosclerosis and ED, which explains the association between ED and vascular changes resulted from lipid abnormalities.^[23] A number of lines of investigations^[23,24] determined lipid panel aberration is an independent element of ED^[47] revealed that the elevated proportion of triglyceride to HDL was significantly associated with an increased risk of ED.

Behavioral and Dietary Changes

Developments have been producing behavioral modifications that in turn cause assimilation of unhealthy lifestyles, which are considered to be the principal culprits for various medical conditions such as diabetes T2 and obesity. Obesity is a condition characterized by increased production of proinflammatory elements such as cytokines, adipokinase, free fatty acids, and estrogen. The increase of these proinflammatory elements is often mentioned as a central risk factor of ED by creating vascular endothelial damage and androgen deficiency.^[48] The aromatase enzyme, which is found abundantly in adipose tissue, is responsible for decreased androgen and ED through conversion of testosterone to estradiol. Other studies^[8,25] also revealed further evidence that obesity is strongly related to reduced Leydig cells receptiveness to exogenous gonadotropin stimulation. Several reports have showed an association between high BMI, defined as 25 kg/m² and above, and ED^[15,25,26] though a few studies disregarded this connection.^[8,49]

The critical roles of proper lifestyles, such as physical exercise and good diet, in both vascular NO production and effective

erectile tumescence have been established.^[50] Even though the mechanism is not explained explicitly, it has been highlighted that appropriate lifestyle habits may prevent ED occurrence or reduce the burden of sexual dysfunction by decreasing or preventing vascular inflammation.^[43] Several investigations supported the importance of healthy lifestyles in sexual function and determined the correlation of unhealthy lifestyles and ED. These studies^[17,18,27] discovered the direct association of ED with alcohol^[27] and with tobacco consumption.^[17,18] Wu *et al.* and Banks *et al.* also reported the significant connection between physical activity and improved sexual function.^[17,18] Consistent with the above-mentioned studies, Esposito *et al.* demonstrated modifications in lifestyle was favorable for improving sexual performance in one-third of obese men impacted with erectile impairment compared to baseline status.^[43]

CONCLUSION

This review is dedicated to summarize available evidence concerning the relationship between ED and various risk factors in DM T2 male patients. It is clearly established that ED is a common sexual abnormality that occurs in men diagnosed with DM T2 compared to the general population. As it is the most underreported medical condition, it necessitates regular screening in routine medical practices, as it is applying for other common chronic complications of DM, for early diagnosis, effective management, and complication prevention. Persistent hyperglycemia, dyslipidemia, obesity, and unhealthy lifestyles are now already acknowledged as the main factors of ED. Therefore, this review is strongly recommending that the health personals need to encourage their patients to perform regular physical exercise and to practice healthy lifestyles including proper diet. In addition, this paper warranted patients with DM to control and check their blood cholesterol levels regularly. Fortunately, physical activity is nowadays considered as a protective and therapeutic measure for ED. Consequently, a glycemic control coupled with lifestyle adjustments is essential in preventing ED or impending severity of ED.

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