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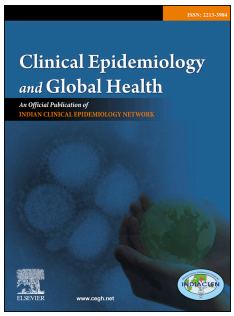

Assessment of erectile dysfunction and other sexual dysfunction in men with type 2 diabetes mellitus: A multicenter observational study in North India

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Assessment of Erectile Dysfunction and other Sexual Dysfunction in Men with Type-2 Diabetes Mellitus: A Multicenter Observational Study in North India

Short Title

Erectile Dysfunction in Men with Diabetes

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Authorship

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Conflict of Interest

All authors declare that there is no conflict of interest.

Assessment of Erectile Dysfunction and Other Sexual Dysfunction in Men With Type 2 Diabetes Mellitus: A Multicenter Observational Study in North India

Abstract

Background: Type 2 diabetes mellitus (T2DM) is one of the major contributing factors of sexual dysfunction in males. Given the presence of limited literature on prevalence of T2DM associated sexual dysfunction in North Indian population, the following study was conducted with aim of investigating the prevalence of ED.

Materials and methods: A multicenter observational study was conducted across 11 centers in Lucknow, North India. A total of 460 patients were asked to fill a validated International Index of Erectile function (IIEF) Questionnaire, and sexual dysfunction was assessed based on scoring for erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction over a period of 4 weeks. Chi-Square analysis was performed to form an association between ED or OFD and other confounding factors.

Results: ED and OFD were found to be prevalent in 32% and 43.3% of patients, respectively. Their presence correlated significantly with T2DM duration (ED, p = 0.0101; OFD, p=002). In Indian context, the prevalence of ED was found to correlate with, presence of macrovascular complications and serum creatinine levels, whereas OFD significantly correlated with T2DM duration, macro– and microvascular complications among other factors.

Conclusion: The prevalence of ED and OFD in men suffering from T2DM is on significant rise, considerably impacting the lives of millions of men worldwide. Thus, the findings of this study highlight the significance of taking follow-up of sexual discomfort and disorders by the clinicians during the visits.

Keywords

Erectile dysfunction, type 2 diabetes mellitus, IIEF Questionnaire, India, prevalence, age of onset, duration of diabetes, orgasmic function defect (OFD)

Introduction

Erectile dysfunction (ED) is a disorder characterized by the inability to attain and/or maintain an erection sufficient to allow satisfactory sexual intercourse.[1] Globally, more than 150 million men are affected by ED, and this figure is expected to reach 322 million by 2025.[2] Type 2 diabetes mellitus (T2DM) is the major risk factor for the development of ED, and it has been observed that as compared to healthy men, diabetic men have a threefold higher risk of developing ED.[1,3] The latest epidemiological data states that the prevalence of ED in T2DM males could be anywhere between 20% and 71%,[4] with huge differences among different studies. The DISCOVER study reported the prevalence of ED as low as 2.7% in diabetic patients from 38 countries all around the globe.[5] As per epidemiological studies, men with both type 1 and type 2 DM are at an increased risk of ED, as compared to the general population.[6] However, 66% of people with T2DM have ED.[7] The incidence of ED in patients with DM is age-related, and ED occurs at a younger age with its incidence increasing with disease duration.[1,3] Although in general cases, ED is age related, it occurs 10–15 years early in men with diabetes. Moreover, ED in patients with DM is more severe and less responsive to conventional oral medication compared to general ED cases, thereby compromising the quality of life.[6]

In 12-30% of men, ED is often the first sign of diabetes,[6] and ED is often one of the under-diagnosed and under-reported complications associated with DM.[8] The pathogenesis of DM-related ED is complex and multifactorial, the key factors being diabetic neuropathy,

macrovascular arterial disease, structural remodeling of the corporeal tissue, psychogenic components, hypogonadism, and adverse drug reactions.[9] The mechanisms of ED in men with DM include vascular diabetic complications, endothelial dysfunction, poor glycemic control, and longer disease duration. Other risk factors for type 2 diabetes mellitus (T2DM) patients include obesity, hypertension, hyperlipidemia, metabolic syndrome, and a sedentary lifestyle.[6,10]

Orgasmic function defect (OFD) is another condition that is commonly associated with ED in patients with T2DM.[10] OFD can be termed as incessant difficult or delay or absence of achieving orgasm post sufficient sexual stimulation leading to personal distress. OFD included delayed orgasms as well as anorgasmia. Anorgasmia is perceived absence of orgasm, independent of the presence of ejaculation. Delayed orgasm is defined as a noticeable delay in ejaculation/ infrequent or absence of ejaculatory response in75% to 100% of occasions of partnered sexual activity without the self-desiring of delay, which persists for at least 6 months. Patients with OFD may also have ejaculatory dysfunction including delayed ejaculations and premature ejaculation and anorgasmia.[11] The prevalence of ejaculatory disturbance in diabetic males is estimated to be around 9%–31%, while that of orgasmic dysfunction is around 7%–8%.[12] The main concern with orgasmic dysfunction in young males is the failure to inseminate, thereby leading to male infertility.[11] Peripheral neurological interruptions as seen in diabetic neuropathy are one of the causes of OFD. Further poor glycemic controls are strongly associated with premature ejaculations in males with T2DM; however, the role of glycemic control in orgasmic dysfunction is not clearly understood.[12]

Endothelial dysfunction plays a key role in DM-associated ED. Alterations in the functionality of the penile endothelium, a specialized component of the vascular system, lead to complications such as ED. Endothelial dysfunction links ED and cardiovascular complications in such patients. Additionally, common comorbidities associated with DM, such as

hypercholesterolemia, hypertension, and obesity, serve as independent risk factors for cardiovascular disease, endothelial dysfunction, and ED.[3] Accumulating pieces of evidence consider ED to be an independent risk factor for coronary artery disease (CAD), particularly in younger men with DM who are already at a higher risk of developing CAD.[13] ED is also associated with poor glycemic control, which in turn is associated with microvascular and macrovascular complications in DM patients. Therefore, DM-associated ED has emerged as the major issue requiring serious attention in the male diabetic population.[14]

DM has become an epidemic over the last two decades, majorly T2DM, which constitutes 90%–95% of all DM cases.[7] Incidence of ED has been extensively associated with T2DM, with a 50% global prevalence in men with T2DM.[15] Despite the clinical importance of ED in men with DM, most clinicians do not enquire about ED, and the prevalence of patient-reported ED is generally very low.[14] When questioned directly by clinicians, patients tend to hide ED and these factors are instrumental in rendering ED as an undiagnosed and underrated problem in male patients with DM.[16] Nevertheless, ED is a diabetic complication that can be prevented; approximately 95% of patients with T2DM-related ED can be treated successfully.[17] In this context, it has been observed that the use of validated questionnaires that are either administered by a third-party interviewer or in an anonymous neutral setting is preferred by patients, thereby aiding the early diagnosis of ED.[16]

Given the attitude of the Indian society toward sexuality, along with the fact that men are usually embarrassed and reluctant to admit having ED, making precise estimates about the prevalence and severity of DM-associated ED in the country is difficult and warrants attention.[17] In this context, the present study aimed at determining the prevalence and risk factors of ED and OFD among men with T2DM at 11 centers in North India. We have included the factors such as sexual stimulation, sexual intercourse, ejaculation and orgasm as sexual dysfunction factors in our questionnaire. The study also assessed the association of ED and

OFD with confounding factors such as age, age of onset of disease, duration of disease, the extent of diabetic control, DM-associated complications (microvascular and macrovascular), and also the use of any prescription drugs.

Materials and Methods

Study Design and Participants

This was a multicenter observational study conducted across 11 centers in Lucknow, North India. This study included sexually active male patients with DM, aged >18 years visiting the study centers for consultation between August 2018 and April 2019. The English and Hindi-translated (regional language) version of the International Index of Erectile Function (IIEF) Questionnaire was used in the study.

Hindi translation was done initially by a qualified translator. Five questionnaires were then filled by subjects who were well versed in both English and Hindi. Changes were made accordingly. This was done 5 times. The fifth revision of the questionnaire was put to test on 50 healthy subjects and consistency was evaluated, which was found satisfactory. Certification for translation was obtained from an appropriate agency. Ethics committee clearance was obtained before the start of the study.

In our study, we have utilized the IIEF-15 questionnaire with lower cut off values. The questionnaire was divided into three sub sections: 0–13 (severe), 14–24 (moderate to mild), 25–30 (without disorder). Based on our study, patients falling under the severe category of ED, that is, if their IIEF scores were less than or equal to 14 out of 30 (functional domain A; Erectile Dysfunction; see attached questionnaire in Supplementary File 1) were included for analysis. In functional domain B corresponding to Orgasmic Dysfunction, patients with a score less than or equal to 5 out of 10 were labeled as having primary orgasmic or ejaculatory dysfunction. Moreover, sexual desire, intercourse satisfaction and overall satisfaction were also included.

During the initial consultation, we recorded patients' demographic and clinical characteristics (age, weight, height, body mass index [BMI], abdominal circumference, and habits such as smoking, tobacco chewing, and alcohol consumption) along with a thorough medical history (for any known systemic diseases such as hypertension and hypothyroidism).

We also collected data on various disease-related parameters, such as duration of T2DM, age of onset of the disease, degree of control of T2DM, medication details, history of hypoglycemia, and microvascular and macrovascular complications.

Upon completion of the initial consultation, all the patients were asked to fill the questionnaire, and the filled copy was collected in a coded envelope to maintain confidentiality. Using the well-validated IIEF Questionnaire, we assessed ED and OFD based on scoring for erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction in the past 4 weeks.

The study protocol was approved by the ethical committee of the participating centers, and written informed consent was obtained from all the enrolled patients.

Statistical Analysis

Descriptive statistics were used to present the baseline characteristics and the prevalence of OFD in T2DM patients. A chi-square test was used for evaluating the association between ED or OFD and other confounding factors. A p-value of <0.05 was considered statistically significant.

Study Outcomes

The primary outcome was to assess the prevalence of ED and OFD in patients with T2DM, while the secondary outcome was to evaluate various parameters associated with these sexual dysfunctions.

Results

Baseline Characteristics of the Study Population

A total of 456 male diabetic patients were included in the study, out of which more than 99% were T2DM patients. No specific selection criteria were used related to the duration of the disease. The age of patients ranged from 22 to 72 years, while the mean age of the study population was 47.64 ± 9.59 years. The mean age (± standard deviation [SD]) of the onset of T2DM was 40.48 ± 10.53. About 38.48% of the study population had T2DM for about 1–5 years, while 25.43% of the patients reported T2DM for ≥5 up to 10 years duration. The majority of the participants did not have hypertension (56.74%) or a history of hypoglycemia (13.26%). Either microvascular or macrovascular complications were seen in 17.17% and 8.04%, respectively. The mean (±SD) Hb_{A1c} of the population was 8.49 ± 2.06. Details of the baseline characteristics of the study population have been represented in Table 1.

Table 1: Baseline characteristics of the study population

Patient Characteristics	Categories/Mean/Median	Values
Age (years)	Mean ± SD	47.64 ± 9.59
	Median	47
Smoking behavior	Nonsmoker	368 (80%)
	Smoker <1 pack	91 (19.78%)
	Smoker >1 pack	0 (0%)
	UNK	1 (0.22%)
Tobacco use	Yes	116 (25.22%)
	No	343 (74.57%)
	UNK	1 (0.22%)

Alcohol consumption	Nonalcoholic	350 (76.09%)
	Alcohol <100 g/week	109 (23.70%)
	UNK	1 (0.22%)
Height (cm)	Mean ± SD	165.80 ± 8.76
Weight (kg)	Mean ± SD	74.64 ± 13.21
Waist circumference (cm)	Mean ± SD	97.06 ± 10.79
BMI (kg/m^2)	Mean ± SD	26.8 ± 3.97
Pulse rate (bpm)	N	412
	Mean ± SD	89.03 ± 12.28
	Median	88
Systolic blood pressure (mmHg)	N	442
	Mean ± SD	131.76 ± 17.29
	Median	130
Diastolic blood pressure (mmHg)	N	442
	Mean ± SD	81.44 ± 10.16
	Median	80
Duration of DM	Total	456 (100%)
	1 = <1 year	71 (15.43%)
	2 = 1–5 years	177 (38.48%)
	3 = 5–10 years	117 (25.43%)
	4 = >10 years	91 (19.79%)
Patients withT2DM	Total	457 (100%)
	Patients with T2DM	456 (99.13%)
Age of onset (years)	N	456

	Mean ± SD	40.48 ± 10.53
	Median	40
Hypertension	Yes	197 (42.83%)
	No	261 (56.74%)
	UNK	2 (0.43%)
Hypothyroid	Yes	58 (12.61%)
	No	400 (86.96%)
	UNK	2 (0.43%)
Other endocrinological disorders	Yes	19 (4.13%)
	No	439 (95.43%)
	UNK	2 (0.43%)
Hypoglycemia	Yes	61 (13.26%)
	No	397 (86.30%)
	UNK	2 (0.43%)
Hb_{A1c} (%)	N	414
	Mean ± SD	8.49 ± 2.06
	Median	8.1
Macrovascular complications	Yes	37 (8.04%)
	No	421 (91.52%)
	UNK	2 (0.43%)
Microvascular complications	Yes	79 (17.17%)
	No	379 (82.39%)
	UNK	2 (0.43%)

BMI: Body mass index; HbA1c: Hemoglobin A1C; SD: Standard deviation; T2DM: Type 2 diabetes mellitus; UNK: Unknown.

Prevalence of ED and OFD in the Study Population

The prevalence of ED was found to be 32.4%, while 43.3% reported OFD. About 27.8% had both ED and OFD, whereas a total of 48.4% of patients suffered from a sexual disorder, that is, having either ED or OFD (Table 2).

Table 2: Prevalence of erectile dysfunction and orgasmic function defect in the study population (N = 460)

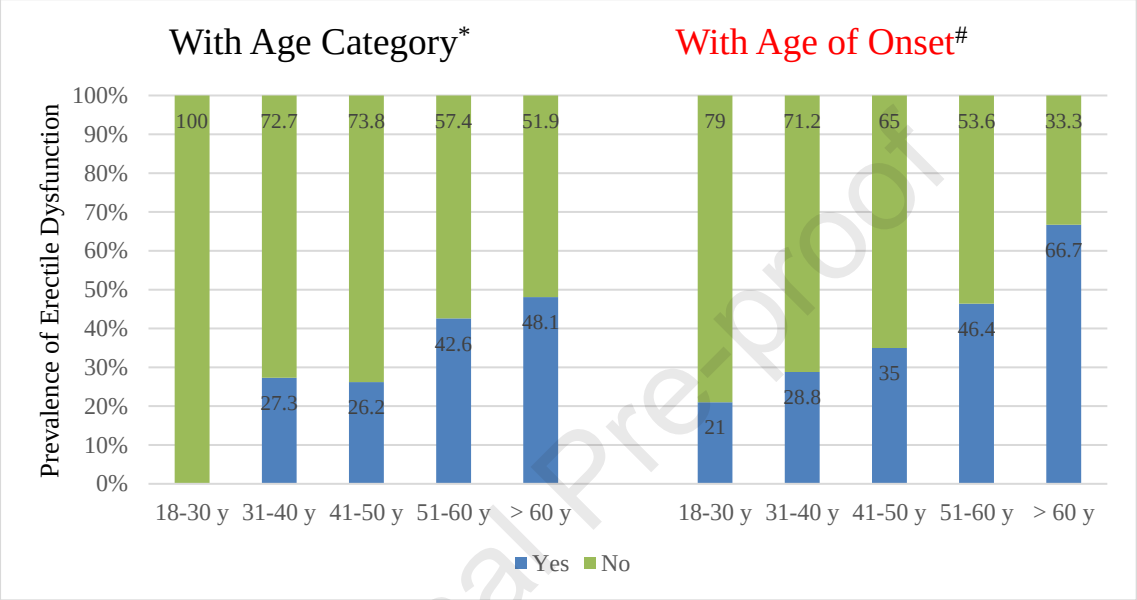
Condition Type	Status	Patient Number (N)	Percentage (%)
Erectile dysfunction	Normal erectile function	308	67.0%
	Erectile dysfunction	149	32.4%
	Unknown	3	0.6%
Orgasmic function defect	Yes	199	43.3%
	No	258	56.1%
	Unknown	3	0.6%

Association of ED and OFD With Different Variables

We also evaluated the association of ED and OFD with different baseline variables. In the case of ED, a significant association was observed between the prevalence of ED and age category ($p = 0.0006$) and the age of diabetes onset ($p = 0.0096$), with ED prevalence gradually increasing with age (Figure 1). There was also a positive association between the prevalence and the duration of T2DM ($p = 0.0101$) (Table 3).

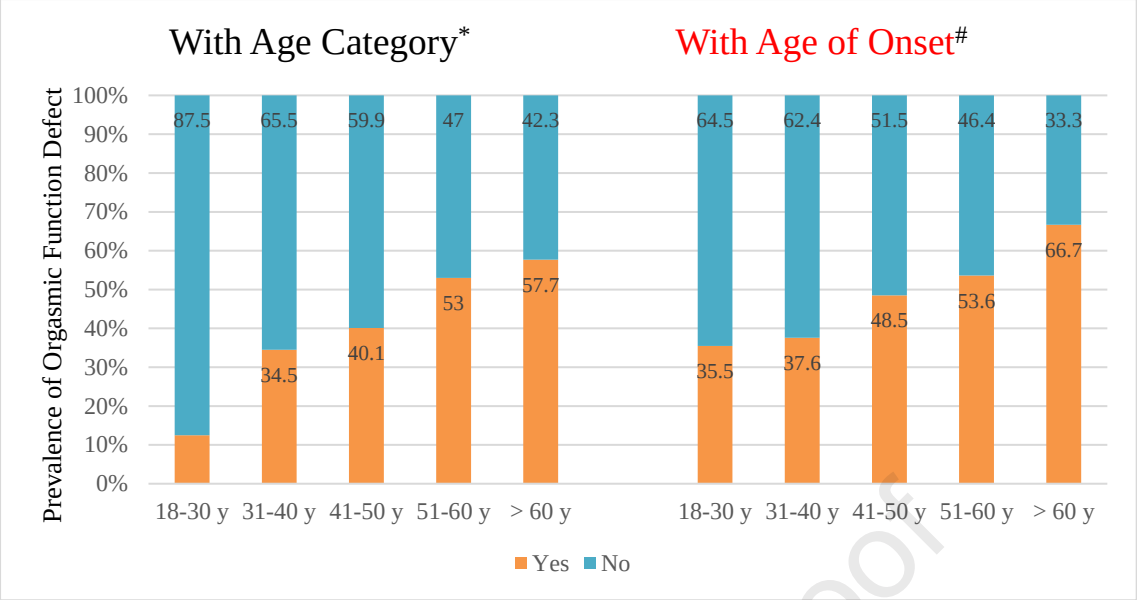
For OFD, the prevalence was found to increase significantly with age (p = 0.003) (Figure 2) and the duration of T2DM (p = 0.0002) (Table 3), whereas no significant association was observed with the age of onset (p = 0.0553) (Figure 2).

Figure 1: Prevalence of erectile dysfunction with age category and age of onset (N = 460).



*p = 0.0006, #p = 0.0096.

Figure 2: Prevalence of orgasmic function defect with age category and age of onset (N = 460).



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194 *p = 0.003, #p = 0.0553.

195 **Table 3:** Association of erectile dysfunction and orgasmic function defect with the duration of

196 T2DM

Duration of T2DM	Erectile Dysfunction			Orgasmic Function Defect		
	No	Yes	p-Value	No	Yes	p-Value
1 (<1 year)	45 (65.2%)	24 (34.8%)	0.0101	44 (63.8%)	25 (36.2%)	0.0002
2 (1–5 years)	136 (76.8%)	41 (23.2%)		117 (66.1%)	60 (33.9%)	
3 (5–10 years)	74 (63.8%)	42 (36.2%)		56 (48.3%)	60 (51.7%)	
4 (>10 years)	52 (57.8%)	39 (42.2%)		39 (42.9%)	52 (57.1%)	

197 T2DM: Type 2 Diabetes mellitus.

198

Among the other variables studied, the prevalence of ED was found to be significantly associated with that of macrovascular complications (p = 0.0032) and serum creatinine levels (p = 0.0141) as shown in Table 04, while there was no significant association with parameters such as hypertension, hypoglycemia, Hb_{A1c} levels, microvascular complications, and mean platelet volume (MPV). Among the medications studied, the prevalence of ED was found to be significantly associated with the use of beta-blocker (p = 0.0326) (Table 4). No significant association was observed between the prevalence of ED and other medications such as oral hypoglycemic agents, insulin, alpha-blockers, and antihypertensives.

The prevalence of OFD was found to be significantly associated with almost all the variables studied, including hypertension (p = 0.0192), hypoglycemia (p = 0.0005), macrovascular (p = 0.0006) and microvascular (p = 0.008) complications, Hb_{A1c} (p = 0.0134) and creatinine (p = 0.0425) levels, beta-blocker (p = 0.0008), and statin (p = 0.0433) (Table 4).

Table 4: Association of erectile dysfunction and orgasmic function defect with different variables

Variables	**Erectile Dysfunction**			**Orgasmic Function Defect**		
	Yes	**No**	**p-Value**	**Yes**	**No**	**p-Value**
Hypertension						
Without hypertension	75 (29.1%)	183 (70.9%)	0.0910	100 (38.8%)	158 (61.2%)	0.0192*
With hypertension	72 (36.5%)	125 (63.5%)		98 (49.7%)	99 (50.3%)	
Hypoglycemia						

Without hypoglycemia	123 (31.2%)	271 (68.8%)	0.2066	159 (40.4%)	235 (59.6%)	0.0005*
With hypoglycemia	24 (39.3%)	37 (60.7%)		39 (63.9%)	22 (36.1%)	
Macrovascular complications						
Without macrovascular	127 (30.4%)	291 (69.6%)	0.0032*	172 (41.1%)	246 (58.9%)	0.0006*
With macrovascular	20 (54.1%)	17 (45.9%)		26 (70.3%)	11 (29.7%)	
Microvascular complications						
Without macrovascular	115 (30.6%)	261 (69.4%)	0.0865	153 (40.7%)	223 (59.3%)	0.008*
With macrovascular	32 (40.5%)	47 (59.5%)		45 (57%)	34 (43%)	
Hb_{A1C}						
≤7	29 (28.7%)	72 (71.3%)	0.3084	34 (33.7%)	67 (66.3%)	0.0134*
>7	106 (34.2%)	204 (65.8%)		148 (47.7%)	162 (52.3%)	
Creatinine						

≤1.2	127 (30.8%)	285 (69.2%)	0.0141*	173 (42%)	239 (58%)	0.0425*
>1.2	22 (48.9%)	23 (51.1%)		26 (57.8%)	19 (42.2%)	
Beta-blocker						
Without beta-blocker	118 (30.5%)	269 (69.5%)	0.0326*	159 (41.1%)	228 (58.9%)	0.0008*
With beta-blocker	27 (44.3%)	34 (55.7%)		39 (63.9%)	22 (36.1%)	
Statin						
Without statin	62 (29.5%)	148 (70.5%)	0.2044	82 (39%)	128 (61%)	0.0433*
With statin	84 (35.1%)	155 (64.9%)		116 (48.5%)	123 (51.5%)	

*p: Significant p-value; T2DM: Diabetes mellitus; HbA1c: Hemoglobin A1C

Discussion

ED serves as one of the major complications of T2DM, yet its presence mostly goes unnoticed in routine clinical practice.[8] In the present study, around 32% and 43.3% of all patients with T2DM were found to suffer from ED and OFD, respectively, while 27.8% had both ED and OFD. A total of 48.4% of patients reported a sexual disorder, that is, having either ED or OFD.

In general, the prevalence of ED among patients with T2DM mostly varies between 20% to 78% across different studies. In a recent cross-sectional study conducted in Northern Sri Lanka, 62.9% of diabetic patients were found to suffer from ED, while 22.4% had severe ED.[17] In a global meta-analysis involving 88,577 male DM patients, the overall prevalence of ED was found to be 59.1%.[1] Several Indian studies have reported a prevalence of T2DM-associated ED in different study populations across the country. A cross-sectional study from Northern India reported ED in 67.4% of patients with diabetes, and 42.4% of them suffered from severe ED.[18] A study from Jaipur, India, reported a very high prevalence of ED (78%) in T2DM patients, while 36% of patients had severe ED.[20] Another study from Jammu, North India, reported a 62.08% prevalence of ED in T2DM patients.[19] The divergent prevalence rates of ED among diabetic patients could be attributed to differences in study populations, including demographic characteristics, type of setting in which the study was done, study population size, severity and duration of T2DM, and presence of other comorbidities.[14] We found an overall low prevalence of ED in our study group. A plausible explanation might be the low cut-off values used in our study. Studies have used a cut-off score of 24 as diagnostic criterion for ED,[20] but IIEF-5 has demonstrated that values between 22-25 reflects no ED, and mild to moderate ED can only be present if the patient's score is between 12 to 16.[21] Also, the original IIEF-15 questionnaire reported a mean cut-off score of 25.8±7.6 for normal population and mean score of 10.7 ± 6.5 for ED patients; similarly, for orgasmic dysfunction, the cut-off value was 8.8 ±2.9 in control group and 5.3 ± 3.2 for study population.[22] So, based on these data, we had chosen a lower cut-off values as diagnostic criteria for ED in our patients, and patients with scoring of >14 were not considered to have ED and >5 were not considered to have orgasmic defect.

A consistent risk factor for ED includes increasing age, in both the diabetic and general population.[12] In the present study, a significant association was observed between age and prevalence of ED; the proportion of ED in diabetic patients increased with age, and the highest

prevalence was observed in the >60-year age category (48.1%) and the lowest in the ≤30-year age category (0.00%). In another Indian study, the prevalence of ED was found to be 10.3% and 54.6% in <40-year and 40–59-year age-groups of patients, respectively.[18] A similar trend was reported by Garg *et al*., where the prevalence of ED was as low as 20% in the <40-year age category and increased to 100% in the >60-year age-group.[23] A study from Jordan reported that the prevalence of ED increased from 26.5% in patients aged <40 years to 91% in patients aged >70 years.[25] Again, Langer *et al*. reported a significant association of age with the prevalence of ED; the majority of ED cases belonged to the 40–60-year age-group.[19] This association between ED and increasing age could be attributed to the prevalence of several common risk factors for ED, such as atherosclerosis, hypertension, and hypogonadism, which become common with increasing age. Also, the presence of T2DM itself increases the risk of developing most of these factors.[14]

In addition to age, the present study also demonstrated the prevalence of ED to be significantly associated with the age of onset of T2DM; the later the age of onset of T2DM, the higher the prevalence of ED. In the study population, the highest prevalence of ED was observed in >60-year age of onset (66.7%), while the lowest prevalence was observed in the ≤30-year age of onset (21%). A similar observation was reported in a study by Anwar *et al.*, showing that the severity of ED increases with a later age of onset of T2DM.[18] This could be attributed to the fact that, generally, patients with ED ignore their symptoms and delay treatment owing to embarrassment and ignorance.[18] Apart from the age of onset, several studies have documented a longer duration of T2DM as an independent risk factor for ED.[14,16–19.23-25]

Our data also confirmed this notion that a longer duration of T2DM increases the prevalence and severity of ED.[24] While 43.3% of patients with >10-year duration of T2DM suffered from ED, 23.2% of patients with <5-year duration of T2DM had ED.

None of the various lifestyle factors evaluated in this study, such as smoking, alcohol consumption, and BMI, were found to be significantly associated with ED. Although smoking is a risk factor for ED associated with T2DM,[13] this was not observed in our study. Our findings are in line with other reports where smoking habit was not related to the prevalence of ED.[14,24] While some studies have found alcohol consumption to be an independent risk factor for ED,[17] other studies did not find any such correlation,[19] similar to our observation. In some studies, as compared to non-ED cases, the BMI of patients with ED has been observed to be higher.[15,17] However, our findings are congruent with several other studies where BMI was not associated with ED.[1,19,23-24] Overall, our study did not reveal any association between lifestyle factors and the prevalence of ED.

Among the various T2DM-associated complications, both microvascular and macrovascular complications have been associated with a high risk of ED. While microvascular complications include medical conditions such as diabetic neuropathy, nephropathy, and retinopathy, macrovascular complications include conditions such as CAD, peripheral vascular disease, and ischemic stroke.[17] Although the present study did not reveal any significant association between the prevalence of ED and microvascular complications, macrovascular complications were found to be significantly associated with the prevalence of ED. In a cross-sectional study on 376 T2DM patients, 81% of patients without ischemic heart disease (IHD) had ED, while 98% of patients with IHD suffered from ED ($p<0.01$).[23] Another study on 988 diabetic men demonstrated that ED was concomitantly present in 80.2% of diabetic patients with CAD.[24] These studies support our findings that macrovascular complications are significantly associated with ED.

297 The findings of the study revealed that apart from macrovascular complications, the prevalence
298 of ED was not associated with other medical conditions such as hypertension and a history of
299 hypoglycemia. Hypertension in diabetic patients increases the risk of atherosclerosis that might
300 affect penile arteries, leading to ED.[17] However, the present study did not reveal any significant
301 association of ED with hypertension., but we found higher non-significant prevalence of ED in
302 hypertensive patients. Similar observations have been reported by Ugwu *et al*. and Goyal *et*
303 *al*., wherein hypertension was not found to be significantly associated with ED in patients with
304 T2DM.[14,16] Other risk factors that were not found to be associated with ED in the study
305 population included hypothyroidism, endocrinological disorders, and MPV. Even the extent of
306 glycemic control (measured by Hb_{A1c}) was not associated with the prevalence of ED in the
307 study population. However, some studies have found a positive correlation between poor
308 glycemic control and the prevalence of ED.[14,16,18,23,24] The prevalence of ED has also been
309 associated with creatinine levels and patients undergoing hemodialysis;[26] although we did not
310 analyze the correlation between estimated glomerular filtration rate and ED in our study, a
311 significant association was observed between creatinine levels and the prevalence of ED.
312 Therefore, patients with chronic kidney disease and DM should be aware of early signs of ED.
313
314 Several medications are known to affect sexual function owing to their long-term side effects.[25]
315 While comparing the association between the type of medications used by the study population
316 and the prevalence of ED, a significant association was observed with beta-blockers. This
317 finding was similar to other studies that have shown beta-blockers to be risk factors for ED.[17]
318 Nisahan *et al*. observed in a study on male diabetic patients that 13 out of 14 users of beta-
319 blockers had ED ($p = 0.019$), thereby indicating that beta-blockers are potential factors for
320 ED.[17] However, none of the other medications used by the patients, including statin, thiazides,
321 alpha-blocker, insulin, oral hypoglycemic agents, and other antihypertensives, were found to

be associated with ED. But in our study, we found a higher prevalence of ED in patients using statin therapy (35% vs. 29%; with statin vs. without statin). Future trials are warranted to assess this correlation further. Similarly, we found higher prevalence of ED in patients with hypoglycemia.

In the present study, patients with T2DM also had a high prevalence of OFD. Assessing the orgasmic function is included as a domain in the IIEF questionnaire. The orgasmic function includes even the process of ejaculation. In our study, we observed that 43.3% of the study population was affected by OFD. Similar to the results of our study, Jakka and Ramesh had reported orgasmic dysfunction in about 38% of their study population, comprising males with T2DM.[12] Further, the study by Malavige *et al.* reported premature ejaculation in 40% of patients with diabetes. They also reported a strong association between ED and premature ejaculation (odds ratio = 4.41; 95% confidence interval = 2.08–9.39) in patients with T2DM.[27] The population-based study by Lindau *et al.* reported a high prevalence of orgasmic dysfunction in patients with diagnosed and undiagnosed diabetes. It was also noted that the rate of ED was not markedly elevated in men with undiagnosed diabetes and hence they reported that orgasmic dysfunction may actually precede ED and not always a consequence of ED.[28] Even in our study, we observed that more T2DM patients reported OFD compared to ED. Moreover, a significant association was observed between the prevalence of OFD and nearly all the variables studied, that is, age, duration of T2DM, microvascular and macrovascular complications, serum creatinine, Hb_{A1c} levels, hypertension, hypoglycemia, and use of beta-blockers and statin. Hence, OFD may be a preceding condition occurring before ED.

Strengths and Limitations of the Study

The key strengths of the study include the large sample size, multicenter location of the specific study group of T2DM, and the assessment of the association of a wide range of variables with

ED and OFD. Being a multicenter study covering 11 centers in North India, the findings of this study depict a wide spectrum in subject selection, hence a better picture of the current scenario of ED and OFD prevalence in T2DM patients, compared to single-center studies that have wide variations in data owing to sociodemographic differences in the study populations. However, some of the limitations of the study include a lack of a healthy control group of individuals for better interpretation of the results and lack of information regarding the proportion of patients receiving treatment of ED and the type of treatment. Moreover, the study did not cover psychological parameters such as depression, which is known to be a contributing factor for ED.[19] Data on the association of ED or OFD with dyslipidemia were also not available for the current study. Lastly, we did not consider the influence of endocrine disorders which are a well-known contributing factor to ED. Findings in this regard should be interpreted with caution.

Conclusion

To conclude, about one-third and nearly half of our study population reported ED and OFD, respectively, which was significantly associated with higher age, longer duration of T2DM, macrovascular complications, and higher creatinine levels. As most patients suffer silently from ED and OFD, periodic screening for these sexual disorders among diabetic men is essential for early diagnosis and proper management.

Conflict of Interest

All authors declare that there is no conflict of interest.

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