

Study of Serum Testosterone Concentration in Men with Type 2 Diabetes and Healthy Control in North West Rajasthan

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Abstract

Background: Diabetes mellitus refers to a group of common metabolic disorders that share the phenotype of hyperglycemia¹. In recent years, androgen deficiency has captured interest of many researchers and they have associated not only with general health of men but also with certain common systemic disorders like abdominal obesity, type 2 diabetes mellitus & others. So we plan to assess serum testosterone concentration in men with type 2 diabetes.

Materials and Methods: This was a cross sectional study. 150 cases of type 2 diabetes mellitus and 50 cases without type 2 diabetes mellitus matched for confounding factors were taken as controls. Serum total testosterone level is assessed by chemiluminiscence metod.

Results: Mean total testosterone in diabetics was 281.67±67.31ng/dl and in controls it was 555.16±126.56ng/dl and the difference was found statistically highly significant (p<0.001).

Conclusions: we concluded that serum total testosterone is low in diabetic than non diabetics.

Keywords: Type 2 Diabetes Mellitus, serum total testosterone.

Introduction

Testosterone is the major male androgen and is produced by the leydig cells in the male testis and in smaller

amounts by the adrenal glands. It is responsible for male secondary sexual characteristics and sperm production. The effects of low testosterone levels include low sex drive, changes in mood, loss of muscle and bone strength, and increase body fat². The amount of testosterone synthesized is regulated by the hypothalamic-pituitary-testicular axis. When testosterone levels are low, gonadotropin-releasing hormone (GnRH) is released by the hypothalamus which in turn stimulates the pituitary gland to release FSH and LH. These latter two hormones stimulate the testis to synthesize testosterone³. This means that when the feedback mechanism is functioning properly, low testosterone level will induce secretion of high FSH and LH levels.

Various mechanisms by which low serum testosterone may be considered a threat for type 2 diabetes mellitus and metabolic syndrome include changes in the body composition, androgen receptor polymorphisms, glucose transport and decreased antioxidant effects. On the other hand, diabetes mellitus may also be considered a risk factor for hypogonadism through visceral obesity, reduced sex hormone binding globulin, inhibition of gonadotropin secretion or production of testosterone by leydig cells, cytokines mediated inhibition (e.g. TNF α , IL-1 β , IL-6) of steroid production and increased aromatase activity resulting in estrogen excess⁴. Further, as suggested by

studies, type 2 diabetes mellitus associated with testosterone dysfunction may exacerbate symptoms of sexual dysfunction by reducing libido, mood & infertility⁵. Hence, circulating serum testosterone measurement may be recommended in patients of type 2 diabetes mellitus having erectile dysfunction.

Several studies linked low testosterone level to type 2 diabetes, but they have not received much attention probably because both type 2 diabetes and low testosterone levels are associated with aging; as a high proportion of older men will have both diabetes and low testosterone levels. However, some clinical studies on men of same age have shown that the level of testosterone is lower in diabetic men as compared to non-diabetic men. These results need to be confirmed in more diabetic men, and studies need to be done to evaluate whether decreased serum testosterone levels in diabetes are related to age or obesity or is influenced by other variables. Hence we plan this study.

Material & Methods

The Cross sectional study was carried out in the department of medicine and diabetes care and research Centre, S.P. Medical College, Bikaner.

Inclusion Criteria

- Healthy subjects (free from any other disease).
- Type 2 diabetic male.
- Patients giving informed consent.

Exclusion Criteria

- Significant comorbidities like liver disease, tuberculosis, smoking, alcoholics, HIV etc.
- Any acute illness.
- Men on hormonal therapy.
- Men who had a surgical or chemical castration (for prostatic cancer)
- Type 1 diabetic male.

- Patients not willing to participate in the study or not giving consent.

Diagnostic criteria for diabetes mellitus¹:

1. Fasting blood sugar > 7.0mmol/L (126mg/dl) or
2. HbA_{1c} > 6.5% or
3. Two hour plasma glucose >11.1mmol/L (200mg/dL) during an oral glucose tolerance test or
4. Symptoms of diabetes plus random blood glucose concentration >11.1 mmol/L(200mg/dL).

Methods

Testosterone Assay- total testosterone level done by chemiluminescence method.

Statistical analysis

All data were analyzed on SPSS 17.0 version of statistical software. Pearson's coefficient level of significance i.e., p value <0.05 kept as significant whereas <0.001 kept highly significant.

Results

Mean total testosterone in diabetics was 281.67±67.31ng/dl and in controls it was 555.16±126.56ng/dl and the difference was found statistically highly significant (p<0.001).(table 1).Mean serum total testosterone (ng/dl) in age group ≤55 years was 360.29±142.21 ng/dl while in age group 56-70 years it was 357.96±152.94 and in age group >70 it was 239.07±61.86 (p<0.01). (table 2 and graph 2).Mean serum total testosterone (ng/dl) in age of onset group ≤50 years was 286.68±70.67 ng/dl while in age of onset group 51-60 years it was 280.55±60.47 and in age of onset group >60 years it was 273.90±73.85 (p>0.05).Mean serum total testosterone (ng/dl) in duration of diabetes group ≤5 years was 298.44±68.13 while in duration of diabetes group 6-10 years it was 268.90±62.06, in duration of diabetes group 11-15 years, it was 243.00±56.15 and in duration of diabetes group >15 years it was

218.00±10.95(p=0.001).Mean serum total testosterone (ng/dl) in BMI group 18-24.99 kg/m² was 455.50±138.14 while in BMI group 25-29.99 kg/m² it was 271.00±58.02, in BMI group 30-34.99kg/m² it was 227.29±34.05 and in BMI group ≥35kg/m² it was 210.00±0.00 (p<0.001). (graph 3).Mean serum total testosterone (ng/dl) in HbA1C group ≤7% was 526.37±141.58 while in HbA1C group 7.1-9.0% it was 292.46± 71.68, in HbA1C group >9% it was 267.97± 63.32 (p<0.001).Mean serum total testosterone (ng/dl) in WHR group ≤0.90 was 458.98±134.89 while in WHR group >0.90 it was 269.53±92.82 (p<0.001).No correlation was found between diabetic complications and serum total testosterone except cardiovascular disease.When we apply regression analysis on overall cases, total cholesterol had a significant change (p<0.05) while age, age of onset and HDL had insignificant difference (p>0.05). Duration of Diabetes, BMI, WHR, HbA_{1c} and LDL cholesterol had a highly significant change (p<0.001).On applying multiple logistic regression analysis, we observed increasing trend of 'r' value all the time when adding different parameters. (graph 4) Age and HbA_{1c} had a significant change (p<0.01) while duration of diabetes, BMI, WHR, TC and LDL cholesterol had highly significant change (p<0.001) and age of onset and HDL had statistically insignificant (p>0.05)(table 3).

Discussion

Each dawn brings new knowledge, new thoughts and new theories to the medical sciences that help man to explore deeper into the complexities of the human body. In present study, Mean serum total testosterone of the non diabetic group was 555.16ng/dl (19.27nmol/l) which was significantly higher than that of the diabetic group 281.67ng/dl (9.78nmol/L) with a p-value of <0.001(table1 and graph 1) and this observation is comparable to that of Mattack et al⁶ where they found that Mean serum total

testosterone of the non diabetic group was 532.41ng/dl (18.88nmol/L) which was significantly higher than that of the diabetic group 293.76ng/dl (10.20nmol/L) with a p-value of <0.0001⁶. In this study, testosterone was significantly lower in men with type 2 diabetics than in non diabetics. This work agreed with Kappor et al⁷, Dhindsa et al⁸ and Al-Hayek⁹. Various mechanisms by which low serum testosterone may be considered a threat for type 2 diabetes mellitus and metabolic syndrome include changes in the body composition, androgen receptor polymorphisms, glucose transport and decreased antioxidant effects. On the other hand, diabetes mellitus may also be considered a risk factor for hypogonadism through visceral obesity, reduced sex hormone binding globulin, inhibition of gonadotrops secretion or production of testosterone by leydig cells, cytokines mediated inhibition (e.g. TNF α, IL-1β, IL-6) of steroid production and increased aromatase activity resulting in estrogen excess¹⁰.

Age was found to be inversely correlated with Serum TT with a age of <55years in mean total testosterone 360.29±142.21ng/dl, 56-70 years in mean testosterone level 357.96±152.94ng/dl and >70 in mean testosterone 239.07±61.86ng/dl and the correlation was extremely significant with p-values of 0.009 as depicted in (Table 2). This finding is in accordance with that of Vikan et al¹¹ Ng Tang Fui et al¹².

Mean serum testosterone in BMI group 18-24.99 kg/m² was 455.50±138.14ng/dl while in BMI group 25-29.99 kg/m² it was 271.00± 58.02ng/dl, in BMI group 30-34.99kg/m² it was 227.29±34.05 ng/dl and in BMI group ≥35kg/m² it was 210.00±0.00ng/dl and this difference was found statistically highly significant (p<0.001) (WHO BMI Classification) Dhindsa et al⁸, Al-Hayek⁹, Kappor et al⁷ shows that BMI was significantly negatively correlated with testosterone levels in men. It has been suggested that

increased visceral adipose tissue in hypogonadal men leads to a further reduction in testosterone concentrations through increased conversion to estradiol by aromatase, which has a direct inhibitory effect on the hypothalamic-pituitary-gonadal axis.

WHR, HbA_{1c}, LDL cholesterol, total cholesterol correlated inversely with total testosterone in a significant manner ($p < 0.001$). In present study, no significant difference were found as we compared complications like neuropathy, nephropathy and retinopathy with total serum testosterone levels ($p > 0.05$) while CAD had a significant relation with low total testosterone ($p < 0.05$). while no correlation found with HDL cholesterol and age of onset.

Conclusion

From our study we concluded that serum total testosterone low in diabetic men than non diabetic. We also concluded that various factors like age, duration of diabetes, body mass index, waist hip ratio, glycated hemoglobin, total cholesterol, LDL cholesterol affect serum total testosterone in which BMI and WHR are more important factors than others. Level of total testosterone correlated inversely with total cholesterol and LDL cholesterol they suggest that total testosterone effect lipid profile but not very well known mechanism thereby increasing cardiovascular disease risk. We also concluded that no correlation of total testosterone with diabetic neuropathy, diabetic retinopathy, diabetic nephropathy. Normally serum total testosterone not routinely done in diabetic patients because of less research work. So we suggest all diabetic patients should be investigate for serum total testosterone test because low serum total testosterone affected many factors like body mass index, waist hip ratio, glycated hemoglobin, duration of diabetes and lipid profile. We suggest that further research required for testosterone therapy and effect of testosterone in diabetics.

Limitations

There are few limitations in the study

1. This was a cross-sectional design which made it impossible to determine whether diabetes preceded or followed the decline in serum testosterone level.
2. Study included only type 2 diabetes patients and type 1 diabetes were excluded
3. To precisely establish the role of testosterone in type 2 diabetes, a more elaborate study with large study group would have been desirable as our study was limited by a small study group.

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>70	239.07	61.86		
Total	281.67	67.31		

Table 3.ANOVA test of different parameters in relation to total testosterone

Parameters	Serum Total Testosterone (ng/dl)						f	P
	≤241		242-400		>400			
	Mean	SD	Mean	SD	Mean	SD		
Age	59.33	11.18	58.08	6.79	53.04	7.50	7.265	0.001
Age of Onset	53.59	9.35	53.21	7.84	44.67	6.42	1.619	0.202
Duration of Diabetes	7.57	4.97	5.02	2.88	8.00	0.00	8.353	<0.001
BMI	30.99	2.50	25.70	4.02	22.55	1.54	87.261	<0.001
WHR	1.23	0.11	1.05	0.19	0.84	0.07	170.79	<0.001
HbA _{1c}	9.07	1.11	8.85	1.23	4.99	0.91	238.687	<0.001
TC	174.13	15.94	189.51	61.99	145.17	42.69	13.888	<0.001
HDL	42.16	8.58	41.63	8.39	43.96	9.43	1.248	0.289
LDL	79.26	14.88	62.47	25.66	48.00	9.66	30.903	<0.001

Table 1

Measurement of serum total testosterone in type 2 diabetic and non diabetic patients

Groups	Total Testosterone (ng/dl)		t	P
	Mean	SD		
Diabetics	281.67	67.31	19.504	<0.001
Controls	555.16	126.56		

Table 2

Statistical analysis of serum total testosterone in relation to age group

Age Group (years)	Serum Total Testosterone (ng/dl)		f	P
	Mean	SD		
≤55 (n=86)	360.29	142.21	4.846	0.009
56-70 (n=99)	357.96	152.94		