A study to evaluate the prevalence of hypogonadism in Indian males with Type-2 diabetes mellitus

Pankaj Kumar Agarwal, Parminder Singh, Subhankar Chowdhury, S. K. Sharma, Anirban Majumdar, Parag Shah, Rakesh Sahay, S. Vageesh Ayyar, Hemant Phatade, Chandar M. Batra, Raeesuddin Syed, Pradeep Shetty

Hormone Care and Research Center, Near St. Mary’s School, Ghaziabad, Uttar Pradesh, 1Department of Endocrinology, Dayanand Medical College and Hospital, Civil Lines, Ludhiana, Punjab, 2Department of Endocrinology, IPGME&R and SSKM Hospital, Ronald Ross Building, 4th Floor, 244, A J C Bose Road, Thyroid and Hormone Clinic, Dhakuria, Kolkata, West Bengal, 3Thyroid and Endocrine Centre, Near 4 No. ESI Hospital, Jaipur, Rajasthan, 4Gujarat Endocrine Centre, 2nd Floor, Silver Brook B, Opposite Doctor House, Near Parimal Crossing, Ahmedabad, Gujarat, 5Department of Endocrinology, Osmania General Hospital, 2nd Floor, Golden Jubilee Block, Afzalgunj, Afzalgunj, Hyderabad, Telangana, 6Department of Endocrinology, St. John’s Medical College and Hospital, Bengaluru, Karnataka, 7Samrat Endocrine Institute of Diabetes, Obesity and Thyroid, Aurangabad, 8Global Medical Affairs, MSD Pharmaceuticals Private Limited, 10th Floor, Platina Building, C-59, G-Block, Bandra Kurla Complex, Mumbai, Maharashtra, 9Department of Endocrinology, Sarita Vihar, Delhi Mathura Road, New Delhi, India

ABSTRACT

Background: A high prevalence of hypogonadism in men with Type-2 diabetes mellitus (T2DM) has been reported worldwide. Objectives: To evaluate the prevalence of hypogonadism in Indian males with T2DM and assess the primary and secondary hypogonadism along with androgen deficiency. Materials and Methods: In this cross-sectional study, 900 men with T2DM were evaluated using androgen deficiency in aging male questionnaire. They were screened for demographic characteristics, gonadal hormone levels, lipid profile, and glycosylated hemoglobin. Results: The prevalence of hypogonadism in T2DM patients was found to be 20.7% (186 out of 900). Hypogonadism was of testicular origin (primary) in 48/186 (25.8%) patients, of pituitary or hypothalamic origin (secondary) in 14/186 (7.53%), and remaining 124/186 (66.67%) patients were found to have low testosterone with the inappropriate normal level of luteinizing hormone and Follicle-stimulating hormone. 451/900 (50.1%) patients were only symptomatic but had normal testosterone levels. Further 263 patients out 900 were asymptomatic, of which 51/900 (5.7%) patients had low levels of testosterone and 212/900 (23.5%) patients had normal testosterone level without symptoms. There were no deaths or other serious adverse events except mild pyrexia which was not related to the study. Conclusion: Hypogonadism diagnosis, at times, might not be validated with the help of androgen deficiency questionnaire or symptoms only. Given the large number of patients of T2DM in India, the incidence of hypogonadism is more in diabetic patients as compared to the general population. Hence, implementation of screening programs in diabetic patients is necessary to understand and detect individuals with low serum total testosterone at any early stage and to supplement testosterone accordingly.

Key words: Androgen, diabetes mellitus, hypogonadism, testosterone

INTRODUCTION

Diabetes is fast becoming the epidemic of the 21st century. Type-2 diabetes mellitus (T2DM), which is more prevalent...
and the main driver of the diabetes epidemic, now affects 5.9% of the world’s population. In India, as per the 2011 estimates reported by the Indian Council of Medical Research, India diabetes study, 62.4 and 77.2 million people have diabetes and prediabetes, respectively.[1]

Hypogonadism is defined as a clinical syndrome which consists of clinical symptoms, with or without signs and associated with biochemical evidence of testosterone deficiency.[2] Male hypogonadism is a recognized medical condition that remains underdiagnosed by clinicians.[3] Several large studies over the last few years have reported a high prevalence of low testosterone levels in men (hypogonadism) with T2DM.[4] It has been demonstrated that free testosterone levels, which are independent of sex hormone-binding globulin (SHBG), are low in one-third of diabetic men.[5]

Visceral obesity is an important cause of insulin resistance which is an important feature of T2DM. Studies have shown that free testosterone levels are low in obese men and correlates inversely with the degree of obesity.[6,7] There is increased deposition of abdominal adipose tissue in hypogonadal patients, which in turn leads to a further decrease in testosterone concentrations, through conversion to estradiol by aromatase estradiol further favors abdominal fat deposition and perpetuates testosterone.[4]

Moreover, when combined with T2DM, obesity has been associated with a 50% prevalence of subnormal testosterone levels compared with 44% in normal weight men with T2DM, 40% in obese men without T2DM, and 26% in normal weight men without T2DM suggesting that both T2DM and obesity may be independent risk factors for hypogonadism and that the two conditions together may have an additive effect on the prevalence of hypogonadism.[8]

Interventional studies have shown a beneficial effect of testosterone replacement therapy (TRT) on insulin resistance.[9] A study in healthy men with low total testosterone reported an improvement in insulin sensitivity with testosterone treatment.[10] TRT has also been shown to reduce insulin resistance in men with obesity,[11,12] men with heart failure,[12] and T2DM patients.[13] Studies in Type-2 diabetic men have shown an improvement in glycemic control with TRT.[13,14]

These findings demonstrate the importance of investigating men with diabetes for testosterone deficiency. However, this data in India are scarce, and it is very important to understand the present disease burden in India. The present study was conducted to assess the prevalence of hypogonadism in Indian men with T2DM.

**Materials and Methods**

**Study design**

This was a multicenter, prospective, epidemiological study which was conducted in 10 centers of India, from five different geographical regions so as to represent the truly national data. The study recorded and evaluated the information of participating patients by means of a study pro forma and laboratory tests. This study involved recruitment of confirmed diagnosed T2DM patients with almost equal number of patients in three age groups (30–39, 40–49, and 50–59 years), and the program was carried out in routine clinical practices of participating health-care practitioners in five regions (Northern, Southern, Central, Eastern, and Western) of India.

The study was approved by the Institutional Review Board/Independent Ethics Committees and was conducted as per the International Conference on Harmonisation good clinical practice, the Declaration of Helsinki, and the Indian Council of Medical Research Ethical Guidelines. The study was registered under Clinical Trials Registry-India (CTRI) (www.ctri.nic.in) with the registration number as (REF/2013/09/005747).

**Patients**

All patients were provided information about the study, and informed consent was obtained before any screening procedure and enrollment into the study. Individuals were enrolled on the fulfillment of eligibility criteria, who were willing to provide informed consent. Patients with known causes of hypogonadism, T1DM, severe diseases such as chronic liver disease, renal disease, advanced malignancy, debilitating diseases such as tuberculosis, malabsorption, inflammatory bowel disease, pyrexia of unknown origin, acquired immunodeficiency syndrome, sickle cell disease, autoimmune diseases such as rheumatoid arthritis, ankylosing spondylitis, any inflammatory disease or infection, and already receiving hormone replacement therapy or with severe psychological symptoms were excluded from the study. Duration of participation of patient was from 1 to 7 days. Participation in the study did not interfere with the routine medical treatment of the patient. No trial medication was administered during the study.

**Data collection**

The patients' demographic characteristics were collected using a prestructured questionnaire. Smoking and alcohol habits were assessed by dividing men into categories
of smokers and nonsmokers and consumers and nonconsumers, respectively. Education status was also assessed by dividing men into categories of illiterate and literate individuals. The study participants were asked to complete the androgen deficiency in aging male (ADAM) questionnaire. A positive response is based on a decrease in libido or the strength of erections, or any three nonspecific questions that may include a decrease in muscle strength, fatigability, mood changes, and loss of height. Blood was withdrawn and the serum was aliquoted to determine serum gonadal hormone levels (total testosterone, free testosterone, SHBG, luteinizing hormone (LH), Follicle-stimulating hormone (FSH), prolactin, and estradiol). These blood aliquots from the patients were analyzed and summarized, using descriptive statistics, according to age ranges, BMI ranges and glycosylated hemoglobin (HbA1c) levels. All the above continuous parameters will be summarized using mean, standard deviation, median, and range. The primary (hypergonadotropic) androgen deficiency is defined as high levels of FSH or LH >10 IU/L, whereas the secondary (hypogonadotropic) androgen deficiency is defined as low levels of FSH or LH <2 IU/L. Similarly, patients in this study, who were positive on ADAM questionnaire and having deranged levels of FSH or LH as per the above statement, were classified as cases of primary and secondary hypogonadism. The prevalence rate of primary (hypergonadotropic) and secondary (hypogonadotropic) androgen deficiency in patients with T2DM according to age ranges, BMI ranges, and HbA1c levels were presented using proportion and 95% confidence interval (CI). The missing data will not be imputed. BMI was computed by dividing the weight in kilograms by the square of height in meters. Overweight was defined as BMI 23-24.9 kg/m², and obesity was defined as BMI ≥25 kg/m². Testosterone deficiency is defined as low free testosterone levels of <0.255 nmol/L with confirmation from a repeat test on separate occasion. In our study, hypogonadism was defined as patients showing as low free testosterone and who were symptomatic hypogonadal assessed through ADAM questionnaire.

Statistical analysis

All the statistical reports including summary tables and listings were generated using a customized reporting Statistical Analysis System (SAS®) Version 9.1.3 for windows (SAS Institute, Cary, North Carolina, USA).

RESULTS

Disposition

Overall 900 patients were enrolled and evaluated in the study excluding the six drop-out patients who were unavailable to provide their repeat free testosterone. All patients were included in the safety populations. In addition, all the patients aged between 30 and 59 years completed the study as per the protocol.

Demographics

The overall mean age (years) ± standard deviation (SD) was 45.2 ± 8.14, mean weight (kg) ±SD was 74.04 ± 13.843, mean height (cm) ±SD was 167.9 ± 6.83, and mean BMI (kg/m²) ±SD was 26.18 ± 4.212 [Table 1]. 199 (22.1%) patients were smokers, 98.2% were literate, and 28.6% patients were consumers of alcohol.

Primary efficacy

The percentage prevalence of hypogonadism (includes patients with positive symptoms evaluated by ADAM questionnaire and patients with low levels of testosterone evaluated by biochemical assay) was 20.7% (186 out of 900) [Table 2]. Hypogonadism was of testicular origin (primary) in 48/186 (25.8%) patients, of pituitary or hypothalamic origin (secondary) in 14/186 (7.53%) patients, and remaining 124/186 (66.67%) patients were found to have normal FSH/LH level with inappropriate low levels of

Table 1: Summary of demographic and baseline characteristics

| Parameter/statistics | Overall (n=900) |
|----------------------|----------------|
| Age (years)          | n=900          |
| Mean (SD)            | 45.2 (8.14)    |
| Range (minimum:maximum) | 30:59      |
| Weight (kg)          | n=900          |
| Mean (SD)            | 74.05 (13.843)|
| Range (minimum:maximum) | 40:131.4   |
| Height (cm)          | n=900          |
| Mean (SD)            | 167.9 (6.83)   |
| Range (minimum:maximum) | 147:190  |
| BMI (kg/m²)          | n=900          |
| Mean (SD)            | 26.18 (4.212)  |
| Range (minimum:maximum) | 15.3:50.0  |
| Marital status (%)   |               |
| Married              | 880 (97.8)     |
| Unmarried            | 20 (2.2)       |
| Dietary habits (%)   |               |
| Vegetarian           | 365 (40.6)     |
| Nonvegetarian        | 521 (57.9)     |
| Other                | 14 (1.6)       |
| Education (%)        |               |
| Literate             | 884 (98.2)     |
| Illiterate           | 16 (1.8)       |
| Smoking habit (%)    |               |
| Smokers              | 199 (22.1)     |
| Nonsmoker            | 701 (77.9)     |
| Alcohol consumption (%) |            |
| Consumer             | 257 (28.6)     |
| Nonconsumer          | 643 (71.4)     |

SD: Standard deviation, BMI: Body mass index
testosterone [Table 3]. Hypogonadism was most prevalent in the 5th and 6th decades \((P = 0.0128\) for 40–50 years age group and \(P < 0.0001\) for 50–60 years age group). The prevalence was higher in underweight patients than those who weighed normal or were obese \((P = 0.0154)\). 451 (50.1%) patients had symptoms but had normal testosterone levels. 451 (50.1%) patients were only symptomatic but had normal testosterone levels.

**Safety results**

Only one patient had one adverse event, i.e., pyrexia. This event was mild and not related to the study which resolved without sequelae. There were no deaths or other serious adverse events reported in this study.

**DISCUSSION**

Hypogonadism is defined as a clinical syndrome which consists of clinical symptoms, with or without signs and associated with biochemical evidence of testosterone deficiency.\(^1\) Hypogonadism may result from testicular disease (primary hypogonadism) or dysfunction of the hypothalamic-pituitary unit (secondary hypogonadism).\(^13\) Recently, the association between late-onset hypogonadism and T2DM\(^{16,23}\) has been demonstrated in numerous studies (indicating that up to 40% of men with T2DM have testosterone deficiency, and up to 75% of them have sexual dysfunction, particularly erectile dysfunction\(^{24,25}\) which is higher than our study.

The prevalence of hypogonadism was around 20.7% in our study which is quite similar to another study by Ganesh *et al.*\(^{16}\) This study was the first study to determine the prevalence of hypogonadism in Indian population. This was done in one center and quoted a prevalence of 15% of hypogonadal patients. Albeit the definition of hypogonadism used in that study was that the patients with calculated free testosterone < 64.8 pg/mL were considered hypogonadal. Probably, the little higher prevalence was due to the higher age of our study cohort (30–59 years) which in the latter was 25–50 years. The higher prevalence can also be attributable to higher mean BMI of 26.18 kg/m², in our

---

**Table 2: Prevalence of hypogonadism (androgen deficiency in aging male positive + low free testosterone) in patients with Type 2 diabetes mellitus-enrolled population**

| Statistics | Overall (n=900) |
|------------|----------------|
| n (%)      | 186 (20.7)     |
| 95% CI     | 18.0, 23.3     |

CI: Confidence interval

**Table 3: Prevalence of primary and secondary hypogonadism among hypogonadal patients**

| Prevalence                               | Overall (n=186) |
|-----------------------------------------|-----------------|
| Primary (hypergonadotropic) hypogonadism | 48 (25.8)       |
| in patients with T2DM, n (%)            |                 |
| Secondary (hypogonadotropic) hypogonadism | 14 (7.53)      |
| in patients with T2DM, n (%)            |                 |
| Low testosterone with inappropriate normal level of LH and FSH, n (%) | 124 (66.67) |

LH: Luteinizing hormone, FSH: Follicle-stimulating hormone, T2DM: Type 2 diabetes mellitus

**Table 4: Prevalence of testosterone deficiency (patients with testosterone deficiency+androgen deficiency in aging male negative) in patients with Type II diabetes mellitus-enrolled population**

| Statistics | Overall (n=900) |
|------------|----------------|
| n (%)      | 51 (5.7)       |

**Table 5: Prevalence of primary and secondary hypogonadism among testosterone deficient patients**

| Prevalence                               | Overall (n=51) |
|-----------------------------------------|----------------|
| Primary (hypergonadotropic) androgen deficiency in patients with T2DM, n (%) | 13 (25.5) |
| Secondary (hypogonadotropic) androgen deficiency in patients with T2DM, n (%) | 3 (5.9)  |
| Low testosterone with inappropriate normal level of LH and FSH, n (%) | 35 (68.6) |

LH: Luteinizing hormone, FSH: Follicle-stimulating hormone, T2DM: Type 2 diabetes mellitus

**Table 6: Prevalence of testosterone deficiency in patients with Type 2 diabetes mellitus (age-wise)**

| Prevalence | Statistics | Age group (years) |
|------------|------------|-------------------|
| Testosterone deficiency | 95% CI  | 30-39 (n=291) | 40-49 (n=305) | 50-59 (n=304) | Overall (n=900) |
| n (%)      |           | 18 (6.2)     | 15 (4.9)     | 18 (5.9)     | 51 (5.7)      |
| 95% CI     |           | 3.4, 9.0     | 2.5, 7.3     | 3.3, 8.6     | 4.2, 7.2      |

CI: Confidence interval
study. Also, another study conducted by Dhindsa et al. was for levels of low testosterone involving 103 patients in the United States of America; the prevalence was around 33% as compared to our study where it was 26.3% (186 + 51). \[4\] In another study in Jordanian population, the prevalence was 18.5% which was also similar to our study. \[27\] Al Hayek et al., in another study (2011), in Jordanian males, found the prevalence to be 36.4% when hypogonadism was defined as total testosterone level of <3 ng/mL in T2DM patients. \[28\]

Gray et al. (1991) reported that serum testosterone and calculated free testosterone levels showed a slight decrease with increasing age which was opposite in our study wherein it showed a little increase with the increasing age cohorts. \[29\] Although SHBG levels showed an increase in both our as well as the study conducted by Ganesh et al. \[26\] Also interestingly, the logistic regression analysis showed that hypogonadism was significantly related to age cohorts 40–49 years and 50–59 years than that of 30–39 years, in our study [Figure 1 and Table 7]. Further analysis showed that the number of patients was more in age group of 40–55 years as compared to other age groups for T2DM patients who were suffering from hypogonadism [Figure 2]. The odds ratio analysis suggests that the covariates age and BMI were statistically significant at 5% level of significance. For every 1 year increase age, there is 1.056 times more chance of getting hypogonadism in T2DM patients as compared to T2DM patients not suffering from hypogonadism. For every unit increase in BMI, there is 1.053 times more chance of getting hypogonadism in T2DM patients as compared to T2DM patients not suffering from hypogonadism [Figure 3]. There is 1.77 times more chance of getting hypogonadal patients with age group of 40–49 as compared to patients with age group of 30–39, which is statistically significant at 5% level of significance and there is 2.96 times more chance of getting hypogonadal patients with age group of 50–59 as compared to patients with age group of 30–39, which

![Figure 1: Prevalence of hypogonadism stratified by age](image1)

![Figure 2: Kernel density plots of Age by hypogonadism status](image2)

**Table 7: Logistic regression-hypogonadism (all patients)**

| Parameter          | T2DM patients with hypogonadism, n=186 | T2DM patients without hypogonadism, n=714 | OR (95% CI) | P      |
|--------------------|----------------------------------------|------------------------------------------|-------------|--------|
| Age (years)        |                                        |                                          |             |        |
| 30–39 (ref)        | 37 (12.7)                              | 254 (87.3)                               | 1.0         |        |
| 40–49              | 61 (20.0)                              | 244 (80.0)                               | 1.77 (1.13, 2.77) | 0.0128 |
| 50–59              | 88 (28.9)                              | 216 (71.1)                               | 2.96 (1.92, 4.56) | <0.0001|
| BMI                |                                        |                                          |             |        |
| Normal (ref)       | 29 (16.6)                              | 146 (83.4)                               | 1.0         |        |
| Underweight        | 8 (61.5)                               | 58 (38.5)                                | 4.51 (1.33, 15.23) | 0.0154 |
| Overweight         | 32 (16.2)                              | 165 (83.8)                               | 0.92 (0.53, 1.61) | 0.7792 |
| Obese              | 120 (23.3)                             | 395 (76.7)                               | 1.55 (0.98, 2.44) | 0.0598 |
| HbA1c (%)          |                                        |                                          |             |        |
| <7 (ref)           | 57 (22.7)                              | 194 (77.3)                               | 1.0         |        |
| 7<8                | 39 (21.0)                              | 147 (79.0)                               | 0.85 (0.53, 1.35) | 0.4884 |
| ≥8                 | 90 (19.4)                              | 373 (80.6)                               | 0.80 (0.54, 1.17) | 0.2450 |

BMI - Normal: 18.5–22.9 (kg/m²), Overweight: 23–24.9 (kg/m²), Obese: ≥25 (kg/m²), Underweight: <18.5 (kg/m²). Age 30–39 years was considered as referenced category for age, normal category was considered as reference for BMI and <7% was considered reference category for HbA1c levels. Ref: Reference category, HbA1c: Glycosylated hemoglobin, BMI: Body mass index, OR: Odds ratio, CI: Confidence interval, T2DM: Type 2 diabetes mellitus.
The prevalence rate of testosterone deficiency in patients of T2DM, without any symptoms, was 5.7% [Table 8]. Out of this 51/900 (5.7%) patients, primary (hypergonadotropic) androgen deficiency was present in 13 (25.5%) patients while secondary (hypogonadotropic) androgen deficiency was present in 3 (5.9%) patients [Table 5]. This result was somewhat similar to the Taiwanese study where and 12% of the study participants had symptomatic androgen deficiency.[31]

### Table 8: Logistic regression-testosterone deficiency (+ androgen deficiency in aging male negative)

| Parameter | T2DM patients with testosterone deficiency + ADAM negative condition, n=51 | T2DM patients without testosterone deficiency + ADAM negative condition n=849 |
|-----------|---------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Age (years) |                                                                             |                                                                           |
| 30-39 (ref) | 18 (6.2)                                                                   | 273 (93.8)                                                               |
| 40-49      | 15 (4.9)                                                                   | 290 (95.1)                                                               |
| 50-59      | 18 (5.9)                                                                   | 286 (94.1)                                                               |
| BMI        |                                                                             |                                                                           |
| Normal (ref) | 8 (4.6)                                                                   | 167 (95.4)                                                               |
| Underweight | 1 (7.7)                                                                    | 12 (92.3)                                                                |
| Overweight | 9 (4.6)                                                                    | 188 (95.4)                                                               |
| Obese      | 33 (6.4)                                                                   | 482 (93.6)                                                               |
| HbA1c (%)  |                                                                             |                                                                           |
| <7 (ref)   | 13 (5.2)                                                                   | 238 (94.8)                                                               |
| 7<8        | 13 (7.0)                                                                   | 173 (93.0)                                                               |
| ≥8         | 25 (5.4)                                                                   | 438 (94.6)                                                               |

BMI - Normal: 18.5-22.9 (kg/m²), Overweight: 23-24.9 (kg/m²), Obese: ≥25 (kg/m²). Underweight: <18.5 (kg/m²). Age 30-39 years was considered as referenced category for age, normal category was considered as reference for BMI and <7% was considered reference category for HbA1c levels. Ref: Reference category, HbA1c: Glycosylated hemoglobin, BMI: Body mass index, OR: Odds ratio, CI: Confidence interval, T2DM: Type 2 diabetes mellitus, ADAM: Androgen deficiency in aging male

**Conclusion**

The percentage prevalence of hypogonadism in patients with T2DM was moderate with highest number of patients belonging to age group 50–59 years. Significant correlation was found between age, BMI, and hypogonadism. Hypogonadism diagnosis, at times, might not be validated with the help of androgen deficiency questionnaire or symptoms only. Given the large number of patients of T2DM in India, the incidence of hypogonadism is more in diabetic patients as compared to the general population. Hence, implementation of screening programs in diabetic
patients is necessary to understand and detect individuals with low serum total testosterone at any early stage and to supplement testosterone accordingly. We recommend screening of all diabetic patients for testosterone evaluation and seeking an opinion from the experts in treating the disease accordingly and building a hormonal range for T2DM patients for future studies.

**Financial support and sponsorship**
This study was sponsored by MSD Pharmaceuticals Private Limited, 10th Floor, Platina Building, C-59, G-Block, Bandra Kurla Complex, Mumbai - 400 098, Maharashtra, India.

**Conflicts of interest**
RaceSuddin Syed and Pradeep Shetty are employees of MSD Pharmaceuticals Private Limited.

**REFERENCES**

1. Anjana RM, Pradeepa R, Deepa M, Datta M, Sudha V, Unnikrishnan R, et al. Prevalence of diabetes and prediabetes (impaired fasting glucose and/or impaired glucose tolerance) in urban and rural India: Phase I results of the Indian Council of Medical Research-India DIABetes (ICMR-INDIAB) study. Diabetologia 2011;54:3022-7.

2. Jones TH. Clinical awareness and diagnosis of male hypogonadism. J Mens Health 2008;5:526-34.

3. Jones TH. Testosterone Deficiency in Men. Oxford, United Kingdom: Oxford University Press; 2008a.

4. Dhindsa S, Miller MG, McWhirter CL, Mager DE, Ghanim H, Chaudhuri A, et al. Testosterone concentrations in diabetic and nondiabetic obese men. Diabetes Care 2010;33:1186-92.

5. Haffner SM, Valdez RA, Stern MP, Kals MS. Obesity, body fat distribution and sex hormones in men. Int J Obes Relat Metab Disord 1993;17:643-9.

6. Kapoor D, Clarke S, Channer KS, Jones TH. Erectile dysfunction is associated with low bioactive testosterone levels and visceral adiposity in men with type 2 diabetes. Int J Androl 2007;30:500-7.

7. 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;30:911-7.

8. Márin P, Holmång S, Jönsson L, Sjöström L, Krist H, Holm G, et al. The effects of testosterone treatment on body composition and metabolism in middle-aged obese men. Int J Obes Relat Metab Disord 1992;16:991-7.

9. Márin P, Krotkiewski M, Björntorp P. Androgen treatment of middle-aged, obese men: Effects on metabolism, muscle and adipose tissues. Eur J Med 1992;1:329-36.

10. Malkin CJ, Jones TH, Channer KS. The effect of testosterone on insulin sensitivity in men with heart failure. Eur J Heart Fail 2007;9:44-50.

11. Sicree R, Shaw J, Zimet P. Diabetes and impaired glucose tolerance. In: Gan D, editor. Diabetes Atlas. International Diabetes Federation. 3rd ed. Belgium: International Diabetes Federation; 2006; p. 15-103.

12. Simon D, Charles MA, Lahlou N, Nahoul K, Oppert JM, Gouault-Heilmann M, et al. Androgen therapy improves insulin sensitivity and decreases leptin level in healthy adult men with low plasma total testosterone: A 3-month randomized placebo-controlled trial. Diabetes Care 2001;24:2149-51.

13. Shaw JE, Sicree RA, Zimet PZ. Global estimates of the prevalence of diabetes for 2010 and 2030. Diabetes Res Clin Pract 2010;87:4-14.

14. Zumoff B, Strain GW, Miller LK, Rosner W, Senie R, Seres DS, et al. Plasma free and non-sex-hormone-binding-globulin-bound testosterone are decreased in obese men in proportion to their degree of obesity. J Clin Endocrinol Metab 1990;71:929-31.

15. Basaria S. Male hypogonadism. Lancet 2014;383:1250-63.

16. Corona G, Mannucci E, Forti G, Maggi M. Following the common association between testosterone deficiency and diabetes mellitus, can testosterone be regarded as a new therapy for diabetes? Int J Androl 2009;32:431-41.

17. Hamdan FB, Al-Matubsi HY. Assessment of erectile dysfunction in diabetic patients. Int J Androl 2009;32:176-85.

18. Selvin E, Feinleib M, Zhang L, Rohrmann S, Rifai N, Nelson WG, et al. Androgens and diabetes in men: Results from the third national health and nutrition examination survey (NHANES III). Diabetes Care 2007;30:234-8.

19. Chen RY, Wittert GA, Andrews GR. Relative androgen deficiency in relation to obesity and metabolic status in older men. Diabetes Obes Metab 2006;8:429-35.

20. Rhoden EL, Ribeiro EP, Teloken C, Souto CA. Diabetes mellitus is associated with subnormal serum levels of free testosterone in men. BJU Int 2005;96:867-70.

21. Pitteloud N, Mootha VK, Dwyer AA, Hardin M, Lee H, Eriksson KF, et al. Relationship between testosterone levels, insulin sensitivity, and mitochondrial function in men. Diabetes Care 2005;28:1636-42.

22. Chandel A, Dhindsa S, Topiwala S, Chaudhuri A, Dandona P. Testosterone concentration in young patients with diabetes, Diabetes Care 2008;31:2013-7.

23. Corrales JJ, Burgo RM, Garca-Berrocal B, Almeida M, Alberca I, Gonzalez-Buitrago JM, et al. Partial androgen deficiency in aging type 2 diabetic men and its relationship to glycemic control. Metabolism 2004;53:666-72.

24. Kelly DM, Jones TH. Testosterone: A metabolic hormone in health and disease. J Endocrinol 2013;217:R25-45.

25. Hackett G, Cole N, Bhartia M, Kennedy D, Raju J, Wilkinson P. Testosterone replacement therapy with long-acting testosterone undecanoate improves sexual function and quality-of-life parameters vs. placebo in a population of men with type 2 diabetes. J Sex Med 2013;10:1612-27.

26. Ganesh HK, Vijaya Sarathi HA, George J, Shioane VK, Bandgar T, Menon PS, et al. Prevalence of hypogonadism in patients with type 2 diabetes mellitus in an Asian Indian study group. Endocr Pract 2009;15:512-20.

27. Al Hayek AA, Khawaja NM, Khader YS, Jaffal SK, Ajlouni KM. The prevalence of hypogonadism among diabetic and non-diabetic men in Jordan. J Diabetes Complications 2014;28:135-40.

28. Al Hayek AA, Khader YS, Jaffal S, Khawaja N, Ajlouni K. Hypogonadism among Jordanian men with type 2 diabetes: Prevalence and associated factor. International Journal of Diabetes Mellitus 2015;3:31-6.

29. Gray A, Feldman HA, McKinlay JB, Longcope C. Age, disease, and changing sex hormone levels in middle-aged men: Results of the Massachusetts male aging study. J Clin Endocrinol Metab 1991;73:1016-25.

30. 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. Baltimore longitudinal study of aging. J Clin Endocrinol Metab 2001;86:724-31.

31. Liu CC, Wu WJ, Lee YC, Wang CJ, Ke HL, Li WM, et al. The prevalence of and risk factors for androgen deficiency in aging Taiwanese men. J Sex Med 2009;6:936-46.