

The relationship between serum levels of prolactin and testosterone in patient with hirsutism

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Abstract

Hirsutism is the presence of excessive terminal hair in androgen dependent areas of woman's body. The aim of this research work was to study the relationship between serum prolactin level and hirsutism. In addition to prolactin, the relation of serum testosterone level to hirsutism was also studied. The aim of this work to study the relationship between serum testosterone and prolactin levels in patients with hirsutism. Total of (90) women were included in this study. Their ages range between (15-45) years. They were classified into 2 groups:

Patients' group (60) women and control group (30) women.

Testosterone and prolactin were measured by using the technique of ELISA for all women in both groups.

العلاقة بين مستوى الهرمون الذكري واللبني في مصل الدم لدى مرضى الشعرانية

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المستخلص

الشعرانية لدى النساء هي وجود كثافة في الشعر القاسي في مناطق الجسم التي تتأثر بالهرمون الذكري. الهرمون الذكري ضروري لتجديد نمو الشعر القاسي. وكذلك يطيل الوقت المتاح لنمو الشعر القاسي في مناطق الجسم التي تعتمد على الهرمون الذكري. الهدف من هذا البحث هو دراسة علاقة مستوى الهرمون اللبني في مصل الدم والشعرانية بالإضافة إلى ذلك، تم دراسة علاقة الهرمون الذكري مع الشعرانية.

شملت هذه الدراسة تسعين امرأة تتراوح أعمارهن بين ١٥-٤٥ سنة، تم تصنيفهن إلى

مجموعتين:

- مجموعة السيطرة (ثلاثون امرأة طبيعية).
- مجموعة المرضى (ستون امرأة شعرانية).

تم قياس الهرمون الذكري والهرمون اللبني بتقنية الاليزا (ELISA) لجميع النساء في

المجموعتين.

Introduction

Hirsutism is defined as the presence of excessive terminal hair in androgen dependent areas of woman's body [1]. This disorder is a sign of increased androgen action on hair follicles, from increased circulating levels of androgen (endogenous or exogenous) or increased sensitivity of hair follicles to normal levels of circulating androgen. Androgen dependent skin sites include upper lip, chin, chest, thigh, upper back, lower back, upper abdomen, lower abdomen [2].

Testosterone and hirsutism

Androgens are necessary for terminal hair and sebaceous gland development and by its effect on the pilosebaceous units (PSUS) which consist of sebaceous gland and sexual hair follicles. Androgen transforms the vellus hair into terminal hair. The most important androgen to stimulate the hair follicles is testosterone, however the hair follicles do not have receptors for testosterone, they have only receptors for 5-dihydrotestosterone (5-DHT). As a consequence, the vellus hair follicles develop into terminal hair follicles in large number in areas of androgen – sensitive skin by increasing the diameter and density of hairs.

Hyperprolactinemia and hirsutism

Hyperprolactinemia is a biochemical description and not a clinical state [3]. It is due to an increase in pituitary secretion of prolactin. In women hyperprolactinemia presents most commonly with galactorrhea, menstrual disturbance such as secondary amenorrhea, oligomenorrhea, menorrhagia and anovulation with infertility [4].

Galactorrhea is a persistent discharge of milk in the absence of parturition or beyond postpartum by six months in a non-nursing mother [5].

Failure to demonstrate galactorrhea does not exclude hyperprolactinemia [6]. Normal serum level of prolactin in females is between 1.2-19.5ng/ml [7]. Prolactin level does not change significantly during menstrual cycle [5]. Androgen excess and hirsutism were found in a significant number of patients with classical galactorrhea and anovulation in original report [8]. The cause of this hyperprolactinemia is pituitary adenoma. Other conditions in which prolactin levels may be elevated and that may lead to hirsutism are phenothiazine intake and hepatorenal failure [2].

In normal female the synthesis and secretion of prolactin is from acidophilic lactotrophs of the anterior pituitary gland [9].

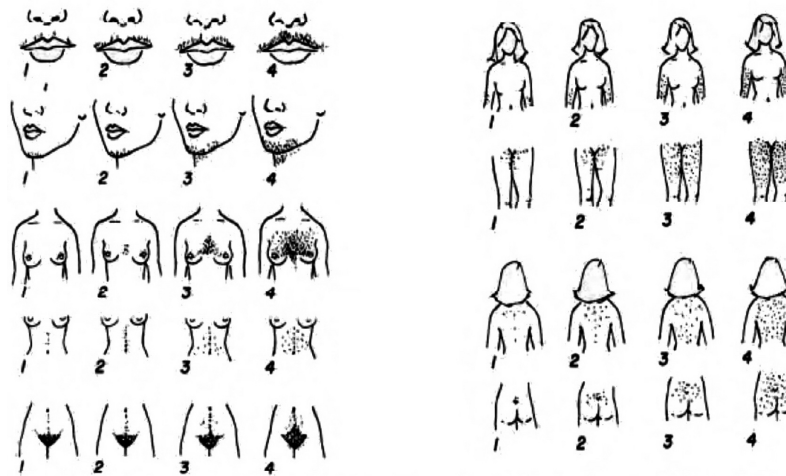
The synthesis and secretion of prolactin occur in a pulsatile manner every 20 minutes and are regulated by hypothalamic hormones namely prolactin inhibitory hormone PIH and prolactin releasing hormone PRH [10].

Subjects and methods

This study was conducted over a period of six months; from October 2017 to April 2018. The females included in this study were single or married but not pregnant. The subjects involved in this study were two groups:

1-Patients

Sixty females with hirsutism (according to Ferryman and Gallwey scoring system of hirsutism) as shown in Figure (1).



Visual method of scoring hair growth in women

Figure (1)
Ferryman and Gallwey scoring system

This system grades hair growth over nine body areas from 1-4. A cut off score of eight was taken as presence of significant hirsutism. Because it is normal for most females to have some hair growth in androgen sensitive sites (but the score is less than eight), a score equal or above eight suggests an excess of androgen-mediated hair growth [11].

The age of these females was within the reproductive age ranging from 15-45 with a mean of 26.82 ± 7.16 years. These females complain either from hirsutism or they have hirsutism but they came to these dermatological and gynecological units complaining from other dermatological or gynecological problems as acne, alopecia, amenorrhea or infertility. The patients were examined first by gynecologist and dermatologist to find out any abnormality that may be related to hirsutism and to refer suitable patients for this study.

2-Controls

Thirty non-hirsute females who have score less than eight according to (Ferryman-Gallwey scoring system) were taken as controls. The age of these females ranges between 15-45 years with a mean of 27 ± 6.24 years.

Methods**- Testosterone assay**

Testosterone assay by enzyme immune assay for the quantitative determination of testosterone concentration in human serum.

- Elisa testosterone kit

Elisa testosterone kit including the following reagents:

1. Goat Anti-Rabbit IgG coated microtiter well, 96 wells.
2. Testosterone reference standards: 0, 0.1, 0.5, 2.0, 6.0 and 18.0 ng/ml.
3. Rabbit Anti Testosterone Reagent.
4. Testosterone-HRP.
5. Testosterone control 1.
6. Testosterone control 2.
7. TMB reagent.
8. Stop solution.

Prolactin assay

Prolactin assay was done by Elisa which is a microplate monosymmetric assay.

Elisa prolactin kit

The contents of each kit are:

1. Prolactin calibrators: six vials of references for prolactin antigen in human serum at levels of 0(A), 5(B), 10(c), 25(D), 50(E) and 100 (f) ng/ml.
-

2. Prolactin enzyme reagent.
3. Streptavidin coated microplate.
4. Wash solutions concentrate.
5. Substrate A.
6. Substrate B.
7. Stop solution.

Results There was a significant positive relationship between serum level of testosterone and the number of Ferryman and Gallwey score of hirsutisms at $P < 0.001$ in the studied groups with a correlation coefficient of ($r = 0.420$) Figure (2), which favors a cause and effect relationship between testosterone level and hirsutism.

When serum testosterone level was studied in each group in detail, we find that 40 patients out of sixty had serum testosterone level equal or higher than the normal level (≥ 0.8 ng/ml) as in Table (1).

The remaining 20 patients had serum testosterone level within the normal value (< 0.8 ng/ml), as shown in Table (1). In the control group only 2 out of 30 females had serum testosterone level equal or higher than the normal value (≥ 0.8 ng/ml); while the majority of the control group (28 out of 30) had serum testosterone level within the normal value (< 0.8 ng/ml), as shown in Table (1).

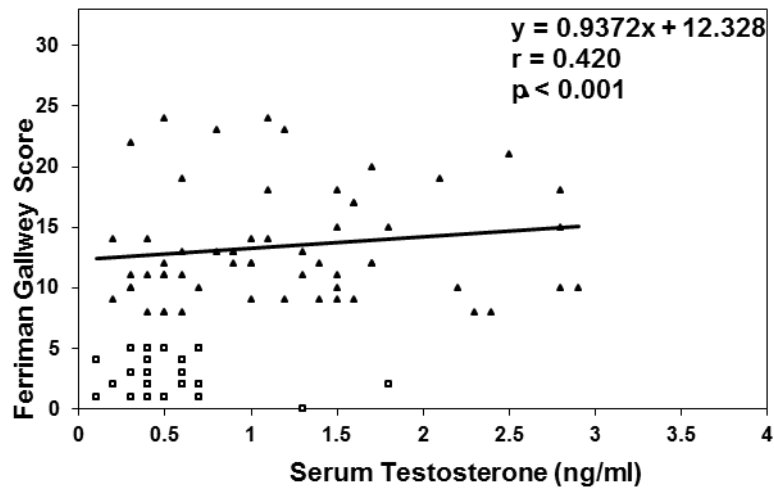


Figure (2)

The relationship between serum level of testosterone and Ferriman -Gallwey score of hirsutisms in studied groups

Table (1)

Comparison of serum level of testosterone between individual patients and individual controls

Serum Testosterone ng/ml	Patients		Control		p-value
	No.	%	No.	%	
≥ 0.8	40	66.7	2	6.66	<0.001****
<0.8	20	33.3	28	93.34	
Total	60	100.0	30	100.0	

**** Highly significant

Prolactin

The mean value of serum level of prolactin in thirty non-hirsute females (control group) was (14.10 ± 9.28) ng/ml, Table (2). This value was within the normal range of serum prolactin level in females which is 1.2-19.5 ng/ml [7].

If we look to mean value of serum level of prolactin in hirsute females (patients' group), we find that it was (11.88 ± 9.96) ng/ml, Table (2).

This value was within the normal range of serum prolactin level.

If we compare the mean value of serum level of prolactin in the control group (14.10 ng/ml) with the patients' group (11.88 ng/ml), we find that there was a slight difference between the two groups, but this difference was statistically not significant ($p > 0.05$) as shown in Table (2). And both values are within the normal range of prolactin level in females.

There was a very weak correlation if any, between serum level of prolactin and Ferryman and Gallwey score of hirsutisms, which is not significant statistically, $P > 0.05$ and $r = 0.054$ Figure (3).

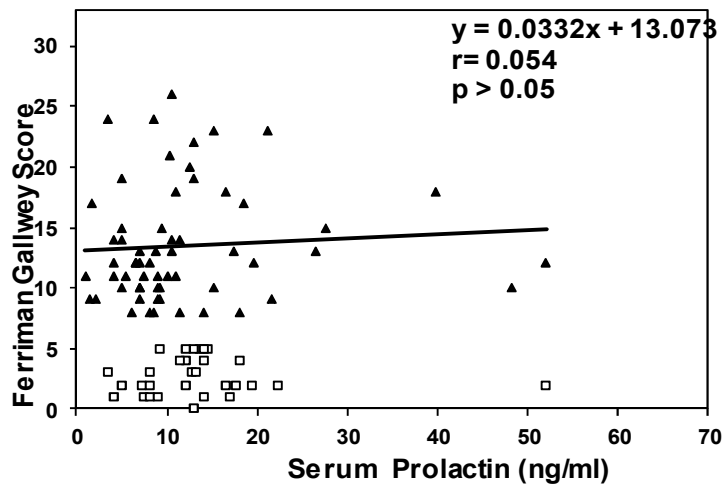


Figure (3)

**The relationship between
Serum level of prolactin and Ferriman -Gallwey score of
hirsutism in the studied groups**

When serum prolactin level is studied in each group in detail, we find that, 8 cases out of 60 patients have serum prolactin level (≥ 19.5 ng/ml) as shown in Table (2). The remainder 52 patients have serum prolactin level within the normal value (< 19.5 ng/ml).

Table (2)

**Comparison of serum level of prolactin between individual
patients and individual controls**

Serum prolactin ng/ml	Patients		Control		p- value
	No.	%	No.	%	
≥ 19.5	8	13.3	2	6.66	$>0.05^*$
< 19.5	52	86.7	28	93.34	
Total	60	100.0	30	100	

***Not significant**

There is statistically significant direct positive relationship between serum prolactin and serum testosterone levels ($P < 0.01$, $r = 0.257$) Figure (4).

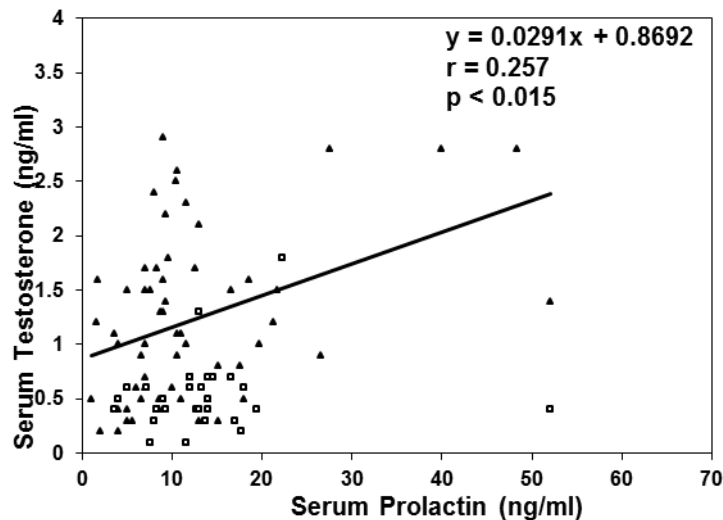


Figure (4)
The relationship between
Serum level of prolactin and testosterone in the studied
groups

Although there were 8 hirsute patients having serum level of prolactin above normal, only 3 of them had galactorrhea. On the other hand, there were 2 hirsute patients having galactorrhea, yet the biochemical result shows normal serum prolactin level.

In the control group only 2 out of 30 having serum prolactin level equal to or higher than the normal value (≥ 19.5 ng/ml), while the majority of the control group (28 out of 30) have serum prolactin level within the normal value (< 19.5 ng/ml), as shown in Table (2).

Discussion**Prolactin and Hirsutism**

We were unable to find a statistically significant difference in the serum prolactin level between the control group and patients group Table (1).

Also, the correlation between serum prolactin level and hirsutism is weak and statistically not significant Figure (2).

Only 8 patient (13%) hirsute women have high serum level of prolactin Table (1).

High serum level of prolactin causes hirsutism by increasing the level of testosterone and testosterone precursors, namely (DHEAS) and (DHEA), whereas TeBG is reduced [12], [13].

The androgen changes are probably secondary to the persistent anovulatory state induced by the elevated prolactin. Anyway, direct prolactin effects on the adrenals, ovaries or TeBG (testosterone binding globulin) are possible [14].

Our finding is in agreement with finding of AL-Rushdi 2002 who found that only 3patients out of 60 hyperprolactinemic women (5%) have got hirsutism [15]. Malik and et.al 2007 [16] found that 8 patients out of 74 (10%) hirsute females had high serum level of prolactin.

Prolactin and testosterone

There is statistically significant direct positive correlation between serum prolactin and serum testosterone levels Figure (3).

A similar result obtained by Olive 1999 who found that about 40% of hyperprolactinemic women have an androgenic abnormality and the most characteristic abnormality is elevated serum level of testosterone [17].

This finding was verified by subsequent publications, which demonstrated that almost 40% of patients with pituitary

adenomas and hyperprolactinemia had abnormal secretion and metabolism of androgen (8).

Androgens are necessary for terminal hair and sebaceous gland development and by its effect on the pilosebaceous units (PSUS) which consist of sebaceous gland and sexual hair follicles. Androgens mediate differentiation of PSUS into either a terminal hair follicle or a sebaceous gland. In the former case, androgen transforms the vellus hair into terminal hair. In the latter the sebaceous component proliferates and the hair remains vellus. The amount of terminal hair growing is determined by the level of androgens, the duration of exposure to these androgens and the sensitivity of the end organ, which is determined among other things by the number of androgen receptors in the hair follicle [18]. The most important androgen to stimulate the hair follicles is testosterone, however the hair follicles do not have receptors for testosterone, they have only receptors for 5-dihydrotestosterone (5-DHT) [19]. Inside the cells of the hair follicles, testosterone is converted to DHT by the enzyme 5-alpha reductase and subsequently binds to the receptors [20].

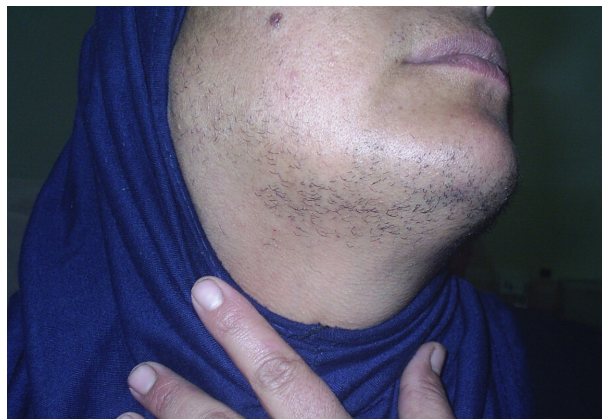


Figure (5)
Patient with Hirsutism

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