



Hypogonadism among Type 2 Diabetes Mellitus Patients with Male Erectile Dysfunction

Dhahir J. Kadhim¹ Ammar MS Almomin¹ Abbas A. Mansour¹

¹Faiha Specialized Diabetes, Endocrine and Metabolism Center (FDEMC), University of Basrah, Basrah, Iraq

Address for correspondence Ammar MS Almomin, MD, Faiha Specialized Diabetes, Endocrine and Metabolism Center (FDEMC), University of Basrah, Basrah, Iraq
(e-mail: Ammar.Mohammed@uobasrah.edu.iq).

Ibnosina J Med Biomed Sci 2023;15:117–120.

Abstract

Introduction Testosterone levels and erectile function are known to decline as men age, leading to hypogonadism and erectile failure. Men with type 2 diabetes mellitus (T2DM) have a high prevalence of hypogonadism and erectile dysfunction. We aimed to estimate the prevalence of hypogonadism in T2DM patients complaining of erectile dysfunction.

Patients and Methods A cross-sectional study was conducted at Specialized Diabetes, Endocrine, and Metabolism Center from early September 2021 to the end of January 2022. The study included 115 fully anonymized randomly selected patients. Patients with diabetes were assessed for erectile dysfunction through a questionnaire derived from “The International Index of Erectile Function (IIEF).” Additionally, hypogonadism has been diagnosed with serum testosterone levels lower than 264 mg/dL according to the Endocrine Society 2018 criteria for the diagnosis of male hypogonadism.

Results The average duration of diabetes was 6.2 years, and the mean glycated hemoglobin value was 9.3%. Dyslipidemia was the most prevalent chronic comorbid condition (84.3%) accompanying diabetes and erectile dysfunction, followed by hypertension (56.5%). An approximately similar rate of hypogonadism was observed in patients with diabetes and erectile dysfunction regardless of whether the other chronic disease was also present. From 115 patients included in this study, hypogonadism was diagnosed in 26% of patients with diabetes and erectile dysfunction.

Conclusion A significant number of hypogonadisms occur in patients with diabetes and erectile dysfunction, which require particular emphasis.

Keywords

- ▶ erectile dysfunction
- ▶ hypogonadism
- ▶ testosterone
- ▶ type 2 diabetes mellitus

Introduction

Diabetes mellitus (DM) is a chronic disease that affected 9.3% of the world's population in 2019 and is expected to increase in prevalence.¹ Sexual dysfunction in men with diabetes includes male erectile dysfunction and ejaculatory

failure. Nearly 20 to 30% of males have at least one episode of erectile dysfunction per year.² A higher prevalence is seen in patients with diabetes, where erectile problems are encountered in 49.2%.³ DM is considered a significant risk factor for erectile dysfunction⁴ and patients with DM are more likely to require more

article published online
June 16, 2023

DOI <https://doi.org/10.1055/s-0043-1769493>.
ISSN 1947-489X.

© 2023. The Libyan Biotechnology Research Center. All rights reserved.

This is an open access article published by Thieme under the terms of the Creative Commons Attribution-NonDerivative-NonCommercial-License, permitting copying and reproduction so long as the original work is given appropriate credit. Contents may not be used for commercial purposes, or adapted, remixed, transformed or built upon. (<https://creativecommons.org/licenses/by-nc-nd/4.0/>)

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

aggressive therapy for erectile dysfunction and even they may deteriorate rapidly.⁵

Erectile dysfunction has different etiologies, which might be present simultaneously. DM, aging, dyslipidemia, hypertension, atherosclerosis, obesity, metabolic syndrome, physical inactivity, smoking, low testosterone level, and psychological factors are all recognized contributing factors.⁶⁻⁹

Hypogonadism mediates reduced sex drive, and testosterone replacement may benefit erectile dysfunction with low testosterone levels. However, scientific knowledge tries to clarify all underlying etiologies, especially for patients with diabetes.¹⁰ Early identification and treatment of erectile dysfunction will improve mood, quality of life, and cholesterol levels and exert some cardiovascular protection. Moreover, phosphodiesterase inhibitors commonly used to treat erectile dysfunction require good testosterone availability for effective action.^{11,12}

In developing countries, sex is stigmatized. Patients with type 2 diabetes mellitus (T2DM) may find it challenging to bring up such topics to their doctors, especially in the presence of others.¹³ Knowing the size of the problem will allow clinicians to expect the disorder and pose pointed questions to identify, diagnose, and properly manage the problem. This study aimed to estimate the contribution of hypogonadism in T2DM patients with erectile dysfunction.

Patients and Methods

Design and Settings

A cross-sectional study assessed the extent of hypogonadism among patients with diabetes and erectile dysfunction who attended Faihaa Specialized Diabetes, Endocrine, and Metabolism Center in Basrah, Iraq, from early September 2021 to the end of January 2022.

Study Population

Cases are randomly selected from patients with diabetes who attend a diabetic center. Each one has the same chance of being selected and considered as the group's representative. A total of 115 fully anonymized patients were included in the study. All the participants were selected between the ages of 40 and 65. Patients who had previous spinal trauma were explicitly excluded from the study.

Assessments

Patients diagnosed with diabetes had been assessed for erectile dysfunction before being involved in the study. This is done using "The International Index of Erectile Function (IIEF)." It is a multidimensional self-report questionnaire to assess male sexual function. It had been considered the "gold standard" test to evaluate the severity of erectile dysfunction. It is composed of 15 precise questions with scored multiple answers from 0 to 5.¹⁴ Hypogonadism was diagnosed according to the Endocrine Society 2018 criteria for diagnosing male hypogonadism, which includes symptoms and signs consistent with testosterone hormone deficiency (serum testosterone less than 264 mg/dL).¹⁵

Data Collection

Questionnaires with direct supervision were provided to the patients to avoid the difficulty associated with several medical terms that could be uncomprehending to the patients. Three to five milliliters of venous blood were taken from the patient using a clot activator-containing tube in a fasting state at about 9 to 10 am. The sample was immediately transferred to the laboratory, allowed for clotting, and then centrifuged prior to the estimation of total testosterone by (COBAS e411 analyzer, Roche Company, Switzerland).

Statistical Analysis

Statistical Package for the Social Sciences version 25 (IBM SPSS Statistics for Windows, Version 25.0., IBM Corp, Armonk, New York, United States) was used for data analysis. Categorical data are expressed as numbers and percentages, and continuous data are expressed as mean \pm standard deviation.

Results

The demographic and clinical characteristics and select relevant comorbidities are presented in **Table 1**. The mean age of the included individuals was 53.1 ± 6.9 years, with a mean body mass index of 29.1 ± 3.9 kg/m², and the mean duration of DM was 6.2 ± 3.8 years. The hemoglobin A1c (HbA1c) was $9.3 \pm 2.3\%$; furthermore, the smoking rate was 21.1%, and depression was reported by 1.3% of patients. Over half (54.5%) of the patients had hypertension, 84.3% had dyslipidemia, and 7.8% had a history of ischemic heart disease. Additionally, 5.2% were on beta-blockers that may affect erectile function (**Table 1**).

Table 1 Demographic and clinical characteristics and the frequency of comorbidities (in decreasing frequency)

Feature	Results ^a
A. Demographic and clinical features (mean \pm standard deviation)	
Age (y)	53.1 \pm 6.9
Body mass index (kg/m ²)	29.1 \pm 3.9
Duration of diabetes (y)	6.2 \pm 3.8
HbA1c (%)	9.3 \pm 2.3
B. Comorbidities (n [%])	
Dyslipidemia	97 (84.3%)
Hypertension	65 (56.5%)
Smoking	24 (21.1%)
Ischemic heart disease	9 (7.8%)
Depression	2 (1.3%)
C. Medications relevant to erectile dysfunction: (n [%])	
Beta-blockers (any)	6 (5.2%)

Abbreviation: HbA1c, hemoglobin A1c.

^aResults are presented as (mean \pm standard deviation) or count (percentage).

Table 2 The frequency of risk factors and comorbid chronic conditions in patients with low testosterone erectile dysfunction by the serum testosterone level

Comorbidities	Low testosterone	Normal testosterone
No disease	13 (26%)	37 (74%)
Any disease (all)	17 (26%)	48 (74%)
Dyslipidemia	23 (23.7%)	74 (76.3%)
Hypertension	17 (26.1%)	48 (73.9%)
Obesity (BMI > 30)	12 (31.6%)	26 (68.4%)
Ischemic heart disease	2 (22.2%)	7 (77.8%)
Drugs (beta-blockers)	2 (33%)	4 (67%)
Depression	0 (0%)	2 (100%)

Abbreviation: BMI, body mass index.

The frequency of risk factors and comorbid chronic conditions in patients with diabetes and erectile dysfunction by the serum testosterone level is shown in **Table 2**. In patients with DM and male erectile dysfunction, 26% had low testosterone levels, while 74% had normal testosterone. This was not significantly different regardless of whether the patient had other chronic diseases or not (chi-squared $p = 0.985$). In a subgroup of patients with additional comorbidities, the testosterone level was normal in 76.3% of patients with dyslipidemia, 73.9% of the patients with hypertension, 77.8% of patients with ischemic heart disease, 67% of patients using beta-blockers, and 100% of patients with depression had a normal testosterone level.

Discussion

Even in healthier men, declining testosterone level is frequently connected to aging.¹⁶ Serum testosterone level was found to be subnormal in 28% of those more than 40-year-old in a longitudinal investigation on aging.¹⁷ In another study, although the variations in testosterone levels between diabetes and nondiabetes individuals were shown to be significant in the sixth decade, they subsequently vanished. Karakas et al in 2018 found that age did not affect the condition risk, and testosterone levels had no substantial correlation with age.¹⁸ Hypogonadism is not more common in diabetes individuals over 60 years old than in their younger equivalents.¹⁹

Male patients with diabetes have lower blood testosterone and a higher risk of developing hypogonadism than patients without diabetes. The underlying processes that govern low testosterone levels might be linked to aging, obesity, and insulin resistance, which are frequently encountered in patients with diabetes.²⁰ As research on DM with erectile dysfunction progresses, the prevalence of diabetes-related endocrine dysfunction becomes more updated and accurate.

In the current study, 26% of patients with diabetes suffering from erectile dysfunction were diagnosed with hypogonad-

ism. Low testosterone level was linked to an increased incidence of T2DM and vice versa in 43 trials, including 6,427 males.²¹ DM was linked to classic hypogonadism symptoms such as lower libido, fewer sexual attempts, and a high risk of sadness.²² The size of the testes and luteinizing hormone (LH) levels were also reduced, indicating that the condition had a central origin.²³

In men with diabetes, the penile and testicular systemic vascular flow was also severely decreased. Madhu et al examined the rate of hypogonadism in T2DM and its link to cardiovascular disease; hypogonadism was more common in T2DM patients with cardiovascular disease (40%) than in T2DM patients without cardiovascular disease (32%).²⁴ Total testosterone level was considerably lower in cardiovascular disease patients than in noncardiovascular individuals. They discovered a significant link between hypogonadism and coronary artery disease ($r = 0.177$, $p = 0.030$).

Our results concur with Al Hayek et al's study of 157 Saudi patients with T2DM revealing a significant rate of clinical hypogonadism. At least 25% of men with T2DM have abnormal testosterone and abnormally low LH and follicle-stimulating hormone (FSH) levels.²⁵

This study found no significant association between serum HbA1c level and hypogonadism. Serum testosterone levels have previously been found to be inversely linked with HbA1c readings.²⁶ Insulin resistance has been linked to low blood testosterone levels in males.²⁷ However, this study found no significant association between the patient's BMI level and the hypogonadism state, although the mean body mass index (BMI) value was slightly higher in the hypogonadism group. This is at variance with Al Hayek et al, who found that BMI was an independent risk factor for hypogonadism.²⁵ Hypogonadism was shown to be prevalent in 32% of 161 adult men with a median age of 45 years, in which 75% with extreme obesity (BMI > 40 kg/m²) had hypogonadism.²⁸ In obesity, testosterone to estradiol and androstenedione to estrone transformation is enhanced; estrogens reduce testosterone synthesis by inhibiting gonadotropin hormone-releasing hormone secretion from the hypothalamus and LH and FSH secretion from the pituitary by negative feedback.²⁹

This study is limited by inquiries concerning sexual health and its symptoms. It needs tremendous empathy and rapport-building with patients to openly reveal their concealed symptoms and worries to the treating physician. Additionally, the study is limited in part by not including enough patients with comorbidities to draw firm conclusions on the effect of these conditions on erectile function in patients with diabetes.

Conclusion

Low testosterone level is frequently encountered in individuals with diabetes and erectile dysfunction that may be overlooked. Particular emphasis on the extent of the problem should be available, particularly in our region where discussion of sexuality may be taboo. Further studies in this field are required to clarify the details of the problem and strengthen the treatment decision.

Authors' Contributions

A.M.S.A was involved in the collection of data and conduct of the work. D.J.K.A collected data and drafted the manuscript. A.A.M. designed the study and supervised the work. All authors reviewed and approved the final version of the article.

Compliance with Ethical Principles

The study was approved by at Faiha Specialized Diabetes, Endocrine, and Metabolism Center (FDEMC) ethical committee under Reference number 56/35/22 on 18/07/2018.

Funding and Sponsorship

None.

Conflict of Interest

None declared.

References

- 1 NIH Consensus Development Panel on Impotence. NIH consensus conference. Impotence. *JAMA* 1993;270(01):83–90
- 2 Lewis RW, Fugl-Meyer KS, Bosch R, et al. Epidemiology/risk factors of sexual dysfunction. *J Sex Med* 2004;1(01):35–39
- 3 Mohamid AR, Mousawi A, Abbas SH, et al. Erectile dysfunction in diabetic patients in the holy Kerbala/Iraq in 2018. *Karbala J Pharmaceut Sci* 2018;9(15):1–10
- 4 Corona G, Giorda CB, Cucinotta D, Guida P, Nada E, Gruppo di studio SUBITO-DE Sexual dysfunction at the onset of type 2 diabetes: the interplay of depression, hormonal and cardiovascular factors. *J Sex Med* 2014;11(08):2065–2073
- 5 Walsh TJ, Hotaling JM, Smith A, Saigal C, Wessells H. Men with diabetes may require more aggressive treatment for erectile dysfunction. *Int J Impot Res* 2014;26(03):112–115
- 6 Gandaglia G, Briganti A, Jackson G, et al. A systematic review of the association between erectile dysfunction and cardiovascular disease. *Eur Urol* 2014;65(05):968–978
- 7 Besiroglu H, Otuntemur A, Ozbek E. The relationship between metabolic syndrome, its components, and erectile dysfunction: a systematic review and a meta-analysis of observational studies. *J Sex Med* 2015;12(06):1309–1318
- 8 Yafi FA, Jenkins L, Albersen M, et al. Erectile dysfunction. *Nat Rev Dis Primers* 2016;2(01):16003
- 9 Brotto L, Atallah S, Johnson-Agbakwu C, et al. Psychological and interpersonal dimensions of sexual function and dysfunction. *J Sex Med* 2016;13(04):538–571
- 10 Malavige LS, Levy JC. Erectile dysfunction in diabetes mellitus. *J Sex Med* 2009;6(05):1232–1247
- 11 Kapoor D, Malkin CJ, Channer KS, Jones TH. Androgens, insulin resistance and vascular disease in men. *Clin Endocrinol (Oxf)* 2005;63(03):239–250
- 12 Zhang XH, Morelli A, Luconi M, et al. Testosterone regulates PDE5 expression and in vivo responsiveness to tadalafil in rat corpus cavernosum. *Eur Urol* 2005;47(03):409–416, discussion 416
- 13 Traish AM, Guay A, Feeley R, Saad F. The dark side of testosterone deficiency: I. Metabolic syndrome and erectile dysfunction. *J Androl* 2009;30(01):10–22
- 14 Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A. The international index of erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. *Urology* 1997;49(06):822–830
- 15 Bhasin S, Brito JP, Cunningham GR, et al. Testosterone therapy in men with hypogonadism: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab* 2018;103(05):1715–1744
- 16 Corona G, Bianchini S, Sforza A, Vignozzi L, Maggi M. Hypogonadism as a possible link between metabolic diseases and erectile dysfunction in aging men. *Hormones (Athens)* 2015;14(04):569–578
- 17 Kapoor D, Aldred H, Clark S, Channer KS, Jones TH. Clinical and biochemical assessment of hypogonadism in men with type 2 diabetes: correlations with bioavailable testosterone and visceral adiposity. *Diabetes Care* 2007;30(04):911–917
- 18 Karakas M, Schäfer S, Appelbaum S, et al. Testosterone levels and type 2 diabetes-no correlation with age, differential predictive value in men and women. *Biomolecules* 2018;8(03):76. Doi: 10.3390/biom8030076
- 19 Harman SM, Metter EJ, Tobin JD, Pearson J, Blackman MR Baltimore Longitudinal Study of Aging. Longitudinal effects of aging on serum total and free testosterone levels in healthy men. *J Clin Endocrinol Metab* 2001;86(02):724–731
- 20 Costanzo PR, Knoblovits P. Male gonadal axis function in patients with type 2 diabetes. *Horm Mol Biol Clin Investig* 2016;26(02):129–134
- 21 Ding EL, Song Y, Malik VS, Liu S. Sex differences of endogenous sex hormones and risk of type 2 diabetes: a systematic review and meta-analysis. *JAMA* 2006;295(11):1288–1299
- 22 Corona G, Mannucci E, Petrone L, et al. Association of hypogonadism and type II diabetes in men attending an outpatient erectile dysfunction clinic. *Int J Impot Res* 2006;18(02):190–197
- 23 Schoeller EL, Schon S, Moley KH. The effects of type 1 diabetes on the hypothalamic, pituitary and testes axis. *Cell Tissue Res* 2012;349(03):839–847
- 24 Madhu SV, Aslam M, Aiman AJ, Siddiqui A, Dwivedi S. Prevalence of hypogonadism in male type 2 diabetes mellitus patients with and without coronary artery disease. *Indian J Endocrinol Metab* 2017;21(01):31–37
- 25 Al Hayek AA, Robert AA, Alshammari G, Hakami H, Al Dawish MA. Assessment of hypogonadism in men with type 2 diabetes: a cross-sectional study from Saudi Arabia. *Clin Med Insights Endocrinol Diabetes* 2017;10:1179551417710209. Doi: 10.1177/1179551417710209
- 26 Fukui M, Soh J, Tanaka M, et al. Low serum testosterone concentration in middle-aged men with type 2 diabetes. *Endocr J* 2007;54(06):871–877
- 27 Farooq R, Bhat MH, Majid S, Mir MM. Association between T2DM and the lowering of testosterone levels among Kashmiri males. *Arch Endocrinol Metab* 2021;64(05):528–532
- 28 Luconi M, Samavat J, Seghieri G, et al. Determinants of testosterone recovery after bariatric surgery: is it only a matter of reduction of body mass index? *Fertil Steril* 2013;99(07):1872–9.e1
- 29 Liu Y, Ding Z. Obesity, a serious etiologic factor for male subfertility in modern society. *Reproduction* 2017;154(04):R123–R131