

Assessment of Gonadotropins and Androgens among Pubertal Overweight and Obese Girls

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Abstract

Background: Previous studies have suggested an association between adiposity, androgen and gonadotropin in late pubertal girls. Aim: Assessment the levels of gonadotropin and androgens among pubertal overweight and obese girls. Subjects and Methods: It was a cross-sectional study, carried out in the Obesity Clinic of the Diabetes, Endocrine and Metabolism Pediatric Unit (DEMPU), Pediatric Hospital, Cairo University. It included 40 overweight and obese girls and 40 age-matching normal weight (control) girls, aged (12- 18) years. Anthropometric assessment; weight and height; was recorded, and BMI was calculated. Laboratory investigations: serum luteinizing hormone (LH) and serum total testosterone were measured.

Results: Hypogonadotropins (LH) and hyperandrogenaemia (total testosterone) were significantly prominent among obese girls. Gonadotropin had significant negative correlations, and androgens had significant positive correlations with BMI.

Conclusion: Obese girls had hypogonadotropins and hyperandrogenaemia. Gonadotropin and androgen had significant opposing correlation with the anthropometric obesity markers defined as BMI.

Key words: Gonadotropin, androgens, pubertal girls, overweight, obesity.

تحديد مستويات الجوناوتروبيز والأندروجينات لدى الفتيات اللاتي تعانين من زيادة الوزن والسمنة في مرحلة البلوغ

الخلفية: أقرحت الدراسات السابقة وجود علاقة بين السمنة والجوناوتروبيز والأندروجين في الفتيات في أواخر البلوغ. وكان الهدف من هذه الدراسة تقييم مستويات الجوناوتروبيز والأندروجين لدى الفتيات اللاتي تعانين من زيادة الوزن والسمنة في مرحلة البلوغ.

الحالات وطرق البحث: هذه الدراسة هي دراسة مقطعية مستعرضة، تم إجراؤها في عيادة النمو السكري والغدد الصماء- وحدة طب الأطفال- مستشفى طب الأطفال- جامعة القاهرة. اشتملت هذه الدراسة على عدد 40 فتاة في مرحلة البلوغ تعانين من السمنة أو زيادة الوزن وعدد 40 فتاة من الصحيحات وجميعهن تتراوح أعمارهن بين (12- 18) عام. تم أخذ قياسات أنثروبومترية معينة للفتيات محل الدراسة مثل (الطول، الوزن)، كما تم حساب مؤشر كتلة الجسم. تم قياس تركيزات هرمون الأندروجين وهرمون الجوناوتروبيز.

النتائج: أظهرت الدراسة أن الفتيات البدينات لديهن أعلى القيم في مستوى الأندروجين (التستوستيرون الكلي) وأقل القيم في مستويات الجوناوتروبيز. ووجد ارتباطاً معنوياً سلبياً بين مستوى الجوناوتروبيز وبين مؤشر كتلة الجسم، بينما كان ارتباط مستوى الأندروجين بتلك المتغيرات ارتباطاً معنوياً إيجابياً.

الاستنتاج: الفتيات البدينات تعانين نقص مستوى الجوناوتروبيز وزيادة مستوى الأندروجين. وكانت الارتباطات بين مستوى كل من الجوناوتروبيز والأندروجين مضادة مع المعايير الأنثروبومترية للسمنة ممثلة في مؤشر كتلة الجسم.

Introduction:

Hyperandrogenaemia represents the most common endocrine disorder in females during reproductive age. Moreover, androgen excess affects different tissues and organ systems, thus resulting in a wide range of clinical conditions, e.g. acne, hirsutism, frank virilization... etc. (Lebbe& Woodruff, 2013; Lizneva et.al., 2016).

Although, the etiology of hyperandrogenemia in some obese girls is unclear, but insulin resistance (IR) with compensatory hyperinsulinemia may play a key role. However, syndromes of severe IR may be associated with marked ovarian hyperandrogenemia. In addition, Hyperinsulinemia may promote both excessive adrenal androgen production and excessive IGF- 1 bioavailability; thus stimulating the production of both adrenal and ovarian androgen (Klenov et.al., 2014).

Gonadotropin are hormones secreted from the gonadotrophs of the anterior pituitary and they stimulate the gonads (the testes in males, and the ovaries in females), and hence the name "Gonadotropin" (Mullen et.al., 2013; Cahoreau, et.al., 2015). Unfortunately, few studies; on early pubertal girls (Tanner stages 2 and 3); suggest that excessive body weight is associated with suppression of gonadotropin secretion, with blunted sleep- related rise of LH (Bordini, et.al., 2009; Lee et.al., 2016).

Reviewing the literature, few studies addressed the assessment of gonadotropins and/or androgens among pubertal overweight and obese girls. (Burt et.al., 2010; Vilmann et.al., 2012; Ibanez et.al., 2014; Kang, 2016). Therefore, the current study represents one of the important studies comparing both androgens and gonadotropins levels among obese, overweight and normal- weight pubertal girls.

Hypothesis:

There is an association between overweight/ obesity and the levels of gonadotropin and androgens among pubertal girls.

Aim:

The present study aims to assess the levels of gonadotropin and androgens among pubertal overweight and obese girls.

Subjects:

This study was a case- control type, carried out in the "Obesity Clinic of the Diabetes, Endocrine and Metabolism", "Pediatric Unit (DEMPU)", Pediatric Hospital, Cairo University. It included 40 overweight and obese girls and 40 age matching normal weight (control) girls, aged (12- 18) years.

Inclusion Criteria:

1. Girls with pubertal stages 2 up to 5 according to Marshall and Tanner (1969).
2. Exogenous Obesity.
3. BMI for obesity is greater than 15th percentile, as the BMI of normal (control) girls ranges between 15th up to 85th percentile, overweight BMI is greater 85 percentile and obese BMI is greater 95 percentile (Coles et.al., 2016).

Exclusion Criteria:

1. Girls with chronic illness which may affect their physical growth (e.g.,

chronic renal failure, celiac disease).

2. Girls with pubertal stage 1 according to Marshall and Tanner (1969), because stage 1 was considered prepubertal.
3. Girls under any regular medication.
4. Overweight and obesity due to endocrinal or syndromatic cause.

Ethical Consent:

Ethical approvals were obtained from the Ethical Committee of "Faculty of Postgraduate Childhood Studies". A verbal approval was taken from every girl participated in the current study, in addition to a written informed consent from one of her parents after explanation of the aim of the study and its possible benefits for identifying the effect of obesity on health.

Methods:

For each girl participated in the study, detailed history, clinical examination, anthropometric, laboratory and hormonal assessment were done.

1. Detailed History: Detailed questionnaire was filled about onset, duration, risk factors, and complication; e.g. symptoms suggestive of secondary diabetes mellitus like polyuria, polydipsia and loss of weight, and symptoms suggestive of hypertension; such as headache or epistaxis... etc; of overweight and obesity among participated girls. History of practicing sports was also evaluated, in addition to family history of early or delayed puberty, and existence of any chronic disease, especially diabetes mellitus "DM".
2. Clinical Examination:
 - a. Complete clinical examination; including cardiac, chest and abdominal; to exclude chronic and genetic disorders that might interfere with the anthropometric measurements of the girl under study; with special emphasis on endocrinal diseases; that would interfere with the type of obesity.
 - b. Pubertal stages assessment was done according to Marshall and Tanner (1969).
3. Anthropometric Assessment: For every girl in the study, body weight (Wt) and height (Ht) were measured. Then, BMI was calculated. Three consecutive measurements were taken and when the difference between the readings was acceptable, the mean was recorded. The landmarks, instruments used and techniques followed were those recommended by the international biological program I.B.P (Hiernaux& Tanner, 1969).
4. Laboratory Investigations:
 - a. One venous blood sample (5ml) was collected between 8:00am to 10:00am after fasting 10 hrs. After clotting the blood samples, they were centrifuged and the sera was separated and kept at- 80 °C for batch assessments.
 - b. Serum LH and total testosterone concentrations were measured using Electro chemiluminescence (ECLIA).
 - c. Luteinizing hormone (LH) was assessed using Enzyme Immunoassay Test Kit Catalog No.C29- 118. (Immunespec

Corporation).

- d. Total Testosterone was assessed using Enzyme Immunoassay Test Kit. Catalog No. KN09I. (XEMA)

Results:

The study included 40 overweight and obese pubertal girls and 40 normal (control) pubertal girls; their age was ranged between (12- 18) years, the age and sex matched with controls.

Comparisons between the 3 groups regarding anthropometric measurements, and laboratory findings were presented in the figures. The age had insignificant difference between the 3 groups under study. The obese girls had the highest significant values than the other 2 groups; followed by the overweight girls then control; in body weight, BMI and androgen (total testosterone); control group: mean= 5.3, SD= 1.7/ overweight group: mean= 7.4, SD=0.79/ obese group: mean= 8.04, SD= 1.05}. They also had the least significant values than the other 2 groups in gonadotropin (LH) (control group: mean= 19.6, SD= 3.6/ overweight group: mean= 18.1, SD= 3.9/ obese group: mean= 12.7, SD= 2.4.

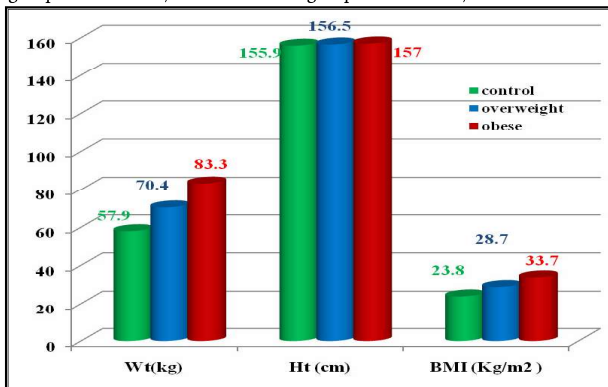


Figure (1) Comparisons between the 3 groups regarding anthropometric measurements

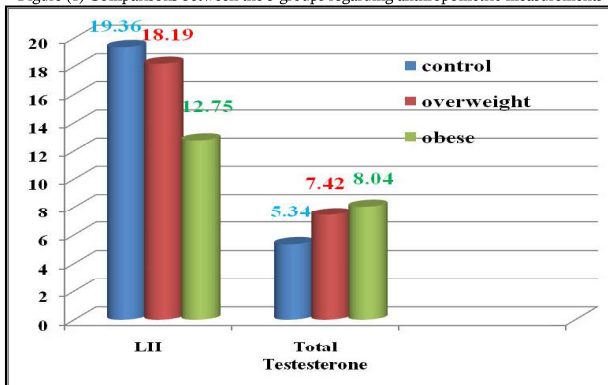


Figure (2) Comparisons between the 3 groups regarding sex hormones

Correlations between BMI; as the most important obesity marker; and gonadotropin and androgen for obese girls were presented in table (1) and the figures. BMI had significant positive correlation with androgen (total testosterone), and significant negative correlation with gonadotropin (LH).

Table (1) Correlation between BMI and gonadotropin and androgen for obese girls

Hormones:		BMI (Kg/ m2)	
		r	p
Gonadotropins:	LH(mIU/ml)	-0.895	0.000*
Androgens:	Total Testosterone (nmol/l)	0.914	0.000*

P* <0.05 is significant

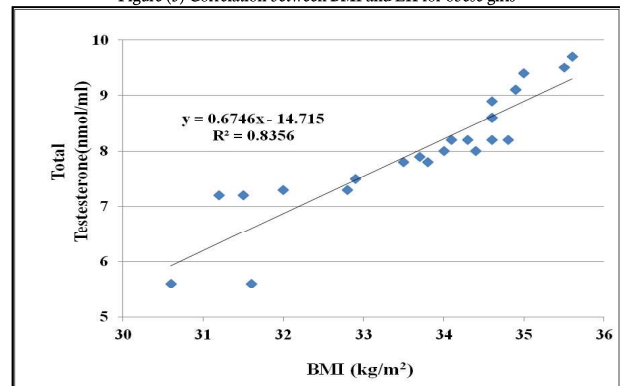
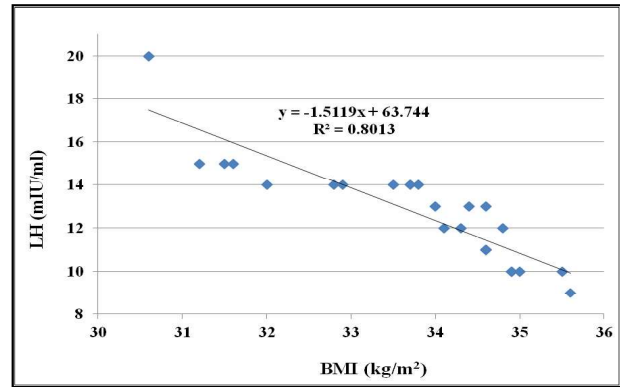


Figure (4) Correlation between BMI and Total Testosterone for obese girls

Descriptive statistics (mean± standard deviation) were calculated for the anthropometric, laboratory and hormonal assessment. Frequency distribution of the girls according to different variables was presented as number and percentage. In order to find out whether there are group differences, independent t- test was carried out to compare between 2 groups, and ANOVA was used to compare between 3 or more groups for the parametric data (quantitative). While for the non- parametric (qualitative) data, Chi- square test was used.

Pearson's correlation was used to assess the association between the gonadotropin, androgen, obesity markers and all the studied variables. Standards of probability were set to P< 0.01; which considered highly significant; and P< 0.05; which considered statistically significant; in all analyses.

Discussion:

Current results showed that, obese girls had the highest significant values than the other 2 groups; followed by the overweight girls then control; regarding in body weight, BMI and androgen (total testosterone).

Although, little and controversial information is available on androgen levels in pubertal obese girls, yet it has been reported that ovarian hyperandrogenaemia is a common consequence of obesity (Coviello et.al., 2006; Marshall JC, 2006). Results of the current study thus consistent with those of Bernstein, (2002) and Heather et.al. (2007) who reported positive association between adiposity and androgen levels (Coviello et.al., 2006; De Leonibus et.al., 2012).

McCartney et.al. (2006& 2007) demonstrated significantly marked hyperandrogenaemia throughout puberty, and concluded that, during early pubertal stages (Tanner 1- 3), obese girls had significantly higher

serum total and free testosterone levels, and lower circulating LH, compared to control/ normal- weight girls. Also, the mean total testosterone levels, in obese girls (Tanner 2 and 3) were higher 1.6 and 3.3 fold respectively. Similarly, when compared with their normal- weight counterparts, obese pre- pubertal and pubertal girls had higher total testosterone levels that were elevated 4- and 1.75- fold, respectively (Bordini et.al., 2009). These abnormalities improved with weight loss (Reinehr et.al., 2005; De Leonibus et.al., 2012). Also, obese girls were found to have increased total testosterone levels, but reduced hepatic sex hormone binding globulin "SHBG" (Dunger et.al., 2005; Jasik& Lustig, 2008; Lee et.al., 2016).

The current results revealed that obese girls had the least significant values of LH. These findings are consistent with De Pergola et.al., (2006), McCartney et.al. (2007), Corbould (2008), Chang (2009) and Wei et.al. (2009) who found that obese and overweight pubertal girls had significantly lower LH levels compared with normal- weight peers. In concordance to current results, Lee et.al. (2016) concluded that in pubertal girls (Tanner stages 1- 3), LH levels were higher among normal- weight than in overweight, and obese girls, whereas, in Tanner 4 girls, LH levels were not significantly different among the 3 groups. In the contrary, some studies revealed that excessive weight was associated with elevation in LH levels in early pubertal girls (Bordini et.al., 2009; McCartney et.al., 2009; Christine& Burt, 2010), and in late pubertal girls (McCartney et.al., (2009).

Conclusion:

Obese girls had hypogonadotropins and hyperandrogenaemia. Gonadotropin and androgen had significant opposing correlation with the anthropometric obesity markers defined as BMI.

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