

Review

Erectile Dysfunction in Type 2 Diabetes – A Short Review

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ABSTRACT

Erectile dysfunction (ED) is a problem of getting or keeping an erection hard enough to achieve satisfactory sexual performance. The global prevalence of ED is 3–76.5%. ED constitutes a large burden on society given its high prevalence and impact on quality of life. Diabetes is a common cause of organic ED. Prevalence of ED in diabetes rate range from 35 % to 85% depending on the study, versus 26% in general population. ED occurs 10-15 years earlier in men with diabetes than it does in sex-matched counterparts without diabetes. The pathophysiology of diabetes-induced erectile dysfunction is multi-factorial. It is related to age, duration of diabetes, body mass index and diabetic complications.

KEYWORDS: Erectile dysfunction, impotence, sexual inadequacy, BM

INTRODUCTION

Erectile dysfunction (ED) also referred to as “impotence,” is a problem of not getting or keeping an erection hard enough for satisfactory sexual performance. It is defined as the persistent inability to achieve and/or maintain penile erection sufficient for satisfactory sexual performance¹.

Age is a strong determinant of occurrence of ED and epidemiological studies indicate a strong relationship between ED and advancing age. While men aged 50–59 years have a 3.6 times higher risk of developing ED as compared to those aged 18–29 years, the risk is even higher (6–7 times) among males older than 70 years².

The causes of ED are numerous but generally fall into two categories: organic or psychogenic. The organic causes can be subdivided into five categories: vascular, traumatic/post-surgical, neurological, endocrinologic and drug-induced¹.

Diabetes is a common cause of organic ED. Both vascular and neurologic mechanisms are implicated for ED in people with diabetes. Vascular includes atherosclerosis of penile and pudendal arteries leading to decreased blood supply to corpus cavernosum and neurological mechanisms involves autonomic neuropathy.

Studies of ED suggest that its prevalence in men with diabetes ranges from 35–75% versus 26% in general population and the onset of ED occurs 10–15 years earlier

in men with diabetes than it does in sex- matched counterparts without diabetes³.

The wide variation in the prevalence of disease is due to use of different definitions in different populations, different diagnostic tools and varied study designs. Precise percentages are difficult to estimate because many men fail to seek help from a doctor about this problem because of embarrassment and being a taboo topic among society. Thus, despite ample evidence that ED is among the major complications in Diabetes mellitus in men, its presence remains poorly evaluated in the routine clinical practice³.

Diabetic men are likely to have comorbidities like hypertension, obesity, metabolic syndrome, atherogenic dyslipidaemia, coronary artery diseases, etc. and each of them could be an independent risk factor in pathogenesis of ED.

The mechanisms involved in the various diseases that lead to erectile disorder include general endothelial dysfunction or dysfunction of the penile endothelium specifically, atherosclerosis, dysregulation of nitric oxide synthase, decrease of nitric oxide, low testosterone levels due to hyperprolactinemia-influenced changes in the hypothalamic–pituitary axis, vasculopathy, autonomic neuropathy, and disruption of neural proerectile processes⁴. The literature reveals that emergence and severity of ED are related with markers and mediators of inflammation and endothelial dysfunction. However, no specific marker has been identified so far that could identify this⁵.

Diabetic neuropathy can similarly cause autonomic and somatic neural disorders which are of importance for erection. Besides diabetes can bring about disorders in relaxation of cavernous smooth muscles as a result of the nitric acid produced from endothelium, which may be a side effect of glycosylated products^{2,3}.

Recent evidence indicates that men with diabetes may be in growing danger of reduction of testosterone levels (hypogonadism) in addition to problems related to arteries and nerves supporting the penis^{4,5}. Although an exact mechanism of this effect has not been completely identified, hypogonadism in such men may indirectly mitigate levels of pituitary hormones, responsible for stimulating testosterone production in testicles⁶. Low levels of testosterone may also lead to loss of sex drive or cause ED either directly or indirectly⁷.

Proper sexual functioning is one of the most important components of quality of life⁸. The presence of ED is associated with grave psychosocial and clinical consequences including poor quality of life and depression⁹. However, it should be noted that ED is the most treatable complication of diabetes; over 95% of cases can be successfully treated¹⁰.

The prevalence rates of sex drive, orgasmic disorders, and ejaculation problems have not been exactly determined. ED occurs in a considerable number of diabetic men, and its incidence estimation is very high in different studies, ranging from 20 to 71%. ED significantly affects quality of life in men

with diabetes¹¹.

The magnitude of erectile dysfunction is usually underestimated in many developing countries because of several reasons. Firstly, ED is not a life- threatening condition, thus not reported. Secondly, it is associated with stigma attached to the problem, men with the problem rarely seeking help. There is also the problem of early detection and management of factors responsible for the development of erectile dysfunction¹².

Erectile Dysfunction (ED)

ED is defined as the persistent inability to achieve or maintain penile erection for successful sexual intercourse causing decreased quality of life in men^{13,14}. ED is detected by having male patients' complete standardized questionnaires investigating their sexual function. One of the most practical questionnaires that is administered is the International Index of Erectile Function (IIEF)⁵ which consists of items 5, 15, 4, 2 and 7 from the full scale IIEF 15; a sum score of 21 or less indicates the presence of ED¹⁵.

Epidemiology of Diabetic Erectile Dysfunction

The overall prevalence of ED has been reported to be 16%–25% in the general population depending on the cohort of study and the definition of ED being applied¹⁶. The prevalence of ED in diabetes has been reported to be 60%–80% in many studies. Age is a strong determinant of occurrence of ED and epidemiological studies indicate a strong relationship between ED and advancing age. While men aged 50–59 years have a 3.6 times higher risk of developing ED as compared to those aged 18–29 years, the risk is even higher (6–7 times) among males older than 70 years³. Age related hormonal, metabolic and inflammatory, as well as increased prevalence of other risk factors for ED in the older population may be responsible for increased prevalence. When ED occurs in younger males, it is associated with a greater increase in the risk of future cardiac events as compared to its first detection in older males¹⁷. Therefore, younger men with early onset ED may be the ideal candidates for intensive CV risk factor screening and medical interventions.

Etiology of Erectile Dysfunction in Diabetes

The causes of ED are numerous but fall into two major categories: organic and psychogenic ED in diabetic men is primarily one of organic origin rather than psychogenic. ED occurs insidiously and is progressive. It is not always a late complication of the disease but can occur at any time. The organic causes fall into four principle categories: neurogenic, vascular, endocrinologic, and drug induced [Table 1].

Table 1: Etiology of Erectile Dysfunction in Diabetes

Organic
<i>-Neurogenic</i>
Peripheral/autonomic neuropathy
<i>-Vascular</i>
Atherosclerotic vascular disease
Veno-occlusive dysfunction
<i>-Endocrinologic</i>
Adrenal insufficiency
Hypogonadism
Hyperprolactinemia
Thyroid disorders
<i>-Drug induced</i>
Beta-blockers
Thiazide diuretics
Mechlodypa
Clonidine
Spironolactone
Cimetidine
Flutamine
Alcohol
Methadone
Heroin
Cocaine
Psychiatric drugs
Psychogenic
Performance anxiety
Depression
Psychological stress
Chronic illness
Relationship problems

Neurogenic Impotence

Erectile dysfunction is more common in diabetic men with peripheral and autonomic neuropathy than men without. Studies have also shown that the development of impotence is associated with the appearance of neuropathy. Indirect testing has shown some correlation between ED and autonomic neuropathy. Two such examples are the presence of bladder areflexia and bladder or bowel dysfunction, which is also more common in patients with diabetes compared to age-matched potent patients¹⁸. Studies have also documented abnormal vascular reflexes as noted by single beat-to-beat variation in diabetic patients with impotence¹⁹. Intracavernosal electromyographic needles or electrodes on the surface of the penile shaft can be used in direct testing of the autonomic innervations. The recorded electrical activity identifies the neurologic abnormalities at the level of the autonomic neuron corporal smooth muscle interface. Diabetic men with impotence have potentials that are either of short duration, high amplitude, or of low amplitude²⁰.

Perineal electromyography, sacral latency testing, dorsal nerve somatosensory-evoked potential evaluation, and vibration perception sensitivity testing can all be used to detect neuropathy in the sensory afferent nerves from the penile skin and the motor efferent nerves to the perineal skeletal musculature. An abnormal result in these tests suggests that there may be coexistence of the autonomic neuropathy in the corpora cavernosa.

Other research has found that diabetics have diminished levels of norepinephrine and acetylcholinesterase tissue levels in the corpus cavernosum²¹ and have decreased autonomic nerve-mediated relaxation of the penile smooth muscle²². These studies

demonstrated that the longer the duration of diabetes, the less the ability of the cholinergic nerves to synthesize acetylcholine, supporting the notion that long-standing diabetics are more likely to present with autonomic neuropathy, and therefore ED. Diabetes also impairs relaxation of the corpus cavernosum smooth muscle to nitric oxide, decreases the synthesis and activity of nitric oxide synthase, and decreases the efficacy of nitric oxide secondary to the oxidizing conditions caused by the advanced glycation end products²³.

Vasculogenic Impotence

Diabetes has been associated with corpus cavernosum smooth muscle changes, such as increased connective tissue synthesis and atrophy of smooth muscle within the corpus cavernosum bodies in humans and animal models. These structural changes are correlated with an increased incidence of veno-occlusive dysfunction and erectile failure consistent with peripheral vascular disease seen in diabetes. Diabetes is associated with intimal, medial, and luminal changes within the artery leading to atherosclerosis. Atherosclerosis can affect the penile and pudendal arteries limiting blood flow to the corpus cavernosum. Among the men with significant peripheral arterial disease, 40% to 50% complain of some degree of erectile dysfunction²⁴. Diabetic men may also have other cardiovascular risk factors, such as smoking, hypertension, and hyperlipidemia that cause an increased development of atherosclerosis in the cavernous arteries. Many invasive and non invasive tests have been developed to measure cavernosal artery systolic occlusion pressure and cavernosal arterial flow in both the erect and flaccid state. It has been found that vascular pathology in ED is related to arterial inflow, penile microvasculature, lacunar space endothelium, and penile fibroelastic frame¹⁸.

Erectile failure can also occur secondary to venous insufficiency or veno-occlusive mechanisms. Direct injury to the sinusoidal endothelium and smooth musculature limits the ability of the smooth muscle to relax within the corpora, resulting in lack of sinusoidal dilatation. Any factor affecting the fibroelastic frame and causing inability to expand the trabeculae against the tunica albuginea and compress the subtunical venules can result in incomplete venous occlusion and subsequent venous leakage and erectile failure. The combination of low arterial flow and loss of compliance of the cavernous trabeculae causing excessive outflow of lacunar blood results in decreased penile rigidity and a diminished ability to sustain an erection. Diabetic men have an abnormal diffuse pattern of venous drainage as documented by pharmacocavernosography¹⁸.

Endocrinologic Impotence

Hormonal causes are related to ED. Hypogonadism, hyper or hypothyroidism, adrenal insufficiency, or excessive levels of adrenal corticosteroids and prolactin may all be associated with ED in a diabetic man²⁵.

Drug-induced Impotence

Both prescription and over-the-counter medications have been shown to be the cause of erectile problems in as many as 25% of the general population with ED²⁶. Patients with diabetes also have other cardiovascular conditions and are normally on multiple medications in order to control the above problems. Antihypertensive medications such as spironolactone, thiazides, methyldopa, clonidine, and beta-blockers all cause impotence. Antihypertensive medications may cause ED by drug-specific effects or by decreasing systolic blood pressure and compounding the already low intracavernosal penile pressure.

Even non prescription medications such as antihistamines or decongestants can affect erectile function. Medications such as cimetidine and flutamine may block the peripheral androgen receptor²⁶. Most psychotropic drugs can increase prolactin levels or decrease testosterone levels and cause ED. Alcohol, methadone, heroin, and cocaine can also ED.

Pathophysiology of Erectile Dysfunction in Diabetes

Diabetes causes several changes in the neuromuscular system, all of which can contribute to ED. In men with diabetes, there is good evidence that ED is due to failure of nitric oxide (NO)-induced smooth muscle relaxation due to both autonomic neuropathy endothelium dysfunction²⁷. The endothelium which is the innermost single layer of our vascular bed and also considered to be the brain of the vascular system has an important role in vascular homeostasis. It has many sensors and mediators. It secretes numerous mediators such as NO, prostacyclin and endothelin that regulate vascular tone, platelet activity and coagulation factors but also influence vascular inflammation and cell migration.

Besides hyperglycaemia, hypertension, dyslipidaemia, obesity and smoking also causes endothelial dysfunction. Endothelial dysfunction is a single most predictor of atherosclerosis, coronary artery disease and stroke.

The dynamics of erection in men is 3-fold. First, it is the neurologically mediated arterial inflow, second, there is relaxation of the corpora spongiosa smooth muscles to allow the blood to flow in the penile vasculature, and finally, there is venous obstruction which allows the blood to remain in the penile vasculature and let the penis remain erect. Any disturbance in any of the above three stages can result in ED. The vascular endothelium in the penile vasculature produces Endothelial NO synthase eNOS, and the neuronal tissues produce neuronal NO synthase nNOS. Both these synthases transport, the NO in the corpora spongiosa smooth muscle and convert the Guanosine triphosphate into cyclic guanosine monophosphate (cGMP), with the help of an enzyme guanylate cyclase. This cyclic GMP relaxes the smooth muscle and allows the blood to flow in. cGMP also potentiates Protein kinase G which inhibits calcium conduction and opens up potassium ion channels which further relaxes the smooth

muscles. The cGMP soon hydrolyses into guanosine monophosphate GMP with the help of an enzyme Phosphodiesterase 5 which is present in the penile smooth muscles and the smooth muscle contracts and leads to detumescence. Hence for proper erection, one needs to have basically a good functional endothelium which produce good amount of eNOS and also nNOS, we also need NO, which we all are aware is the chemical currency which initiates the erectogenic mechanism and also reduces as we age. There should be adequate guanylate cyclase activators and stimulators, cGMP in the more bioavailable form to keep the penile smooth muscle in a relaxed state, and something to block the phosphodiesterase type 5 (PDE5) like PDE5 inhibitors to sustain the erection²⁸.

Rho A/Rho-Kinase pathway is the key pathway which inhibits relaxation of the penile smooth muscle vasculature. Rho-associated protein kinase (ROCK) is a kinase which induces the formation of stress fibers and focal adhesions by phosphorylating myosin light chain. Due to this phosphorylation, the actin binding of myosin II and contractility increases. Protein kinase C and ROCK are involved in regulating calcium ion intake and these calcium ions, in turn, stimulate a myosin light chain kinase forcing contraction. Hence, inhibition of these pathways will help in relaxation of the cavernous smooth muscle and produce a sustained erection.

Diabetic neuropathy is the most common diabetic complication, affecting 10%–90% of people with diabetes, depending on the diagnostic criteria and the age and duration of DM. Some studies showed an earlier development of DN in men, compared to women. Neuropathy is a very important pathogenetic factor in the development of ED. Because DN affects all levels of the neural system, disturbances could happen at all levels in the complex process of erection from the central initiation to the penis. In the literature, much more attention is paid to the vascular aspects of ED compared to the neural ones.

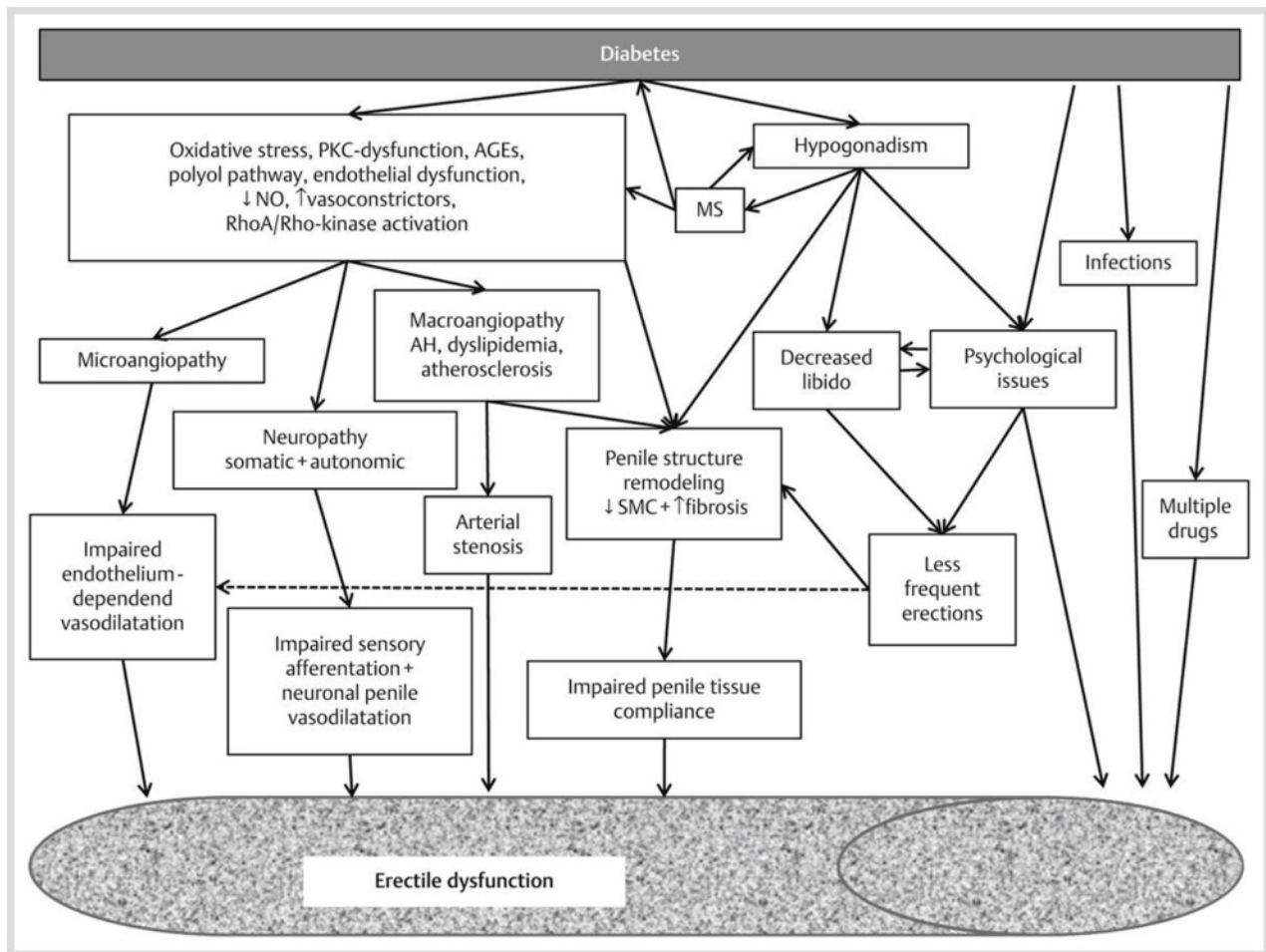


Figure 1: Pathogenesis of DED.

AGEs – advanced glycation end products; PKC – protein kinase C; NO – nitric oxide; MS – metabolic syndrome; SMS – smooth muscle cells; AH – arterial hypertension²⁹

Diagnosis of Erectile Dysfunction

The diagnosis of ED starts with the patient's interview. When the anamnesis suggests the presence of ED, the administration of a validated questionnaire can be useful to objectively assess its presence and severity. In this regard, the International Index of Erectile Function (IIEF) represents a useful and validated tool³⁰. In patients with DM referred for ED, the diagnostic flow-chart should include the evaluation of both TT serum levels and penile echo-color Doppler ultrasound (PCDU) examination after intracavernous injection (ICI).

According to the Endocrine Society, the diagnosis of hypogonadism can be made in the case of TT serum levels below the cut-off of 264 ng/dL (9.2 nmol/L) in at least two different measurements³¹. However, it must be considered that DM has been listed among the conditions that lower either SHBG or TT below the normal range. In these cases, the clinician has to consider that a value of free T < 64 pg/mL (220 pmol/L) confirms the presence of hypogonadism³¹.

PCDU examination after ICI with prostaglandin (Pg) E1 or derivatives (e.g., alprostadil) is a second-line diagnostic test in patients with ED. Despite the lack of standardization of sampling location³² and cut-off values, a major effort has been made over the decades to identify PCDU waveforms predicting arterial or venous ED.³³ The PCDU allows the measurement of the peak systolic velocity (PSV) and end-diastolic velocity (EDV) of the cavernous arteries in response to ICI drug administration (most often alprostadil). Both of these parameters describe the characteristics of blood flow in the cavernous arteries during erection and are currently used for the diagnosis of vasculogenic ED. Consequently, a restriction of the lumen of the cavernous artery (e.g., due to an arterial plaque or to a greater media-intima thickness) causes arterial blood flow to slow down and the PSV value decreases accordingly. In this regard, a PSV cut-off value between 25 and 35 cm/s is used as the cut-off. Conversely, in the case of dysfunction of the veno-occlusive mechanism (blood is drained too quickly from the dorsal vein of the penis), the EDV increases (>5 cm/s)³³. In particular, a retrospective study of up to 300 patients with ED followed for 10 years reported that morphological abnormalities of the cavernous arteries (e.g., stenosis, atherosclerotic plaques, and intima-media thickness) were closely associated with cardiovascular disease. In fact, the risk for MACE was three times higher in patients with morphological abnormalities of the cavernous arteries than in those with normal morphology³⁴. Once again, this evidence highlights the crucial importance of correct diagnosis and management of ED, given its consequences on cardiovascular health, especially in patients with DM.

Prevalence and Risk Factors for ED in Diabetes

In a multicentre study, the prevalence and risk factors for developing erectile dysfunction were investigated by Cho et al. in 1312 Korean men with diabetes. They used the modified International Index for Erectile Function-5 criteria to identify mild, moderate and complete ED. The mean age and median

duration of diabetes were 53.8 ± 6.65 and 6 years (range 1–43), respectively. The mean HbA1c and fasting glucose levels were $7.9 \pm 1.65\%$ and 8.6 ± 2.82 mmol/l, respectively. The overall prevalence of mild, moderate, complete ED and all ED (mild-to-complete) were 20.1, 19.5, 25.8 and 65.4%, respectively. ED was more common with age, reaching 79.3% in men aged > 60 years. Subjects aged > 60 years and with a duration of diabetes > 10 years were at greatest risk for all ED (OR = 10.4, 95% CI 5.8–18.5, $P < 0.001$) and complete ED (OR = 13.2, 95% CI 7.3–23.9, $P < 0.001$) when compared with the reference group (age 40–50 years with duration < 6 years). Age, duration of diabetes, HbA1c, insulin use, neuropathy and macrovascular complications were positively associated with ED, but alcohol consumption and exercise habits were negatively associated³⁵.

A study to determine the prevalence of and risk factors for erectile dysfunction in men newly diagnosed with type 2 diabetes mellitus (DM) was conducted by Hunayan et al.³⁶. All consecutive samples of men newly diagnosed with type 2 DM attending the diabetes centre in the capital of Kuwait were included in the study. Of 323 men with newly diagnosed type 2 DM, 31% had ED; comparing potent men and men with ED, there were statistically significant differences for smoking, duration of smoking, hypertension, education level, body mass index and serum glycosylated haemoglobin level. Among these, age was the most important risk factor identified by multivariate logistic regression. Study concluded that about a third of men with newly diagnosed type 2 DM had ED; this was associated with many variables, but most notably with age at presentation³⁶.

A cross-sectional study was planned to assess cardiovascular risk of DM2 men with ED by Cleveringa et al. During annual check-up, the practice nurse asked 1823 DM2 men: “Do you have erection problems? Yes/ No.” ED prevalence rate was calculated. The prevalence of ED in DM2 patients was 41.3%. When categorizing by age, following prevalence was found: 40 years, 3.0%; 40–49 years, 19.2%; 50–59 years, 34.1%; 60–69 years, 45.7%; 70–79 years, 51.5%; and N80 years, 49.4%. There was no independent association between ED and HCVD [adjusted OR, 1.2 (95% CI, 0.9–1.5)]. The 10-year UKPDS CHD risk difference between men with and without ED was 5.9% (95% CI, 3.2–8.7), but after adjustment for age, this association disappeared [adjusted risk difference, 0.6% (95% CI, –1.5 to 2.7)]. The ED prevalence rate assessed by a single question was comparable to that assessed by questionnaires. ED neither did independently relate to patients' cardiovascular history nor to cardiovascular risk³⁷.

Awad et al. tried to explore the role of glycemic control, and its correlation to sexual function in one hundred patients with diabetes type2. The selected patients were evaluated for sexual function by asking the patients to complete the abridged form of the International Index of Erectile Function (IIEF). Results indicated that in the group with good glycemic control, the greater percentage of patients had good potency (53%), whereas a lesser percentage had fair potency (20%) and poor

potency (26%). The level of HbA1c is significantly higher with declining degrees of potency (P -value=0.003). Also, there is an association between potency degree and glycemic control ($P=0.002$). Study concluded that glycemic control is independently and inversely associated with ED in men with diabetes³⁸.

The prevalence of ED in Chinese men with type 2 diabetes mellitus was investigated by Yang et al.³⁹. They also evaluated the efficacy and safety of sildenafil citrate in these patients. Patients from 42 outpatient diabetes clinics with type 2 diabetes mellitus and ED as defined by the International Index of Erectile Function (IIEF)-5 were studied. Participants with ED received three doses (100mg each) of sildenafil citrate for use over 3 months. Efficacy of sildenafil citrate was assessed using the IIEF-5 and the Global Efficacy Questionnaire (GEQ). A total of 5477 participants were evaluated, and 75.2% had ED. Age, duration of diabetes and glycosylated hemoglobin (HbA1c) 46.5% were independently and significantly associated with the presence and degree of ED. Patients who received pharmacotherapy reported significant improvements. The rate of erections as determined by the GEQ was also significantly improved following treatment. ED is a common complication in Chinese men with type 2 diabetes mellitus, and certain risk factors are associated with the presence of ED and severity³⁹.

A study was designed by Giugliano et al. to evaluate the prevalence and correlates of ED in a population of diabetic men⁴⁰. Consecutive patients with type 2 diabetes were recruited among outpatients regularly attending Diabetes Clinics. A total of 555 (90.8%) of the 611 men were analyzed in this study. ED was assessed by the IIEF-5 instrument. Approximately, 6 in 10 men in their sample of diabetic men had varying degrees of erectile dysfunction: mild 9%, mild to moderate 11.2%, moderate 16.9% and severe 22.9%. The prevalence of severe ED increased with age. Higher hemoglobin A1c (HbA1c) levels were associated with ED; similarly, the presence of metabolic syndrome, hypertension, atherogenic dyslipidemia (low levels of HDL-cholesterol and high levels of triglycerides) and depression was associated with ED. Physical activity was protective of ED; men with higher levels of physical activity were 10% less likely to have ED as compared with those with the lowest level. In conclusion, among subjects with type 2 diabetes glycemic control and other metabolic covariates were associated with ED risk, whereas higher level of physical activity was protective. These results encourage the implementation of current medical guidelines that place intensive lifestyle changes as the first step of the management of type 2 diabetes⁴⁰.

A study was undertaken to find out prevalence of erectile dysfunction in Type-2 diabetic patients and its association with various risk factors. Fifty Type-2 diabetic patients fulfilling the inclusion criteria were recruited amongst outpatients regularly attending OPD of MGMCH, Jaipur. They were assessed for erectile dysfunction using International Index of Erectile Dysfunction (IIEF-5). The prevalence of erectile dysfunction

in type-2 diabetics was very high (78%). Mild, moderate and severe ED was present in 6, 36 and 36% patients respectively. Prevalence of ED was found to increase with age, duration of diabetes, fasting blood sugar level, HbA1c level, hypertension and dyslipidaemia. A definite correlation between various complications and prevalence of erectile dysfunction was found⁴¹.

A cross-sectional hospital based study was conducted among 312 diabetic patients attending diabetic clinic at Muhimbili National Hospital between May and December 2011 to determine the prevalence of ED and associated risk factors. More than half (55.1%) of the patients were found to have some form of ED (12.8% had mild dysfunction, 11.5% moderate and 27.9% severe dysfunction). The severity of ED was correlated with increased age. Multivariate logistic regression revealed that ED was significantly predicted by old age (odds ratio (OR) = 7.1, 95% CI 1.2-40.7), evidence of peripheral neuropathy (OR) =5.9, 95% CI 1.6-21.3), and evidence of peripheral vascular disease (OR =2.5, 95% CI 1.2-5.3). Also longer duration of DM was marginally associated with ED ($p=0.056$). Patients with ED were also more likely to suffer other sexual domains ($p<0.001$). No lifestyle factor was associated with ED. The prevalence of ED was high among DM patients¹³. It was recommended that early diagnosis and detection of DM and its complications, and adherence to treatment to prevent complications should be implemented¹³.

The prevalence and risk factors for ED among men with type 2 DM in a Nigerian tertiary healthcare centre was conducted by Ugwu et al.⁴². This was a cross-sectional study of 160 male type 2 DM adults, aged 30–70 years, attending a tertiary healthcare clinic. Demographic and relevant clinical information was documented. Erectile function was assessed using an abridged version of the International Index of Erectile Function (IIEF-5). 152 (95%) patients with a mean age of 60.3 ± 8.8 years completed the study. 71.1% had varying degrees of ED, while 58.3% suffered from a moderate-to-severe form. Independent predictors of ED were longer duration of DM, PAD, autonomic neuropathy, poor glycemic control, and testosterone deficiency. Study concluded that the prevalence of ED and its severe forms was high in this patient population. Poor glycemic control and testosterone deficiency were the strongest risk factors for ED, making it possibly a preventable condition⁴².

Anwar et al. assessed the prevalence of ED among diabetic men and to compare the DM patients with severe ED with those having a normal erection on various sociodemographic and clinical correlates. In the study, a total of 184 diabetic patients were assessed, and 67.4% (124/184) of the participants were found to be suffering from ED and 42.4% from severe ED. Those with severe ED were found to have poor glycemic control, worse lipid profile, higher body mass index, later age of onset, and longer duration of untreated diabetes as compared to non-ED patients. ED patients also scored higher on depression rating scale, had poorer general health and quality of life (QOL). Early attention to ED in diabetic patients can improve general health and QOL of the sufferers. Author

concluded that DM patients with poor glycemic control and advanced age have a higher propensity of developing severe ED, which further deteriorates the already compromised health & QOL⁴³.

A systematic review and meta-analysis to assess the relative prevalence of erectile dysfunction in diabetes searching major databases from inception to November 2016 for studies reporting erectile dysfunction in men with Type 1 and Type 2 diabetes mellitus was done by Kouidrat et al. They conducted a meta-analysis of the prevalence [and 95% confidence intervals (95% CIs)] of erectile dysfunction in diabetes compared with healthy controls, calculating the relative odds ratios (ORs) and 95% CIs. A random effect model was applied. From 3747 initial hits, 145 studies were included representing 88 577 men (age: 55.8±7.9 years). The prevalence of erectile dysfunction in diabetes overall was 52.5% (95% CI, 48.8 to 56.2) after adjusting for publication bias, and 37.5%, 66.3% and 57.7% in Type 1, Type 2 and both types of diabetes, respectively (P for interaction < 0.0001). The prevalence of erectile dysfunction was highest in studies using the Sexual Health Inventory for Men (82.2%, 17 studies, P for interaction < 0.0001). Studies with a higher percentage of people with hypertension moderated the results (beta = 0.03; 95% CI, 0.008 to 0.040; P = 0.003; R2 = 0.00). Compared to healthy controls (n = 5385) men with diabetes (n = 863) were at increased odds of having erectile dysfunction (OR 3.62; 95% CI, 2.53 to 5.16; P < 0.0001; I2 = 67%, k = 8). Erectile dysfunction is common in diabetes, affecting more than half of men with the condition and with prevalence odds of approximately 3.5 times more than controls. Findings suggested that screening and appropriate intervention for men with erectile dysfunction is warranted⁴⁴.

An epidemiological study of ED in men with DM in a primary health care was done by Tridiantari et al. There were 122 diabetic men who were all included in the study. The results showed that the prevalence of diabetic men with ED was 84.4%. Most men with ED had age of ≥46 years (91.0%), experienced work stress (88.5%), had low physical activity (93.1%), had obesity (88.0%) of which 86.3% had central obesity, smoking (84.6%), had DM >5 years (91.2%), and took antihypertensive drugs (90.0%). The fasting blood glucose level of respondents ≥ 126 mg/dl was 86.0% and 91.7% had sexual desire disorder. The duration of DM and aging are contributing factors of ED in males with DM, with a p-value of 0.016 and 0.013, respectively⁴⁵.

A cross sectional study was conducted from January 2016 to March 2016 by Walle et al. to assess the prevalence of erectile dysfunction and associated factors among diabetic patients. A total of 422 diabetic patients were participated with 100% response rate. The proportion of erectile dysfunction was 85.5% and it was significantly associated with higher age (AOR: 6.46, 95% CI 2.55–16.44) and Diabetic complication (AOR: 3.97, 95% CI 1.06–17.36). Therefore, screening for ED in diabetic patients, particularly for those who are in advanced age and living with DM for more than 10 years is needed for its early detection, prevention and management⁴⁶.

The prevalence and predictors of ED among diabetic patients in a tertiary hospital of Southwest Ethiopia was conducted⁴⁷. It was a hospital-based cross-sectional study was conducted on male diabetic patients on follow-up at the diabetic clinic of Jimma Medical Center (JMC). 350 male diabetic patients were enrolled in the study. The mean (+SD) age of the study participants was 47.9 (+12.2) years. The majority, 212(60.4%) of the diabetic patients had varying degrees of ED and almost all, 207 (97.6%) of the patients were not treated for ED. Independent predictors of ED were older age and longer duration of diabetes⁴⁷.

Bahar et al.⁴⁸ conducted a study in the city of Sari in Mazandaran Province, with the aim of investigating ED in men with type II diabetes. A total number of 350 male patients suffering from type II diabetes referring to endocrinology clinics in the city of Sari. The average period of time in which the patients were facing diabetes was 3.65±5.75 years. The IIEF mean score was equal to 16.98±43.79. Erectile dysfunction (ED) was also evident in 152 patients (62.2%). Moreover, increase in age had significantly decreased the IIEF scores (p<0.001). The chance of being affected with ED among diabetic patients above 50 was 11.21 times as much as those below 50 years of age (odds ratio (OR): 11.21, 95% confidence interval (CI): 6.40-19.62). Author recommended that concerning the high prevalence rate of ED in men suffering from type II diabetes, doctors are required to directly ask them about sexual disorders in follow-up visits. Furthermore, using screening questionnaires can be helpful in identifying this problem⁴⁸.

Hospital based cross-sectional study was conducted on 362 participants in Debre Tabor Comprehensive and Specialized Hospital North West Ethiopia from August - December 2020 using systematic random sampling technique. Three hundred sixty-two diabetes patients participating in the study with the mean age being 44.4 ± 14.47 (range: 18 -78) years were interviewed. The majority (59.7%) of the diabetes patients suffered from erectile dysfunction and 13.3% were found to have severe erectile dysfunction. Bi-variable analysis showed duration of diabetes (>10 years), type of diabetes (type II), physical exercise, drinking alcohol, BMI, blood glucose, and blood pressure were associated with erectile dysfunction at 5% level (p ≤ 0.05). Multiple logistic regression analysis revealed that duration of diabetes 10 years p = 0.001, co-existing hypertension, p = 0.002, physically inactive p = 0.003, unsafe level alcohol intake p = 0.003) and raised blood glucose p = 0.004 were independent risk factors but no association was found with other variables. Study concluded that the magnitude of erectile dysfunction in this study population was 59.7% and associated with the type of diabetes; duration of diabetic, physical exercise, alcohol drinking, increase in blood pressure, and elevated blood glucose level were independently correlated with erectile dysfunction⁴⁹.

Tamrakar et al. aimed to identify the prevalence of erectile dysfunction and its association with other risk factors among type 2 Diabetic males attending the tertiary care hospital in

Nepal. The prevalence of erectile dysfunction with varying degrees of severity was found to be 76.87% among T2 DM male patients. There was a significant negative correlation of the IIEF5 Score with the duration of T2 DM burden ($r = -0.416$, $p < 0.05$) and the level of HbA1c ($r = -0.391$, $p < 0.05$). There was a higher prevalence of erectile dysfunction among T2DM male patients that were also associated with poor glycemic control and the duration of T2 DM burden⁵⁰.

An institutional-based cross-sectional study was conducted involving 462 men diabetic patients at the three hospitals of the northwest Amhara region Ethiopia⁵⁷. The prevalence of sexual dysfunction was found to be 69.5% (95%CI: (65.1–73.9)). The magnitude of sexual dysfunction was prevalently observed among participants who were older (> 50 years) (AOR = 8.7, 95%CI: (3.3–23.1)). Likewise, the odds of sexual dysfunction was significantly higher among men who have lived with diabetes for a longer duration (AOR = 10.8, 95% CI: (5.3–21.9)), with poor metabolic control (AOR = 3.57, 95% CI: (1.81–7.05)), with comorbid illnesses (AOR = 5.07, 95% CI: (2.16–11.9)), and diabetic related complications (AOR = 3.01, 95% CI: 1.31–6.92). On the other hand, participants who were physically active (AOR = 0.41, 95% CI: (0.12–0.7)) and satisfied with their relationship (AOR = 0.15, 95% CI: (0.03–0.7)) showed a lesser risk of experiencing sexual dysfunction⁵¹.

The institution-based cross-sectional study was conducted on 352 adult male diabetic patients randomly selected at Hawassa, Southern, Ethiopia. The prevalence of erectile dysfunction was 72.2% (95%CI, 1.76–3.68). After adjusting all factors, old age, diabetes duration, drinking alcohol, and poor glycemic control had shown significant association with erectile dysfunction. Author recommended that the occurrence of erectile dysfunction in this study community is very high. Drinking alcohol, poor glycemic control, age, and duration of diabetes were predictors of erectile dysfunction in this study area⁵².

Dave et al. conducted a study to evaluate ED in male diabetes patients. It was a hospital-based prospective observational study. According to International Index of Erectile Function (IIEF)-5 questionnaire, patients were divided into 4 categories: mild ED with score 17 to 21, mild-to-moderate ED with score 12 to 16, moderate ED with score 8 to 11 and severe ED with score 1 to 7. Prevalence of ED in male diabetes patients was found to be 72.4%. Among 110 cases with ED, 8 had mild ED (7.2%), 27 had mild-to-moderate (24.5%), 27 had moderate ED (24.5%) and 48 had severe ED (43.6%). Prevalence of ED was found to be proportional to age. Majority of cases in ED group were those with long-standing diabetes. Correlation of ED with complication of diabetes, like nephropathy and retinopathy, was significant, whereas it was not significant with neuropathy. Significant correlation of ED was found with BMI and PLR. Author concluded that ED prevalence was high among the diabetes patients and it increased with age and duration of the disease. Presence of diabetic complications was significantly associated with ED. BMI was significantly associated with development of ED⁵³.

Parmar et al. aimed to determine the prevalence of ED and its predictors among diabetic men. A hospital-based cross-sectional observational study was conducted at a tertiary care centre including 357 diabetic men recruited over one and half years. ED was found in 212 (59.38%) diabetic males. A strong negative correlation was found between potency score and age ($r = -0.647$), and a moderate negative correlation with duration of DM ($r = -0.324$), systolic blood pressure (SBP), and diastolic blood pressure. BMI, fasting blood sugar, serum cholesterol, and serum creatinine showed a weak negative correlation with potency score. Serum testosterone level showed a strong positive correlation with potency score. Age, SBP, duration of diabetes, fasting blood sugar, and serum free testosterone ($P < 0.05$) were independent predictors of ED⁵⁴.

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