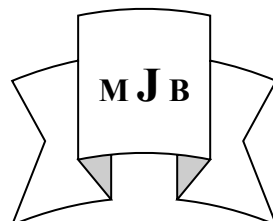


Total , Free Testosterone and Insulin Hormone Levels in Patients with Hirsutism

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Abstract

The aim of this study is evaluated the levels of testosterone hormone (total and free) and insulin hormone in women that suffering with hirsutism; which is defined as the presence of excessive terminal hair in androgen-dependent areas of a woman's body. It may result from various causes including polycystic ovarian syndrome, nonclassic congenital adrenal hyperplasia, adrenal or ovarian tumors. Serum samples were taken from forty women with hirsutism with [mean age $\pm$ SD (29 $\pm$ 7.4)years; body mass index (BMI) 26.95 $\pm$ 6.8 kg/m²] as well as fifteen healthy women with (mean age $\pm$ SD (30 $\pm$ 6.1); BMI, 24.14 $\pm$ 2.2 kg/m²) as a control group. The results showed that the total testosterone hormone and free testosterone are increased significantly (P<0.00) in the female patients with hirsutism compared to control group. Also, basal insulin found to be significantly increased in patients with hirsutism (p<0.05) when compared with control group.

الخلاصة

تهدف هذه الدراسة إلى قياس مستويات هرمون التستوستيرون بشكليه الكلي والحر وكذلك هرمون الانسولين في النساء التي لديهن زيادة في نمو الشعر وتسمى هذه الحالة بالهيرسوتيزم (داء الشعرانية). والهيرسوتيزم يُعرّف بأنه ظاهرة نمو الشعر بشكل مفرط في جسم المرأة في المناطق المعتمدة على الهرمون الذكري. وقد تظهر هذه الحالة نتيجة لوجود العديد من الأمراض الأخرى . ولقد أظهرت نتائج هذه الدراسة وجود زيادة معنوية في مستويات هذه الهرمونات في مصل لدم أربعين امرأة من اللواتي يعانين من الظاهرة المفرطة في نمو الشعر مقارنة بمجموعة السيطرة والتي تتمثل بنماذج مصل الدم من خمسة عشر امرأة لاتعاني المرض كمجموعة السيطرة.

Introduction

Hirsutism is defined as the growth of hair in a woman on the face and body which appears in the same pattern and with the same temporal development as in men[1]. Hirsutism is the excessive hairiness on women in those parts of the body where terminal hair does not normally occur or is minimal - for example, as a beard or chest hair [2]. It refers to a male pattern of body hair (androgenic hair) and it is therefore primarily of cosmetic and

psychological concern. Hirsutism is a symptom rather than a disease and may be a sign of a more serious medical condition, especially if it develops well after puberty. The amount and location of the hair is measured by a Ferriman-Gallwey score [3,4].

Hirsutism affects women, since the rising of androgens causes a male pattern of body hair, sometimes excessive, particularly in locations where women normally do not develop terminal hair within their puberty (chest, abdomen, back and face). The

medical term for excessive hair growth that affects women is hypertrichosis. Hirsutism form of hair growth is dependent on stimulation by androgens. It differs significantly from "hypertrichosis" which is an uniform growth of hair over the entire body and which develops either as part of a congenital or metabolic disorder (eg anorexia nervosa and hypothyroidism) or in response to non-hormonal drugs (eg cyclosporin and minoxidil) [5].

The presence of hirsutism can only be determined by clinical examination of the pattern and timing of the hair growth. The natural development of androgenic body hair begins at puberty with a conversion of vellus to terminal hairs in the pubic area followed by the axillae after an interval of about two years. Facial hair appears at the same time as axillary hair in boys. Terminal hairs start at the corners of the lips and spread over the upper lip before appearing on the chin and then cheeks. An orderly sequence of hair conversion follows on the body: the lower legs, thighs, forearms, abdomen, buttocks, chest, back, upper arms and shoulders [6].

It is estimated that up to 15% of women are affected by the distressing condition of hirsutism or excessive body hair. In the vast majority of cases, there is an underlying hormonal (endocrine) problem, the biggest culprit being polycystic ovarian syndrome (PCOS). The most important hormones determining distribution and thickness of hair are the androgens, also loosely called 'male sex hormones'. This latter term is not strictly correct as women do normally produce androgens even though it is not to the levels seen in men. In conditions such as Polycystic Ovarian Syndrome (PCOS), the level of active androgens in circulation tends to be higher than the normal female physiological range [7].

Types of hirsutism

A- Primary or idiopathic hirsutism- Idiopathic hirsutism is defined as hirsutism with no other clinical abnormalities, particularly no menstrual irregularity; and using the Rotterdam criteria, no evidence of a multifollicular ovary. It may well be a mild variant of PCOS. It is probably hereditary, because there is usually a family history of the disorder [8]

B- Secondary hirsutism - It is most often associated with polycystic ovary syndrome. This type of hirsutism may also be caused by:

- malfunctions of the pituitary or adrenal glands.
- use of male hormones or minoxidil (Loniten), a drug used to widen blood vessels (Causa occasionalis).
- adrenal or ovarian tumors[9-11].

Testosterone is an androgen steroid hormone that is usually linked to male sexuality. It stimulates the growth of normal male sexual organs, leads to deepening of the male voice, stimulates facial and pubic hair growth, and is essential in the sexual behavior of men. Testosterone is made not only in the testes of men but also in the ovaries of women and in the adrenal glands of both men and women [12]. Abnormally high testosterone levels in women can lead to a variety of symptoms. Most often, women with high testosterone levels develop male pattern hair growth, especially on their faces and chests. More rarely, over time some women may experience virilization, which is increased muscle mass, redistribution of body fat, enlargement of the clitoris, deepening of the voice, male pattern baldness, acne, and increased perspiration. It is important to note that some women develop hirsutism without having a high testosterone level. Increased testosterone levels in women are most often caused by polycystic ovaries. Less commonly, when testosterone

levels are very elevated, ovarian cancer is a concern. Adrenal gland problems may contribute as well [13]. Free testosterone represents about one to four percent of the total amount of testosterone in a man's body. The reason why it is called "free" is because it is not bound to any substance or another hormone in the performance of a specific function. Free testosterone is an indicator of good hormone function and a normal level of free testosterone equates to an overall health [14].

Insulin is a hormone produced by the pancreas which is central in regulating carbohydrate and fat metabolism in the body. Insulin causes cells in the liver, muscle, and fat tissue to take up glucose from the blood, storing it as glycogen in the liver and muscle [15].

Insulin stops the use of fat as an energy source by inhibiting the release of glucagons. Insulin is provided within the body in a constant proportion to remove excess glucose from the blood, which otherwise would be toxic. When blood glucose levels fall below a certain level, the body begins to use stored sugar as an energy source through glycogenolysis, which breaks down the glycogen stored in the liver and muscles into glucose, which can then be utilized as an energy source [16-17].

Material and Methods

Control and Patients

Patients

The study was conducted in Hilla city. Forty hirsute females patients [mean age $\pm$ SD (29 $\pm$ 76.4 8)years; with body mass index (BMI) 26.95 $\pm$ 6.8 kg/m²] complained from hirsutism disease, were attended Merjan Teaching Hospital in Hilla city, have been subjected to present study .

Control and Patients

The control group includes fifteen females apparently healthy individuals with mean age $\pm$ SD (30 $\pm$ 6.1) years; with body mass index (BMI) 24.14 $\pm$ 2.2 kg/m²], after having been asked about their health.

Collection of Blood and Serum Preparation

Five milliliters of blood were obtained from patients and healthy persons, then collected in tubes without anticoagulants and were left for 15 minutes at room temperature to clot. After that, the blood samples were centrifuged at 1000 - 2000 x g for approximately 10 minutes. The sera were aspirated and stored at -20°C until time of use.

For hormone samples serum may be stored at 2-8 °C for up to 24 hours, and should be frozen at -10°C or lower for longer periods. Grossly hemolyzed or grossly lipemic specimens were not used.

1. Determination of serum total testosterone hormone done by ELISA using total testosterone kit. Monobind Inc.(USA).

2. Determination of serum free testosterone hormone was done by ELISA using free testos-terone kit Monobind Inc.(USA).

3. Determination of serum Insulin hormone done by ELISA using Insulin kit DRG (Germany).

Statistical Analysis

This study is a case control study. Student's t-test has been used to determine the significant difference between two groups, p values than 0.05 is considered significant.

Results and Discussion

Testosterone is an important hormones in biological system. The changes in the level of this hormone was studied in this work. The study shows significant increases in the mean of total testosterone of females patients

in the comparison with control group as shown in table (1). Also in table (2) there was significant increase in mean

serum level of free testosterone in females patients when compared with control group.

Table 1 The mean serum levels of total testosterone hormone in female patient and control

Female total testosterone (ng/ml)	M	SD	No.	P-value
Patients	1.62	1.4	40	0.00
Control	0.08	0.06	15	

Table 2 The mean serum levels of free testosterone hormone in female patient and control

Female free testosterone (pg/ml)	M	SD	No.	P-value
Patients	4.68	3.7	37	0.001
Control	1.8	1.4	15	

Hirsutism can be caused by either an increased level of androgens, the male hormones, or an oversensitivity of hair follicles to androgens. Male hormones such as testosterone stimulate hair growth, increase size and intensify the growth and pigmentation of hair and these results agree with other studies [18].

The majority of testosterone is bound to transport proteins; weakly bound to albumin (25-65% females - 45-85% males) and tightly bound to sex hormone-binding globulin (SHBG) (females 35-75% - males 14-50%). A small fraction exist as unbound or free testosterone, however this form is biologically active. Therefore, the free hormone concentration is a better indicator of biological activity than total testosterone [19].

Testosterone acts on the hair follicles by converting into its active form called dihydrotestosterone. 5-alpha reductase, the substance which is responsible for this conversion is found in these hair follicles. Testosterone travels in the blood attached to a protein called sex hormone binding globulin or SHBG.

It is taken to the target areas where the protein releases the hormone. In the target areas, it gets converted into the active form – dihydrotestosterone [20].

Insulin hormone

In the present study, there was a significant increase in mean serum level of insulin hormone as shown In the table (3). High insulin levels may increase the availability of testosterone through the suppression of SHBG synthesis and enhance ovarian androgen production. On the other hand, high testosterone levels lead to disturbances in insulin metabolism and cause hyperinsulinemia [21], which is a well-recognized and important risk factor for CHD and hypertension in men as well as in women [22]. Our results agree with other studies [23][24].

Growing evidence implicates high circulating levels of insulin in women for the development of hirsutism. This theory is speculated to be consistent with the observation that obese (and thus presumably insulin resistant hyperinsulinemic) women are at high risk of becoming hirsute. Furthermore,

treatments that lower insulin levels will lead to a reduction in hirsutism[23].

Table 3 The mean serum levels of Insulin hormone in female patient and control

Female insulin (nIU/ml)	M	SD	No.	P-value
Patients	13.3	12.27	37	0.04
Control	7	6.7	15	

It is speculated that insulin, at high enough concentration, stimulates the ovarian theca cells to produce androgens. There may also be an effect of high levels of insulin to activate the insulin-like growth factor-I (IGF-1) receptor in those same cells. Again, the result is increased androgen production[25].

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