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# CORRELATION BETWEEN HYPOTHYROIDISM AND INFERTILITY

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**ABSTRACT:**
**BACKGROUND:** Infertility may occur as a result of a thyroid disease that is neither diagnosed nor treated. Therefore, for fertility and conception the normal functioning of thyroid gland is necessary.

**OBJECTIVE:** To determine an association between hypothyroidism and infertility in females of reproductive age group

**METHODOLOGY:** It was a prospective observation study carried out at outpatient department of Gynecology and Endocrinology, KEMU / Mayo hospital, Lahore. 60 females of reproductive age group were included, i.e. 30 with primary infertility and 30 with secondary infertility and 30 females in control group. TSH, T4 and T3 levels were assessed and compared with control group.

**RESULTS:** The mean age of the patient in the Group A, B and control were 30.97±5.44 years, 30.63±5.46 years and 30.47±5.64 years respectively. The mean serum TSH levels in the group A, B and control were 5.09±2.025 µIU/m, 4.93±1.78 µIU/m and 3.16±1.22 µIU/m respectively. The mean T3 and T4 levels in Group A and B were 0.96±0.27 ng/ml and 12.53±1.9 ng/dl and 0.83±0.20 ng/ml and 11.6± 1.9 ng/dl respectively. Hypothyroidism was present in 66.7% of primary infertility females, 76.7% of the secondary infertility group and 10% of the control group. In secondary infertility group, hypothyroidism had a significant association with age (p value 0.028). Hypothyroidism showed an association with duration of infertility in the primary infertility group with a p value of 0.003. Hypothyroidism and infertility were positively correlated with each other (primary infertility p value 0.000 and secondary infertility p value 0.000).

**CONCLUSION:** Hypothyroidism and infertility are correlated positively with each other.

**KEY WORDS:** Hypothyroidism, Infertility, Correlation

## INTRODUCTION:

Infertility in couples is the inability to conceive after having an unprotected intercourse for a year[1, 2]. It is estimated to be present in 10-15% of general population[2]. Infertility may occur as a result of a thyroid disease that is neither diagnosed nor treated[1]. Abnormalities of thyroid hormones can result in infertility in various manners such as causing anovulation, defect in the luteal phase, raised levels of prolactin and an imbalance in the hormones related to sex[3]. Therefore, for fertility and conception the normal functioning of thyroid gland is necessary. Evaluation of thyroid function should be carried out in every woman who has a history of thyroid problem in the family, has irregularity in the menstrual cycle, has not been conceiving after a year of intercourse that is unprotected or has a history of more than two miscarriages[1,3].

Hypothyroidism is present in 2-4% of the women of reproductive age. Hypothyroidism results in dysfunction in ovulation in females that leads to infertility. It is characterized by the presence of low levels of serum thyroxine (T4) and a reduced negative feedback on hypothalamic-pituitary-ovarian axis[3]. This leads to raised thyrotropin releasing hormone secretion that further causes stimulation of thyrotropes and lactotrophs, resulting in raised levels of thyroid stimulating hormone and prolactin. This raised prolactin level that occurs as a result of hypothyroidism leads to a change in the follicles morphologically that leads to blockage of secretion and action of gonadotropins. 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.

Studies conducted in the past showed that levels of thyroid stimulating hormone significantly predicts fertilization that occurs in vitro, as levels of thyroid stimulating hormone were high significantly in women whose oocytes failed to get fertilized[7]. Hypothyroidism disrupts the metabolism of estrogen and production of sex hormone binding globulin. This effects the signals conducted through feedback loop to the hypothalamic-pituitary axis resulting in disruption and leading to infertility[7].

There is scarce data on association of thyroid disorder and infertility. So the rationale of current study is to determine an association between hypothyroidism and infertility in females of reproductive age group. This will help in creating awareness about the cause of infertility that is manageable and can improve the chances of conception thus reducing the medical, economical and psychological implications that are associated with infertility.

## METHODOLOGY:

### *Study Charactertistics:*

It was an observational prospective study that was carried out in the department of Gynaecology and Endocrinology, of King Edward Medical University / Mayo Hospital, Lahore. The study was carried out over 6 months period i.e. from July, 2023 to December, 2023, after taking ethical approval from internal review board/ethical committee. A total of 60 participants were included in the study keeping expected percentage of hypothyroidism as 4%[4].

### *Selection Criteria:*

All females between the ages of 20-45 years were enrolled in the study, after taking written informed consent, who fulfilled the definition of infertility i.e. defined as inability to conceive after a period of 1 year of unprotected intercourse (either primary or secondary infertility), and were married for more than a year. Females who had tubal blockade, pelvic inflammatory disease, endometriosis, history of other medical illness were excluded from the study. Females who had undergone thyroid surgery previously or took thyroid medicines were excluded. Cases in which infertility was related to male problem were also excluded.

### *Data Collection Procedure:*

The participants were divided into three groups, each comprising of 30 females. Group A included females with primary infertility (unable to conceive despite having regular, unprotected intercourse for a duration of more than a year), Group B included females with secondary infertility (those who

were unable to conceive after having a pregnancy previously) and Group C included females as a control who presented in the outdoor of gynecology department and had normal menstrual cycle. Detailed history, physical examination was carried out. Fasting blood samples were withdrawn from all participants to assess serum TSH,T4 and T3 levels. Hypothyroidism was labeled if the participant has TSH >4.l7 µIU/m.

Data was analyzed using SPSS version 21. Quantitative data such as age, TSH Levels, T4 levels and T3 levels were expressed as mean and standard deviation. Qualitative data such as hypothyroidism, duration of infertility, menstrual cycle regularity was expressed as frequency and percentages. Pearson correlation was applied to assess correlation between hypothyroidism and infertility. A p- value of ≤0.05 was considered as significant. Data was stratified for age, duration of infertility and menstrual cycle regularity to deal with effect modifiers. Post-stratification chi square test was applied and a p value of ≤0.05 was considered as significant.

**RESULTS;**

A total of 60 patients were enrolled in the study with infertility and were categorized as having primary infertility (n=30) and secondary infertility (n=30) and were matched with a control group. The mean age of the patient in the primary infertility group was 30.97±5.44 years, in secondary infertility group it was 30.63±5.46 years and in the control group it was 30.47±5.64 years (Table 1). The mean serum TSH levels in the primary infertility group was 5.09±2.025 µIU/m, in the secondary infertility group it was 4.93±1.78 µIU/m and in the control group it was 3.16±1.22 µIU/m (table 1). The mean T3 and T4 levels in the primary infertility group were 0.96±0.27 ng/ml and 12.53±1.9 ng/dl respectively and in the secondary infertility groups, the levels of T3 and T4 are 0.83±0.20 ng/ml and 11.6± 1.9 ng/dl respectively (Table 1).

Hypothyroidism was present in 66.7% of primary infertility females, 76.7% of the secondary infertility group and 10% of the control group (Table 2). Menstrual cycle were regular in 73.3%, 66.7% and 66.7% of the Group A, Group B and control group respectively (Table 2). In the group of primary infertility, the duration of infertility was short in 43.3% females, long in 43.3% of the females and extremely long in 13.3%, whereas in the secondary infertility group, it was short in 33.3%, long in 46.7% and extremely long in 20% (table 2).

Data was stratified for age, menstrual cycle and duration of infertility. The results showed that in secondary infertility group, hypothyroidism had a significant association with age (p value 0.028). However, it was not associated with age of females with primary infertility. With regards to menstrual cycle, hypothyroidism in primary infertility and secondary infertility groups was not associated with regularity of menstrual cycle as shown by p value >0.05. Hypothyroidism showed an association with duration of infertility in the primary infertility group with a p value of 0.003. However, it was not associated in the secondary fertility group.

Pearson correlation was applied to see correlation between hypothyroidism and infertility and it was found that both were positively correlated with each other and this correlation was statistically significant (primary infertility p value 0.000 and secondary infertility p value 0.000).

**Table 1: Showing Mean And Standard Deviation For Quantitative Variables**

| **N=60 (30 IN EACH GROUP)** | | |
|---|---|---|
| **AGE: (In years)** | **MEAN±STANDARD DEVIATION** | **P VALUE** |
| Group A | 30.97±5.44 | 0.807 |
| | 30.63±5.46 | 0.028* |
| Group B | 30.47±5.64 | 0.280 |
| Control group | | |
| **TSH:** | | |
| Group A | 5.09±2.025 | |
| Group B | 4.93±1.78 | |
| Control group | 3.16±1.22 | |

| | | |
|---|---|---|
| **T4** | | |
| **Group A** | 12.53±1.9 ng/dl | |
| **Group B** | 11.6± 1.9 ng/dl | |
| **Control group** | 5.67±0.9 | |
| **T3** | | |
| **Group A** | 0.96±0.27 ng/ml | |
| **Group B** | 0.83±0.20 ng/ml | |
| **Control group** | 1.24±0.32 | |

**p value <0.05 is significant*

**Table 2: Frequency Of Hypothyroidism, Menstrual Cycle Regularity And Duration Of Infertility And Their Association**

| **HYPOTHYROIDISM** | **GROUP A (%)N=30** | **GROUP B (%)N=30** | **CONTROL (%) N=30** |
|---|---|---|---|
| Yes | 66.7 | 76.7 | 10 |
| No | 33.3 | 23.3 | 90 |
| **MENSTRUAL CYCLE** | | | |
| Regular | 73.3 | 66.7 | 66.7 |
| Irregular | 26.7 | 33.3 | 33.3 |
| *P Value* | 0.770 | 0.222 | 0.197 |
| **DURATION OF INFERTILITY** | | | |
| ***Short Duration*** (>1 year-3 years) | 43.3 | 33.3 | |
| ***Long Duration*** (>3years-5years) | 43.3 | 46.7 | |
| ***Extremely long*** **Duration** (>5years) | 13.3 | 20 | |
| *P Value* | 0.003* | 0.182 | |

*P value <0.05 is significant*

**Table 3: Showing Correlation Of Hypothyroidism With Primary Infertility**

| **PARAMETER** | **PEARSON CORRELATION** | **P VALUE** |
|---|---|---|
| Hypothyroidism And Primary Infertility | 0.583 | 0.000 |

**Table 4: Showing Correlation Of Hypothyroidism With Secondary Infertility**

| **PARAMETER** | **PEARSON CORRELATION** | **P VALUE** |
|---|---|---|
| Hypothyroidism And Secondary Infertility | 0.673 | 0.000 |

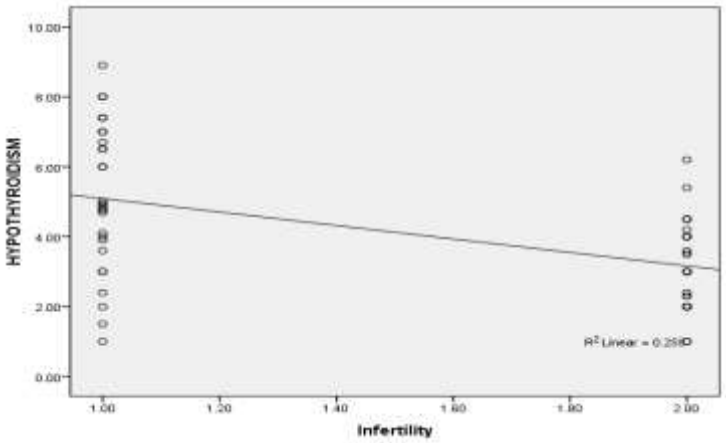


**Figure 1: Showing Linear Correlation Between Hypothyroidism And Infertility**

## DISCUSSION:

Issues related to infertility are challenging for a clinician and can be resolved by managing certain endocrinological conditions such as hypothyroidism. Profound effects have been found of thyroid on reproductive health of females. The data on the association of thyroid disorders and infertility is scare and such an association with a single entity has not been analyzed much. The current study revealed that hypothyroidism was positively correlated with both primary and secondary infertility. Hypothyroidism was significantly associated with age in the secondary infertility group and with duration of infertility in the primary infertility group. The results of current study were similar to those revealed by Valvekar U, et al. in 2016. The authors enrolled 120 females which were divided into three categories, i.e. primary infertility, secondary infertility and control. Thyroid hormones and levels of prolactin were assessed and the authors found that both these hormones were correlated positively with infertility (both primary and secondary). So the authors concluded that all women presenting with infertility should be screened for these hormones[3].

Another study conducted by Sharma P,et al. in 2017 also assessed the effects of thyroid on fertility and also evaluated the prevalence of hyperprolactinemia in females with infertility. They included 150 patients with primary infertility, secondary infertility and control. They found that 41% of infertile females had hyperprolactinemia and 6% of the control group had hyperprolactinemia. Hypothyroidism was present in 18% of the patients with primary infertility and 16% females with secondary infertility and in 8% of the control. They concluded that positive correlation is present between hypothyroidism, hyperprolactinemia and ovulatory failure. So the authors concluded that all patients with infertility should undergo screening for these hormonal issues. The results were similar to our study results as well in terms of positive correlation of hypothyroidism with primary and secondary infertility[10].

Lal RZ, et al. in 2016 also assessed the association of thyroid hormones with LH, FSH and prolactin levels in infertile females. The results showed that thyroid stimulating hormone and prolactin was correlated positively. Negative correlation was found between FSH, LH and T3 in infertile females. The authors concluded that both hypothyroidism and hyperprolactinemia have an important role in the pathophysiology of infertility. Similar results were yielded by our study. However, the current study did not evaluated the role of prolactin levels on fertility.

The current study had certain limitations. Firstly, the same size was small so it can not represent the whole general population. Secondly, it was carried out in a single center, so the results cannot be generalized. Lastly, infertility issues related to only females were assessed, however, the effects of male infertility was not taken in to account.

## CONCLUSION:

Hypothyroidism was highly prevalent in the current study in both primary infertility females and secondary infertility females. All women who present with issues of infertility must be screened for abnormality of thyroid hormones, and appropriately intervened to prevent further morbidity.

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**Ethical approval:** The study was approved by the Institutional Ethics Committee

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