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ORIGINAL ARTICLE

Frequency and Correlation of Hypogonadism in Men with Type 2 Diabetes

ADNAN ALI[1], AFAQ NAEEM[2], LAIBA NASEER[3], NADEEM NAEEM[4], SHAHID WAHEED[5], MARYAM MASTOOR[6]
[1]*Fellow Endocrinology, Bahria International Hospital, Lahore*
[2]*House Officer Internal Medicine, Jinnah Hospital, Lahore*
[3]*House Officer, Shaikh Zayed Hospital, Lahore*
[4]*Consultant Endocrinologist and Physician, MMIH, Karachi*
[5]*Assistant Professor, Department of Family Medicine, University of Lahore*
[6]*Assistant Professor Biochemistry, Amna Inayat Medical College, Lahore*
Corresponding author: Adnan Ali, Email: adnanali126dr@gmail.com

ABSTRACT

Aim: The present study aimed to determine the frequency and association of hypogonadism in men with type 2 diabetes mellitus.

Material and Methods: This cross-sectional study was conducted on 242 type 2 DM male patients in the Department of General Medicine, Bahria International Hospital, Lahore from 16th January 2022 to 15th July 2022. The Androgen deficiency in aging male (ADAM) questionnaire was used for screening hypogonadal symptoms in the study group. The presence of low serum testosterone below 3 ng/mL and positive ADAM score was referred to as hypogonadism. T2DM patients with and without hypogonadism had their clinical and biochemical variables compared. Total testosterone, BMI, free testosterone, waist circumference, and sex hormone–binding globulin were measured. SPSS version 26 was used for data analysis.

Results: Of the total 242 T2DM male patients, the prevalence of hypogonadism was 24.8% (n=60). The most prevalent symptoms in T2DM patients were hypogonadal symptoms. The overall mean age was 45.8± 9.63 years with range (25-70 years). Mean BMI value was 24.8 ± 3.64 kg/m2. The incidence of overweight and obese patients were 17.8% and 49.3% respectively. The prevalence of erectile dysfunction, reduced libido, and work performance deterioration in hypogonadism were 94.8%, 68.2%, and 56.3% respectively. T2DM patients without hypogonadism had lower a) incidence of diabetic neuropathy (18.6% vs. 43.8%; p=0.021), b) T2DM duration (5.3± 3.82 vs. 9.2± 4.9 years; P=0.002), c) occurrence of diabetic retinopathy (26.9% vs. 57.8%; P=0.006), and d) HbA1c (8.9± 1.53% vs. 9.9 ± 2.54%: P=0.005), and insulin therapy (21.5% vs. 45.8%: P=0.031) compared to those with hypogonadism.

Conclusion: The present study found that prevalence of hypogonadism was 24.8% in type 2 diabetes mellitus. Patients with hypogonadism had higher HbA1c, higher prevalence of neuropathy and retinopathy, longer diabetic duration, and predominantly used insulin therapy than those T2DM patients without hypogonadism.

Keywords: Hypogonadism, Type 2 diabetes mellitus, Androgen deficiency in aging male (ADAM).

INTRODUCTION

Type 2 diabetes and reduced insulin sensitivity are associated with low testosterone levels in men [1]. Type 2 diabetes is characterized by insulin resistance. Men with healthy testosterone levels have lower insulin levels [2]. Insulin resistance and type 2 diabetes are also predicted by low testosterone levels [3]. Furthermore, insulin resistance and adipose tissue in the upper abdomen were associated with low testosterone. Type 2 diabetes (T2D) is associated with low testosterone (T) in large epidemiological studies [4, 5]. A biological marker T was used in these studies and found to be frequently low in males with T2DM, often in conjunction with dyslipidaemia and abdominal fat. The testosterone levels of diabetic men are also lower than those of nondiabetic subjects [6]. As a result of the mean testosterone levels measured by equilibrium dialysis, the most commonly used and clinically relevant testosterone assay, being significantly lower in 33% of men with type 2 diabetes, Asaduzzaman et al. [7] identified a significant decrease in the free testosterone levels of 33% of these men. Cross-sectional studies have consistently shown that males with T2DM have a higher prevalence of hypogonadism [8]. Though the pathogenic mechanisms remain unclear, there is an increasing amount of discussion around its association with type 2 diabetes mellitus and hypogonadism [9].

The presence of hypogonadism in T2DM subjects appears to have significant health consequences. Male hypogonadism is related to sexual and reproductive dysfunction, decreased energy levels, decreased bone mineral density, sadness of mood, decreased insulin sensitivity, visceral adiposity, and increased cardiovascular risk [10]. Type 2 DM patients were screened using biochemical features and clinical variables for the presence of hypogonadism. The Androgen deficiency in aging male (ADAM) questionnaire was used for the clinical evaluation of hypogonadism symptoms [11]. The hypogonadism diagnosis was confirmed based on positive score with measurement of serum total testosterone on ADAM [12]. Limited investigations have been carried out on T2DM patients for the presence of hypogonadism in Pakistan [13, 14]. There is scarcity of data regarding biochemical and clinical features related to hypogonadism in male patients. Therefore, the present study aimed to evaluate the prevalence and correlation of hypogonadism in T2DM adult male patients.

METHODOLOGY

This cross-sectional study was conducted on 242 type 2 DM male patients in the Department of General Medicine, Bahria International Hospital, Lahore from 16th January 2022 to 15th July 2022. Research and ethical committee approved the study protocol. Written informed consent was taken from each individual. The Androgen deficiency in aging male (ADAM) questionnaire was used for screening hypogonadal symptoms in study groups. The presence of low serum testosterone below 3 ng/mL and positive ADAM score was referred to as hypogonadism. T2DM patients with and without hypogonadism had their clinical and biochemical variables compared. Total testosterone, BMI, free testosterone, waist circumference, and sex hormone–binding globulin were measured. T2DM patients with age 25 to 70 years fulfilling the eligibility criteria were enrolled. Patients suffering from advanced malignancy, major psychiatric illness, chronic liver disease, tuberculosis, and patients receiving testosterone replacement therapy were excluded. Clinical data, demographic details, and anthropometric information were gathered. Based on BMI, all the patients were classified as follows: underweight BMI<18.5 kg/m2, normal weight BMI 18.5-23.0 Kg/m2, overweight BMI 23.1-25 kg/m2. Glycated hemoglobin (HbA1c), fasting plasma glucose (FPG), serum creatinine, and postprandial plasma glucose (PPG) were determined. ADAM questionnaire confirmed the diagnosis of hypogonadism based on their symptoms.

SPSS version 26 was used for data analysis. Numerical variables were described as mean and standard deviation. Qualitative variables were expressed as frequency and percentages. Chi-square test was used for comparing the T2DM patients with hypogonadism and without hypogonadism taking 95% confidence interval and 5% level of significance.

RESULTS

Of the total 242 T2DM male patients, the prevalence of hypogonadism was 24.8% (n=60). The most prevalent symptoms in T2DM patients were hypogonadal symptoms. The overall mean age was 45.8± 9.63 years with range (25-70 years). Mean BMI value was 24.8 ± 3.64 kg/m2. The incidence of overweight and obese patients were 17.8% and 49.3% respectively. T2DM patients without hypogonadism had lower a) incidence of diabetic neuropathy (18.6% vs. 43.8%; p=0.021), b) T2DM duration (5.3± 3.82 vs. 9.2± 4.9 years; P=0.002), c) occurrence of diabetic retinopathy (26.9% vs. 57.8%; P=0.006), and d) HbA1c (8.9± 1.53% vs. 9.9 ± 2.54%: P=0.005), and insulin therapy (21.5% vs. 45.8%: P=0.031) compared to those with hypogonadism. Demographic details and baseline characteristics are shown in Table-1. Figure-1 illustrates the distribution of patients based on their age. Distribution of patients on the basis of BMI as underweight, normal, overweight, and obese are depicted in Figure-2. Biochemical and clinical details are shown in Table-II. The incidence of diabetic retinopathy, hypertension, neuropathy, CAD, and insulin therapy is demonstrated in Figure-3. HbA1c levels (%) and diabetes duration in different T2DM patients are shown in Table-III. Based on ADAM scores, the prevalence of erectile dysfunction, reduced libido, and work performance deterioration in hypogonadism were 94.8%, 68.2%, and 56.3% respectively as shown in Figure-4. Different biochemical and clinical features of T2DM patients with and without hypogonadism are compared in Table-IV.

Table-1: Demographic details and baseline characteristics

Variables	Value
Age (years) Mean ± SD	45.8± 9.63
Marital Status N (%) Single Married	 14 (5.8) 228 (94.5)
Smoking History N (%)	129 (53.3)
Height (cm)	165.8±5.71
Weight (kg)	66.9±4.6
BMI (kg/m2)	24.8 ± 3.64
Waist circumference (cm)	91.6±11.8

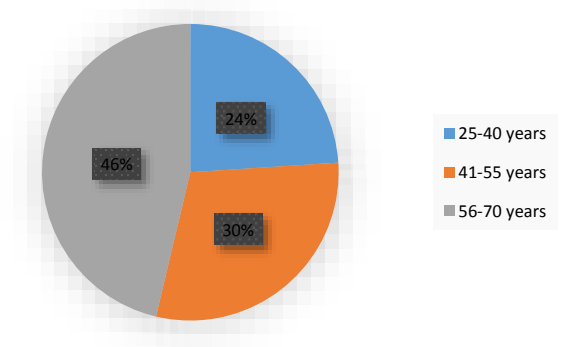

Figure-1: Age-wise distribution of patients

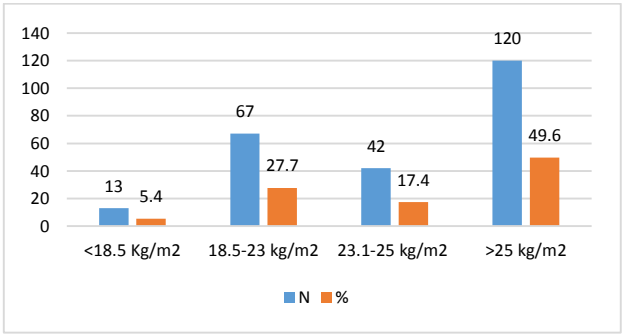

Figure-2: Distribution of patients based on BMI

Table-2: Biochemical and clinical details

Variables	Value
Serum creatinine (mg/dL)	0.8±0.51
SBP (mm Hg)	124.8±16.9
DBP (mm Hg)	76.2±9.6
Reduced eGFR (<60 mL/minute/1.73 m2)	16 (6.6%)
FPG (mg/dL)	193.8±69.9
PPG (mg/dL)	259.2±91.32

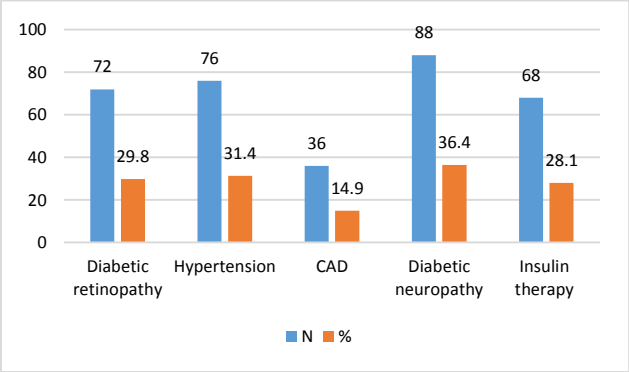

Figure-3: incidence of diabetic retinopathy, hypertension, neuropathy, CAD, and insulin therapy

Table-3: HbA1c levels (%) and diabetes duration in different T2DM patients

Variables	Frequency (N)	Percentage (%)
HbA1c (%) <8 8-10 >10	 68 70 116	 28.1 28.9 47.9
Diabetes Duration (years) <5 6-10 >10	 128 72 42	 52.9 29.8 17.4

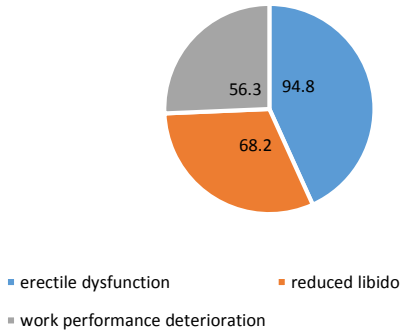

Figure-4: Based on ADAM scores, the prevalence of erectile dysfunction, reduced libido, and work performance deterioration in hypogonadism

Table-4: Comparison of Different biochemical and clinical features of T2DM patients with and without hypogonadism.

Variables	T2DM with hypogonadism (%)	T2DM without hypogonadism (%)	P-value
SBP (mm Hg)	125.3±16.64	126.88±20.25	0.418
DBP (mm Hg)	76.7±10.34	79.3±9.82	0.541
CAD	14 (23.3)	24 (13.2)	0.132
Hypertension	26 (43.3)	50 (27.5)	0.124
Diabetic neuropathy	43.8	18.6	0.021
Diabetic retinopathy	57.8	26.9	0.006
Insulin therapy	45.8	21.5	0.031
HbA1c (%)	9.9 ± 2.54	8.9± 1.53	0.005
Serum creatinine (mg/dL)	1.2±0.49	0.8±0.43	0.082

DISCUSSION

The present study mainly investigated the prevalence and correlation of hypogonadism in type 2 diabetes mellitus and reported that the incidence of hypogonadism was 24.8%. Frequency of diabetic neuropathy, retinopathy, CAD, hypertension, insulin therapy, and HbA1c (%) was lower in T2DM patients without hypogonadism than without hypogonadism. The prevalence of erection dysfunction was the most prevalent health issue in male adult T2DM patients followed by reduced libido, and work performance deterioration in hypogonadism. Kizilay et al [15] reported that the incidence of hypogonadism was 15% in T2DM patients which is lower than the reported 24.8% in the current study. Agarwal et al [16] found that hypogonadism was present in 20.7% T2DM patients. Another study by Madhu et al [17] reported that about 32% T2DM patients had lower serum testosterone without CAD and 40% with CAD. However, Bajaj et al [18] found that lower testosterone was 44.5% in T2DM patients. The overall prevalence of hypogonadism varied from 7% to 51% in T2DM reported worldwide [19, 20].

Numerous studies showed that hypogonadism is significantly associated with T2DM in adult male [21, 22]. Hypogonadism presence in T2DM patients is due to the most significant contributor known as overweightness and obesity which in turn cause lower testosterones [23]. In T2DM patients with hypogonadism, erectile dysfunction was the most common symptom (94.8%) followed by reduced libido in 68.2%. Similar findings were reported by White et al [24] and Ugwa et al [25]. Both studies commonly reported that erectile dysfunction was the most affirmative answer given on ADAM questionnaire.

In the present study, higher diabetes duration was observed in T2DM patients with hypogonadism than without hypogonadism. Zheng et al [26] and Hu et al [27] reported similar findings in their study on hypogonadism in type 2 diabetes mellitus patients. The higher prevalence of hypogonadism was mainly due to HbA1c and DM higher duration in underweighted T2DM patients.

The HbA1c level was higher in T2DM patients with hypogonadism compared to without hypogonadism. Lee et al [28] reported similar results in terms of lower serum testosterones with HbA1c >6.5% than the control group. The pathogenic mechanisms responsible for lower testosterone are yet to be determined [29]. The role of hyperglycemia in the development of hypogonadism, in addition to the role of insulin resistance, is not well understood. Laird et al.[30] used a cell culture model to show that high glucose concentrations have a negative effect on the expression of genes that mediate the function of GnRH neurons.

CONCLUSION

The present study found that prevalence of hypogonadism was 24.8% in type 2 diabetes mellitus. Patients with hypogonadism had higher HbA1c, higher prevalence of neuropathy and retinopathy, longer diabetic duration, and predominantly used insulin therapy than those T2DM patients without hypogonadism.

REFERENCES

1. Gangwar SK, Verma SK, Modi S. Frequency and correlates of hypogonadism in adult males with type 2 diabetes mellitus. Indian J Endocr Metab 2021;25:320-5.
2. Li Y, Zhang M, Liu X, Cui W, Rampersad S, Li F, et al. Correlates and prevalence of hypogonadism in patients with early- and late-onset type 2 diabetes. Andrology 2017;5:739–43.
3. Herrero A, Marcos M, Galindo P, Miralles JM, Corrales JJ. Clinical and biochemical correlates of male hypogonadism in type 2 diabetes. Andrology 2018;6:58–63.
4. Selim S, Lona H, Imran S, Rahman M, Mahjabeen S, Mustari M. Frequency and Determinants of Hypogonadism and Erectile Dysfunction in Men with Newly Detected Type 2 Diabetes. Bangladesh Journal of Endocrinology and Metabolism¦ Volume. 2022 Sep;1(1).
5. Handelsman DJ. History of androgens and androgen action. Best Pract Res Clin Endocrinol Metab. 2022:101629. doi: 10.1016/j.beem.2022.101629. Epub ahead of print. PMID: 35277356.
6. Bhasin S, Brito JP, Cunningham GR, Hayes FJ, Hodis HN, Matsumoto AM, et al. Testosterone therapy in men with hypogonadism: An endocrine society clinical practice guideline. J Clin Endocrinol Metab 2018;103:1715-44.
7. Asaduzzaman M, Kamrul-Hasan AB, Islam A, Kabir MA, Chanda PK, Islam MA, et al. Frequency and risk factors of erectile dysfunction among Bangladeshi adult men with type 2 diabetes mellitus. Mymensingh Med J 2020;29:66-72.
8. Khodarahimi S, Mazraeh N, Bougar MR, Sheikhi S. Hypogonadism and Sexual functioning in males with and without Diabetes Type II. Sexologies. 2022 Jun 1;31(2):138-44.
9. Corona G, Isidori AM, Aversa A, Bonomi M, Ferlin A, Foresta C, et al. Male and female sexual dysfunction in diabetic subjects: focus on new antihyperglycemic drugs. Rev Endoc Metab Disord 2020;21(1):57—65, http://dx.doi.org/10.1007/s11154-019-09535-7.
10. Esteghamati A, et al. Diabetes in Iran: prospective analysis from first nationwide diabetes report of national program for prevention and control of diabetes (NPPCD-2016). Sci Rep 2017;7(1):13461.
11. Grinspon RP, Bergadá I, Rey RA. Male hypogonadism and disorders of sex development. Front Endocrinol 2020;11:211, http://dx.doi.org/10.3389/fendo.2020.00211.
12. Guariguata L, Whiting DR, Hambleton I, Beagley J, Linnenkamp U, Shaw JE. Global estimates of diabetes prevalence for 2013 and projections for 2035. Diabetes Res Clin Pract 2014;103(2):137—49.
13. Kaiser AB, Zhang N, Derplutijm WV. Global prevalence of type 2 diabetes over the next ten years (2018—2028). Diabetes 2018;67(1):202—10, http://dx.doi.org/10.2337/db18-202-LB.
14. Raza MT, Sharif S, Khan ZA, Naz S, Mushtaq S, Umer A. Frequency of hypogonadism in type 2 diabetes mellitus patients with and without coronary artery disease. Cureus 2019;11(12):e6500, http://dx.doi.org/10.7759/cureus.6500.
15. Kizilay F, Gali HE, Serefoglu EC. Diabetes and sexuality. Sex Med Rev 2017;5(1):45—51.
16. Agarwal PK, Singh P, Chowdhury S, Sharma SK, Majumdar A, Shah P, et al. A study to evaluate the prevalence of hypogonadism in Indian males with type -2 diabetes mellitus. Indian J Endocrinol Metab 2017;21:64-70.
17. 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 Endocr Metab 2017;21:31-7.
18. Bajaj S, Srivastava A, Varma A, Tiwari A. Serum testosterone in males with newly diagnosed type 2 diabetes mellitus and microvascular complications. Sri Lanka J Diabetes Endocrinol Metab 2016;6:18-22.
19. Liu Q, Zhao Y, Gu Y, Shang X, Zhou Y, Zhang H, et al. The association of age-related differences in serum total testosterone and sex hormone-binding globulin levels with the prevalence of diabetes. Arch Gerontol Geriatr 2020;88:104040, http://dx.doi.org/10.1016/j.archger.2020.104040.
20. Maiorino MI, Bellastella G, Esposito K. Diabetes and sexual dysfunction: current perspectives. Diabetes Metab Syndr Obesity: Targets Ther 2014;7:95—105, http://dx.doi.org/10.2147/DMSO.S36455.
21. Mushtaq S, Khan K, Abid S, Umer A, Raza T. Frequency of hypogonadism and erectile dysfunction in type II diabetic patients. Cureus 2018;10(5):e2654, http://dx.doi.org/10.7759/cureus.2654.
22. Shiferaw WS, Akalu TY, Aynalem YA. Prevalence of erectile dysfunction in patients with diabetes mellitus and its association with body mass index and glycated hemoglobin in Africa: a systematic review and meta-analysis. Int J Endocrinol 2020;2020:5148370, http://dx.doi.org/10.1155/2020/5148370.
23. Travison TG, Vesper HW, Orwoll E, Wu F, Kaufman JM, Wang Y, et al. Harmonized reference ranges for circulating testosterone levels in men of four cohort studies in the United States and Europe. J Clin Endocrinol Metab 2017;102(4):1161—73, http://dx.doi.org/10.1210/jc.2016-2935.
24. White H, Sabarwal S. Quasi-experimental design and methods, methodological briefs: impact. Evaluation 8. Florence: UNICEF Office of Research; 2014.
25. Ugwu TE, Ikem RT, Kolawole BA, Ezeani IU. Clinicopathological assessment of hypogonadism in men with type 2 diabetes mellitus. Indian J Endocrinol Metab 2016;20:667-73.
26. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nat Rev Endocrinol 2018; ;14(2):88—98, http://dx.doi.org/10.1038/nrendo.2017.151.
27. Hu X, Han X, Chen Y, Xiang P, Wei X, Gong T, He Z, Su Y, Chen G, Liu C. Factors Defining the Association Between Vitamin D and Testosterone in Males With Type 2 Diabetes and Hypogonadism. Frontiers in Endocrinology. 2022;13.
28. Christakos S, Dhawan P, Verstuyf A, Verlinden L, Carmeliet G, Vitamin D. Metabolism, Molecular Mechanism of Action, and Pleiotropic Effects. Physiol Rev (2016) 96:365–408. doi: 10.1152/physrev.00014.2015.
29. Holick MF. The Vitamin D Deficiency Pandemic: Approaches for Diagnosis, Treatment and Prevention. Rev Endocr Metab Disord (2017) 18:153–65. doi: 10.1007/s11154-017-9424-1
30. Laird E, O'Halloran AM, Carey D, Healy M, O'Connor D, Moore P, et al.. The Prevalence of Vitamin D Deficiency and the Determinants of 25(OH)D Concentration in Older Irish Adults: Data From The Irish Longitudinal Study on Ageing (TILDA). J Gerontol A Biol Sci Med Sci (2018) 73:519–25. doi: 10.1093/gerona/glx168.