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Study of Hormonal levels changes in women's serum with polycystic ovaries syndrome (PCOS)

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ABSTRACT

This study was done in Fallujah Hospital and AL-Jameaa medical Lab in Fallujah city since the beginning of February of 2009 until June 2009. Hormonal changes in the serum of polycystic ovary syndrome (PCOS) infertile women in Fallujah city and there countryside's were studied. Forty infertile women affected with increase of testosterone were selected, twenty of them with (PCOS) compared with twenty normal women. All of the women in this study from Fallujah city and surrounded area with different ages. All women showed the same symptoms, like hair growth in face, bold voice with an increase in testosterone and increase in LH while there no differences in FSH level. The levels of Prolactin was increased at (12.5%) .In conclusion the high levels of testosterone is responsible of hirsutism studeid in women lead to presence of the secondary characters of men in women and this because of high levels of in free androgens which lead to the increase estrogen in esteron form that make a appositive feedback on LH secretion which lead to increase testosterone secretion from the ovary.

Introduction

In 1935, Doctors Irving Stein and Michael Levental (US gynecologists), were the first Physicians described the a presentation signs and symptoms that were observed in a group of female patients, these patients exhibited irregularities in their menstrual cycles (anovulation/amenorrhea, oligomenorrhea, dysmenorrhea, infertility), presence of enlarged ovaries with polycists (2 to 5 times normal size which morphologically showed numerous fluid filled cysts with an "pearl like" distribution just inside the outer ovarian wall of the ovaries. The outer wall presented as a thickened shiny white sclerotic capsule surrounding the ovary). Other they noted was hirsutism and obesity.1. Stein and Leventhal also found that, after ovarian biopsy, the women began to menstruate regularly which provided the basis for current radical surgical techniques that reintroduce ovulation in women with PCOS. Due to their initial literary contributions this syndrome became known as "Stein-Leventhal Syndrome". Later, alternate names were coined such as; Sclerocystic Ovarian Disease, Functional Ovarian Hyperandrogenism, PCO and of course the most commonly accepted name PCOS (polycystic ovarian syndrome (1)

PCOS: is one of the most common disorders in women of reproductive age affecting up to 10% of population (2) the exact causes of PCOS is unknown (3) certainly a miscommunication occur among the hypothalamus, pituitary gland ovaries and fatty tissue (4) The condition was defined in 1999 and revised in 2003 by the European Society for Human Reproduction and Embryology (ESHRE) and the American Society of Reproductive Medicine (ASRM) sponsored workshop group (5).

Estimates of prevalence vary through 5-10 percent of reproductive age females and variations have been found across ethnic origins

LH luteinizing hormone: is elevated while FSH (follicular stimulate hormone) usually normally (6) at ratio at 2:1 or 3:1 (7). Estrogens level is high. SHBG is low while the androgens especially testosterone

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hormone are abnormally high (8). The abnormally high levels of androgens (9) primarily testosterone and androstendione are responsible for the development of acne, excessive facial and body hair and male pattern hair distribution and further loss of ovulation. (10) Women with PCOS- are at risk of hyperinsulinemia and insulin resistance (11) alteration in B- cells function and at high risks of glucose intolerance(2). Administration of insulin to women with PCOS increase circulation androgens levels (12).

According to Hopkinson and co-workers in 1998, the aetiology of PCOS is uncertain although there is evidence of a genetic link(13).and also explain that insulin resistance increases as part of puberty but that it should decline in early adulthood. They suggest that women who are genetically predisposed to PCOS fail to resume normal insulin
resistance and continue to 'express metabolic and endocrine features usually confined to puberty' (13).

Ehrmann (2005) agrees that there is no clear aetiological factor which causes the range of symptoms and suggests that the thecal cells in the ovaries of affected women are better at converting precursors into testosterone (14)

Women with PCOS often develop symptoms during puberty although sometimes later depending on environmental and lifestyle factors such as weight gain. The symptoms are caused by the imbalance of hormones in the body (14).

Although both lean and obese women with the syndrome show decreased sensitivity to the hormone insulin, the resistance is more marked in obese women (15).

Central fat tissues become resistant to insulin which means that the body produces more insulin to compensate. Patients are often found to have high levels of insulin circulating in their blood (hyperinsulinaemia). (Figure 1) show how hyperinsulinaemia contributes to the condition by reducing the amount of sex hormone binding globulin (SHBG) available to bind to excess androgens and stimulating the thecal cells of the ovary to produce more androgens (13).

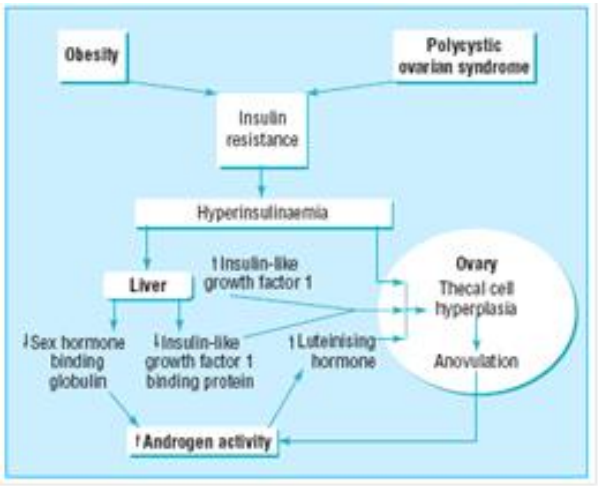

Figure 1 – Probable mechanisms whereby defects in insulin metabolism promote increased androgen activity at the level of the ovary.Source (Hopkinson et al, 1998)

The higher levels of circulating androgens produce various physiological changes such as the development of hirsutism and male pattern baldness. The measurement of androgens in the blood as a part of a diagnosis is not recommended because of the variability of androgenaemia in the normal population and limitations of testing (12).

The production of androgens such as testosterone is also a result of abnormalities in the interactions between the hypothalamus, pituitary and ovary. The hypothalamus produces pulses of gonadotrophin-releasing hormone (GnRH) which stimulates the pituitary to produce luteinising hormone (LH). Ehrmann (2005) explains that there may be an 'intrinsic abnormality' which favours LH production over follicle-stimulating hormone (FSH).

The ratio between LH and FSH is important because a) LH promotes androgen production in the ovary and b) FSH cannot stimulate the ovarian follicle to mature in the presence of high levels of LH. When the follicles do not mature and they fail to release eggs, small cysts form on the ovaries giving the condition its name (16)

Several conditions can produce the same signs and symptoms as PCOS and would need to be excluded if clinically suspected (ESHRE/ASRM 2003).
Hyperprolactinemia (17)

High levels of Prolactin in the blood.
Causes infertility, irregular menses and can stimulate

lactation.

Can be caused by prolactinoma (pituitary gland tumour which secretes Prolactin), drugs, severe head trauma and acromegaly.

Blood tests would show elevated Prolactin levels and prolactinoma would be diagnosed following magnetic resonance imaging scan and biopsy.

Testosterone is one of androgens; the major circulating androgens in women are testosterone, dihydrotestosterone, dihydroepiandrosteendione (DHEA) and Dihydroepiandrostenodione – sulphate (DHEA-s) both of adrenal gland and ovaries normally synthesize and secret testosterone, and the other androgens (18) approximately 50% of testosterone arises from the peripheral conversion of androstendione and 25% is secreted by adrenal gland. (10)

Testosterone is the circulating androgens while testosterone circulating in the blood it is bound to protein carrier in known a sex Hormone binding globulin (SHBB) and produced in the liver, (19) it is glycoprotein containing a single binding site for testosterone (10) about 80% bound to SHBG (18). Another 19% is loosely bound to albumin, leaving only 1% unbound "free (11) (10). The testosterone binding capacity is decreasing by androgens.

It is deleted as the presence of hair in androgen – dependent sites in which hair does not normally appear in women (11), (23). Or it a male pattern hair growth in women. Androgens are the major determinants of hair distribution, these androgens must be converted testosterone to dehydratesosteron by 5 α reeducate (3) before the can bind to the receptor of target cell and induce an androgens response. (12)

In hirsute women only 25% of the circulation testosterone arises from peripheral conversion and most is due to direct glandular secretion, the ovary is the most important source of increased testosterone and androsteindione in hirsute women. (10)

Patient and Method

The study was perform in Al-Fallujah city, (60) married women, there are (20-40)years old were selected (in infertility unit at Fallujah hospital and Al-Jameaa medical Laboratory in Al-Fallujah from February 2009 to June 2009) The women included in this study were classified to three groups as follows:

Twenty Women were normal married and fertile. They were taken from normal women accompanying the fertile patients attending the infertility unit. This group served as a control. Complete history and clinical examination were carried out serum levels of testosterone, FSH, LH were determined in this group. The blood samples were drawn in the mid follicular phase of the cycle. Twenty women complaining of infertility for more than (one) year with signs and symptoms of hypertestosteronemia such as hirsutism or with out menstrual disturbances, complaining of infertility. Twenty women complaining of infertility. The patients were examined first by gynecologist who conducted a clinical examination to rule out any abnormality and to refer suitable patient for this study. The level of testosterone, FSH, LH were determined in this group also, the blood samples were drawn in the 2nd half of follicular phase (day-2 to day -8)

4. The level of Prolactin was also studied.

Blood samples were obtained from the control and patients. Disposables syringes and plain plastic tubes were prepared and labeled. Each women has a special form written on it the name date, serial number and history. Blood samples of (5ml) were taken by an antecubital vein puncture in the morning between 9 - 12:00 am. The blood was allowed to clot in plain plastic tubes in incubator at temperature of (37c) for about (10) minutes. After that centrifugation was done at (300) RPM to separate the serum, the serum was transferred by pipette in to plastic tubes for hormones (testosterone, FSH, LH and Prolactin) assay by minividas samples of sera were a quoted and stored at (-20) until the assay was done .

Results & Discussion

The patient were divided in to two groups, one have hypertestosteronemia without PCOS others have hypertestosteronemia with PCOS they are compare with normal health as control as shown in table (1) and figure(2).

Hypertestosteronemia with out pcos (1.25 + 00. 7) ng / m1 is higher significantly ($P < 0.05$) that control (0.5+0.02)ng/m1, while group (2) (hypertestosteronemia

with pcos) the mean levels of testosterone (1.77 + 0.12) ng/ml is higher than group1 significantly (P0< 0.05). While the mean of FSH levels showed no difference in all groups. The mean levels of LH group (2) (8.95+0.35) mIU/ml is higher significant (P< 0.05) the group 1 (7.13+ 0.20) mIU /ml. Table (2) and figure (3) shows no significant differences at (P>0.05). In those to subgroups of infertile women (a,b) that divided according to presence of hirsutism or not.

There is an increase in Prolactin level in some patients in this study as which represented by 12.5% of the patients.

Testosterone level is increasing significant in groups (hyper testosteronemic women with PCOS). This finding is an agreement with finding of previous studies. (20). Yen (4) shows that women with pcos raised serum testosterone and LH levels and enlarged ovaries, franks (21). Finds that normal weight women with pocs elevated serum level of testosterone and had normal SHBG level. Rittmaster (22) also find that pocs women have higher serum level of free testosterone and this level is usually no more than twice the upper normal range.

Increasing of testosterone level associated with LH department ovarian over production of androgens (23), and at a base line women with pcos had higher LH pulse response to GnRH, this higher LH lead to hyperplasia of the theca cells and increased androgens production (24),(25).

There was no significant difference between FSH in control group and others. This finding in agreement with yen (4) and Golzicher (26). They found that the serum FSH, prolactin, endometrial thickness were not different from those of control group.

LH increased significantly in group 3, these may be attributed to the low level of SHBG, that probably facilitate tissue uptake of free androgens leading to increasing peripheral formotion of estrogen primary, (23) (3), the estrogen positive feedback on the central nervous system-hypothalamic – pituitary unit induce inappropriate gonadotropin secretion (23).(27).

The estrogen stimulate GnRH synthesis and secretion in the hypothalamus causing preferential LH release by the pituitary gland, this estrogen may also increase GnRH decreasing hypothalamic dopamine, like increase in LH secretion stimulates theca cells to produce excess androgen (23) Eden et al (26) found that the pcos group had higher medicine follicular phase LH, Eden testosterone free androgen index than the control. There is an agreement with the finding of Darweish et al. whose find that there is an increase in Prolactin levels in polycystic ovaries woman and this may refers to pituitary gland disorders (28). In conclusion the high levels of testosterone is responsible of hirsutism studeid in women lead to presence of the secondary characters of men in women and this because of high levels of in free androgens which lead to the increase estrogen in esteron form that make a appositive feed back on LH secretion which lead to increase testosterone secretion from the ovary

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Table (1) the concentration of testosterone FSH and LH in (hypertestosteronemia women with or without PCOS).

Hormone Concentration	Control	Group 1	Group 2
Testo ng/ml	0.50 ± .0029a	1.25± 0.076 b	1.77± 0.12c
FSH (mIU/ml)	5.00± 0.169 a	5.34±0.12 9a	5.60± 0.23a
LH(mIU / ml)	4.2± 0.159a	7.13± 0.206 b	8.95± 0.35c

Group1 = without PCOS , Group2 = with PCOS
Means with different letters horizontally has significant difference as compared with the control at P 0>0.05

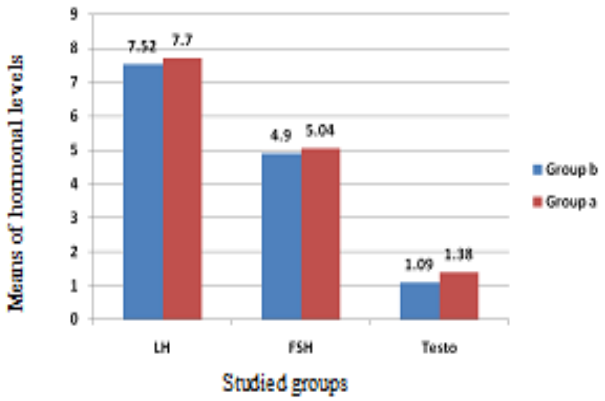

Figure (2): Hormonal Level in Hypertestosteronemic Women with or without PCOS.

Table (2): The hormonal levels in hirsutism.

Hormone Concentration		Mean ± SD	
	Group a	Group b	
Testo Ng/ml	1.090 ± .0.16a	1.38± 0.26a	Group a: infertile women with out hirsutism Group b: Infertile women with Hirsutism
FsH (mIu/ml)	4.90± 0.69a	5.040±0.89a	
LH(mIu / ml)	7.52± 0.40a	7.70± 1.70a	

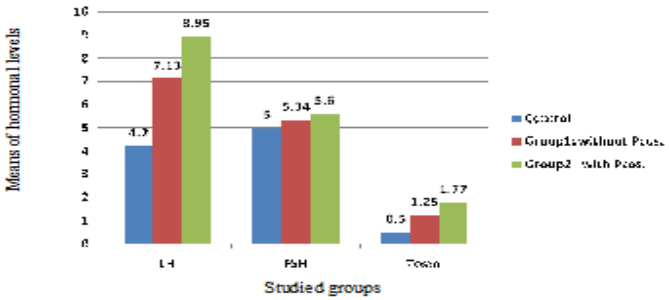

Figure (3): Hormonal levels in hirsute women, (3) The effect of age:

As shown in table (3) and figure (4). The patients were classified in to three groups.
20 years old Between 21-30 years. Between 31- 40 years.
The effect of age shown little variation in all parameters but not significant level at (P >0.05)

Table (3) the effect of age on hormone levels.

parameters	Age (year)Mean ± SE		
	Group 1	Group 2	Group 3
Testo ng/ml	1.15 ± 0.109	1.42± 0.09a	1.43± 0.13a
FSH (mIU/ml)	5.40± 0.15a	5.5± 0.15a	5.52± 0.21a
LH(mIU / ml)	7.00± 0.269	7.75± 0.36a	7.75± 0.36a

Means with different letters vertically has significant difference with the control according to Duncan test at P>0.05
Group 1: 20years. Group 2: 21 – 30 years Group 3: 31 – 40 years

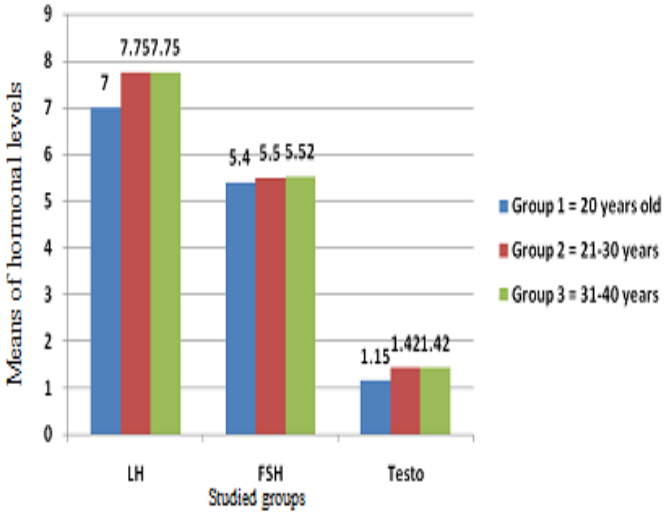

Figure (4): The effect of age on the hormonal levels

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دراسة بعض التغيرات الهرمونية في مصل النساء المصابات بتحوصل المبيض

نافع أحمد سعود **مصطفى نهاد جمعة**

الخلاصة

تمت الدراسة في مستشفى الفلوجة وكذلك في مختبر الجامعة في الفلوجة منذ بداية شهر شباط 2009 لغاية شهر حزيران 2009 بهدف دراسة بعض التغيرات الهرمونية في مصل النساء المصابات بمرض تحوصل المبيض في مدينة الفلوجة ونواحيها.أربعون امرأة عقيمة مصابة بمرض ارتفاع الهرمون الذكري, منهم عشرون امرأة مصابة بتحوصل المبيض قورنت مع عشرون امرأة طبيعية. جميع النساء الخاضعات للدراسة في الفلوجة والمناطق المحيطة بها. وكانوا بأعمار مختلفة.جميع النساء العقيمات اظهرن نفس الأعراض تقريبا مثل زيادة نموا الشعر في الوجه وصوت خشن مع زيادة في هرمون الشحمون الخصوي وزيادة في هرمون LH وعدم تغير في مستوى هرمون FSH . وقد سجل ايضا ارتفاع في مستوى هرمون prolactin في 12.5% من بين جميع النساء المصابات في هذه الدراسة . وتم الاستنتاج بانه زيادة هرمون الشحمون الخصوي تؤدي إلى ظهور الصفات الثانوية للرجال في النساء والذي يعد بسبب زيادة الاندروجينات الحرة التي تؤدي إلى زيادة التحول في هرمون الاستروجين Estrogen الى الاسترون estron الذي يعمل كعامل محفز للغدد النخامية لزيادة افراز هرمون LH الذي يحفز المبيض على إفراز هرمون الشحمون الخصوي testosterone.