Original article:

Correlation of thyroid hormones with infertility in reproductive age group women

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Abstract

Introduction: The infertility problem is more common phenomenon among the women now days and has increased over past 30 years. The present study was carried out to correlate thyroid hormones with infertility in the reproductive age group of women. The aim of this research work was to correlate thyroid hormones with infertility in the reproductive age group of women.

Material and methods: Total 120 infertile women, and 80 normal fertile women volunteers were selected on OPD basis between age group of 19 to 45 years. Out of 120 infertile women, 80 were of primary infertility and 40 of secondary infertility. They were screened for thyroid hormone status by Chemiluminescence Immunoassay (CLIA).

Result: There was a higher prevalence of hypothyroidism in the infertile women as compared to the fertile ones in the study group. Prevalence of hypothyroidism was more in secondary infertility. Both hypothyroidism and hyperprolactinemia may result in menstrual disorders. Oligomenorrhea was most common in infertile women. Hypothyroidism is commonly associated with ovulatory failure. Hence, assessment of serum TSH is mandatory in the work up of all infertile women, especially those presenting with menstrual irregularities. So the basic approach should be to identify those hypothyroid individuals who have greatest risk for the development of infertility. Long standing hypothyroidism may develop ovulatory dysfunction, and hyperprolactinemia. So identifying and treating hypothyroidism at an earlier stage before the appearance of ovulatory dysfunction and hyperprolactinemia, can have potentially great preventive value.

Key words: Infertility, Thyroid hormones, Chemiluminescence, Hypothyroidism

Introduction

Hormonal disorders of female reproductive system are comprised of a number of problems resulting from dysfunction of hypo-thalamic-pituitary ovarian axis. These relatively common disorders often lead to infertility. Parenthood is undeniably one of the most universally desired goals in adulthood, and most people have life plans that include children. However, not all couples who desire a pregnancy will achieve one spontaneously and a proportion of couples will need medical help to resolve underlying fertility problems. Infertility has been recognized as a public health issue worldwide.

Many people may be infertile during their reproductive years. They may be unaware of this infertility. Many parameters are outlined for the cause of infertility like age, lifestyle and physical problems etc. The infertility problem is more common phenomenon among the women now days and has increased over past 30 years. The prevalence of infertility is estimated to be between
It thus represents a common condition, with important medical, economic and psychological implications. Proper evaluation of these disorders involves a multidimensional diagnostic approach. Despite the fact that infertility is common in both men and women, it differs from life threatening diseases including cancer or AIDS, so no one worries about the possibility that he or she may be infertile or makes an effort to prevent infertility. The reason for this may be that, even if the individual is infertile, various organs of the cardiovascular system, alimentary system, etc., which are important for the health and life sustaining of the individual are normal and cause no problems in daily living activities. Therefore, individual patients generally do not recognize abnormalities of the reproductive system until they marry and attempt to conceive a child.

Thyroid dysfunction is known to affect all aspects of reproductive function in the female. Hypothyroidism or hyperthyroidism can produce infertility, abortions, stillbirths, failure of lactation and menstrual abnormalities; measurement of prolactin and thyroid hormones has been considered an important component tests for infertility. The increased prevalence of upper normal limit of serum TSH and raised anti-thyroperoxidase antibody titer indicate relatively more frequent occurrence of compensated thyroid function in infertile women than normal women of reproductive age. This necessitates considering such cases a subgroup of women in which all aspects of pituitary-thyroid axis should be thoroughly investigated than merely do with TSH testing. The present study was carried out to correlate thyroid hormones with infertility in the reproductive age group of women. The aim of this research work was to correlate thyroid hormones with infertility in the reproductive age group of women.

Material and methods
Study design - Cross sectional Study
Time period – 2010-2012
Institute – department of Biochemistry, Government Medical College, Aurangabad
Age group- 19-45 years

After written and informed consent, total 120 infertile women, and 80 normal fertile women volunteers were selected on OPD basis between age group of 19 to 45 years. Out of 120 infertile women, 80 were of primary infertility and 40 of secondary infertility.

Participants were selected on the basis of detailed history, clinical examination and laboratory investigations. Detailed history of participants including age, menstrual history, obstetric history, history of any medications, addictions, was taken.

Inclusion criteria:
1. Infertile women age between 19 to 45 years.
2. Normal fertile women age between 19 to 45 years.

Exclusion criteria:
1. Male factor infertility.
2. Patient who received medication that could alter TFT. (amiodarone an phenytoin excluding β-blockers, heparin & dopamine)
3. Amongst the female factors were tubal factor, any congenital anomaly of the urogenital tract, or any obvious organic lesion.
4. Any history of thyroid disease or previous thyroid surgery.

Biochemical investigations:
After written informed consent, 12 hour fasting venous blood samples were collected from all participants in there early follicular phase of menstrual cycle i.e. between day 3rd to 5th in plane bulbs. Serum was separated after 1 hour by centrifugation at 3000 rpm for 10 minutes, and was tested for following parameters.
Serum FT₃
Serum FT₄
Serum TSH

Method:
Quantitative estimation of all hormones done by Chemiluminescence Immunoassay (CLIA) using Acculite CLIA microwells.
Assay kits from Monobind INC., Lake Forest, CA 92630, USA.

Result

Table 1: Showing number of study subjects and their groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Subjects</th>
<th>Number (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Infertile women (cases)</td>
<td>120</td>
</tr>
<tr>
<td>II</td>
<td>Normal fertile women (control)</td>
<td>80</td>
</tr>
</tbody>
</table>

Table 2: Showing number of subgroups in group I

<table>
<thead>
<tr>
<th>Group</th>
<th>Subjects</th>
<th>Number (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IA</td>
<td>Primary infertile women</td>
<td>80</td>
</tr>
<tr>
<td>IB</td>
<td>Secondary infertile women</td>
<td>40</td>
</tr>
</tbody>
</table>

Table 3: The mean age distribution of subjects

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group IA n= 80</th>
<th>Group IB n= 40</th>
<th>Group II (Control) n= 80</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>23.525 ± 2.48</td>
<td>27.575 ± 1.94</td>
<td>27 ± 2.12</td>
</tr>
</tbody>
</table>

Table 4: Menstrual pattern in study groups:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group IA n=80</th>
<th>Group IB n=40</th>
<th>Group II n=80</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular</td>
<td>30</td>
<td>14</td>
<td>66</td>
<td>110</td>
</tr>
<tr>
<td>Oligomenorrhoea</td>
<td>36</td>
<td>20</td>
<td>14</td>
<td>70</td>
</tr>
<tr>
<td>Amenorrhoea</td>
<td>14</td>
<td>6</td>
<td>0</td>
<td>20</td>
</tr>
<tr>
<td>Total</td>
<td>80</td>
<td>40</td>
<td>80</td>
<td>200</td>
</tr>
</tbody>
</table>
Graph 1: Graphical comparison of menstrual pattern:

![Graph showing menstrual pattern comparison](image)

Table 5: Thyroid profile in Cases and Controls

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group IA n=80</th>
<th>Group IB n=40</th>
<th>Group II Control n=80</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FT3 (1.4 - 4.2pg/ml)</td>
<td>2.24 ± 1.8</td>
<td>2.16 ± 0.97</td>
<td>2.9 ± 1.14</td>
<td>&lt; 0.001*</td>
</tr>
<tr>
<td>FT4 (0.8 - 2ng/ml)</td>
<td>1.45 ± 0.67</td>
<td>1.4 ± 0.52</td>
<td>1.53 ± 0.57</td>
<td>0.53</td>
</tr>
<tr>
<td>TSH (0.39-6.16µIU/ml)</td>
<td>4.56 ± 2.54</td>
<td>4.77 ± 2.6</td>
<td>3.39 ± 1.52</td>
<td>&lt; 0.001*</td>
</tr>
</tbody>
</table>

This table shows that there is a highly significant difference in Thyroid profile components in the studied groups (P< 0.001), except FT4. Mean value of FT4 is slightly lower in infertile group than control but difference is not statistically significant. Mean value of TSH is increased in infertile women as compared to control, the difference is highly significant in control & infertile group (P< 0.001). Comparing primary and secondary infertile group TSH is slightly higher in secondary infertile women; the difference is not statistically significant.
Thyroid function status in the study population is presented in Table 6. Cases and control further divided in Euthyroid, Hyperthyroid & hypothyroid according to their thyroid hormones status. Most of the infertile women 93/120 (77.5%) and control 68/80 (85%) were euthyroid. The prevalence of hyperthyroidism in the cases and the controls were 5/120 (4%) and 6/80 (7.5%), respectively. Hypothyroidism was seen in 22/120 (18%) of the infertile women whereas in the control group it was found to be 6/80 (7.5%). The crude prevalence of hypothyroidism was higher when compared to hyperthyroidism in the infertile group.

Significantly higher serum TSH levels were noted in the infertile cases with euthyroid (p<0.5) and hypothyroidism (p<0.01) when their distributions were compared to their respective control groups.

The rise in serum FT4 and FT3 in the infertile group with hyperthyroidism was found to be non significant as compared to the control group with hyperthyroidism. The current study was designed to evaluate thyroid status in infertile women and its correlation with infertility. The individuals were divided in 2 groups according to fertility i.e. Group I Infertile women (cases), Group II Normal healthy fertile women (controls); Cases are further sub classified as Group IA (Primary infertile women) and Group IB (secondary infertile women). It is well known that in both sexes thyroid hormones influence sexual development and reproductive function. Hypothyroidism from infancy, if untreated, leads to sexual immaturity and hypothyroidism beginning before puberty causes a delay in onset of puberty followed by anovulatory cycles. It is stated in
different textbooks that in adult women, hypothyroidism results in changes in cycle length and amount of bleeding. Thyroid dysfunction is a condition known to reduce the likelihood of pregnancy and to adversely affect pregnancy outcome. Data on the relationship between thyroid disorders and infertility remain scarce and the association with a particular cause of infertility has not been thoroughly analyzed\textsuperscript{11}. Likewise, Goswami Binita et al (2009)\textsuperscript{1}, study revealed that 62.5 % of hypothyroid cases had menstrual disturbances. Kunkumet\textsuperscript{2}, had reported the menstrual abnormality to be 57.6% in their study. Oligomenorrhea was observed in (50%). In the study done by Krasses et al (1999)\textsuperscript{10}, the prevalence of menstrual irregularities (mainly Oligomenorrhea) reached 23% among 171 hypothyroid patients, while being only 8% in 214 controls (p<0.05). The authors had shown an association between the severity of menstrual abnormalities and higher serum TSH concentrations. Taken together, these findings indicate that the frequency of menstrual disturbances in hypothyroidism is approximately three times greater than in the normal population. The main menstrual irregularity observed in hypothyroid women was Oligomenorrhea,

**Thyroid profile:**

In this study, the majority of infertile (77.5%) as well as fertile (85%) women were euthyroid. However, the distribution of thyroid dysfunction in the study group was somehow different – hypothyroidism was more prevalent in the infertile group (18%) as compared to control (7.5%). The prevalence of hyperthyroidism in the cases and the controls were 4% and 7.5%, respectively. Our findings correlates with the study by Goswami Binita et al (2009), in their study they investigated 160 women with primary infertility and 80 fertile women with similar age and socioeconomic status were enrolled as the controls. The association between thyroid dysfunction and levels of serum prolactin, LH and FSH as their menstrual status were reviewed. They found most of the control (86%) and infertile women (87%) were euthyroid. Prevalence of Hypothyroidism was seen in 8% of the infertile subjects whereas in the control group it was found to be 5%. Hyperthyroidism was found in 5% of the infertile patients\textsuperscript{1}.

Elahi et al (2007)\textsuperscript{7}, in their study of infertile (140) and fertile women (152), also found most of the infertile women (89.3%), & control women (93.4%), were euthyroid. The incidence of hypothyroidism (6.4%) was slightly higher as compared to hyperthyroidism (4.3%). N. Akhter & S. A. Hassan (2009)\textsuperscript{11}, in their study of 113 infertile women, they found that prevalence of sub-clinical hypothyroidism was 6.5% and 15%, in primary and secondary infertility respectively. Where as in our study we found 16.2 & 22.5% hypothyroid women in primary and secondary infertility respectively.

These findings of above studies correlate with findings of our study in which we get high prevalence of hypothyroidism in infertile as compared to control. The prevalence of hypothyroidism in women of reproductive age (20–40 years) varies between 2% to 4%\textsuperscript{73}. Relatively higher prevalence rate of hypothyroidism in the infertile women found in our study could be due to special referral pattern of the patients who were referred to the hospital based on suspicion of thyroid abnormalities and due to exclusion of other causes of infertility i.e. tubal factor, any congenital anomaly of the urogenital tract, or any obvious organic lesion and male infertility. A relatively higher occurrence of hypothyroidism in infertile women, when compared to the control group in this study, reflects the tendency of infertile patients towards thyroid insufficiency or the vice versa.

**Conclusion:** Hypothyroidism is strongly associated with infertility, than hyperthyroidism.
Cause of infertility in Hypothyroidism: Altered peripheral estrogen metabolism, hyperprolactinemia, defects in homeostasis, and disturbances in GnRH secretion that result in an abnormal pulsatile release of LH are some of the main causes to explain the high frequency of infertility in hypothyroid women. Moreover, both Gn and T4 appear necessary to achieve maximum fertilization rates and blastocyst development.

Cramer et al showed recently that serum TSH levels are a significant predictor of fertilization failure in women undergoing In Vitro Fertilization (IVF). These data support the importance of the role of thyroid hormones in oocyte physiology.

Conclusion
The present study was carried out in 200 women classified according to fertility in normal fertile women (control), primary infertile women and secondary infertile women. The concept behind our work was to correlate thyroid hormones with infertility. There was a higher prevalence of hypothyroidism in the infertile women as compared to the fertile ones in the study group. Prevalence of hypothyroidism was more in secondary infertility. Both hypothyroidism and hyperprolactinemia may result in menstrual disorders. Oligomenorrhea was most common in infertile women. Hypothyroidism is commonly associated with ovulatory failure. Hence, assessment of serum TSH is mandatory in the work up of all infertile women, especially those presenting with menstrual irregularities.

Long standing hypothyroidism may develop ovulatory dysfunction, and hyperprolactinemia. So identifying and treating hypothyroidism at an earlier stage before the appearance of ovulatory dysfunction and hyperprolactinemia, can have potentially great preventive value. So TSH screening of all females of early reproductive age group should be done so as to detect subclinical thyroid problem and to prevent infertility risk.

References

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