Correlation of BMI with Hormonal and Lipid Profile A mong Women with Polycystic Ovary

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Abstract:

Background: It is estimated that 5-10% of women in the reproductive age have PCOS. It occurs in 85-90% of women with oligomenorrhea and in 30-40% of women with amenorrhea. Fifty percent of women with PCOS are obese with an android pattern.

Objective: to correlate between BMI and various hormones and lipids among women with polycystic ovary syndrome.

Methods: this cross-sectional study was conducted in AL-Elwiya Maternity Teaching Hospital during the period from October 2004 through December 2005. A total number of 41 women with PCO was studied; an ultrasound examination was done to confirm the polycystic appearance of the ovary. Height and weight were measured to calculate the body mass index. A series of hormonal and biochemical analysis was done to the women including FSH, LH, estradiol, free serum testosterone, fasting insulin, fasting High density lipoprotein-Cholesterol (HDL/Cholesterol) and fasting triglyceride level in addition to total cholesterol/ HDL ratio and Progesterone. Women were sub-divided into 4 groups according to their body mass index.

Results: The mean of HDL/Cholesterol decreases progressively as BMI increases. The mean of total serum cholesterol, of TC / HDL- Cholesterol ratio and of free triglycerides levels was increasing proportionally with BMI. Estradiol and FSH are the only two hormones which showed non significant relationship with BMI (P values are 0.24 and 0.88 respectively). Both LH and LH/FSH ratio are significantly correlated to BMI (P<0.0001). The slope of fasting insulin level curve with BMI was positive which indicates a proportional relationship between them.

Conclusion: women with PCO (whether with normal or high BMI) have high levels of fasting serum insulin, testosterone, and free cholesterol in addition to low HDL-Cholesterol which may expose them to major health problems like diabetes mellitus, ischemic heart disease, and other related metabolic disorders.

Keywords:

Introduction

Since the original description of the baffling triad of (obesity, hirsutism and polycystic appearance of the ovary) in 1936 by Stein and Leventhal, polycystic ovary syndrome (PCO) remained an amazing disorder among females and practicing physicians for almost decades in the last century [1,2]. In the last 20 years many abnormalities became evident. Polycystic ovary syndrome was found to be one of the insulin resistance disorders accompanied by a wide variety of clinical, hormonal and biochemical changes. The diagnostic criteria of polycystic ovary has witnessed dramatic changes from the simple non invasive (history, physical examination and abdominal ultrasound) to the full assessment of different hormonal profiles like fasting serum insulin, testosterone and LH/ FSH ratio [3,4,5]. The clinical issue of polycystic ovary syndrome has been linked to later liability of wide spectrum major health problems like diabetes mellitus, atherosclerosis, ischemic heart diseases, cerebrovascular diseases and endometrial carcinoma[6,7,8]. However, in clinical practice, history and clinical examination (namely oligomenorrhea, hirsutism and obesity –measured by BMI-) remained the main key points that attract the clinician's minds to the possibility of diagnosis of PCO. In normal daily practice two of the above mentioned findings represent the justification to send the woman for further investigations by ultrasound, hormonal and biochemical analysis. The aim of this study is to correlate between BMI (as an independent variable) with various hormones and lipids (dependent variables) among women with polycystic ovary syndrome.

Patients & Methods

Setting: The study was conducted in AL-Elwyia Maternity Teaching Hospital during the period from October 2004 through December 2005.

Design:

This is a cross sectional study with an analytic element.

Sampling:

A total number of 41 women with PCO was chosen from the outpatient and infertility clinic of Al-Elwiya Maternity Teaching hospital, The sample was a consecutive one by pooling all the patients attended the mentioned hospital during a fifteen month period, the women were told about the aim (and the method) of the study, a consent was taken from each one of them.

Methods:

All patients were first screened for menstrual disturbances and hirsutism. Women included in the study were never have any form of treatment previously for infertility nor taking contraceptive, aldactone, cyproterone acetate or insulin sensitizing drugs; as those drugs may modify the hormonal and

biochemical interpretation of the investigations. The patients then were sent for ultrasound examination to confirm the polycystic appearance of the ovary. In addition accurate measurement of the height and weight was done to calculate the BMI. The weight was measured by using a well-calibrated digital scale with an accepted error of (0.1 Kg) and the height was measured by a stadiometer with an accepted error of (0.1 cm), BMI was estimated from the equation: BMI = Wt. (kg)/ Ht. (m^2).

The women then were sent for a series of hormonal and biochemical analysis at AL-Kindy Center for Diabetes and Endocrinology. At day 3-5 of the menstrual cycle they were sent for FSH, LH, estradiol, free serum testosterone, fasting insulin level, fasting High density lipoprotein-Cholesterol (HDL/Cholesterol) and fasting triglyceride level in addition to total cholesterol/ HDL ratio. While at the mid- luteal phase (calculated by subtracting 7 days from the next expected menstrual cycle) they were sent for progesterone level at the same center. LH/FSH ratio more than 2 was used to confirm the diagnosis of PCO.

After collection of data, the women were sub-divided into 4 groups (in the analysis stage); the normal weight group, the over- weight, the obese and the grossly obese group, according to their BMI of <25, 25- <30, 30 - < 35 and >35 respectively.

Statistical analysis:

The body mass index was used as an independent variable to construct a series of linear formulas by the least square fit technique. The general form of the formula has the following equation {y = a1+ a2 * x}, where x is universally the BMI, while y represents the various hormonal and biochemical parameters that were measured. The constant (a1) is the (intercept) which represents the point on y axis where the regression line intercepts. The constant a2 represents the (slope) of the curve that represents the tangent of the angle between the x-axis and the constructed regression line. F test was calculated. P value less than 0.05 was considered as a cut-off point for statistical significance. Microsoft Excel Software 2003 was used to compute the different statistical parameters.

Results

Table 1 shows the various hormonal and lipid profiles versus BMI sub groups. The mean of both LH and LH/ FSH ratio increases progressively as BMI increases, while mean progesterone levels decrease with BMI increment. The mean of HDL-Cholesterol was inversely related to BMI. While the mean of total serum cholesterol, of TC/HDL/Cholesterol ratio and of free triglycerides levels was increasing proportionally with BMI. Estradiol and FSH were the only two hormones that have non significant relationship with BMI (P = 0.24 and 0.88). Both LH and LH/FSH ratio were significantly associated with BMI (P<0.0001). The slopes of the line constructed were 0.6104 and 0.1317 respectively. While the coefficients of determination were 0.8969 and 0.8824 respectively, this indicates a linear correlation with BMI. The slope of progesterone line was negative (-0.0236) which indicates an inverse relationship with BMI, the coefficient of determination was 0.8945 indicating a linear relationship with BMI (P<0.0001). The slope of testosterone curve was positive (0.1544) that indicates a proportional relationship with BMI, while the coefficient of determination was 0.9484 indicating a strong positive linear relationship with BMI (P < 0.0001). The slope of fasting insulin level curve with BMI was positive 1.8258 which indicates a proportional relationship between them. The coefficient of determination was 0.9229 pointing to a strong positive linear relationship with BMI (P < 0.0001). The slope of HDL/ Cholesterol was negative (-0.0573) that means an inverse relationship with BMI, the Coefficient of determination was 0.9240 which indicates a strong negative linear relationship with BMI increment (P <0.0001). The slopes of total cholesterol, TC/ HDL- Cholesterol ratio and free triglycerides are all positive (0.1232, 0.3394 and 0.0632 respectively). The positive slopes' values indicate direct and proportional relationship with BMI increment. Their coefficients of determination were 0.8404, 0.9114 and 0.9530 respectively, all with P values less than 0.0001. Table.2

Table 1: Mean (±SD) of hormonal and lipid profiles among 4 sub groups according to BMI

Characteristics	Normal weight N=(7)	Over weight (N=15)	Obese (N=7)	Grossly obese (N=12)	Total (N=41)
Weight (Kg)	54+1.41	64+1.41	75+2.16	84.5+3.60	70.17+11.71
Height (meter)	1.54+0.020	1.52+0.080	1.52+0.036	1.47+0.024	1.51+0.058
BMI (kg/m^2)	22.77+0.69	27.60+1.52	32..48+1.52	39.12+2.73	30.98+6.28
FSH (U/L)	4.44+0.13	4.76+0.42	4.57+0.26	4.63+0.30	4.63+0.33
LH (U/L)	9.7+0.55	12.42+0.99	13.94+0.26	19.31+3.53	14.24+4.05
LH/ FSH ratio	2.19+0.13	2.62+0.29	3.05+0.24	4.17+0.77	3.07+0.88
Estradiol (pmole/L)	141.71+2.28	142.66+3.15	144+4.28	141.25+4.39	142.31+3.64
Progesterone (nmole/L)	1.99+0.050	1.85+0.050	1.74+0.20	1.61+0.13	1.78+0.15
Testosterone (nmole/L)	0.71+0.24	1.74+0.37	2.28+0.058	3.41+0.32	2.15+0.99
Insulin (IU/L)-fasting	15.14+3.57	29+4.47	40.57+2.07	47.25+2.13	33.95+11.94
HDL-Cholesterol (mmole/L)	1.87+0.021	1.76+0.047	1.58+0.125	0.98+0.15	1.52+0.37
Total Cholesterol (TC) (nmole/L)	5.50+0.21	6.59+0.44	7.46+0.069	7.72+0.068	6.88+0.84
TC/HDL – Cholesterol ratio	2.94+0.14	3.74+0.35	4.75+0.448	8.08+1.61	5.05+2.23
Triglycerides (mmole/L)	0.733+0.098	1.093+0.18	1.484+0.056	1.75+0.19	1.29+0.40

Table: 2 Correlation coefficients of equations between BMI and hormones/lipids

Variables	Slope (a1)	Intercept (a^2)	Coef. of det. (r^2)	F value	P value
FSH	0.001289	4.598824	0.000572	0.022333	NS p=0.88
LH	0.610483	-4.672836053	0.896992	339.6101	P<0.0001
LH/ FSH ratio	0.131789	-1.00512	0.882436902	292.7367509	P<0.0001
Estradiol	-0.10721451	145.639154	0.034202154	1.381121339	NS P=0.24
Progesterone	-0.02366801	2.520825431	0.894574434	330.9292438	P<0.0001
Testosterone	0.154423437	-2.63361768	0.948486804	718.0875594	P<0.0001
Insulin	1.825873383	-22.62413254	0.922907206	466.883855	P<0.0001
HDL/ Cholesterol	-0.05739200	3.30007562	0.924026351	474.3358791	P<0.0001
Total Cholesterol	0.123294101	3.065760529	0.840463412	205.4580304	P<0.0001
TC/HDL-Choles. ratio	0.339493562	-5.466108449	0.911417995	401.2700098	P<0.0001
Triglycerides	0.063288506	-0.667471063	0.953028943	791.2985358	P<0.0001

Discussion

It is estimated that 5-10% of women at reproductive age have PCOS [2]. Around 50% of PCOS women are obese and tend to have an android pattern of obesity [3]. PCOS occurs in 85 to 90% of women with oligomenorrhea and in 30-40% of women with amenorrhea [4]. Anovulation in PCOS women is associated with steady increase in gonadotropins and ovarian steroids, thus they are in a "chronic estrous state". Constant estrogen exposure leads to hyperplasia of the endometrium and to unpredictable bleeding episodes.

In this study; there was a significant correlation between BMI and abnormal hormonal profile, namely elevated LH, LH/ FSH ratio, testosterone and insulin. Still in the same context there was an abnormal lipid profile mainly with reduced HDL/Cholesterol, total cholesterol/HDL ratio and elevated free cholesterol and triglyceride levels. The elevated serum fasting insulin levels found in our study can be directly linked to the insulin resistance among women with PCO. In a study done by Panidis D; one hundred and twenty-six PCOS women with wide scale body mass index were investigated for various hormonal profiles, they found that elevated serum testosterone, LH, LH/ FSH ratio are significantly correlated with BMI which is related to insulin resistance and can be the key disorder in PCOS-associated metabolic abnormalities [9]. Our results are in agreement with another study where serum levels of luteinizing hormone were assessed, follicle stimulating hormone, estradiol, testosterone, prolactin, sex-hormone-binding globulin, progesterone, fasting plasma glucose and fasting insulin were collected from women with PCOS; obese PCOS women were found to have more severe insulin resistance and hyperinsulinism than normal-weight PCOS women, which may have some health implications later in life [10]. The royal college of obstetricians and gynecologists has recommended that all patients presenting with PCOS, particularly if they are obese, should be offered measurements of fasting blood glucose and urinalysis for glycosuria and abnormal results should be confirmed by a glucose tolerance test. Such patients are at an increased risk of developing type II diabetes mellitus [11]. On the other hand, lipid abnormalities which have been shown in the current study (mainly with reduced HDL/Cholesterol and increased levels of free

cholesterol) were not uniformly obtained by some researchers. Topcu S in his study found that fasting insulin levels and insulin resistance index were higher in the PCOS group than in matched controls [12]. Still the LH, LH/FSH ratio, total testosterone, free testosterone and androstenedione were higher in the PCOS group than the controls, in his study; however, FSH, estradiol, prolactin, progesterone, cholesterol, triglyceride and C-reactive protein were similar between the two groups. The explanation of the widely variable abnormal lipid profiles among women with PCO can be explained by the variable generally elevated levels of free serum testosterone in their blood. It is well known that normal females differ from normal males in the sense that they have higher HDL, lower LDL and free triglycerides levels as well as free cholesterol. It is also known that this difference in normal females is mediated by the estradiol level in their blood which comes from the ovary during normal ovulation. However, once they reach menopause they loose this privilege upon the reduction of free estradiol levels. This explains why women in the pre-menopausal age have lower incidence of ischemic heart diseases as well as cerebrovascular accidents compared to males. As far as women with PCOS have higher testosterone than average normal females, they have though variable, yet abnormal lipid profile. The higher testosterone level in their blood, the more disturbed lipid profile will be present The measurement of fasting cholesterol, lipids and triglycerides should be offered to patients with PCOS, since early detection of abnormal levels might encourage PCOS women to change their dietary habits and to practice more exercise [11]. In the current study; though body mass index was not significantly related to FSH and free Estradiol level, yet there is evidence that the continuous exposure of estrogen due to prolonged un-ovulation can ultimately linked with a probable development of endometrial carcinoma among women with PCO later on in their life [13,14,15]. Oligo- and amenorrhoeic women with PCOS may develop endometrial hyperplasia and later carcinoma so it is a good practice to recommend progestogens treatment to induce a withdrawal bleed at least every three to four months to prevent endometrial hyperplasia [11].

It could be concluded from this study that women with PCO (whether with normal or high BMI) have statistically significant high levels of fasting serum insulin, testosterone, and free cholesterol in addition to low HDL-Cholesterol that may expose them to wide scale major health problems like diabetes mellitus, and IHD. It is recommended that all PCO patients (regardless of their BMI values) should be investigated with full scale hormonal and lipid profiles preferably on regular and scheduled basis so as to catch any alarming changes at an early (treatable) stage.

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