

# Correlation of Prolactin and Thyroid Hormones levels with Menstrual Patterns in Infertile Women

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**Abstract-** This study was undertaken to review the impact of thyroid status on the menstrual function and fertility of the subjects. we investigated 44 women with primary infertility aged(22-35)years and Forty four fertile women with similar age and socioeconomic status were enrolled as the controls. The association between thyroid dysfunction and levels of serum prolactin,; The majority of the infertile women were euthyroid(79.5%) . The infertile women had significantly higher prolactin levels control , infertile women with raised serum prolactin levels were 29.5 % had hyperprolactinemia mean serum prolactin level was (39.45 ±3.22) ng/ml , present study revealed incidence of thyroid dysfunction in hyperprolactinemia was 20.45% had hypothyroidism, TSH (10.653±0.44)  $\mu$ iu/l, T4(0.553±0.05) ng/dl, T3( 0.421±0.11) nmol/l while it was not in the control group there were positive correlation between prolactin and TSH ( r=0.7) and negative correlation between T4 and prolactin was ( r=0.30) ,T3 and prolactin was ( r=0.08) .

also we record 30.7% of hyperprolactinemia with oligomenorrhea , Amenorrhea were detected in 15.38%.

The aims of the present study were to find the incidence and corelation of hyperprolactinemia in female infertility with hypothyroidism .

**Key Words-** hypothyroidism, hyperprolactinemia, Infertility women



## 1 INTRODUCTION

Infertility is defined as the inability to conceive after one year of regular intercourse without contraception. [1] Infertility may be caused by an underlying medical condition that may damage the fallopian tubes, interferes with ovulation, or causes hormonal complications. These medical conditions include pelvic inflammatory disease, endometriosis, polycystic ovarian syndrome, premature ovarian failure, uterine fibroids and environmental factors. Other causes of infertility in females include ovulation problems, tubal blockage, age-related factors, uterine problems, previous tubal ligation and hormone imbalance while the main cause of male infertility is poor semen quality.

Also The etiological importance of environmental factors in infertility has been stressed [2].Toxins such as glues, volatile organic solvents or silicones, physical agents, chemical dusts, and pesticides are implicated in infertility [3]. exposure to such chemicals have high chances of having primary or secondary infertility as the case may be. Estrogen-like hormone-disrupting chemicals such as phtalates are of particular concern for effects on babies of women.

Ovarian dysfunction could be caused by weight loss and excessive weight gain with body mass index (BMI) greater than 27 kg/m<sup>2</sup> [4]. Excess weight has also been found to have effect on treatment efficacy and outcomes of assisted reproductive technique [5]. Estrogen is produced by the fat cells and primary sex organs and thus, state of high body fat or obesity causes increase in estrogen production which the body interprets as birth control, limiting the chances of getting pregnant [6]. Also, too little body fat causes insufficient estrogen production and thus menstrual irregularities with anovulatory cycle [5]. Proper nutrition in early life had been linked to be a major factor for later fertility [7].

Fertility declines with age, female fertility is at its peak between the ages of 18 and 24 years [8], while, it begins to decline after age 27 and drops at a somewhat greater rate after age 35 [9]. In terms of ovarian reserve, a typical woman has 12% of her reserve at age 30 and has only 3% at age 40 [10]. 81% of variation in ovarian reserve is due to age alone [10], making age the most important factor in female infertility. Ovulatory dysfunction is more common in younger than old couples [11].

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. 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.[12] However many infertile women present with normal menses despite a raised serum prolactin level. Pituitary hormones such as TSH, prolactin or growth hormone may act synergistically with FSH and LH to enhance the entry of non-growing follicles into the growth phase [13]. Morphological changes observed in the follicles in hypothyroidism can be a consequence of higher prolactin production that may block both secretion and action of gonadotropins [14 ,15]

The prevalence of hypothyroidism in women in the reproductive age (20-40years) varies between 2%to 4%.Hypothyroidism is associated with a broad spectrum of reproductive disorder ranging from abnormal sexual development through menstrual irregularities to infertility [16].

## 2 MATERIALS AND METHODS

The study was conducted on 88 women with primary infertility (age group 22–35 years) who attended to fertility center in Al-Sadder Medical City at Al-Najif province from January 2014 to September 2014. The forty four infertile patients were diagnosed by specialist doctors. The control group included forty four healthy married women. Five milliliters of fasting venous sample obtained in the morning of day three of menstrual cycle for serum biochemical analysis. Serum was separated and stored for further analysis. All the hormones were estimated by using immunoassay methods of TSH, T3, T4 and prolactin, (ELISA kits from Monobind, USA). The normal range of serum prolactin and TSH, were 2–25 ng/ml and 0.5–4.7 mIU/L respectively, as per kit supplier's instruction. Therefore, (The upper range of normal serum prolactin level was considered 23 ng/ml); hyperprolactinemia at PRL levels of >25 ng/ml and hypothyroidism was considered at TSH levels of > 4.7  $\mu$ IU/ml. Patients with subclinical hyperthyroid as well as those with hyperthyroidism were not included in the study. Statistical analysis was done by using Mega stat and SPSS software, version 12 (SPSS Inc, Illinois, USA) a P-value <0.05 was considered statistically significant.

### 3 RESULT.

The infertile female patients were compared with the fertile females (controls) for prolactin and thyroid profile. Both Serum PRL and TSH levels were found to be increased in infertile females as compared to controls as shown in Table 1. This increase was statistically highly significant ( $p < 0.000$ ).

**Table 1:** TSH and PRL levels in control (fertile) and infertile women:

Parameter	Control		Case		P.value
	Mean	$\pm$ SE	Mean	$\pm$ SE	
<b>Prolactin ng/ml</b>	8.63	$\pm$ 0.63	20.16	$\pm$ 2.36	<0.000
<b>TSH <math>\mu</math>u/l</b>	0.86	$\pm$ 0.098	4.05	$\pm$ 0.57	<0.000
<b>T4 ng/dl</b>	1.21	$\pm$ 0.13	0.77	$\pm$ 0.034	<0.000
<b>T3 nmol/l</b>	0.714	$\pm$ 0.058	1.130	$\pm$ 0.06	<0.000

**Table 2:** Thyroid and prolactin status in infertile women (n=44)

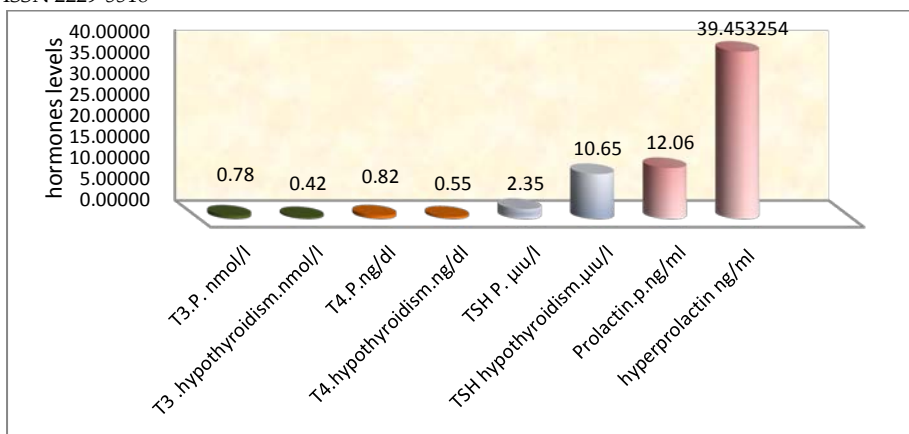
Case	No.	Hypothyroidism		Euthyroidism		Hyper prolactinemia	
		No.	%	No.	%	No.	%
<b>Infertility women</b>	44	9	20.4	35	79.5	13	29.5

**Table 3:** Thyroid status in hyperprolactemia infertile women (n=13)

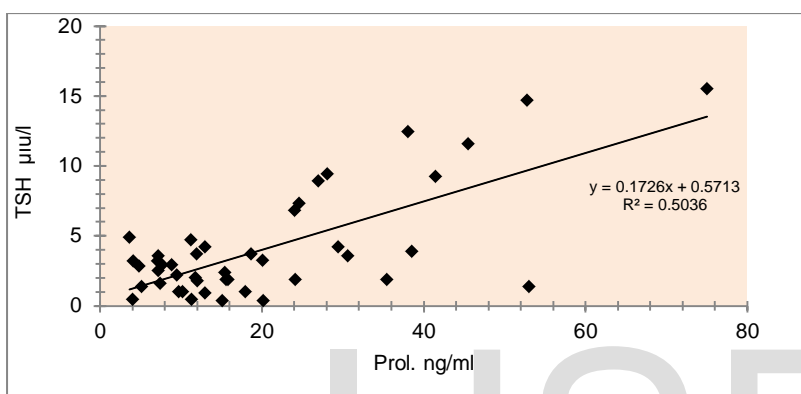
Parameter	No.	%	Mean $\pm$ SE
<b>Prolactin ng/ml</b>	13	29.5	39.45 $\pm$ 3.32
<b>TSH <math>\mu</math>u/l</b>	9	20.45	10.65 $\pm$ 0.44
<b>T4 ng/dl</b>	9	20.45	0.55 $\pm$ 0.05
<b>T3 nmol/l</b>	9	20.45	0.42 $\pm$ 0.11

**Table 4:** Menstrual disturbance in infertile women (n=44).

Clinical condition	Normal prolactine (n=31)		Hyperprolactinemia (n=13)	
	No.	%	No.	%
<b>Regular menses</b>	26	83.9	7	53.8
<b>Oligomenorrhea/ yomenorrhea</b>	4	12.9	4	30.7
<b>Amenorrhea</b>	1	3.2	2	15.38
<b>Menorrhagia</b>	0	0	0	0
<b>total</b>	31		13	

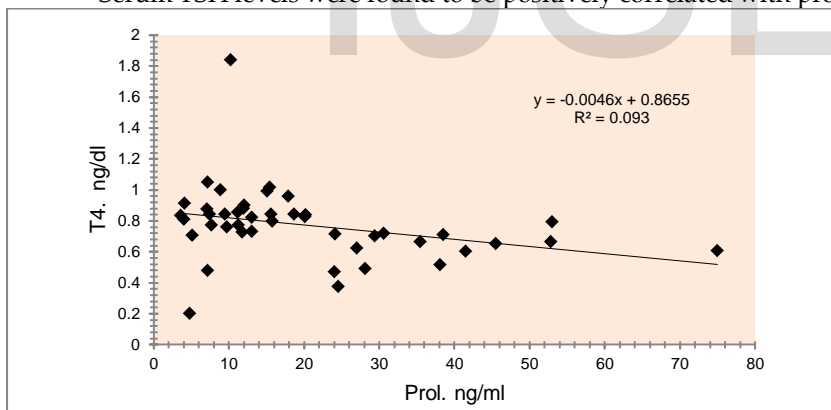


**Figure 1:** Comparison between hyperprolactinemia infertile women(n=13) and infertile women(p) (n=31).



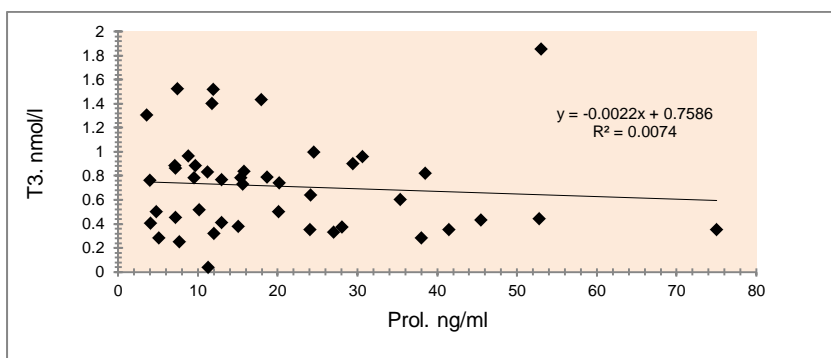
**Figure 2:** Correlation between prolactin and TSH in infertile women.

Serum TSH levels were found to be positively correlated with prolactin levels in the cases ( $r=0.7$ ,  $p=0.0189$ ).



**Figure 3:** Correlation between prolactin and T4 in infertile women .

Serum T4 levels were found to be negatively correlated with prolactin levels in the cases ( $r=0.30$ ,  $p=1.15E-18$ ).



**Figure 4:** Correlation between prolactin and T3 in infertile women .

Serum T3 levels were found to be negatively correlated with prolactin levels in the cases ( $r=0.08$ ,  $p=1.84E-09$ ).

## 4 DISCUSSION

In this study all patients under present study belong to reproductive age group (22-35) years were infertile. Table 1 show significant increase in serum TSH and prolactin hormone in infertile women as compared with control group. This result agrees with [17,18]. This finding may be due to environmental factors such as, diet, sedentary lifestyle and stress. This result goes in line with [19]. The hypothalamus, through the release of gonadotrophin releasing hormones, controls the pituitary gland which directly or indirectly controls most other hormonal glands in the human body. Thus, alterations in the chemical signals from the hypothalamus can affect the pituitary gland, ovaries, thyroid, mammary gland and hence, hormonal abnormalities. Hormonal anomalies not produce enough follicles that affect ovulation include hyperthyroidism, hypothyroidism, polycystic ovary syndrome and hyperprolactinemia [17]. Table 2 shows thyroid and prolactin status in infertile women. The percentage of women with Hyperprolactinemia about 29.5%. This result was in agreement with the [17,20]. Hyperprolactinemia (HP) is the presence of abnormally-high prolactin levels in the blood. Prolactin is produced by the anterior pituitary gland and is primarily associated with breast development during pregnancy and induces lactation. However, prolactin also binds to specific receptors in the gonads, lymphoid cells, and liver [20]. Hyperprolactinemia causes infertility by increasing the release of dopamine from the hypothalamus which inhibits gonadotrophin-releasing hormone (GnRH) and thus gonadal steroidogenesis and eventual infertility [19]. Table 2 and table 3 show percentage of Hypothyroidism about 20.4% agree with [18] who was recorded 25.5% suffering from hypothyroidism. This may be due to Hypo- and hyperthyroidism affect metabolism of sex steroids and ovarian function in women, which is often seen as menstrual irregularities [21] and about 79.5% with euthyroidism. Other workers also depicted the same pattern but indifferent level concentration of thyroid profile association with infertility women [18,22,23]. In present study, the percentage of patients who had irregular cycle in hyperprolactinemic groups was highly percentage (46.08%) increase than control women (table.4) agree with [20,23,24]. Hyperprolactinemia resulting from longstanding primary hypothyroidism has been implicated in ovulatory dysfunctions ranging from inadequate corpus luteal progesterone secretion when mildly elevated to oligomenorrhea or amenorrhea when circulating prolactin levels are high. It is demonstrated by menorrhagia or oligomenorrhea, pregnancy loss and/or infertility [23,21,24].

Fig. 1 revealed no. of infertile women (P) with normal prolactin and thyroid profile. Due to there are other factors effect infertility in women may be caused by an underlying medical condition that may damage the fallopian tubes, interferes with ovulation. These medical conditions include pelvic inflammatory disease, endometriosis, polycystic ovarian syndrome, premature ovarian failure, uterine fibroids and environmental factors. Other causes of infertility in females include ovulation problems, tubal blockage, age-related factors, uterine problems [2,3,25].

Figure 2 shows positive correlation between prolactin and TSH in infertile women [24]. Fig. 3, 4 show negative correlation between prolactin and T4, T3. Hypothyroidism itself may contribute to infertility since thyroid hormones may be necessary for the maximum production of both estradiol and progesterone [22].

## 5 CONCLUSION

In the present study there is high prevalence of hypothyroidism in infertile female. These disorders may lead to menstrual irregularities resulting in infertility. This is also associated with hyperprolactinemia and these patients are commonly associated with ovulatory failure. Hence, assessment of serum TSH and prolactin levels are mandatory in the work up of all infertile women, especially those presenting with menstrual irregularities.

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