Correlation of Prolactin and Thyroid Hormone Levels of Infertile Women
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ABSTRACT: Hyperprolactinemia is the most prevalent endocrine disorder in hypothalamic-pituitary axis especially among reproductive age female, affecting about one-third of infertile women. The prevalence of hyperprolactinemia in hypothyroidic patients is considered as a cause for reproduction disorder (infertility) and for early diagnosis and treatment of this problem. Sixty infertile female patients with primary hypothyroidism and sixty age matched (35-42 years old) apparently healthy control group, were selected from outpatients clinic of the specialized center for endocrinology and diabetes. Thyroid hormones (total triiodothyronin TT3 and tetraiodothyronin TT4), thyroid stimulating hormone (TSH) and prolactin were measured by electrochemiluminescent immunoassay method using automated analyzer and Vidus. In this study both serum TT3 and TT4 levels are significantly decreased (p<0.01) and serum TSH and prolactin levels are significantly elevated (p<0.01) in infertile group in comparison to healthy control group, in addition to a strong negative correlation was found between TT4 and prolactin hormone in infertile group.

Conclusion: measurement of TSH and thyroid hormones should be done at early stage of infertility and recommended as a routine check up in these cases.

Key words: hypothyroidism, hyperprolactinaemia, women infertility

How to cite this article: Abdullah AH, Jaafar AK, et al (2020): Correlation of prolactin and thyroid hormones levels of infertile women, Ann Trop Med & Pub Health; 23:S399. DOI: http://doi.org/10.36295/ASRO.2020.23113

INTRODUCTION
Hypothyroidism or hyperthyroidism in females along with subclinical thyroid dysfunction have been found to be associated with anovulatory cycles, decreased fecundity and increased morbidity during pregnancy1,2). Primary hypothyroidism lead to hyperprolactinemia and pituitary hyperplasia, both causes prolactinoma which limit the ability of hypothalamic dopamine to inhibit prolactin production3). This is confirmed in a study by Chafik A, et al. who administrated dopaminergic therapy and the evolution is normalization of prolactin levels4). Also pituitary tumors secreting prolactin lead to amenorrhea and infertility5). Hyperprolactinemia adversely affects the fertility potential by impairing secretion of GnRH and hence interfering with ovulation1,6). This disorder has been implicated in menstrual and ovulatory dysfunctions like amenorrhea, oligomenorrhea, anovulation, inadequate corpus luteal phase and galactorrhea7,8). 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 phase9). Morphological changes observed in the follicles in hypothyroidism can be a consequence of higher prolactin production that may block both secretion and action of gonadotropins10). Adequate thyroid supplementation restores prolactin levels as well and normalizes ovulatory function11). Even in the absence of hyperprolactinemia, hypothyroidism itself may contribute to infertility since thyroid hormones may be necessary for the maximum production of both estradiol and progesterone, Prolactin secretion is controlled by prolactin inhibitor factor that releasing hormone thyrotrophin releasing hormone (TRH) which cause
increase prolactin secretion\textsuperscript{(12)}. In fact, TRH in addition to increasing TSH raises prolactin level\textsuperscript{(13)} and in concomitant with the presence of primary hypothyroidism, the increased level of TRH can lead to galactorrhea\textsuperscript{(14)}. Previous studies reported the high incidence of hyperprolactinemia in female infertility and its correlation with hypothyroidism and a positive correlation of 1:4 was found between hypothyroidism and hyper prolactinemia\textsuperscript{(15)}.

**Aim of the study** is to evaluate the correlation between the deficiency in the thyroid hormones (TT3 and TT4) levels and the increase in the anterior pituitary gland activity throughout measurements of serum levels of (TSH) and (Prolactin) hormones in relation to the infertility.

**MATERIALS AND METHODS**

**Subjects, material and method**

This study was performed on sixty primary hypothyroid infertile female were enrolled as patients group, compared with sixty apparently healthy volunteers as control group. All participants were selected randomly from the outpatients clinic of the specialized center for endocrinology and diabetes diseases. Verbal approvals were taken from all participants prior to the study in addition to the approval of the ethics committee in the department of clinical biochemistry, College of Medicine, Al-Iraqia University and the Iraqi Ministry of Health. The studied groups, were matched in term of age range (35-42 years old). Exclusion criteria from participation in this study include pregnant and lactating women, renal failure and primary hyperprolactinemia. Five ml of venous blood aspirated from each subscriber for the measurement of serum levels of thyroid stimulating hormone (TSH), total tri-iodothyronine (TT3) and thyroxine (TT4) following the instructions in the Biomerux kit for the analysis by Vidus apparatus; whereas, measurement of serum prolactin level is done by electrochemiluminescent immunoassay method using automated analyzer apparatus.

**Statistical Analysis**

Social process statistical system (SPSS) was used to compare between the results in the studied groups, $p$ value $<0.05$ and $<0.01$ was considered to be statistically significant. Student t-test was applied and correlation coefficient ($r$) test is used to describe the association between different parameters.

**RESULTS AND DISCUSSION**

The mean serum levels of TT3 and TT4 in the patients group was significantly highly decreased in comparison to healthy control group ($P <0.01$), as shown in table (1); meanwhile, the mean serum levels of prolactin hormone and TSH in the patients group was significantly highly increased compared to control group ($P <0.01$).
Table (1): Comparison of mean serum levels of TT3, TT4, TSH and prolactin hormone between the studied groups.

<table>
<thead>
<tr>
<th>PARAMETERS</th>
<th>STUDIEDGROUPS</th>
<th>P VALUE</th>
<th>SIGNIFICANCY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PATIENTS GROUP</td>
<td>CONTROL GROUP</td>
<td></td>
</tr>
<tr>
<td>TT3 nmol/L</td>
<td>1.13±0.48</td>
<td>1.69±0.34</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>TT4 nmol/L</td>
<td>51.68±17.30</td>
<td>89.07±10.15</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>TSH mIU/ml</td>
<td>14.38±3.19</td>
<td>3.48±0.63</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Prolactin ng/ml</td>
<td>64.80±29.16</td>
<td>24.00±4.69</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

This results are agree with a study done by Lunenfeld et al who suspected that the patient with increased prolactin level is often have hypothyroidism, and hyperprolactinemia which results from a longstanding primary hypothyroidism has been implicated in ovulatory dysfunctions due to an inadequate corpus luteal progesterone secretion resulting in oligomenorrhea or amenorrhea.\(^{(16)}\). Kumkum A stated that amenorrhea occurs in hypothyroidism due to hyperprolactinemia which results from a defect in the positive feedback of oestrogen on leutinizing hormone (LH), and because of the suppression of LH and follicle stimulating hormone (FSH), and the prevalence of ovulatory dysfunction is one of the causes of female infertility\(^{(17)}\). These findings were similar to a report by Raber et al indicating that menstrual disorder was seen in 26% of the hyperprolactinemia patients\(^{(18)}\). Therefore, thyroid hormones have profound effects on reproduction, and thyroid dysfunction is implicated in a broad spectrum of reproductive disorders ranging from abnormal sexual development to menstrual irregularities and infertility, this is conducted throughout the hypothyroidism which is associated with increased production of TRH that stimulates pituitary to secrete TSH and prolactin\(^{(19)}\). In another manner, hyperprolactinemia adversely affects fertility potential by impairing GnRH pulsatility throughout lowering kisspeptin expression, and may be due to cortisol releasing hormone mediated pathway and thereby ovarian function\(^{(16 \text{ and } 20)}\).

Figure (1) shows that serum level of TT4 of the patients is negatively but strongly correlated \((p=0.001)\) with their serum level of prolactin hormone \((r=0.336)\). This finding is coincide with a results by Sharma N and et al, that a high prevalence of hyperprolactinemia was determined in infertile female and a positive association between hyperprolactinemia and hypothyroidism was detected\(^{(21)}\).
CONCLUSION

Measurement of TSH and thyroid hormones should be done at early stage of infertility and recommended as a routine check up in these cases and in hyperprolactinaemia disorder.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES


