Diabetes & Metabolic Syndrome: Clinical Research & Reviews 7 (2013) 129–132

Contents lists available at SciVerse ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

# Gonadal function in young adult males with metabolic syndrome

Bipul Kumar Choudhury *, Sarojini Dutta Choudhury, Uma Kaimal Saikia, Dipti Sarma

*Gauhati Medical College & Hospital, India*

ARTICLE INFO

*Keywords:*
Metabolic syndrome
Gonadal function
Hypogonadism
Testosterone
Sex hormone binding globulin

ABSTRACT

*Aims:* Aim of the study was to assess the gonadal function of young adult males with metabolic syndrome and to compare them with healthy age matched controls.
*Methods:* Forty young male subjects of age group 20–40 years who fulfilled the IDF criteria (2005) for diagnosis of metabolic syndrome were included in the study. Thorough evaluation of the subjects was done and history of sexual dysfunction if any was noted. Pooled blood samples were collected from each subject in fasting state for total testosterone, SHBG, FSH, LH, prolactin and insulin levels. All hormonal analyses were done by radio immune assay (RIA). Hypogonadism was defined as total testosterone less than 3 ng/ml. Eighteen healthy age matched controls were also taken for the study.
*Results:* Twenty percent of subjects with metabolic syndrome had eugonadotropic hypogonadism compared to 5.5% controls. Subjects with metabolic syndrome also had significantly lower SHBG level compared to the controls.
*Conclusion:* From this study it has been observed that eugonadotropic hypogonadism with low total testosterone and normal or low normal gonadotropin levels may be a feature of the metabolic syndrome in young adult males. Significant low SHBG levels as compared to controls could be one of the factors responsible for various biochemical alteration seen in these cases. This study highlights the importance of evaluating gonadal function in young adult males with the metabolic syndrome and has therapeutic implications in the management of such subjects with gonadal dysfunction.


## 1. Introduction

The metabolic syndrome is a cluster of metabolic and physical abnormalities that includes central obesity, elevated triglycerides, reduced HDL cholesterol, hypertension, increased fasting plasma glucose and hyperinsulinaemia. These cluster of abnormalities increases the risk of cardiovascular disease and diabetes mellitus. Besides cardiovascular risk and the risk of developing diabetes, metabolic syndrome has also been implicated in sexual dysfunction [1,2]. On the other hand androgen deficiency has been linked to development of metabolic syndrome. Low testosterone and sex hormone binding globulin (SHBG) levels are considered risk factors for metabolic syndrome in men [3,4].

It has been well established that with aging testosterone level falls [5]. Aging is also associated with increased prevalence of metabolic syndrome [6]. Blouin et al. in 2005 and 2006 studied whether the aging process itself or declining androgen level with aging is responsible for the development of metabolic syndrome and found that the effect of declining testosterone level on metabolic parameters was not age dependent [7,8]. Laakosen et al. in 2003 had already shown an inverse relationship between total testosterone levels and odds ratios for having metabolic syndrome in nondiabetic patients [9]. Most of these studies have been done in middle aged and elderly people. It has been observed that the incidence of metabolic syndrome is increasing in the younger population. With increasing evidence of a link between androgen deficiency and metabolic syndrome we designed this study to assess the gonadal function in young adult males with metabolic syndrome.

## 2. Material and methods

The present study was conducted in Gauhati Medical College and Hospital, a tertiary care hospital in Assam, India. Forty young male subjects of age group 20–40 years who fulfilled the IDF criteria (2005) for diagnosis of metabolic syndrome were included in the study. Exclusion criteria were chronic illness, hypopituitarism, hypo or hyperthyroidism, nephrotic syndrome, steroid use or use of any drug causing hypogonadism. Waist circumference was measured as per National Heart, Lung, and Blood Institute (NHLBI) practical guide recommendation [10]. Blood pressure was recorded in supine position with the B.P cuff applied in the right arm. Fasting plasma glucose and fasting lipid profile were done by autoanalyzer Vitros 5600. Fasting glucose was done by glucose

* Corresponding author. Tel.: +91 9864037328.
*E-mail address:* bipulchoudhury@sify.com (B.K. Choudhury).

1871-4021/$ – see front matter © 2013 Diabetes India. Published by Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.dsx.2013.06.013

oxidase–peroxidase method, HDL by phosphotungstic acid and magnesium chloride, cholesterol oxidase method and triglyceride by lipase-glycerol kinase method. Thorough evaluation of the subjects was done and history of sexual dysfunction if any was noted. Pooled blood samples, separated by 20 min, were collected from each subject in fasting state for total testosterone (RADIM diagnostics, Pomezia, Italia; normal range: 2.5–8.5 ng/mL), SHBG (IZOTOP – Institute of Isotopes Company Ltd., Budapest; normal range: 7.7–81 nmol/L), FSH (RIAKEY, Shinjin medics Inc., Seoul; normal range: 1.1–13 mIU/ml), LH (RIAKEY, Shinjin medics inc., Seoul; normal range: 0.8–11.1 mIU/ml), prolactin (RIAKEY, Shinjin medics inc., Seoul; normal range: 1.1–13 ng/ml) and insulin (IZOTOP – Institute of Isotopes Company Ltd., Budapest; normal range: 6–44 μIU/ml) levels. All hormonal analyses were done by radio immune assay (RIA). Eighteen healthy age matched controls were also taken for the study. Hypogonadism was defined as total testosterone less than 3 ng/ml.

## 3. Statistical analysis

Data are presented as mean ± SD. The IBM SPSS Statistics version 19 was used for statistical analysis. Chi square test, Chi square with Yates correction and Fisher's exact test, wherever applicable was done to test the association between two findings. Student's *t*-test was done to find the significance of difference between means when ever applicable. One tailed Pearson's correlation test was done to find the correlation between various variables. Linear regression analysis was done whenever appropriate.

## 4. Results

The cases (subjects with metabolic syndrome) and the controls were equally matched for age with mean age 33.2 ± 4.6 years and 31.7 ± 4.7 years ($p = 0.286$) respectively. Eleven cases (27.5%) gave history suggestive of sexual dysfunction in contrast to none in the control group and it included history of premature ejaculation, erectile dysfunction and decreased libido. None of the cases however had signs of hypogonadism. Comparison of the clinical characteristics of cases and controls are shown in Table 1.

In this study we have taken a value of total testosterone less than 3 ng/ml to diagnose hypogonadism. Accordingly out of forty cases, eight (20%) had total testosterone value less than 3 ng/ml compared to only one (5.5%) control. The mean total testosterone, FSH and LH of these eight cases were 2.35 ± 0.34 ng/ml, 2.7 ± 1.9 mIU/ml and 3.4 ± 2.7 mIU/ml respectively. On the other hand the total testosterone, FSH and LH of the lone control with testosterone less than 3 ng/ml was 2.81 ng/ml, 1.95 mIU/ml and 2.99 mIU/ml. When all the cases with metabolic syndrome were taken together the respective values were 4.03 ± 1.08 ng/ml, 3.57 ± 2.0 mIU/ml and 2.74 ± 1.5 mIU/ml. In comparison the mean total testosterone, FSH and LH of the controls were 5.3 ± 1.03 ng/ml ($p < 0.001$), 3.7 ± 2.1 mIU/ml ($p = 0.75$) and 2.95 ± 1.1 mIU/ml ($p = 0.15$) respectively. The mean prolactin level in cases and controls were 5.05 ± 3.4 ng/ml and 7.0 ± 3.4 ng/ml respectively ($p = 0.46$). This shows the presence of eugonadotropic hypogonadism in 20% cases. The mean SHBG level was significantly lower in cases (22.5 ± 13 nmol/L) compared to the controls (37.36 ± 15.1 nmol/L). Comparison of the biochemical and hormonal profile of cases and controls are shown in Table 2.

**Table 1**
Comparison of the clinical characteristics of cases and controls.

| | Case | Control | *p* value |
|---|---|---|---|
| *N* | 40 | 18 | |
| Age (years) | 33.2 ± 4.61 | 31.7 ± 4.7 | 0.286 |
| Waist (cm) | 102.7 ± 9.9 | 90.7 ± 3.6 | <0.001 |
| BMI (kg/m$^2$) | 30.2 ± 5.63 | 23.6 ± 2.5 | <0.001 |
| Hypertension (%) | 65 | 11.11 | |
| Acanthosis (%) | 37.5 | 5.5 | |
| H/O sexual dysfunction (%) | 27.5 | None | |

**Table 2**
Comparison of the biochemical and hormonal profile of cases and controls.

| | Case (40) | Control (18) | *p* value |
|---|---|---|---|
| FPG (mg/dl) | 148.7 ± 54.2 | 79.8 ± 10.0 | <0.001 |
| HDL (mg/dl) | 38.4 ± 8.2 | 50.5 ± 9.4 | <0.001 |
| Triglyceride (mg/dl) | 198.3 ± 92.7 | 114.1 ± 22.9 | 2.08 |
| Fasting insulin (μIU/ml) | 24.4 ± 18.4 | 12.5 ± 8.3 | 0.001 |
| T. testosterone (ng/ml) | 4.03 ± 1.08 | 5.3 ± 1.03 | <0.001 |
| FSH (mIU/ml) | 3.57 ± 2.0 | 3.7 ± 2.1 | 0.75 |
| LH (mIU/ml) | 2.74 ± 1.5 | 2.95 ± 1.1 | 0.15 |
| SHBG (nmol/L) | 22.5 ± 13 | 37.36 ± 15.1 | 0.001 |
| Prolactin (ng/ml) | 5.05 ± 3.4 | 7.0 ± 3.4 | 0.46 |

Using the the $\chi^2$ test and Fisher's exact p value we could not find out any association of occurrence of metabolic syndrome with total testosterone value less than 3 ng/ml. On the other hand we got a significant association between metabolic syndrome and SHBG value less than 30 nmol/L ($p < 0.05$). In our study we got a significant negative correlation between total testosterone and waist circumference ($r = -0.274$, $p = 0.04$) which is shown in Fig. 1 and between total testosterone and BMI ($r = -0.297$, $p = 0.03$). There was also a negative correlation of SHBG with waist circumference and BMI but these were not statistically significant. The mean fasting insulin level of cases was 24.4 ± 18.4 μIU/ml compared to 12.5 ± 8.3 μIU/ml of controls ($p = 0.001$). There was a negative correlation between total testosterone and fasting insulin level and between SHBG and fasting insulin level with both correlation being statistically significant ($p < 0.05$) as shown in Figs. 2 and 3.

## 5. Discussion

Metabolic syndrome is a cluster of metabolic and physical abnormalities that includes increased central obesity, elevated triglycerides, reduced HDL cholesterol, hypertension, increased fasting glucose and hyperinsulinaemia. Worldwide the metabolic syndrome shows a prevalence of 20–30% in most countries [11]. The prevalence increases with age, but high prevalence of metabolic syndrome in over weight adolescents has also been

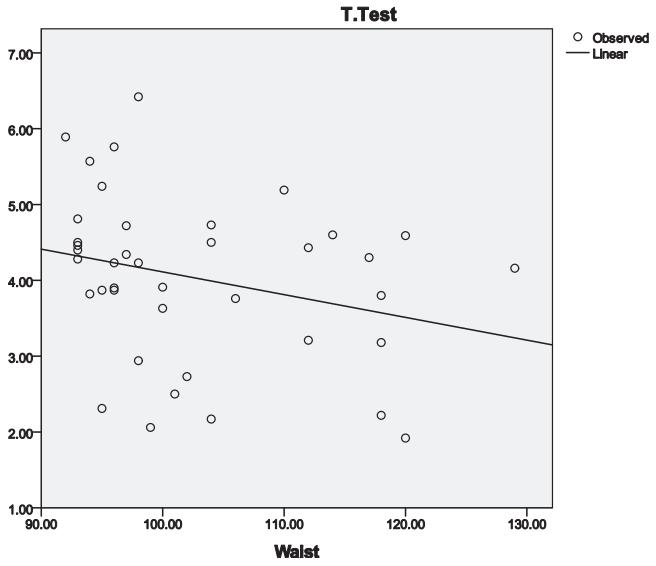


**Fig. 1.** Inverse relation of total testosterone with waist circumference.