Relationship of Sex Hormon Binding Globulin, Thyroid Stimulating Hormone, Testosterone and Prolactine with Body Mass Index (BMI) Value among Iraqi Females in Reproductive Age

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Abstract

Background: The purpose of this study was to determine the relation between increasing in the body mass index (BMI) value and sex hormones level represented by sex hormon binding globulin (SHBG), Thyroid stimulating hormone (TSH), testosterone and prolactine in 51 women in reproductive age aiming following the life quality of these females.

Method: Participants were 51 women from center of Baghdad city. Every female full a questionnaire and sex hormone concentration from each female were measured. Level of FBS and HbA1c test was estimated and designed as exclusion criteria for diabetic mellitus and other metabolic disorders. Body mass index value was compared by demographic properties, Pearson's correlation coefficient and A stepwise method in linear regression statistic test was applied to detect the association of BMI (kg/m2) with serum sex hormon binding globulin (SHBG), Thyroid stimulating hormone (TSH), testosterone and prolactine and predict the most affected factor.

Results: The mean and standard deviation level of most studied parameter were not differences between case study and control females group (obese vs non-obese) in compared with normal value of each test. BMI value were negatively correlated with age and SHBG (nmol/l) level (r = 0.156; P= 0.274) and (r = 0.578; P = 0.00) respectively. While BMI were moderately positive correlated with testosterone (nmol/l), TSH (µIU/mL) and prolactin (ng/ml) (r = 0.388; **P =** 0.005), (0.354; **P = 0.011**) and (0.37; **P =** 0.006) respectively. Depending on the stepwise method in linear regression analyses, the SHBG (nmol/l) and testosterone (nmol/l) were the most independent predictor factors for BMI in the studied groups (β = 0,484; P = 0.001) and (β = 0.348; P = 0.001) respectively.

Conclusions: The most factors affecting obesity identified in the study were SHBG, Testosterone. However, other variables such as age, did not impact the BMI value of participants.

Keywords: *Iraq; Sex hormone binding globulin, Testosterone; obesity.*

Introduction

Obesity can be defined a complicated and multifactorial disease that occurs due to the interaction of social, behavioural, metabolic, genetic and impact of cultural behavioral. Obesity offers a cause for many health problems, reduces life's duration, effect the quality of life and increased mortality. As a result, it has become an important public health affair on a global scale [(1)]. Gender specific issues in female with obesity start with initial puberty, menstrual disturbances and dysovulation, and then they go forward with polycystic ovary syndrome (PCOS), obstetric problems, infertility , endometrial and breast cancer incidence which rise after

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menopause [2]. Hormonal changes are associated with gradually increasing BMI are slow, therefore a certain "adaptation mechanism" could improve and might clarify why the BMI-associated sex hormone alterations were not proven to be a significant role in anxiety pathogenesis in overweight individuals. Hormonal changes which were associated with obesity could be "protective" against anxiety.

The term "sex steroid-binding globulin (SSBG)" are also called "Sex hormone-binding globulin (SHBG)" structurally are homodimer glycoprotein which are able to binds both estrogens and androgens hormones [1]. SHBG structurally are synthesis from the liver with different binding affinity values for different hormones such as five high affinity with dihydrotestosterone (DHT), testosterone (T) while less bindings values with17β -estradiol (E2) hormones [2]. Therefore, (SHBG) regarded as the major vehicles for transporting these sex steroids hormones, also to non-specific carriers such as albumin, primarily the concentration of SHBG control the availability of the aforementioned steroids hormone [3]. The literature indicated that the influence of genetic, different hormonal, and lifestyle-related factors on circulating SHBG levels. The estrogen/ androgen balance was typically the key feature in the regulation of SHBG synthesis. SHBG regulation is considered currently as multifactorial and other non-steroidal factors have a significant character in the circulating levels of this binding protein. [4]. The rise in body fat ratio in premenopausal women, can lead to an imbalance in sex steroids. Estrogen aromatization of androgens rises the estrogen amount in stromal vascular cells in fatty tissue. On the other hand, the estrogen/androgen ratio rises in obese individuals, there is a fall in sex hormone- binding globulin (SHBG).

Materials and Method

Participant

The present study was a cross-sectional types of cases and control. The studied population included female patients with gynecological health problems in Baghdad teaching hospital department of gynocology in Iraq between September 2018 and February 2019. The age of participants was 19 years or greater. The participants in the present study were chosen by simple random sampling method from among female patients with gynecological health problems. Thirty-one female patients were chosen as cases (BMI 30 and above) and twenty female patients (BMI ≤ 29.9) were chosen as controls. Inclusion criteria were being females free from some health problems such as polycystic ovary disease, thyroid disorder, chronic renal diseases, chronic hepatopathy, and tumors and any metabolic syndrome (MetS,). As well as, females who were undergoing to hormone treatment. The sample size was calculated by this formula:

$$n = \frac{2(z_1 + z_2)^2 s^2}{d^2}$$

=51 participants The research council and ethics committee of Baghdad health directorate in Iraq approved this study. Written informed consent was completed by all the patients before starting this study. The data collection tools in this study included: demographic characteristics, anthropometric measurements and Biochemical tests. Each participant woman in this study was undergoes to biochemical tests.

Hormonal and another parameter assay

A blood sample for biochemical test was drawn from each participant at day of experiment and after 12 hours overnight fasting. Blood samples were divide into two tubes one for serum collection the other was transferred in test tubes containing EDTA substances. Questionaries' was obtained from the participants before starting this study. All samples were sent to the medical city complex for teaching laboratories institute for assessments. The SHBG, testosterone, prolactin and TSH were detected by using IMMULITE® 2000 immune assay system (IMMULITE, SIMENS, USA). While the FBS and HbA1c were assessed by using (Dimension® RxL Max®, USA) integrated system, and analyzer by using (Arkray, ADAMS, JAPAN) respectively.

Statistical Analyses

Statistical analyses were calculated using the Statistical Package for Social Sciences (SPSS) software (SPSS version 22. Inc., Chicago, IL, USA, 2013) and the level of significance was established at a p-value 0.05 or less. Descriptive analysis was conducted to determine the means, standard deviations, percentages and frequencies. Shapiro walk test for normality was

carried out on each continuous variable because of the sample size less than 100.

Result

Frequency and biochemical test descriptive of studies groups

The demographic properties of participants' biochemical measurement were summarized in Table 1 and Table 2. The frequency of obese group was 31 in number which account (60.8 %) in comparison with non-obese groups females which has normal body mass values which account 20 cases (39.2%) of total participants from total study count. When categorized the BMI (kg/m2) values of studied groups the resulted group were (obese vs overweight normal weight) the mean value was (35.7±4.2 vs 19.35±1.26) as arranged in (Table 1). There are no obvious differences in the mean values of the four types of sex hormones level which includes SHBG (nmol/l), Testosterone (nmol/l), TSH (μIU/mL) and Prolactin (ng/ml) for both groups when compared with normal value of each test. The result of this study also revealed the level of both test FBS (mg/dl) and HBA1c level % which designed primarily as exclusion criteria for studied the normal health status of both groups were within normal range (97.6+7.05 vs96.3±7.1) and (5, 14±0, 3 vs 5, 1±0, 5) respectively when compared with normal value of each test as arranged in (Table 2). Subsequently, on bivariate correlation analysis, the BMI of participants was found to be significant associated with the independent variables which include SHBG, Testosterone, TSH, prolactin and which are significant predictors as declared in (Table 3). The results revealed that correlation of BMI (kg/m2) had strong negative significant correlation with SHBG (nmol/l) hormone (r= -0.578, P= 0.00). While the rest hormones such as Testosterone (nmol/l), TSH (μIU/mL) and Prolactin (ng/ml) were showed moderate positive significant correlation (r= 0.388, P=0.005), (0.354, P= 0.011) and (0.37, 7, P= 0.006) respectively as shown in (Table 4). We excluded the HbA1c and FBS tests from predicator test because we regarded it in the design of our study as exclusion tests of diabetic status. Four-predictor multiple linear regression models are proposed to explain the variation of BMI(Y). The four-predictor variables proposed are SHBG (X1), Testosterone (X2), TSH (X3), and Prolactin (X4). A stepwise method in linear regression has been used (Table 5). Therefore, the variables already in the equation are removed if their p-value becomes larger than the default limit due to the inclusion of another variable. The result of regression revealed highly significant model ($p < 0.001$). For addressing the multicollinearity, the researcher has been used collinearity statistics to remove the offending variables, where they represented clearly multicollinears, which indicated a problem in the statistics. The result of regression revealed significant model {$F = 25$, $df = (3, 47)$ $p < 0.001$}.

Table 1: Frequencies of BMI of Study Groups

Group of Categorical BMI	Frequency	Percentage (%)
< 24.9 (control)	20	39.2
25 and above (case)	31	60.8
Total	51	100

Table 2: Descriptive statistic of studies group

No	Parameter	(M±SD) of obese	(M±SD) of non-obese	Norma value
1	Age (years)	29.90 ±6.2	30.9±5.1	-
2	(BMI) kg/m2	35.7±4.2	19.35±1.26	24.9< non-obese 30 obese ≥ 30 overweight
3	SHBG (nmol/l)	31.7±14.2	52±10.23	27-109

Cont... **Table 2: Descriptive statistic of studies group**

4	Testosterone (nmol/l)	21.7±6.5	18.51±0.51	17.2- 50
5	TSH (µIU/mL)	3.2±2.1	1.73±0.5	0.4-4
6	Prolactin (ng/ml)	12,2±7.4	13,±5,5	4.6 – 37
7	FBS level (mg/dl)	97.6+7.05	96.3±7.1	74-106
8	HBA1c level %	5,14±0,3	5,1±0,5	**4 % and 5. 6 %**

BMI, Body mass index; SHBG, sex hormone binding globulin; TSH, thyroid stimulating hormone ,FBS; fasting blood sugar, HBA1c, glycosylated hemoglobin

Table 3: Correlations between BMI and other variables

Pearson correlation						
Dependent variable		**Age (Years)**	**SHBG (nmol/l)**	**Testosterone (nmol/l)**	**TSH (IU/ml)**	**Prolactin (ng/ml)**
BMI (Kg/m2)	Correlation –r	-0.156	-0.578**	0.388**	0.354*	0.377**
	P-value	0.274	0.000	0.005	0.011	0.006
	N	51	51	51	51	51
**Correlation is significant at the 0.01 level (2-tailed)						
**Correlation is significant at the 0.05 level (2-tailed)						

Table 4: Interpretation of correlation result of BMI with other independent variables

No	**Variables**	**Correlation**	**p-value**	**Interpretation**
1	SHBG (nmol./l)	-0.578	0.000	Strong negative significant correlation
2	Testosterone (nmol/l)	0.388	0.005	Moderate positive significant correlation
3	TSH (IU/mL)	0.354	0.011	Moderate positive significant correlation
4	Prolactin (ng/ml)	0.377	0.006	Moderate positive significant correlation

Table 5: Multiple linear regression analysis of BMI and associated with the predicator variable

Model	Unstandardized Coefficients B	Standardized Coefficients B	t-statistic	Sig.	Collinearity Statistics	
					Tolerance	VIF
SHBG (nmol/l)	-0.264	-0.484	-3.511	0.001	0.869	1.151
Testosterone (nmol/l)	0.578	0.348	-4.992	0.001	0.938	1.066
Dependent Variable: BMI (Kg/m2)						

Discussion

Hepatocyte SHBG production is under the influence of several factors which can either increase (thyroid hormones, estrogens) or reduce its levels (obesity, progestogen, growth hormone, prolactin) [4,5]. The mechanism by which obesity is associated with decreased SHBG has not been fully explained, but may involve inhibition of hepatic source of SHBG due to increased levels of insulin hormone (7, 8). Sex hormone-binding globulin (SHBG), are regarded as a major transporter protein of testosterone hormone, the level of (SHBG) are one indicator of risk for metabolic syndrome in both men and women [9]. Another publisher who indicated that a low circulating level of SHBG was not associated with high concentration of insulin level(10) but was associated with dyslipidemia and obesity conditions that are strongly associated with fatty liver in humans [11-13]. Women with MS showed increased testosterone and lower SHBG independently of menopausal status (9). Our result was disagreement with previous study, so the level of the FBS level (mg/dl) and HbA1c % range was within normal range (97.6+7.05, 96.3±7.1,5,14±0,3,5,1±0,5%) respectively. Obesity is documented as one causes which leade to insulin resistance state which in turn lead to development of diabetus mellitus disease [10], increase the risk of Metabolic syndrom state [11] also associated with hypercortisolism condition [12], and elevated level of estrogen hormones [13]. The result of regression analysis represented by stepwise method revealed the SHBG (nmol/l) and testosterone (nmol/l) were the most independent predictor factors affected due to increased in the BMI (kg/m2) value in the studied groups (β = -0,484; P = 0.001) and (β = 0.348; P= 0.001) respectively. Obesity is linked with lower serum levels of SHBG in both men and women [14,15]. Some studies, that has been applied on typically small samples of peri-menopausal women, indicate either a decreas or no substantial age-related changes in SHBG concentration [16-18]. There is increasing evidence that low SHBG levels are strongly associated with metabolic syndrome and also an independent risk factor for development for diabetes, especially in postmenopausal women [19,20].

Conclusion

The main objective of this study, are to follow the healthy status of obese females under reproductive stage aiming to protect them from and metabolic syndrome which may lead to impair their quality of life also to predict the most biochemical test which may predict the hormonal disturbances for those females who are nor married.

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the Middle Technical University and all experiments were carried out in accordance with approved guidelines.

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