



Hyperprolactinemia Causes Primary and Secondary Infertility in Women of Iraqi Patients

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Abstract

In this study; a total of 150 hyperprolactinemic women their ages (20-50) years are collected from Kmal Al-Samaraee hospital and 50 for normal healthy women used as control. The patients were divided into two groups, those who suffer from primary infertility and those who suffered from secondary infertility, then the 150 patient groups were divided into three age groups (20-30), (31-40) and (41-50) years. Test of fertility hormones, which is (LH and FSH) was done for all patient groups to check the effect of high prolactin levels on the level of other hormones. It was found that there is a significant difference in all hormones concentrations (LH,FSH,PRL) for patients when compared with normal healthy groups hormones, according to type of fertility, both in primary and secondary infertile women. The results show that the prolactin levels in both infertile groups were higher than in normal, healthy, fertile women which lead to decrease the concentration of fertility hormones. Also, it is obvious that the prolactin level in secondary infertile women higher than its level in the primary infertile patients. The results indicate that the higher prolactin levels were in the age group (31-40) years, than of the other two groups.

Keywords: Hyperprolactinemia; Infertility; Prolactin.

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1. Introduction

There is a wide range of studies considering the infertility problem and causes among women's. Prolactin(PRL) hormone is a peptide hormone which synthesized by lactotropes that produced by the pituitary gland, which located in the base of the brain and that can highly effected on women's reproduction due to its effect on fertility hormones[1]. It starts its activity via binding to a specific receptor which a single membrane bound protein [2]. The other extra-pituitary sources are breast tissue, brain and immune cells [3,4,5].

Hyperprolactinemia is a condition in which presence of abnormally high level of prolactin hormone in the blood of non-lactating and nonpregnant women in which the normal levels are typically 10–35 ng/ml and 1ng is equivalent to 21.2 mU/ml [6]. Hyperprolactinemia is the major cause of female infertility, the elevated prolactin level affects a women's ovulation and menstrual cycles this by inhibiting the fertility hormone which is follicle stimulating hormone and leutilizing hormone

An excessive PRL secretion decreases the pulsatile release of GnRH impairing the pituitary production of FSH and LH. Furthermore, it may directly impair the endocrine activity of ovarian follicles. As a consequence defective luteal phase, inconstant ovulation and chronic an ovulation are conditions frequently observed in young hyperprolactinemic patients [7]. Primary infertility was defined as those cases in whom conception had never occurred and secondary infertility was defined as those cases in whom there was an inability to conceive after a previous successful conception.

2. Aim of the work

Identification of the effect of high prolactin hormone level (hyperprolactinemia) on two other fertility hormones, leutilizing hormone (LH) and follicle stimulating hormone (FSH) in Iraqi women patients and to check the effect of this effect on three ages group in two type of fertility (first and second infertile women).

3. Materials and methods

Blood samples were collected from 150 randomly selected hyperprolactinemic infertile women, blood specimens also collected from fertile non-pregnant and non-lactating 50 healthy women with no past history of hyperprolactinemia. All these samples were obtained from infertility hospital of Kamal AL-Samraee starting from March 2014 to Septembers 2014. Hormonal assay of fertility hormone levels was measured using Bio-merieux (France) and data was recorded which is age, detailed medical history, duration of the infertility problem and type of infertility suffered by the patients.

Then the 150 patients were arranged depending on ages into three groups which is (20-30), (30-40) and (41-50) years old, to check in which age group the effect is. Statistical analysis for all values were expressed as Mean± Standard Deviation of the ($M \pm SD$). P value are 0.05 was regarded as statistically significant.

Statistical analysis for both groups was carried out on the data obtained using Minitab 15 software. ANOVA test was used first to compare two infertile groups to check the effect of hyperprolactinemia in these two groups then

also used to compare different age groups among each other and with control

4. Result

A total of two hundred samples was taken, of whom one hundred fifty sample of hyperprolactinemic infertile women this group screened as case group and fifty were fertile healthy group as a control. There were 75% infertile hyperprolactinemic women in case group which include Group 1 comprised 64.6% primary infertile women and Group 2 include 35.09% secondary infertile hyperprolactinemic patients. These groups distributed as shown in table 1 and figure 1, as 200 represent whole group study, 97(64.6%) were primarily infertile women, 53(35.4%) as secondary infertile women and 50 as healthy control.

Table 1: Frequency and percent of the whole group, control group, first infertility and second infertility case group.

Sample	Frequency	Percent
Study group	200	100%
Control	50	25%
Hyperprolactinemia	150	75%
First infertility	97	64.6%
Second infertility	53	35.4%
Chi-square (χ^2)	---	9.673 **
P-value	---	0.0139

** (P<0.01).

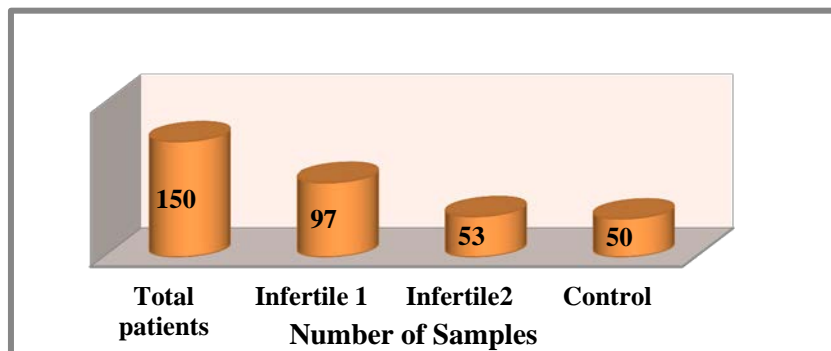


Figure 1: Distribution study of groups

The patients were divided into two groups, those who suffer from primary infertility and those who suffered from secondary infertility, then the 150 patient groups were divided into three groups according to age, which is (20-30), (31-40) and (41-50) years. Test of fertility hormones, which is (LH and FSH) was done for all patient groups to check the effect of high prolactin levels on the level of them.

Effect of hyperprolactinemia on fertility hormones.

Screening of hyperprolactinemia according to fertility hormones which is (LH, FSH) that affected by increased prolactin level, give the results as shown in table (2).

Table 2: Measurement of prolactin, LH and FSH in females with hyperprolactinemia.

Hormone type	Normal concentration	Measured concentration	No. of total cases.	Ages
Prolactin	1.3-25 ng/ml	30-114 ng/ml	150	20-50
LH	1.5-8 mIU/ml	1-4.5mIU/ml		
FSH	3.9-12 mIU/ml	0.8-3.59 mIU/ml		

The prolactin hormone level was increased in hyperprolactemic patients and have effect on decreasing the two fertility hormones (LH and FSH), is clear in table (3), and it's shown that the mean of prolactin hormone level in hyperprolactemic patients is 42.18 ± 12.64 , while for control healthy is 10.84 ± 4.67 , this higher difference is statically significance as the difference between mean value of two group (control and patients) is higher than the LSD value which is 8.306. For LH hormone the decrease of level of this hormone in hyperprolactemic patient is highly significance as the difference of mean value for both group (Patient and control) is higher than LSD for this hormone which is 1.941, also same was for the other fertility hormone (FSH), in which it decreased in hyperprolactemic patients than in healthy control groups when the difference of mean value is higher than LSD which is 2.853.

Table 3: Effect of hyperprolactinemia on the fertility hormones level in comparison with control group

Hormone	Mean \pm SD		LSD value
	Control	Patients	
Prolactin	10.84 \pm 4.67	42.18 \pm 12.64	8.306 **
LH	5.700 \pm 1.809	2.60 \pm 0.937	1.941 **
FSH	8.251 \pm 2.477	3.71 \pm 1.077	2.853 **

** (P<0.01).

Hyperprolactinemic patients, according to type of infertility

Screening of 150 hyperprolactinemic female, according to their type of infertility with their fertility hormones gave the results shown in table (4).

As shown in table (4), the measurements of fertility hormones for both first and second infertile women and on comparison of the prolactin levels and fertility hormones in primary and in secondary infertile women, and the p value was obtained. It was found increase in prolactin level in secondary infertile women than in first infertile women when the mean is 41.1 ± 11.8 in first infertile group and 44.0 ± 16.1 in second infertile group, but the difference of PRL hormone level between two groups (first and second infertile), is 3.1 and this value is statically non-significant as its less than T-value which is 8.029. For FSH hormone its clear that the level of it is decrease in second infertile group in which its mean is 3.55 ± 1.43 , but its higher in first infertile group when its mean is 3.80 ± 1.13 . This increase is not significant as the difference between the level of this two hormone is 0.25 which is less than T-value (0.972). Also for the other fertility hormone (LH), it's clear from the table above that its level is higher in first infertile group in which the mean is 2.61 ± 1.05 but in second group is 2.59 ± 1.18 , and the difference between this two groups is 0.02 and its less than T-value 0.619 so the decreases in hormone level in second infertile women is not significant.

Table 4: Group Statistics of first and second infertile women by mean, Std. Deviations and T-Value >0.05, N= number).

Fertility type		N	Mean	St.Dv	T- value
Prolactin	Primary	97	41.1	11.8	8.029 NS
	Secondary	53	44.0	16.1	
FSH	Primary	97	3.80	1.13	0.972 NS
	Secondary	53	3.55	1.43	
LH	Primary	97	2.61	1.05	0.619 NS
	Secondary	53	2.59	1.18	

NS: Non-significant

A graphical representation of fertility hormones according to type of infertility is shown in figures (2),(3) and (4) regarding to PRL, FSH and LH respectively.

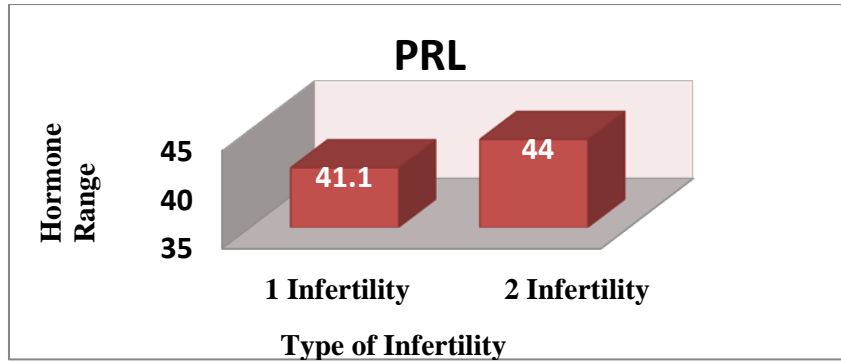


Figure 2: Prolactin levels in hyperprolactinemic infertile women categorized according to infertility type, (35, 40, 45) refers to hormone range

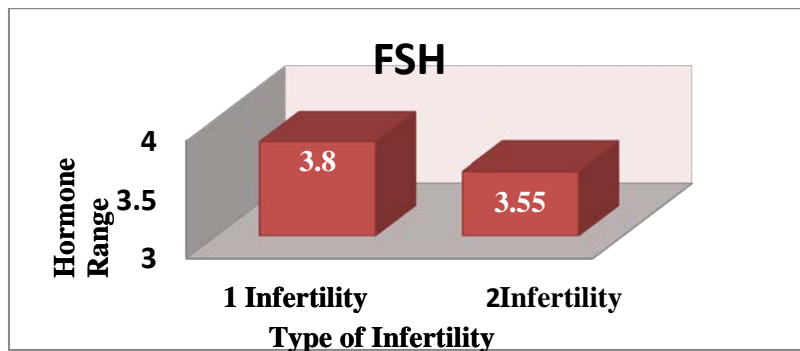


Figure 3: FSH levels in hyperprolactinemic infertile women categorized according to infertility type. (3, 3.5 and 4) refer to hormone range.

Hyperprolactinemic patients according to three age groups and types of fertility hormones.

The results in table 5, show the measurements of prolactin hormone were increased with each infertile group while the fertility hormones (LH and FSH) were decreased compared with the control group.

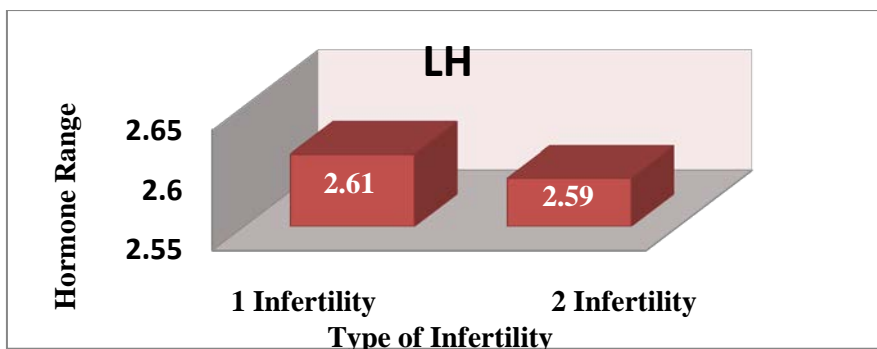


Figure 4: LH levels in hyperprolactinemic infertile women categorized according to infertility type.(2.55, 2.6 and 2.65 refers to hormone range).

The serum prolactin means and SD is 38.56 ± 12.59 , 44.10 ± 14.98 and $43.87 \pm 12.12.49$ in the three ages infertile

groups while its 10.84 ± 4.67 in the control group. It was shown from the table (3- 5), that the elevation in prolactin hormone is more in age group (31-40) years old among those other two groups (20-30), (41-50), with mean \pm standard deviation of 44.10 ± 14.98 , but the elevation is less in group 20-30 in which the mean is 38.56 ± 12.59 and noticing age group 41-50 years old the prolactin level is with mean of 43.87 ± 12.49 only in comparison with age group 31-40 years old. This differences in PRL hormone level with three ages group is not significant as the difference between hormone level in above ages group is less than the LSD value which is 9.337. For the LH hormone, the decrease in level of it is more in age group 41-50 years old, with mean 2.451 ± 1.078 , and also decreased in the other two ages group (20-30), (31-40) years old, but the decrease in hormone level between three ages group is non significant as the difference between levels of hormone for this three groups is less than LSD value which is 0.502. In contrast for the third hormone FSH its noticed that this hormone is decreased significantly in all ages group as the difference of level of this hormone is more than the LSD value which is 0.638.

Table 5: Statistical analysis of fertility measurement of hyperprolactemic females categorized according to age.

Hormone	Age group			LSD value	Control (Mean \pm SD)
	20-30 (Mean \pm SD)	31-40 (Mean \pm SD)	41-50 (Mean \pm SD)		
Prolactin	38.56 \pm 12.59 A	44.10 \pm 14.98 A	43.87 \pm 12.49 A	9.337 NS	10.84 \pm 4.67
LH	2.756 \pm 0.925 A	2.594 \pm 1.256 A	2.451 \pm 1.078 A	0.502 NS	5.700 \pm 1.809
FSH	3.915 \pm 0.956 A	4.007 \pm 1.436 A	3.199 \pm 1.168 B	0.638 *	8.251 \pm 2.477

5. Discussions

The result of this study revealed elevated prolactin concentrations in infertile subjects. By comparison between two infertile groups it was found that prolactin value of (44.0 ± 16.1) in secondary infertile women was higher than the prolactin value in primary infertile women which is (41.0 ± 11.8) . The result is coinciding with the study of Solomon *et al* (2013) stated that the concentration of prolactin has been always higher in secondary infertile women than the primary infertile women. (7). Also, according to Al- Muhammadi *et al* (2012) this is probably due to that the patients with secondary infertility consult a specialist less frequently than others because they are in less urge for seeking medical help since they already got children.(8). This delay in the treatment could be due to the fact that these cases had a marginal elevation of the prolactin and were not having any additional symptoms except infertility, so they waited for a longer period.

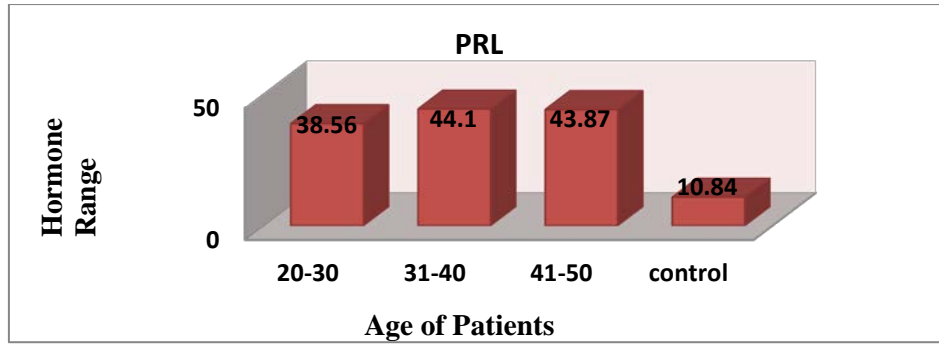


Figure 5: PRL level in three patient groups according to age and control group.(0, 20, 40 and 60 ng/ml) referred to hormone range.

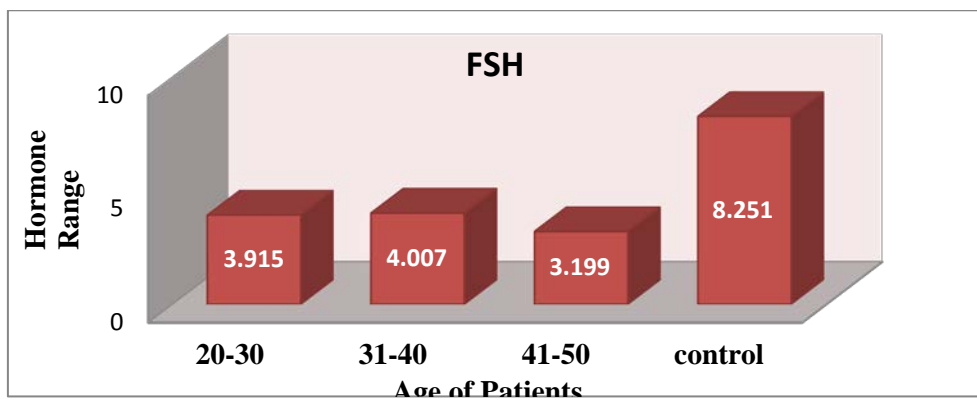


Figure 6: FSH level in three patient groups according to age and control group.(0, 2, 4, 6, 8 and 10 mIU/ml), referred to hormone range.

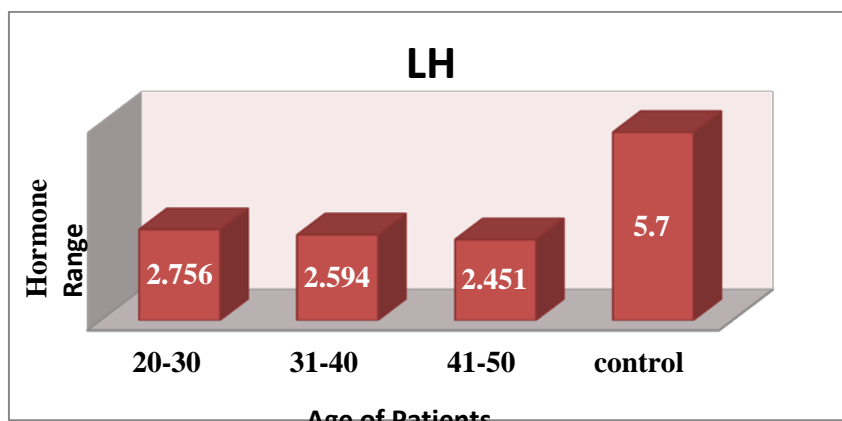


Figure 7: LH level in three patient groups according to age and control group.(0, 1, 2, 3, 4, 5 and 6 mIU/ml), referred to hormone range.

Also the obvious results showed that the highly significant increase in serum prolactin level in both infertile groups will lead to a significant decrease in serum LH and FSH as the mean of FSH is (3.80), (3.55) (mIU/ml)

for both infertile groups, respectively, and of LH (2.61)(2.59) (mIU/ml) for primary and secondary infertility group respectively, so in different groups of hyperprolactinemic women an increase in serum prolactin level and a decrease in other fertility hormones and this happened more in women with secondary infertility than women with primary infertility. Also in different age groups of hyperprolactinemic women, an increase in serum prolactin level and variation in other hormonal levels was observed, and its clear that this happened more in women with group age 30-40 years, as it shown in the figures (3-3) and (3-4).

This result coincides with the study of Lee *et al.*, (2012) that showed hyperprolactinemia decreases the pulsatile secretion of gonadotrophin-releasing hormone impairing the release of LH and FSH (9), It's clear the more increase in prolactin level among different age group was happening in age thirties, and its well-known that age plays an important role in female infertility, however, in this study the correlation between them is clear as the mean value of increasing prolactin level was in one age group than in another one (10).

This support that, when abnormal elevation started it will continue and may remain in women(10).

6. Conclusion

In conclusion, it can conclude from this study that in different groups of hyperprolactinemic women an increase in serum prolactin level and a decrease in other fertility hormones and this happened more in women with secondary infertility than women with primary infertility. Also the present study revealed that in different age groups of hyperprolactinemic women, an increase in serum Prolactin level and variation in other hormonal levels was observed, and it's clear that this happened more in women with group age 30-40.

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