Correlation Of Prolactin Hormone With The Thyroid Gland Hormones And The Female Sexual Hormones In Infertility Women

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Abstract

Background: infertility is defined as not being able to get pregnant. Hormonal disorders of female reproductive system are comprised of a number of problems resulting from aberrant dysfunction of hypothalamic- pituitary-ovarian axis. These relatively common disorders often lead to infertility.

Aims: This study aimed to evaluate the concentrations of a group of hormones, They acted as a marker to make the functional changes in ovaries or caused the infertility or Sub Infertility in some women . the study involved estimating the concentration of the prolactin (PRL) , follicle stimulating hormone (FSH) , luteinizing hormone (LH) , estrogen (E2) and cortisol in addition to assess the concentrations of thyroid stimulating hormone (TSH) , thyroxin (T4) and Triodeothyronin(T3) as well as find the correlations between prolactin hormones and the studied hormones, the study covered (30) samples of infertility women ranged their age between (28-48) compared with (15) healthy samples treated as a control group .

Result :The results of study showed a significant increase ($P<0.05$) in concentrations of prolactin (PRL) , follicle stimulating hormone (FSH) , luteinizing hormone (LH) , cortisol and the thyroid stimulating hormone (TSH) in the patients whereas these results also indicated to a significant decrease ($P<0.05$) in concentrations of estrogen (E2) , (T4)and (T3) .The results of the correlations showed a positive correlation between prolactin hormone and (TSH) at probability level ($p <0.01$) and with (FSH) (LH)، and cortisol at probability level ($p<0.05$) whereas the correlation was negative between prolactin hormone and estrogen (E2) , (T4) and (T3).

Key Words :Infertility , prolactin , FSH, LH ,Estrogen, Thyroid hormones

Introduction

Infertility defined as a state of the biological inability of woman and man to achieve a pregnancy(1,2). It is a diseases happened for many causes including the hormone troubles(3) or genetic or immunological causes, (4,5),or biological ones as the chromosome deviations and congenital deformities as well as the acquired factors represented the geographical variance like the environmental factors(6) and bacterial infections (7).The infertility is classified into two main types: the infertility that means an inability to achieve absolutely a pregnancy due to non - treating causes (8), The sub - infertility that means there were some problems can be treated (9,10) ,since the physiological changes occurred in women by producing the sexual

hormones according to some steps that began by secretion the gonad hormones from the anterior lobe of pituitary (follicle stimulating hormone FSH) and (luteinizing hormone LH). They stimulated the ovary to produce periodically the ovum and secreted the female sexual hormones (progesterone, estrogen) (11).

Prolactin hormone(PRL) is a protein hormone consisting of (199) amino acids with a molecular weight of (23.000) , Dalton. It is secreted by the acidic cells called (lactotrophs) from the anterior lobe of pituitary gland (12) .PRL is mainly secreted by the lactotrophs, cells that constitute 20-50% of the anterior pituitary cells. There are also many extra pituitary sources of PRL, including lymphocytes, skin fibroblasts, the brain, the breast, and prostate and adipose tissue cells. (13). It has a role in reproduction, calcium metabolism, osmo regulation and behavior (14). This hormone activated in females during the physiological activity in the female puberty period by stimulating the action of growing the female organs, especially the lactic glands in combination with the Estrogen hormone (15). The increase of prolactin hormone ratio (Hyperprolactinemia) in non- pregnant females led to a trouble in the quantity of progesterone hormone in luteinizing phase after the ovulation, menstrual disorder and lactation. These symptoms are accompanied the sterility. (16) has been primarily identified as a major stimulating factor for lactation in the postpartum period However, apart from its classical functions this hormone affects other aspects of human homeostasis, including osmo regulation, metabolism and regulation of both the immune and the nervous system (17).hyperprolactinemia may result in hypogonadism, infertility, and galactorrhea, or it may remain asymptomatic Bone loss occurs secondary to hyperprolactinemia-mediated sex steroid attenuation Spinal bone density is decreased by approximately 25% in women with hyperprolactinemia (18,19) The most frequent symptoms of chronic hyperprolactinémie include reproductive dysfunction, sexual impairment, breast pathology, abnormalities associated with chronic hypogonadism, behavioral and mood alterations, possible immunologic depression(20). The FSH is a Glycoprotein hormone, having molecular weight reached at [33,000]

Dalton. The protein molecule consisted of two units, A and B (21,22). The FSH excreted from the Basophilic cells in the anterior lobe of pituitary (23) by depending on the stimulating hormone (Gn RH) that produced from the hypothalamus (24, 25) and this hormone influenced also on growing and developing the ovarian follicles as well as on developing and completing the Oocyte maturation(26). The LH hormone is as Glycoprotein one, its molecular weight amounted to (26,000) Dalton and consisted of sub units: A and B (27). This hormone produced from [β cells] in the anterior lobe of pituitary gland in response of secreting the free hormone of the hypothalamus (Gn RH), The (LH) activated growing the follicles, supporting the ovulation and stimulating "corpus luteum" to secrete Estrogen and progesterone role in growing the ovum and ovulation (28,29).

The secretion of the hormone LH before ovulation impact of high concentrations of the hormone estrogen during the process of positive feedback mechanism Positive feedback mechanism, but after ovulation , this hormone is inhibited by estrogen and progesterone levels by feeding negative feedback mechanism (30,31). Estrogen Hormone has a key role in the development of primary and secondary genitalia and regulate the menstrual cycle and affects many other organs such as the bones , brain and blood vessels and skin(32). Secreted estrogen -mediated Theca Interna and Granulose cells for Ovarian follicles as well as secreted from Corpus luteum and Placenta and Granulus cells (33).The measurement of the concentration of estrogen in women reflects the activity of the ovaries(34).There are three forms of estrogens in the blood are : Estrone (1E) and β-Estrdiol (2 E), and Esterol (E3), β -Estradiol is most active in the body(35).

Subject &methods

The study aim at knowing some changes occurring in hormones in female with Infertility . (30) samples of blood gathered from the patients and (15) samples of blood were taken from the healthy persons as a control group.

- Estimation of Prolactin Hormone (PRL),Luteinizing Hormone (LH), and Follicle Stimulating Hormone (FSH) were

determined by using AccuBind ELISA (Monobind Inc.,USA).

- Estimation of Estrogen:-

Serum estrogen was determined by using ELISA (Bio ChecK - U.S.A.)

- Estimation of Cortisol:-

Serum cortisol was determined by using ELISA (Bio ChecK - U.S.A.)

statistical analysis:

Results were analyzed statistically using SPSS software and using T- test the statistical test.

Results

figure (1,2,3,5,6) shows the mean & standard deviation of prolactin, Follicle Stimulating(FSH), Luteinizing (LH) , Cortisol and Thyroid Stimulating hormone (TSH) concentration, there is a significant increase in hormones concentrations in the patients with Infertility at significant level ($P< 0.05$) compared with the Control Group. Figure (4,7,8) shows the mean & standard deviation Estrogen (E2), -thyroxin (T4) and Triiodothyronin(T3) hormone concentration, there is a significant decrease in hormones concentration in the patients with Infertility at significant level ($P< 0.05$) compared with the Control Group.

Table (1) shows the correlations of prolactin hormones with Other hormones, The results of showed a positive correlation between prolactin hormone and (TSH) at probability level ($p <0.01$) and with (FSH) (LH)، and cortisol at probability level ($p<0.05$) whereas the correlation was negative between prolactin hormone and estrogen (E2) , (T4) and (T3).

Discussion

In the present study ,results showed that there was a significant increase in Prolactin hormone concentration in female with infertility (22.45 ± 7.57) as compared to control(11.55 ± 4.58) , The results of the recent study agreed with the results of (36,37) , showed the increase in concentration of prolactin hormone in the infertility women. PRL influences the gonads either directly or indirectly. Its direct action results in a decreased sensitivity of the luteinizing hormone (LH) and of the follicle-stimulating hormone (FSH) receptors in the gonads (38). The indirect effect is exerted by a reduction of gonadoliberine (GnRH) secretion, more specifically by its pulsatile secretion inhibition caused by opiate system stimulation. Consequently, suppressed LH and FSH

secretion inhibits ovulation (39). Results of the study showed there was a significant increase in (FSH) hormone concentration in female with infertility (17 ± 5.91) as compared to control(10.05 ± 2.49) , The results of the recent study agreed with the results of (40, 41,42) The increase in concentrations of follicles stimulating hormone in the infertility group may be a marker to the malfunction ovary and losing the feedback It may be a marker to the infertility or approaching meno pause(43). It was also occurred by the psychological stress or disorder in dietic system (44,45), very low estrogen levels, As a result, negative feedback that is normally produced by estrogen in the hypothalamus is reduced Gonadotropin-releasing hormone (GnRH) secretion is improved and stimulates pituitary gonadotropin release. The resulting increase in follicle-stimulating hormone (FSH), in turn, drives ovarian follicular activity (46). Also in the present study there is a significant increase in (LH) hormone concentration in female with infertility(52.5 ± 12.19) as compared to control(30.3 ± 9.69), This is agreed with the mentioned the researcher (47,48,49). It is due to the increase in concentrations of luteinizing hormone. This is indicated to the pituitary dysfunction, or to increase the luteinizing hormone accompanied a decrease in concentrations of progesterone and Estrogen. It is well known that the inhibitions of luteinizing hormone happened when the concentrations of Estrogen and progesterone increased by the negative feedback mechanis. (50). While the results showed there was a significant decrease in estrogen hormone concentration in female with infertility(43.5 ± 28.67) as compared to control(145.85 ± 76.41) , The results of our study agreed with the results of (51).The Estrogen hormone had a great importance to show the activity of ovary, because it was secreted from the Granulus cells of follicles in the ovary, The absence of Estrogen means non - oogenesis and then inability to achieve a pregnancy. This was occurred in meno pause (52). The concentration of Estrogen hormone may decrease due to any pituitary gland disorders, producing an increase in releasing the hormones feeding the gonads : FSH and LH. This led to inhabit secreting the Estrogen by the negative feedback mechanism (53,54) . results of the study showed

there was a significant increase in (TSH) hormone concentration in female with infertility (5±1.68) as compared to control(3.35 ± 1.39), The results of our study agreed with the results of(55,56). Thyroid disease had been shown to be associated with increased risk of prematurity or infertility (57) low serum level of thyroxine (T4) and decreased negative feedback on the hypothalamopituitory axis ، The resulting increased secretion of thyrotropin releasing hormone (TRH) stimulates thyrotrophs and lactotrophs, thereby increasing the levels of both thyroid stimulating hormone (TSH) and prolactin (58) Thyroid dysfunction which is quite prevalent in the population affects many organs including male and female gonads, interferes with human reproductive physiology, which reduces the likelihood of pregnancy and adversely affects pregnancy outcome, thus becoming relevant in the algorithm of reproductive dysfunction(56). While the results showed there was a significant decrease in(T4) and (T3) hormones concentration in female with infertility (5.3 ± 1.25) (0.65± 0.36)sequentially as compared to control(7.2 ± 1.52) (1.15 ± 0.39) sequentially The results of the current study agreed with the results of many studies (13). (GnRH) and T4 are important in achieving maximum level of success of fertilization and blastocyst development(59) .The decrease in concentrations of the thyroid gland hormones caused great morpho changes intra- uterine lining and an oviduct due to many physiological problems (60,61). results of the study showed there was significant increase in Cortisol hormone concentration in female with infertility(10.86 ± 3.14) as compared to control(6.45 ± 2.23) ,he results of the current study agreed with the results of many studies (62) , Cortisol hormone acted as a measure to efficiency of performance of Adrenal gland in its activity because the increase in its concentration indicated to the trouble in this gland or in the other glands (63).Secreting a plenty of cortisol hormone led to secrete LH hormone and then happened the infertility The oxidative stress showed a role in an increase in the cortisol hormone. (64). Several lines of evidence indicate stress-related hormones as immunosuppressive agents, which present a range of effects on the immune system Stress activates neurons that secrete corticotropin-

releasing hormone, which results in higher plasma cortisol levels. Prolactin is also released in response to stressor stimuli, although its exact role in the response to the stress is not known (65).It has long been known that frank hypothyroidism causes elevated cortisol levels ,presumably due to both decreased clearance and blunted negative feedback of cortisol on the hypothalamic pituitary-adrenal axis(66).

About the Correlation of Prolactin hormones with Other hormones The results of the correlations showed a positive correlation between prolactin hormone and (TSH) at probability level ($p < 0.01$) and with (FSH) (LH)، and cortisol at probability level ($p<0.05$) whereas the correlation was negative between prolactin hormone and estrogen (E2) , (T4) and (T3).Hyperprolactinemia is the most prevalent endocrine disorder in hypothalamic- pituitary axis , Pathologic hyperprolactinemia is generally applied for the situation in which prolactin level increases because of some reasons other than physiologic causes. Prolactin secretion is controlled by prolactin inhibitor factor that is secreted from hypothalamus, other factors like vaso active inhibitory peptide (VIP) and Thyroid relising hormone (TRH) cause to increase prolactin secretion, In fact, TRH in addition to increasing TSH causes to rise prolactin level , In patients with hypothyroidism, increased levels of TRH can cause to rise prolactin levels and these patients may have galactorrhea.(13). PRL influences the gonads either directly or indirectly. Its direct action results in a decreased sensitivity of the luteinizing hormone (LH) and of the follicle-stimulating hormone (FSH) receptors in the gonads (67). The indirect effect is exerted by a reduction of gonadoliberine (GnRH) secretion, more specifically by its pulsatile secretion inhibition caused by opiate system stimulation. Consequently, suppressed LH and FSH secretion inhibits ovulation (39). In the cases of hyperprolactinemia hypogonadotrophic hypogonadism is observed.

Conclusion

In the present study, there is high prevalence of hypothyroidism in infertile women, These disorders may lead to menstrual irregularities resulting in infertility, In hypothyroidism, increased(TRH)

production leads to hyperprolactinaemia and altered (GnRH) secretion, This leads to a delay in(LH) response and inadequate corpus luteum leading to abnormal follicular development and ovulation.

Therefore the study recommended that to pay attention for serum(T3, T4, TSH) and prolactin level should be evaluated in all infertile women.

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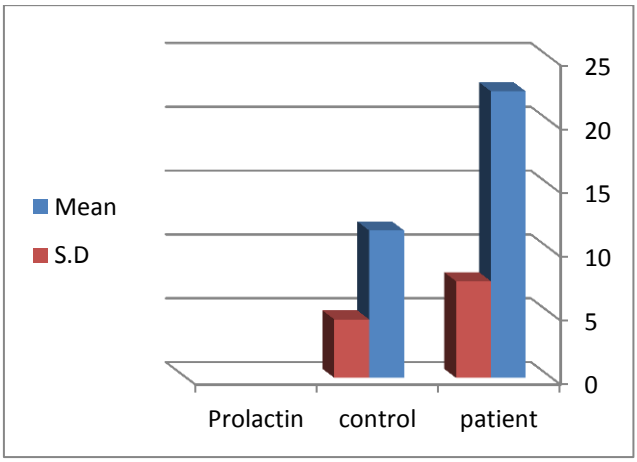
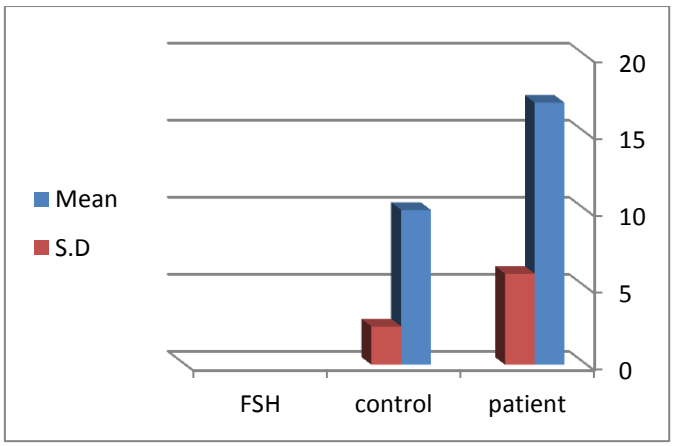
Table (1): correlation between prolactin hormone with other hormones in women with infertility

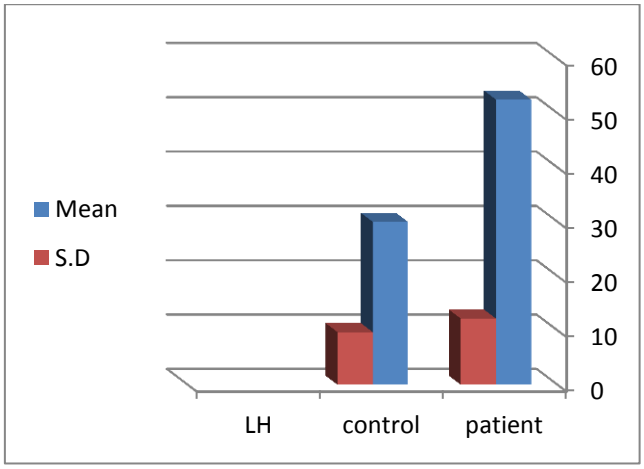
	Prolactin	
	r	P value
TSH	0.57	0.01
T3	-0.46	0.01
T4	-0.47	0.01
FSH	0.39	0.05
LH	0.37	0.05
Esradiol	-0.36	0.05
Cortisol	0.35	0.05



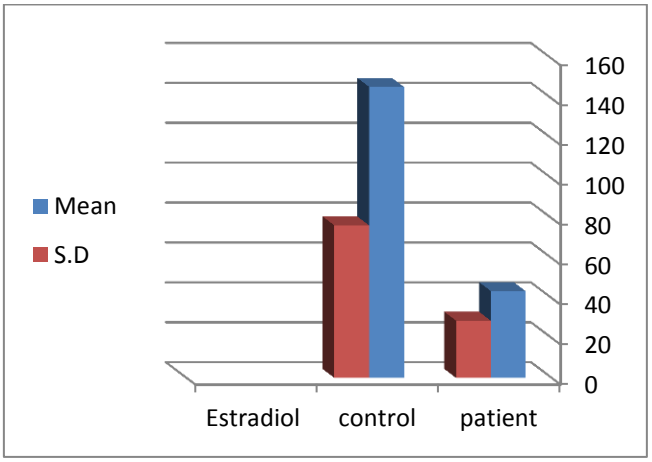
The figure (1) explained there is a significant increase in prolactin hormone concentration (ng/ml) in the patients with Infertility at significant level (P< 0.05) compared with the Control Group.



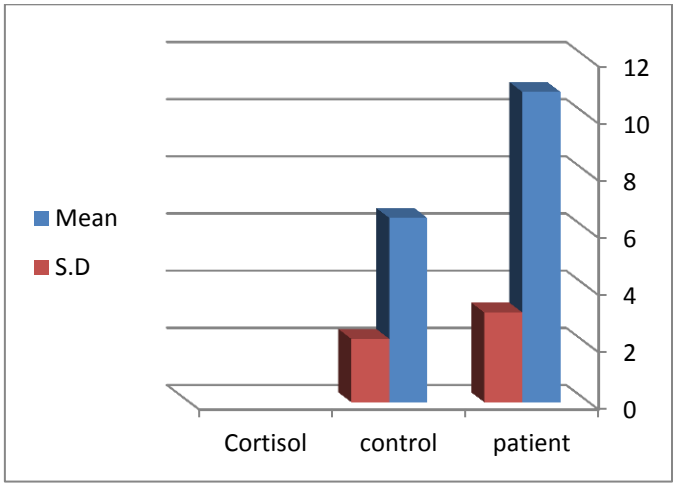
The figure (2) explained there is a significant increase in (FSH) hormone concentration in the patients with Infertility at significant level (P< 0.05) compared with the Control Group.



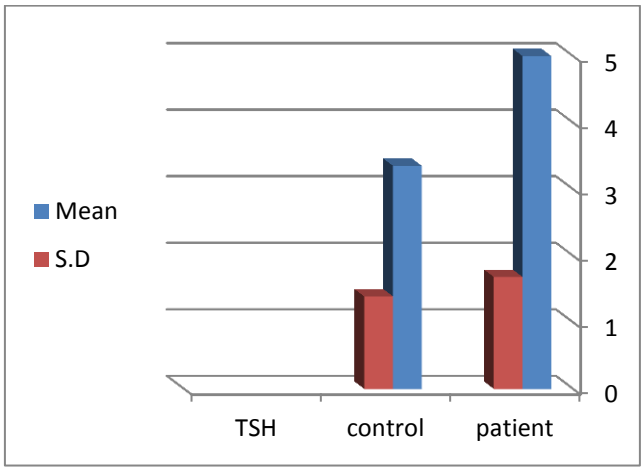
The figure (3) explained there is a significant increase in (LH) hormone concentration in the patients with Infertility at significant level (P< 0.05) compared with the Control Group



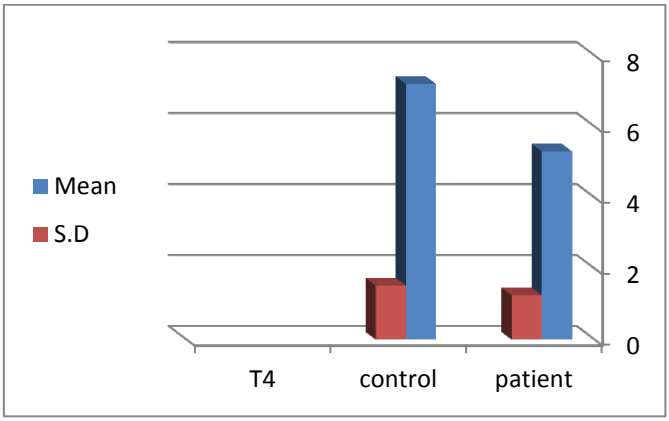
The figure (4) explained there is a significant decrease in (E2) hormone concentration (pg/ml) in the patients with Infertility at significant level (P< 0.05) compared with the Control Group



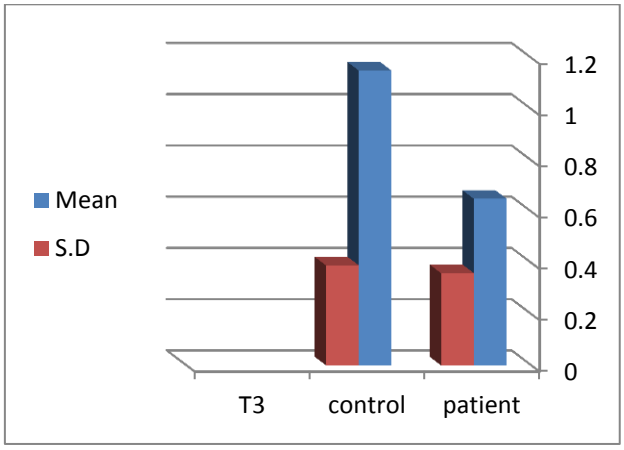
The figure (5) explained there is a significant increase in cortisol hormone concentration(µg/dl) in the patients with Infertility at significant level (P< 0.05) compared with the Control Group



in The figure (6) explained there is a significant increase in (TSH) hormone concentration(Mlu\ml) in the patients with Infertility at significant level ((P<0.05) compared with the Control Group



in the The figure (7) explained there is a significant decrease in (T4) hormone concentration(ng\ml) patients with Infertility at significant level (P< 0.05) compared with the Control Group



The figure (8) explained there is a significant decrease in (T3) hormone concentration(ng\ml)in the patients with Infertility at significant level (P< 0.05) compared with the Control Group