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The effect of obesity and smoking on testosterone level in middle age Sudanese men in Shendi town, North Sudan

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Abstract
Obesity is a major health problem in this century, and is associated with many endocrine disorders and metabolic diseases.
It was reported that obesity is associated with male infertility anddecreased testosterone and increased estradiol level.
Testosterone (C19H28O2) is the most important androgen in potency and quantity and required in high testicular concentration for spermatogenesis.

Objectives
The study aimed to examine the association between obesity and serum total testosterone level in middle-aged healthy Sudanese men.

Methods
It was a cross sectional, descriptive, case control study; conducted in Shendi town, River Nile State,north Sudan from April 2018 to August 2018. It included sixtymiddle aged healthy Sudanese men.Twenty of them were normal (BMI ≤25). Twenty were overweight (BMI ≥25) and twenty were obese (BMI ≥30), Testosterone level was measured by ELISA technique and its concentration was expressed as ng/ml.

Result
The study revealed significant inverse correlation of serum total testosteronewith BMI(r = - 0.787, P value = 0.000), waist circumference (WC) (r = - 0.717, P value = 0.000) and waist to hip ratio (WHR) (r = - 0.580, P value = 0.000).
The study also found insignificant relationship between age and serum total testosterone level with (P value = 0.061). It also demonstrated statistically significant decreased of serum total testosterone level with smoking with (P. value = 0.017).

Keywords: Obesity, BMI, WC, WHR, Testosterone, Fertility, Smoking.

Introduction

Obesity is excess weight gain for a given height (WHO), and having a body mass index (BMI) of 30 or more is considered as Obesity (Pellitero et al. 2012). The BMI is a measure of relative weight based on an individual's mass and height. BMI (kg/m^2) = Body weight (kg) / Height $(m)^2$. It is commonly used to classify underweight, overweight and obesity (Frank Q. Nuttall. 2015). Obesity is a key pathological contributor to themetabolic syndrome (Diaz-Arjonilla et al. 2009). It is well known that plasma testosterone level in the obese decline with increasing body weight, particularly in men with central obesity (Osuna C et al. 2006; Lima N, 2000; Shamim et al. 2015).

Measurement of central adiposity is performedby waist circumference (WC). and waist-to-hip ratio (WHR), and have been adopted as more accurate predictors of obesity-related cardiovascular risk and have replaced BMI in several definitions for clinical diagnosis of metabolic syndrome.(Crystal Man Ying Leea. 2008) For male the normal (WC):- ≤ 102 cm andhigh (WC) :- >102 cm, whereas the normal (WHR):- ≤ 0.9, and thehigh (WHR) :- > 0.9. Obesity currently represents one of the most common medical conditions in the United States. Obesity among adults in the developed world is defined as a body mass index (BMI) over 30 (kg/m2), and morbid obesity constitutes a BMI of 40 or higher. Almost a third of adults in the United States are considered obese on the basis of current measured weights and heights.(M Diaz-Arjonilla. 2009) Obesity is associated with diabetes, hypertension and renal dysfunction. Hypogonadism and sub -fertility are also other prevalent endocrine dysfunctions amongobese people. Obesity in itself contributes to loss of muscle mass and function, with escalating effects on mobility, leading to disability and functional impairment. Moreover the pro-inflammatory cytokines released by adipose tissue may contribute to loss of muscle mass and function, leading to inactivity and further weight gain in a vicious cycle (Fui MNT, et al.2014).

Increase in the adipose tissue mass, which is the prominent feature of obesity is a key pathological contributor to themetabolic syndrome. High BMI, central adiposity, and the metabolic syndrome are associated with and predict low serum total and to a lesser extent free testosterone and steroid hormone binding protein (SHBG) levels. It has been suggested that obesity-associated male hypogonadismis related to the central inhibition of gonadotropinsecretion. Obesity and related concomitant metabolic abnormalities are among the proposed causes of male infertility(Brugo-OlmedoS, et al. 2001).Infertilityis considered as a one year of unwanted non-conception with unprotected intercourse in the fertile phase of the menstrual cycles (Gnoth C, et al.2005). Approximately 30–40% of infertility cases can be attributed to problems with the male partner (Phillips and Tanphaichitr, 2010).

Testosterone (17b-hydroxy-4-androstene-3-one) is a 0.288kD C19 sex steroid hormone produced from cholesterol via a series of enzymatic conversions. (Vingren, et al.2010)**.** This process takes approximately 20–30 minutes.Testosteroneis a sex hormone that plays important roles in the body.It is essential to maintain spermatogenesis and male fertility.It regulateslibido, bone mass, fat distribution, production of red blood cells, and muscle mass and strength(FinkelsteinJS,etal2013 ;Walker WH. 2010).Testosterone is converted to dihydrotestosterone (DHT) by the action of 5α-reductase in target tissues; although it is about one-tenth as abundant as testosterone it accounts for most of testosterone's biological action(Ragini Srinivasan. 2001;Brinkmann. 2011)**.** A small amount of circulating testosterone is converted to estradiol in peripheral tissues by the action of aromatase enzyme complex. Aromatase activity is present in adipose cells and also in liver, skin, and other tissues. Increased activity of this enzyme may contribute to the estrogenization that characterizes such diseases as cirrhosis of the liver, hyperthyroidism, aging, and obesity (Weil PA. 2018).The concentration of testosterone declines with increasing age. Human has a plasma β-globulin that binds testosterone with specificity, relatively high affinity, and limited capacity sex-hormone-binding globulin (SHBG), which is produced in the liver.Measurement of free testosterone or (SHBG) level is helpful in determining bioavailable testosterone because many systemic conditions are associated with changes in SHBG level(Kalyani et al, 2007).

Testosterone is oxidized to androstenedione and then reduced to androsterone and 5/3-androsterone, which are conjugated with both glucuronic and sulfuric acid before excretion in the urine (Baulieu and Mauvais-Jarvis. 1964).Several studies demonstrated that the serum testosterone concentration declines with increasing age (Snyder. 2001).Testosterone replacement therapy is necessary in all hypogonadal patients (Seftel A.2006). Androgen replacement comprises injectable forms of testosterone as well as implants and transdermal systems (Zitzmann and Nieschlag. 2000; Kumar et al. 2018; Dandona P, Rosenberg M.2010).

Low serum total testosterone predicts the development of central obesity and accumulation of intra-abdominal fat (Wang et al. 2011). Obesity and related concomitant metabolic abnormalities are among the proposed causes of male infertility (Phillips and Tanphaichitr. 2010).

Material and Methods

The study was a cross sectional, descriptive, case control study conducted in Shendi town, River Nile State, north Sudan,from April 2018 to August 2018.

It included sixty middle aged (18-50 years) healthy Sudanese men. Twenty of them were normal (BMI ≤25) and considered as control group. Twenty were overweight (BMI ≥25) and twenty were obese (BMI ≥30), Adultmaleswho had diseases which may affect testosterone levelswere excluded from the study. Data were collected by preformed questionnaire and 5ml of bloodwere collected from each participant through venipuncture technique into plain container each blood specimen was centrifuged at 3000 round per minute for five 5minutes to obtain the serum, which was collected gently into plain container and stored in at -20 °C until serological analysis.

The serum was analyzed for quantitative detection of testosterone level by commercially available enzyme–linked immune sorbent assay, BXE0862A(96 tests)" kit produced by (Fortress Diagnostics Limited, unit 2C Antrim Technology Park, Antrim, BT41 1QS United Kingdom).The assays were performed following the instructions of the manufacturer.Testosterone concentration was expressed as ng/ml.

According to the information included in the kit's insert, the immunoassay used has 98.0% sensitivity and 99.3% specificity.

The reference values for testosterone concentration were;Low(< 2.5 ng/ml),normal(2.5-10 ng/ml), high(>10 ng/ml)

Anthropometrics values of weight, height, and hip and waist circumference were measured to calculate the waist to hip ratio (WHR) and BMI.

All collected data was analyzed using SPSS for windows, version 21, Pearson Chi-Square test was used for categorical data with p value ≥ 0.05 as significant. Analysis of variance (ANOVA) was used for continuous data and the statistical results were presented as means ± SD.

Ethical clearance

Ethical approval for the study was obtained from the Board of the Faculty of Graduates Studies and Scientific Research in Shendi University. Verbal informed consent for participation in the study was obtained from each participant before recruitment into the study.

Results

Table (1):-Correlation between testosterone level, BMI, WC & WHR

	BMI(kg/m2)	**WC**(cm)	**WHR**
Mean	27.02	101.53	.9115
SD	6.601	19.101	.07921
Testosterone PearsonCorrelation	- 0.787	- 0.717	- 0.580
	0.000	0.000	0.000

Table (2):- Mean and standard deviationof testosterone level with BMI

BMI	**No**	**Mean**(ng/ml)	**SD**	***P*. value**
Normal	20	7.34	2.57	
Over weight	20	3.62	2.05	0.000
Obese	20	2.08	0.58	

* *P*.value is significant

Table (3):-Mean and standard deviation of testosterone level with WC

WC Level	**No**	**Mean(ng/ml)**	**SD**	***P*. value**
Normal	32	5.85	3.21	0.001
High	28	3.03	1.89	

*** *P*. value is significant**

Table (4):-Mean and standard deviation of testosterone level with WHR

WHR Level	**NO**	**Mean**(ng/ml)	**SD**	***P*. value**
Normal	32	5.43	3.52	0.045
High	28	3.51	1.89	

* *P*. value is significant

Table (5):-Mean and standard deviation of testosterone level with age.

Age(years)	**No**	**Mean**(ng/ml)	**SD**	***P*.Value**
18-28	27	5.048	3.2570	0.061
29-39	18	4.994	3.1791	
40-49	15	2.943	1.3903	
Total	60	4.506	2.9789	

* *P*.value is insignificant.

Table (6):- Mean and standard deviation of testosterone levels with social status

Social status	**No**	**Mean**(ng/ml)	**SD**	***P*.value**
Single	30	5.83	3.35	0.000
Married	30	3.18	1.79	

* *P*. value is significant (ANOVA)

Table (7):-Mean and standard deviation of Testosterone level in smokers and non-smokers.

Smoking	**No**	**Mean**(ng/ml)	**SD**	***P*. value**
No	36	5.09	±3.47	0.017
yes	24	4.12	±2.59	

* *P*. value is significant (ANOVA)

Table (8):- the effect of exercise ontestosterone levels

Exercise	**N**	**Mean**(ng/ml)	**S. D**	***P*.Value**
Never	27	4.53	3.57	0.474
Regular	24	4.90	2.68	
Irregular	9	3.44	1.34	
Total	60	4.51	2.98	

* *P*.value is Insignificant (ANOVA).

Table (9):- Mean and standard deviation of testosterone level with family history of obesity.

Family history of obesity	**No**	**Mean**	**SD**	**P. value**
Yes	27	3.00	±1.84	0.000
No	33	5.73	±3.20	

* *P*. value is significant

Discussion

This study examined testosterone levels among middle aged apparently healthy men with different ages and weights (normal, overweight and obese).

The mean and SD of testosteronelevel in different weight (normal, overweight and obese) were (7.34± 2.57, 3.62 ± 2.05, 2.08 ± 0.58) respectively as appeared in table (2) And the study found that (66.7% = 40/60) who were overweight and obese hadrelatively low testosterone level, which was statistically highly significant (*P*.value <0.000).

Significant inverse correlation of serum total testosteronewith BMI(r = - 0.787, *P*.value = 0.000), WC(r = - 0.717, *P*. value = 0.000) and WHR (r = - 0.580, *P*.value = 0.000) was observed in this study.

The findings of this study agreed partially with result obtained in Pakistan by Shamim MO, et al.2015, who demonstrated statistically significant difference in the mean value of testosterone against BMI and WHR. Significant difference of serum total testosteronewith BMI (r = -0.311, *P*.value = 0.000) was observed in that study. However testosterone was not significantlycorrelated with waist to hip ratio.(r = 0.126, *P*. value = 0.076) Middle age men working at Dow University of Health Sciences (DUHS) in Pakistan, who have low level of serum total testosterone are moreobese than individuals with normal total testosterone level.(Shamim et al., 2015)

The results of this study were also consistent with those observed by Osuna C J. et al.2006), who found that testosterone and SHBG serum concentrations decreased as the BMI increased. (Osuna C et al. 2006)

Table (3) showed the meanof testosterone level for normal and high (WC) was (5.85± 3.21, 3.03± 1.89) respectively. Table (4) demonstrated that the meantestosterone level was (5.43± 3.52, 3.51± 1.89) for the normal and high (WHR) respectively. Significant decreased of serum total testosterone with increasedof(WC) with (*P*.value = 0.001) and (WHR) with (*P*. value = 0.045).

The data displayed in table (5) illustratedinsignificant relationship between age and serum total testosterone level. (5.05 ±3.30) (4.99±3.17), (2.94±1.39) for the age group (18-28), (29-39), (40-49) years respectively, with (*P*. value = 0.061).although there was apparent decline in the mean testosterone level with increasing age.

The figures appeared in table (6) highlighted statistically significant effect of marital status onserum total testosterone level where as the mean was (5.81±3.35), (3.18±1.79) for single and married respectively with (*P*.value =0.000).

Table (7) revealed statistically significant decreased ofserum total testosterone levels with smoking were mean and SD of smokers and non-smokers (4.12,±2.59), (5.09,±3.47), respectively, with *P*. value (0.017),

In table (8), data presented no statistically significant effect of exercise on meanserum total testosterone level.

Conclusion

The study revealed statistically significant inverse correlation between serum total testosteronewith BMI, WC and WHR.It also showed no statistically significant relationship between age and serum total testosterone levels.The findings of study demonstratedlower serum total testosterone levels in married compared to single ones. The study also illustrated statistically significant decreased of serum total testosterone levels with smoking .No statistically significant effect ofexerciseonserum total testosterone level.

Recommendation

The authors highly recommend augmentation of efforts to control body weight as this century witness unprecedented global obesity crisis. Smoking cessation is also strongly recommended as these two conditions have serious impact on testosterone level and hence human fertility.

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