Hormonal Study of Primary Infertile Women

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Abstract:

Approximately (15 %) of couples attempting their first pregnancy meet with failure. Most authorities define these patients as being primary infertile if they unable to achieve a pregnancy after one year of unprotected intercourse. The aim of this study was to evaluate the serum levels of Luteinizing hormone, Follicle stimulating hormone, Prolactin and Testosterone in (410) primary infertile women in Sulaimani city. The results obtained compared with that of (240) age matched fertile women. The results showed, higher incidence of primary infertility was in the age range (26-37) years and hormonal imbalance plays an important role in primary female infertility.

Keywords: Primary female infertility, LH, FSH, PRL, Testosterone.

INTRODUCTION:

Conception normally is achieved within (12) months in (80-85) of couples who use no contraceptive measures. Females presenting after this time should therefore be regarded as possibly infertile and should be evaluated .Data available over the past (20) years reveal that in approximately (30%) of cases, pathology found in the women alone, and in another (20%) both the man and woman are abnormal [1-2].

The women reproductive years begin when she starts her menstrual cycle during puberty (about the age 13) years, and the ability to have a child usually ends around the age (45) years, although it is potentially possible for a women to be pregnant until her periods end with menopause (about the age 51) years [3].

Born girl already carries in her body about (400000) immature eggs (oocytes). These are stored in her ovaries in tiny fluid-filled sacs called follicles. Once she enters her reproductive years, she starts having monthly one egg (or, less commonly, more than one), which may join with a male motile sperm cell during fertilization and being a pregnant [4].

The development and release of the egg depend largely on a delicate balance of hormones (chemicals that signal the body organs to do a particular task). Some of these hormones are produced in the ovaries, others from the two glands in the brain, the hypothalamus and the pituitary [5].

Primary infertility is a term used to describe a couple that has never been able to conceive after a minimum of one year of attempting to do so through unprotected intercourse. Causes of primary infertility include a wide range of physical as well as emotional factors [6]. The principal causes are:

1. Ovulatory or hormonal abnormality: Failure of ovulation is the single most common cause of infertility in females. The normal ovarian cycle is so complex that even small deviations may disrupt the cycle and prevent ovulation [7]. Ovulatory disorders are most often caused by abnormality in one of the controlling hormone. However, problems can also arise if the ovaries themselves are resistant or non responsive to normal levels of hormones. In addition, absent, damaged or diseased ovaries will prevent ovulation [8]. The principal symptoms associated with ovulatory disorders are: Amenorrhea, Oligomenorrhoea, Irregular menstrual cycle, Obesity, Excessive weight loss Galactorrhoea, Hirtism and Acne [9].
2. Anatomical disorders: Disorders of the female sex organs are much more common than those of the male. This is especially true of infection and inflammatory conditions [10].
3. Chromosomal disorders: Infertility can arise when there are abnormal chromosomes or abnormal numbers [11].
4. Unexplained infertility (Idiopathic): This is a diagnosis of exclusion.

FSH is synthesized and secreted by gonadotropins in the anterior pituitary gland; it is a glycoprotein that regulates the development, growth, pubertal maturation and reproductive processes of the human body. In females, it initiates follicular growth, specifically affecting granulose cells. With the concomitant rise in inhibin B (a complex protein that down regulates FSH synthesis and inhibits its secretion). FSH levels then decline in the late follicular phase. This seems to be critical in selecting only the most advanced follicle to proceed to ovulation [12].

LH is produced also by the anterior pituitary gland; it is a glycoprotein and essential for reproduction. In females, at the time of menstruation, LH initiates follicular growth, specifically affecting granulose cells [13].

Testosterone is a steroid hormone from the androgen group. It is the principal male sex hormone, produced by testes in men and by thecal cells of the ovaries and placenta in women.

Testosterone is also synthesized by zona reticulais of the adrenal cortex in both sexes. In general, Testosterone has both anabolic and virilizing effects [14-15].

Prolactin (PRL) is mainly synthesized in the pituitary gland and involved in many different biological functions including behavior, immunology, endocrinology, metabolism and reproduction [16].

More than (300) different biological functions have been attributed to PRL, the major ones being induction of differentiation and growth in mammary epithelia and stimulation of milk protein secretion [17].

PRL is secreted mainly by lactotrope cells, breast deciduas and immune system [18]. Hyperprolactinemia is one of the most common endocrine disorders of the hypothalamic pituitary axis. It is more commonly diagnosed in women than in men and if it persists, it usually causes infertility, amenorrhea, galactorrhea, oligomenorrhea, hyperandrogenism, hirsutism, acne, regular menses; but with anovulatory cycles [19].

In the light of these data and to extent the understanding the hormonal effects on female infertility, this study was undertaken to investigate the serum levels of LH, FSH, PRL and Testosterone in primary infertile women and comparing the results obtained with that of age

matched fertile women in order to explore the role of hormonal abnormality in female infertility.

SUBJECTS AND METHODS:

Subjects: This study was conducted over a period of two years, from January 2007 to July 2009 at the department of chemistry/ College of Science/ Sulaimani University/ Sulaimani/ Iraq. Informed consent was obtained verbally from all participants. All participants were carefully screened to exclude evidence of congestive heart failure hepatic and renal diseases. The present study included (650) females, which were divided into two groups:

I. Control group (Fertile women group): Included (240) apparently healthy fertile women.

II. Case group (Primary infertile women group): Included (410) primary infertile women, diagnosed by gynecology and obstetrics consultants. Details of the number and age of the two groups are illustrated in Table (1):

Table (1): Details of number, and age of the studied groups.

Groups	Number	Range of age (years)
Control (Fertile women) group	240	22-40
Case (Infertile women) group	410	22-40
Total	650	22-40

Samples: Five ml of venous blood was withdrawn from the cubital vein of each participant using disposable syringes during the second day of menstrual cycle.

The blood samples were allowed for (15) minutes at room temperature to clot and serum was separated by centrifugation at 3000 rpm for (10) minutes. Serum samples were either analyzed immediately or stored at (-28 ˚C) until they were analyzed.

Methods: The serum levels of LH, FSH and PRL were determined by immunoradiometric assay and that of testosterone by a radioimmunassay as described by Ban M.R. [20].

Statistical analysis: The means, standard deviations, T-test and P-value were used to compare the significance of different data.

The overall predicted values for the results in both studied groups were performed using SPSS 16.0 program.

RESULTS:

The mean serum levels of LH, FSH, PRL, and Testosterone in fertile women are all within their normal means. On the other hand there was a clear difference between the primary female infertility according to their age ranges. Those of the age range between (26-37) years represented the highest percentage.

The results indicated also highly significant differences ($P < 0.05$) in the mean serum levels of LH, FSH, PRL and Testosterone between control and case groups, Table (2).

Table (2): Serum levels (Mean ± S.E.) of LH, FSH, PRL and Testosterone in control and case groups.

Studied Hormones	Control group	Case group	P-values
LH (mIU/ml)	3.18 ±1.34	8.79±10.01	< 0.05
FSH (mIU/ml)	4.99 ±2.6	12.95 ±17.53	< 0.05
PRL (ng/ml)	7.28 ±3.34	12.85±16.89	< 0.05
Testosterone (nmole/L)	1.91 ±0.59	2.27 ±1.32	< 0.05

DISCUSSION:

Female infertility may be either primary (refers to the biological inability of a woman to contribute to conception after one year of unprotected intercourse) or secondary (describes women who have been pregnant at least once, but have not been able to achieve a pregnancy again) and the simplest evaluation of a female infertility is the hormonal analysis.

The data obtained in this study for serum levels of LH, FSH, PRL and Testosterone in control group are all within their normal means. Similar results were obtained by Davis and Tran [14], Scott and Ledenson [21], Griswold [22], and Casanueva [23].

The results of the present study showed also that among (410) infertile women, there was a significant difference of infertility according to age. Those of the age range (26-27) years represented (50.24%). This finding is in agreement with other international studies which showed that the number of infertile couples rises with increasing age. The same authors reported also that women are born with a finite number of eggs. Thus, as the reproductive years progress, the number and quality of the eggs diminish. The chances of having a baby decreased by (3-5 %) per year after the age of (30). This reduction in infertility is noted to a much greater extent after age (40) [24-26].

The results of the present study indicated a significant difference ($P<0.05$) in the mean serum levels of LH, FSH, between control and case groups. LH and FSH in females are intricately involved in the reproductive cycle. LH stimulates the ovarian theca to produce several androgen precursors of estradiol, whereas FSH, in turn, induces the conversion of these androgens to estradiol by the ovarian granulose cells [27-28]. Serum measurements of LH and FSH are frequently used in the evaluation of disorders of infertility and puberty, such as, hypo-gonadism, ovulation timing and infertility studies, monitoring ovulation induction and the clinical administration of gonadotropins. Generally, elevated LH levels indicate ovarian dysfunction, whereas that of FSH indicates poor follicle development and consequently anovulatory cycles [29-30]. The primary function of PRL is the development and maintenance of lactation. Several physiological conditions induce the release of PRL, the most notable being the stimulation of the breast and nipple during nursing [31]. Two other conditions giving rise to PRL release are severe stress and major surgery involving general anesthesia. The release of PRL into the blood stream is thought to be under the control of a prolactin-inhibitory factor produced by the hypothalamus [32].

Several other clinical conditions have been associated with abnormal levels of PRL in women, such as galactorrhea, anovulation with amenorrhea, hypoestrogenism and hyperprolactinemia [33]. The results of the present study indicated a significant ($P> 0.05$) difference in the serum level of PRL in infertile women compared to fertile women. This finding is in agreement with the results of other studies [34]. The data obtained revealed also a significant ($P < 0.05$) increase in the serum level of Testosterone in primary infertile women compared with fertile women. This finding is similar to that obtained by Shirtcliff et al [35]. Testosterone is produced in small quantities by the ovaries in women and elevated levels can lead to infertility. The commonest cause of hair growth in women with abnormal periods is polycystic ovary syndrome, which cause hyperandrogenaemia. The appropriate test for hyperandrogenaemia is estimation of serum total testosterone [36].

CONCLUSIONS:

The conclusions can be summarized as follows:

1. The results of this study showed that the higher incidence of primary female infertility was in the age range between (26-37) years.
2. The data obtained revealed also that the serum levels of LH, FSH, PRL, and Testosterone in primary infertile women were significantly higher than that of control group, so hormonal imbalance plays an important role in primary female infertility.

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لیکولینەوەی هورمونی لە ژنانی نەزوك – جوری سەرەکی

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پوختە

نزیکەی 15٪ خیزان تووشی نالەبارى ئەبن لە منداڵ بوون لە ژنان. زۆربەی لیکولینەوەکان لە سەر نەخوشی نەزۆکی سەرەکی، وا پینا سە ئەکەن، کە بریتیە لە نەتوانینی ژن و میرد بو وەچە خستنەوە دوای یەك سال هاوسەرگیری بە مەرجیك هیچ بەربەستیك ئە نجام نەدرابیت لە کاتی جووتبوندا. مەبەست لەم تویژینەوەیە بریتیە لە خەملاندنی بری هە یەك لە هورمونی (LH, FSH, PRL, Testosterone) **لە شلەی خوینی** (410) **ژنی نەزوك لە شاری سلیمانی. ئە نجامەکان بەراورد کرا لە گەڵ ئە نجامەکانی** (240) **ژنی ئاسایی کە هەمان تەمەنی ژنانی نەزوکیان هەبوو. ئە نجامی ئەم تویژینەوەیە دەریخست کە زورترین ژنە نەزوکەکان تەمەنیان لە** (26-37) **ساڵیدایە، وە لە لایەکی ترەوە بری هەر چوار هورمونە خەملیوراوەکان بەرەکیان لە ژنانی نەزوکدا بەرز تربوو بە بەراورد لە گەڵ ژنانی ئاسایی.**