Greener Journal of Medical Sciences
Vol. 11(2), pp. 137-142, 2021
ISSN: 2276-7797

https://gjournals.org/GJMS

Assessment of Hypogonadism in Men with Type 2 Diabetes Mellitus

Etawo U.S*; Aleme B.M**

Departments of Surgery* and Chemical Pathology**
University of Port Harcourt Teaching Hospital, PMB 6173, Port Harcourt

ARTICLE INFO

Article No.: *101421104*
***Type*:** *Research*
Full Text: *HTML, EPUB*

Accepted: *14/10/2021*
Published: *18/10/2021*

Corresponding Author
Dr. U S Etawo
E-mail: *dr_etawo@yahoo.com*
Phone: *+234 803 312 2701*

Keywords: *Diabetes Mellitus; Hypogonadism; Testosterone*

ABSTRACT

Background: There is an established relationship between type 2 diabetes and Hypogonadism. Testosterone, the main gonadal steroid in men is lower in diabetic men when compared with healthy subjects. Currently, very few diabetic men with testosterone deficiency are diagnosed and treated worldwide. Knowledge of testosterone levels of patients will reveal those with androgen deficiency so that appropriate treatment will be offered.

Objective: The aim of this study was to assess the prevalence of Hypogonadism based on biochemical measures of total testosterone deficiency in men with type 2 diabetes in Port Harcourt.

Methods: Type 2 diabetic patients attending the Medical Out-Patient Clinic of University of Port Harcourt Teaching Hospital (UPTH) between April and May, 2012 were used for this study. Fasting blood sugar was measured using Randox kit, Testosterone was measured using Enzyme Linked Immunoassay. Data were analyzed using the SPSS package (Version 20.0.0). The mean levels of testosterone for the patients as a group and also according to age, glycemic state and duration of disease were computed. Values were expressed as a percentage of each group or as mean $\pm$ 2SD. Comparisons between groups were made using the student t-test at 95% confidence interval. Results were significant if $P < 0.05$.

Results: One hundred and forty two (142) patients were tested within the study period. 31.7% (45) of the 142 diabetic patients had a lower than normal testosterone level (Testosterone<3.0ng/ml). The mean testosterone levels decreased significantly in the older men (>70 years). The percentages of patients with low testosterone levels were increasingly higher as the age increased. 10.7% of patients aged 41-50 years had low testosterone levels. Their mean was 3.51$\pm$ 0.54 ng/ml. 12.8% of patients aged 51-60 years had low testosterone and their mean level was 3.35$\pm$0.58 ng/ml. 25.0% of the patients aged 61-70 years had low testosterone levels. Their mean was 2.89$\pm$0.68, while 92.3 of the patients >70 years had low testosterone with a mean of 1.57$\pm$0.70 ng/ml. The percentage of patients with low testosterone was not altered by the degree of rise in blood sugar level. 32.2% of the patients whose fasting blood glucose level were <10.0mmol/L had low testosterone levels and their mean was 2.99$\pm$0.83ng/ml while 28.0% of the patients with fasting blood glucose level >10mmol/L had low testosterone levels and their mean was 3.0$\pm$0.67 ng/ml. There was no significant difference between the two groups. 17.4% of the patients whose disease has lasted for 1-5 years had low testosterone level and their mean was 3.27$\pm$0.58 ng/ml while 74.1% of the patients with disease duration between 6-10 years had low testosterone levels and a mean of 2.23$\pm$0.78ng/ml. 83.3% of the patients with disease duration >10years had low testosterone levels and their mean level was 1.62$\pm$1.81ng/ml.

Conclusion: Testosterone levels are low in type 2 diabetic men. These levels are further affected by age and duration of disease. Glycemic status had no statistically significant.

INTRODUCTION:

Hypogonadism is a clinical condition comprising both symptoms and biochemical evidence of testosterone deficiency. It is generally accepted by endocrinologists that if biochemical testosterone deficiency is associated with symptoms of hypogonadism, then testosterone substitution should be considered unless contraindicated[1].

Hypogonadism is a lack of testosterone in adult men. It can be of central (hypothalamic or pituitary) or testicular origin or a combination of both and is increasingly common in the aging population. Hypogonadism due to testicular failure arising from genetic disorders, trauma or other conditions is known as primary Hypogonadism. A variety of conditions including disease and damage to the hypothalamic-pituitary axis could lead to secondary Hypogonadism. These include cancer, acquired immuno-deficiency syndrome, hyperthyroidism or hypothyroidism, several medical agents, morbid obesity and so many others including diabetes mellitus[2, 3, 4].

There has been long known, an association between type 2 diabetes and Hypogonadism. Insulin resistance is an important feature of type 2 diabetes and it's been increasingly recognized that low levels of testosterone, are associated with reduced insulin sensitivity and type 2 diabetes[5] (Kapoor et al. 2005). Simon and his fellow workers observed an inverse relationship between testosterone levels and insulin concentrations in healthy men.[6] Low testosterone levels have also been found to predict insulin resistance and the future development of type 2 diabetes [7,8,9]

Several studies document the fact that testosterone levels are lower in diabetic men compared with non-diabetic subjects. [10,11] Testosterone is the major gonadal steroid in men. It has been suggested that normal levels of testosterone are necessary to maintain normal sexual function, whereas increases in fat-free and lean-tissue mass rise in a dose-dependent manner over the normal range of circulating testosterone [3] In a recent study of androgen-deficient patients undergoing subdermal testosterone implantation, thresholds for total and free testosterone below which symptoms of androgen deficiency returned as testosterone levels declined were determined. Reduced libido and lack of motivation and/or energy recurred when testosterone reached approximately 2.8ng/ml in patients with secondary (hypogonadotropic) Hypogonadism, and 3.37ng/ml in patients with primary (hypogonadotropic) hypogonadism. Testosterone appears to play a role in maintaining sexual function, especially libido, although androgen deficiency per se is infrequently the sole cause of erectile dysfunction in hypogonadal males, particularly elderly men. [12]

Testosterone may also promote bone formation and cognitive performance, including mental-rotational tasks. [3]

Interventional studies have shown a beneficial effect of testosterone replacement therapy on insulin resistance. A study in healthy men with low total testosterone reported an improvement in insulin sensitivity with testosterone or dihydrotestosterone treatment. [13] Testosterone treatments have also been shown to reduce insulin resistance in obese men [14], men with heart failure, and type 2 diabetic subjects. There have also been reports of improvements in glycemic control in type 2 diabetic patients with testosterone replacement therapy [1].

Andersson and his group postulated that, currently, few diabetic men with testosterone deficiency are diagnosed and treated worldwide.[11] This appears to be the subsisting condition at the as there exist barely any records of type 2 diabetic patients routinely coming for testosterone assay. The reason for this according to additionally, most patients will not disclose their sexual concerns and state of erectile dysfunction to their physicians.

These findings and conditions demonstrate the importance of investigating men with diabetes for androgen status. In addition to recognizing presenting symptoms, conducting appropriate laboratory testing is central to diagnosing male Hypogonadism[3]. The aim of this study therefore was to assess the prevalence of Hypogonadism in men with type 2 diabetes attending University of Port Harcourt Teaching Hospital Medical Out-patient clinic, based on biochemically measurable total testosterone level.

METHODS:

All diabetic men who developed diabetes Mellitus after the age of 30 years seen in the Medical outpatient Clinic of the University of Port Harcourt Teaching Hospital between April and May 2012 were recruited for the study. Patients with type 1 diabetes Mellitus, men on androgen deprivation therapy were excluded from the study. Patients were confirmed diabetics who were coming for their routine check and/or follow-up. Information about the age of patient, year of diagnosis, medication, sugar level, testosterone level were obtained. The samples were collected at the Phlebotomy unit of Chemical Pathology Department as the patients came for their routine fasting blood glucose tests. Testosterone levels were also matched with glycemic levels, age and duration of disease to see if these variables affected testosterone levels.

Assessment: Samples were collected between 8:00 and 11:00 a.m. in line with the WHO guidelines. Samples were collected by veni-puncture into plain bottles for testosterone assay and fluoride oxalate bottle for the glucose test. Glucose samples were run almost immediately while sample for testosterone were centrifuged at 2,000g and serum obtained were stored in a frozen state for not more than one week before assay.

All assays were done at the Chemical Pathology Laboratory. Fasting blood glucose was analyzed using Glucose Oxidase kit from Randox (Randox Laboratories LTD, Ardmore, Diamond Road, Crumlin, Co. Antrim, UK BT29 $QY). Testosterone was assayed using Enzyme Linked Immunoassay kits obtained from BioCheck (Vintage Park Dr., Foster City, CA).

Statistical analysis: Data were analyzed using the SPSS package (Version 20.0.0). Values were expressed as a percentage of each group or as mean ± 2SD. The mean levels of testosterone according to age, glycemic state and duration of disease was computed. Comparison between groups was made using the student t-test at 95% confidence interval.

RESULT

One hundred and forty (142) patients qualified for the study. 18 patients were on insulin and the rest were on oral hypoglycemic agents .The baseline data are shown in Table 1. Mean age was 58.0 ±0.1 years. Duration of disease was 4.0 ±2.8 years. Mean fasting blood glucose was 8.0 ± 2.2 mmol/L while mean testosterone level was 2.99 ± 0.82 ng/ml. Mean testosterone level for the general patient group was just on the borderline of normal (Normal range of testosterone is 3-10 ng/ml.)

Table 2 is the mean testosterone levels of the patients according to age (in decades). The patients were divided into 4 groups by age (in decades): 41-50, 51-60, 61-70, and >70 years. The mean testosterone level for patients aged 41-50 years was 3.51±0.54ng/ml. The mean testosterone level for the patient group 51- 60 and 61-70 years were not significantly different from that of the lowest group (age 41-50 years), though they were slightly lower (3.35±0.58 and 2.89±0.68ng/ml respectively). Testosterone level in the >70 years age group was significantly different from that of the lowest (41-50 years) age group; 1.57±0.70 ng/ml (p< 0.05).

Table 3, is the mean testosterone level of the patients divided into two groups according to glycemic state: Group1, FBS 5-10 mmol/L and Group 2, FBS >10 mmol/L). The mean testosterone levels in the two groups were not significantly different. (P> 0.05).

Table 4, shows the mean values of testosterone in the patients according to duration of disease in years. Patients were divided into 3 groups: 1-5, 6-10, and >10years. The mean testosterone levels progressively fell substantially as the duration of disease increased. (3.27±0.58, 2.23±0.78 and 1.62±0.81 ng/ml for the 1-5, 6-10, and >10 years of disease duration respectively.

45 of the 142 diabetic patients or 31.7% had their testosterone level below the normal range (Testosterone <3.0ng/ml). The percentage of patients that had their testosterone level falling below the normal range according to age (in decades), glycemic state (FBG level) and duration of disease in years is displayed in Table 2, 3 and 4.

Table1. Mean values of measured parameters in Type 2 diabetic patients

Age (Years)	**58 ± 0.1**	**-**
Duration of Disease (Years)	4.0 ± 2.8	-
Fasting blood glucose (mmol/L)	8.0± 2.2	3.5 – 5.5 **
Testosterone (ng/ml)	2.99± 0.80	3 – 10 **

** Normal Range for healthy men.

Table 2. Mean testosterone level according to age group (in decades)

Age (Years in decades)	Mean Testosterone (ng/ml)	Percentage below normal range (Testosterone) 3.0ng/ml)	p value*	Significance
41-50 (n=37)	3.51±0.54	10.7%	-	
51-60 (n=50)	3.35±0.58	12.8%	0.26	P >0.05
61-70 (n=41)	2.89±0.68	25.0%	0.02	P >0.05
>70 (n=14)	1.57±0.70	92.3%	3.60	P <0.05

*P values were obtained by comparing mean testosterone value of the successive age groups with that of the lowest age group (age 41-50 years)

Table 3. Mean testosterone levels according to glycemic state

Fasting Blood Glucose (mmol/L)	Testosterone (ng/ml)	Percentage below normal range (Testosterone< 3.0ng/ml)	P Value*	Significance
5.0-10.0 (n=117)	2.99±0.83	32.2%	-	
>10.0 (n=25)	3.00±0.67	28.0%	0.99	P >0.05

Table 4. Mean Testosterone levels of patients according to duration of disease

Duration of Disease (Yrs)	Mean Testosterone ng/ml	Percentage below normal range (Testosterone< 3.0ng/ml	P value*	Significance
1-5 (n=109)	3.27±0.58	17.4%		
6-10 (n=27)	2.23±0.78	74..1%	2.39	P <0.05
>10 (n=6)	1.62±0.81	83.3%	5.12	P <0.05

*P values were obtained by comparing mean testosterone value of the successive age groups with that of the lowest group (Duration of disease 1-5 years)

DISCUSSION

The prevalence of low testosterone among type 2 diabetic men in this study was 34.8%. This is in keeping with other studies from Nigeria and United Kingdom where their total prevalence of testosterone deficiency among type 2 diabetic men were 35.3%, 25% and 33% respectively [2,15,16]

It is already known that a low testosterone level is common in diabetic men. Insulin resistance is an important feature of type 2 diabetes mellitus. Testosterone plays an significant role in glucose homeostasis [17]. Low testosterone levels will lead to increased insulin resistance and therefore increased risk of type 2 diabetes mellitus. This will explain the high prevalence of testosterone defiency in our study. Furthermore, interventional studies have shown a beneficial effect of testosterone replacement therapy on insulin resistance.[17]this will explain the high prevalence of testosterone defiency in our study.

In this study, we observed that decrease in testosterone levels was significantly affected by age. The percentage of patients with low testosterone increased as the age of the patients increased. This increase was very significant in the >70 years age group. This is in agreement with previous works. [2,3,4] The aging male patient can present with signs of low testosterone, including loss of libido, erectile dysfunction, depression, lethargy, loss of muscle mass and strength and diminished intellectual capacity[18,19]

We also observed a significant decrease in level of testosterone among type 2 diabetic men as duration of the disease increased. This though, could be linked to the age effects on testosterone level in these patients as those patients with longer duration of disease also generally fell into the older age groups. The possibility that this could be an independent or compounding effect of duration of disease cannot however be ruled out. Also, longer exposure to hyperglycemia means greater possibility of insulin-resistance.

In this study, the hyperglycemic state of the patient did not appear to affect their testosterone levels. There was no substantial difference in the testosterone levels of patients whose fasting blood sugar level fell between 5-10mmol/L and those whose fasting blood sugar levels were >10mmol/L.

In this study, we did not correlate the low testosterone levels found in these diabetic patients with symptoms. There could be other predisposing factors. Recent studies have demonstrated that free testosterone levels which are independent of serum hormone binding globulin (SHBG), are low in one-third of diabetic men. A confounding factor is that SHGB rises with age and thus, free testosterone decreases more rapidly than total testosterone in older men. Thus, it is important to

measure also bioavailable or free testosterone in men with diabetes.

CONCLUSION

Testosterone status has become increasingly important in the management of patients with type 2 diabetes. The evidence that testosterone therapy improves insulin resistance, glycemic control and cholesterol levels in diabetic men with low testosterone, and together with the findings that testosterone improves symptoms in men with heart conditions, suggests that normalization of testosterone status in type 2 diabetes has important clinical consequences besides benefits on libido. We suggest that further studies are required to establish the benefit of testosterone replacement therapy on the diabetic state and over all well-being of men with type 2 diabetes.

Conflict of interest

There was no conflict of interest

Funding/Grant

There was no grant for this research work

Acknowledgement

The Mother, Baby and Adolescent Care Global Foundation

REFERENCES

1. Kapoor D, Goodwin E, Channer KS, Jones TH: Testosterone replacement therapy improves insulin resistance, glycaemic control, visceral adiposity and hypercholesterolaemia in hypogonadal men with type 2 diabetes. Eur J Endocrinol. 2006; 154:899–906.
2. Kapoor D, Aldred H, Clarck S, Chanee K and Jones T.H. Clinical and Biochemical Assessment of Hypogonadism in Men with Type 2 Diabetes: Correlations with bioavailable testosterone and visceral adiposity. Diabetes Care. 2007; 30(4): 911-917.
3. Seftel A. Male Hypogonadism. Part II: Etiology, Pathophysiology, and Diagnosis. Int. J Impot Res. 2006; 18(3):223-228.
4. Carnegie C. Diagnosis of Hypogonadism: Clinical Assessments and Laboratory Tests. Rev. Urol. 2004; 6(6): S3-S8.
5. Kapoor D, Malkin CJ, Channer KS, Jones TH: Androgens, insulin resistance and vascular disease in men. Clin Endocrinol (Oxf). 2005; 63: 239–250.
6. Simon D, Preziosi P, Barrett-Connor E, Roger M, Saint-Paul M, Nahoul K, Papoz L: Interrelation between plasma testosterone and plasma insulin in healthy adult men: the Telecom Study. Diabetologia. 1992; 35:173–177.
7. Oh JY, Barrett-Connor E, Wedick NM, Wingard DL: Endogenous sex hormones and the development of type 2 diabetes in older men and women. Diabetes Care. 2002; 25:55–60.
8. Stellato RK, Feldman HA, Hamdy O, Horton ES, McKinlay JB: Testosterone, sex hormone binding globulin and the development of type 2 diabetes in middle aged men. Diabetes Care. 2000; 23:490–494.
9. Haffner SM, Shaten J, Stern MP, Smith GD, Kuller L: Low levels of sex hormone binding globulin and testosterone predict the development of non insulin dependent diabetes mellitus in men. Am J Epidemiol. 1996; 143:889–897.
10. Barrett-Connor E, Khaw KT, Yen SS: Endogenous sex hormone levels in older men with diabetes mellitus. Am J Epidemiol. 1990; 132:895–901.
11. Andersson B, Marin P, Lissner L, Vermeulen A, Bjorntorp P: Testosterone concentrations in women and men with NIDDM. Diabetes Care 17:405–411, 1994
12. Bremner WJ, Vitiello MV, Prinz PN. Loss of circadian rhythmicity in blood testosterone levels with aging in normal men. J ClinEndocrinolMetab. 1983; 56(6):1278–1281.
13. Simon D, Charles MA, Lahlou N, Nahoul K, Oppert JM, Gouault-Heilmann M, Lemort N, Thibult N, Joubert E, Balkau B, Eschwege E: Androgen therapy improves insulin sensitivity and decreases leptin level in healthy adult men with low plasma total testosterone. Diabetes Care. 2001; 24:2149–2151.
14. Marin P, Holmang S, Jonsson L, Sjostrom L, Kvist H, Holm G, Lindstedt G, Bjorntorp P: The effects of testosterone treatment on body composition and metabolism in middle-aged obese men. Int J Obes Relat Metab Disord. 1992; 16:991–997.
15. Dhindsa S, Prabhakar S, Sethi M, Bandyopadhyay A, Chaudhuri A, Dandona P: Frequent occurrence of hypogonadotropichypogonadism in type 2 diabetes. J Clin Endocrinol Metab. 2004; 89:5462–5468.
16. Ogbera OA, Sonny C, Olufemi F, Wale A: Hypogonadism and Subnormal levels in men with type 2 diabetes mellitus. J coll Physicians Surg Pak. 2011; 21(9):517-21.
17. SaadFarid and Gooren J. L. The role of Testosterone in the Etiology and Treatment of Obesity, the Metabolic Syndrome and Diabetes Mellitus Type 2. Journal of Obesity. www.hindawi.com/journals/jobes/2011/471584/abs/
18. McCulloch DK, Campbell IW, Wu FC, Prescott RJ, Clarke BF: The prevalence of diabetic impotence. Diabetologia. 1980; 18:279–283.
19. Leifke E, Gorenoi V, Wichers C, Muhlen A, Buren E, Brabant G: Age-related changes of serum sex hormones, insulin-like growth factor-1 and sex-

hormone binding globulin levels in men: cross-sectional data from a healthy male cohort. Clin Endocrinol (Oxf). 2000; 53:689–695.

Cite this Article: Etawo, US; Aleme, BM (2021). Assessment of Hypogonadism in Men with Type 2 Diabetes Mellitus. *Greener Journal of Medical Sciences*, 11(2): 137-142**.**