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## **Correlation of hypothyroidism and reproductive health problems: A cross sectional study**

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**Abstract**--Background: Thyroid dysfunction is 10 times more common in women than in men. Hypothyroidism among women of reproductive age group is linked to menstrual irregularities, polycystic ovarian syndrome (PCOS), miscarriage and infertility. Several studies are available in the literature reporting regarding impact of hypothyroidism on one or the other isolated problems of reproductive health problems. Objectives: This study is undertaken to correlate hypothyroidism and reproductive health problems like menstrual irregularities, infertility, PCOS, recurrent pregnancy loss. Materials & Methods: Study Population: All women of age between 18-45 years with reproductive health problems like menstrual irregularities, infertility, PCOS, early pregnancy loss, recurrent pregnancy loss attending Gynaecology OPD in Vinayaka Mission's Kirupananda Variyar Medical College Hospital between March 2022-August 2022. Sample Size: 100 patients. Results: Majority (30%) in the study were belonging to the 18-24. Age group with mean age being 30.31 and median age 29 years. The study shows that majority of participants having normal BMI fall between 18-24 years of age group. Hypothyroidism with infertility was associated in 14% cases, but Test Statistic and P- Value which is found to be 1.315 and 0.711 respectively, are not statistically significant. (Fisher Exact Chi-Square Test Used). However, there was an observed clinical difference with the increased presence of infertility among hypothyroid patients. Conclusion: In present study the occurrence of hypothyroidism was found to be 16.89%. Since hypothyroidism has close association with

problems like menstrual irregularities, PCOS, miscarriages and infertility, thyroid function test should be routinely recommended for these women. Thyroid dysfunction can be corrected with simple, cost-effective treatment. This will help in improvement in pregnancy outcome and also avoid subjecting women for major surgeries for menorrhagia.

**Keywords**--estradiol, follicular stimulating hormone, hypothyroidism, infertility, menstrual irregularities, miscarriages, PCOS, reproductive age.

## Introduction

Thyroid dysfunction is a common endocrine disorder. In the US National Health and Nutrition Examination Survey, the prevalence of hypothyroidism was 4.6%(0.3 overt and 4.3% subclinical) and the prevalence of hyperthyroidism 1.3%(0.5 overt and 0.7% subclinical) in people without known thyroid disease or a family history of thyroid disease.[1] A study from eight major Indian cities have shown the prevalence of hypothyroidism in the urban India is 10.95% in which 3.47% were previously undetected, and 7.48% were self-reported cases.[2]. Thyroid dysfunction is usually acquired and may occur anytime in life. In the reproductive age women, thyroid autoimmunity is the most prevalent cause of thyroid dysfunction.[3,4] Thyroid hormones (TH) are secreted by follicular cells of the thyroid gland of which thyroxine (T4) is the major form and triiodothyronine (T3) is the predominant active form present in the circulation.

At the tissue level, TH actions are regulated by a family of intracellular deiodinases (DIOs): Hepatic type 1 DIO mediates peripheral T4 to T3 conversion; DIO2 converts T4 to T3 in the hypothalamus and pituitary, thereby playing a central role in negative feedback regulation of the hypothalamic-pituitary-thyroid axis; in contrast DIO3 converts T4 to reverse T3 and T3 to T2, thereby limiting TH action.[5] Although nongenomic actions of TH are recognized but its major actions are mediated by binding to specific receptors which are called thyroid hormone receptors (TRs) in the nucleus of target cells.[6] There are two thyroid hormone receptor genes (TRa, TRb) present on chromosomes 17 and 3, respectively. Each thyroid hormone receptor genes gene undergoes alternate splicing to generate TRa1, TRa2, TRb1, and TRb2 isoforms, each with differing tissue distributions (e.g. TRa1 is predominantly expressed in the central nervous system, myocardium, colon, and skeletal muscle; TRb1 is mostly expressed in the liver and kidney; TRb2 plays a major role in negative feedback regulation at the level of the hypothalamus and pituitary).[7,8,9]

Recently, it was reported that TRs are also present in human ovarian surface epithelium and act on ovarian follicles and shows some slight localization in granulosa cells of ovarian follicles.[10] It has been reported that THs regulate a variety of biological processes including growth, cellular oxygen consumption, metabolism, embryonic development, tissue differentiation, and maturation.[11] In mammals, down-regulation of TRs lower the fertility and decrease follicle number.[12] Hypothyroidism has been associated with the altered ovarian

function, menstrual irregularities, subfertility, and higher (recurrent) miscarriage rates, suggesting that thyroid hormone affects female reproductive axis.[13,14]

Hypothyroidism causes an increase in the levels of thyroid releasing hormone (TRH) which in turn stimulates secretion of thyroid stimulating hormone (TSH) and prolactin (PRL) and PRL inhibits the synthesis and secretion of gonadotrophins. Several studies have also confirmed abnormal menstrual patterns in overt hypothyroidism.[15] The association of hypothyroidism and infertility,[16] polycystic ovarian syndrome,[17] metabolic syndrome,[18] atherosclerosis,[19] heart disease,[20] and cognitive function are well described in the literature but studies that have focused on association in between overt hypothyroidism and female reproductive hormone are sparse particularly from Indian subcontinent. Therefore, present study aimed to intensively evaluate the relationship in between overt hypothyroidism and female reproductive hormone and effect of thyroid replacement therapy.

## **Materials and Methods**

### **Inclusion Criteria**

All women of age between 18-45 years with reproductive health problems like menstrual irregularities, infertility, PCOS, early pregnancy loss, recurrent pregnancy loss attending Gynaecology OPD in Vinayaka Mission's Kirupananda Variyar medical College Hospital.

### **Exclusion Criteria**

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- Pregnant women
  - Women with gynaecological malignancies
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### **Methodology**

The present study is a hospital based cross sectional study which includes patients of age between 18-45 years with reproductive health problems like menstrual irregularities, infertility, PCOS, early pregnancy loss, recurrent pregnancy loss attending Gynaecology OPD in Vinayaka Mission's Kirupananda Variyar Mmedical College Hospital. After getting informed consent the patient details as regard to age, parity, educational status, socio-economic status will be recorded. Detailed clinical history, menstrual history, past medical history, past surgical history, personal history and treatment history will be recorded. After calculating BMI, general physical examination, gynaecological examination, thyroid gland examination will be carried out. The data will be entered in a pre-structured proforma. Participants will be subjected to routine and relevant investigations in addition to thyroid Function Tests. Following reference values will be used to categorise. Normal values:

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- Free T3 - 2.4-4.2pg/ml
  - Free T4 - 0.7-1.24 ng/ml
  - TSH - 0.5-4.5mIU/ml

Patients with normal fT4 and high TSH were considered to have subclinical hypothyroidism (SCH); those with low fT4 and high TSH were considered to have hypothyroidism; those with normal fT4 and low TSH were considered to have subclinical hyperthyroidism; and those with high fT4 and low TSH were considered to have hyperthyroidism. After collecting the data, it will be analysed for correlation.

### Statistical Analysis

For numerical variables, descriptive statistics was performed, and the results were expressed as a mean  $\pm$  standard deviation. Pearson correlation was used for normally distributed variables. Pretreatment comparisons between controls and primary hypothyroid patients were performed by the unpaired *t*-test. The pretreatment and post treatment data of patients with hypothyroidism were compared using the paired *t*-test. The Statistical analysis was performed using the Statistical Package for the Social Sciences Version 20 ([SPSS] IBM Corporation, Armonk, NY, USA).  $P < 0.05$  was considered statistically significant.

### Results

Table 1  
Age distribution

S.No	Age group	N (%)
1	18-24 years	30 (30)
2	25-29 years	27 (27)
3	30-34 years	17 (17)
4	35-39 years	20 (20)
5	40-45 years	6 (6)

Table 1 show that the majority (30%) in the study were belonging to the 18-24. Age group with mean age being 30.31 and median age 29 years. The study shows that majority of participants having normal BMI fall between 18-24 years of age group.

Table 2  
Thyroid status

S.No	Thyroid status	N (%)
1	Normal	79 (79)
2	Subclinical hypothyroid	13 (13)
3	Overt hypothyroid	4 (4)
4	Subclinical hyper thyroid	3 (3)
5	Hyper thyroid	1 (1)

Table 3  
Thyroid status with BMI (%)

S.No	Types of BMI	Euthyroid	Hypothyroid
1	Under weight	85.7	14.3
2	Normal	89.9	10.1
3	Over weight	77.3	22.7
4	Obesity grade 1	65.2	34.8
5	Obesity grade 2	66.7	33.3

Table 4  
Cross-tabulation of status of thyroid vs. duration of bleeding

Types of bleeding	Euthyroid	Hypothyroid	P Value
Normal	56 (85)	10(15)	0.031
Hypo menorrhhea	7 (95)	1 (5)	
Menorrhagia	15 (71)	6 (29)	
Oligomenorrhhea	20 (80)	6 (20)	

Table 5  
Cross-tabulation of status of thyroid vs. PCOS

Thyroid status	PCOS absent	PCOS present	P Value
Euthyroid	66 (85)	12 (15)	0.33
Hypothyroid	12 (71)	5 (28)	

Out of 17 participants having PCOS, in 5 (28%) women were diagnosed to have hypothyroidism and 12 (15%) had normal thyroid status. This difference was found to be statistically significant with Test Statistic and P- Value 6.80 and 0.33 respectively. (Chi-Square Test used).

Table 6  
Cross-tabulation of status of thyroid vs. infertility

Fertility status	Euthyroid	Hypothyroid	P Value
No fertility	83 (70)	17 (14)	0.711
Fertility	10 (78)	3 (22)	

Hypothyroidism with infertility was associated in 14% cases, but Test Statistic and P- Value which is found to be 1.315 and 0.711 respectively, are not statistically significant. (Fisher Exact Chi-Square Test Used). However, there was an observed clinical difference with the increased presence of infertility among hypothyroid patients.

Table 7  
Cross-tabulation of status of thyroid vs. history of pregnancy loss

	Euthyroid	Hypothyroid	P Value
No pregnancy Loss	72 (83)	15 (17)	0.866
Pregnancy Loss	6 (72)	2 (28)	

Out of the 94 normal and hypothyroid patients, the history of previous abortion was not significantly associated with thyroid status with Test Statistic P- Value 0.866 and 0.626 respectively. (Fisher Exact Chi-Square Test Used). However, there was an observed clinical difference with increased abortions among hypothyroid patients.

### Discussion

In the present study having 100 women participants attending gynaecology OPD, it was noticed that (79%) were euthyroid and 13 (13%) subjects were having sub-clinical hypothyroid whereas only 4 (4%) subjects were diagnosed to have overt hypothyroidism. Hyperthyroidism was noticed in only in 1 women. 3 (3%) cases were diagnosed to have subclinical hyperthyroidism and 1(0.3%) woman having clinical hyperthyroidism. The overall occurrence of hypothyroidism accounts to 16.79%, in these rural women.<sup>12</sup> The occurrence of hypothyroidism noticed in present study is low as compared to various study conducted in other parts of India. In the study conducted at Nellore (2015) at tertiary care hospital the prevalence was 21.8%, a study conducted at sea food consuming area of Kerala (2015) it was 26.75%, study conducted in Navi Mumbai tertiary care hospital (2015) was 27%, prospective observational study at secunrabad (2016) was 19% and observational study conducted at Gujarat medical college (2017) was 29% As mentioned earlier this area is coastal, as it is a seafood consuming population the chance of iodine deficiency causing hypothyroid is not very common and so the prevalence of hypothyroidism in the present study must be less when compared to other studies. It may be also due to intake of iodized salt for last more than 3 decades that had improved iodine status overall in general population.<sup>13</sup>

The present study has comparable findings of hypothyroidism in infertility women. A study conducted in a tertiary care hospital showed correlation of hypothyroidism with infertility in 32.3% infertile women which is little high compared to other studies and this study was conducted in coastal area of Pondicherry where sea-food rich in iodine is consumed. In another hospital based descriptive study conducted in Sholapur shows association of hypothyroidism with infertility in 23%.<sup>18</sup> Other similar study conducted for infertile women with hypothyroidism, where the response of treatment was followed up, which has shown the association of increased TSH more than 4.2 mU seen in 23.9% of cases. Out of which 76.6% conceived after treatment with thyroid hormones. Other studies which were conducted at Bangladesh and Mumbai, on evaluating the thyroid status in infertile women which was shown to be associated with hypothyroidism in 22%. Excessive iodine consumption stimulates autoimmune antibodies. In their study autoimmune antibodies are not estimated. Probably these women may have increased autoimmune antibodies.

## Conclusion

Our study demonstrated that hypothyroidism in women causes menstrual irregularities, mostly oligomenorrhea. Hypothyroidism is associated with hyperprolactinemia, and it decreases the serum levels of Estradiol, T, and Glomerulonephritis which increase after achieving euthyroidism.

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