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Comparison Of Ovarian Reserve in Euthyroid and Hypothyroid Infertile Women

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ABSTRACT

Aim: The aim of the present study was to evaluate ovarian reserve in infertile women with euthyroid and hypothyroid conditions, providing insights into how hypothyroidism might influence reproductive potential.

Methods: The present study was conducted in the Department of Obstetrics &Gynaecology of Hindu Rao Hospital and associated NDMC Medical College, Delhi (Tertiary care setup) from March 2023 – Feb 2025. Cases (Hypothyroid infertile women) - 50 Control (Euthyroid infertile women) – 50 were included in the study.

Results: The majority of population (54%) of infertile women belonged to the age group of 26-30 years in both the study groups. The 31- 35 years age group had smallest presentation in both groups. The mean BMI in euthyroid group was 23.81 Kg/m² and in the hypothyroid group was 24.56 Kg/m².The mean period of infertility in euthyroid and hypothyroid group was 2.42 years 2.16 years respectively. The density plot shows similar distribution in both the groups. Euthyroid group had almost equal distribution of primary (46%) and secondary infertility (54%) whereas in hypothyroid group, the incidence of secondary infertility (66%) was twice compared to primary infertility (34%).The mean S.AMH in the euthyroid group was 2.43 ng/ml and 2.19 ng/ml in the hypothyroid group. Since the p value (0.304) was greater than 0.05, it showed that there was no statistically significant difference between the groups in terms of S.AMH.The mean S.FSH in the euthyroid group was 7.03 mIU/ml and the corresponding value in the hypothyroid group was 6.83 mIU/ml.

Conclusion: In this study, we investigated the impact of hypothyroidism on ovarian reserve in infertile women by comparing various ovarian reserve markers (AMH, FSH, E2) between euthyroid and hypothyroid groups. The results found no significant differences in these markers between the two groups, suggesting that hypothyroidism does not have a substantial impact on ovarian reserve in infertile women.

Keywords*: ovarian reserve, infertile women, euthyroid, hypothyroid.*

INTRODUCTION

Infertility has been defined by The International Committee for Monitoring Assisted Reproductive Technologies (ICMART) and the World Health Organization (WHO) as "A disease of the reproductive system defined by the inability to achieve clinical pregnancy after 12 months or more of regular unprotected sexual intercourse".[1] The prevalence of infertility varies globally, but it affects approximately 8-12% of the reproductive-aged population.[2] It is estimated that around 13-19

million couples are expected to be infertile in India at a given point of time.[3] This rate indicates that infertility is a common issue that requires more attention and resources than it often receives. The consequences of infertility are significant and multifaceted, including psychological distress, financial stress, matrimonial disharmony, domestic violence, social discrimination and personal suffering. Infertility may occur due to male factors, female factors and combination of male and female factors or may be unexplained. Despite equal contribution by males, women are blamed for it mostly, considering it as a particular problem among females, part more so in developing countries. Female-related infertility and combined male and female factors account for 33-40% and 30-35% of the causes of infertility respectively.[4]

Besides biologic factors, lifestyle factors such as exposure to pollutants, smoking, excessive alcohol use and obesity have been linked to decreased fertility in both men and women.[5] These factors suggest that infertility can often be a complex interplay of genetic, hormonal, environmental and personal health factors. Thyroid dysfunction is the most common endocrine disease in reproductive age females[6] and has been identified as an important hormonal risk factor for female infertility. The prevalence of hypothyroidism in India is 11%, inland states have a higher prevalence of hypothyroidism compared to coastal states probably due to iodine deficiency.[7] Hashimoto's thyroiditis and congenital hypothyroidism have now taken over iodine deficiency as the major cause of hypothyroidism in India.

The evaluation of the infertile couple requires consideration of all possible etiologic factors in both partners. Analysis of the semen and measurement of reproductive hormones are adequate for assessment of most infertile men, whereas investigation of ovulatory function, hormonal levels, patency of female genital tract, ovarian reserve testing are required for infertile females. Ovarian reserve serves as an indicator of a woman's reproductive potential. A reduced ovarian reserve is linked to lower pregnancy rates, repetitive implantation failure, and high risk of miscarriages.[8] Some studies suggest a negative impact of hypothyroidism on ovarian reserve while others have found no significant associations. This discrepancy in findings highlights the need for further research to clarify the relationship and extent to which thyroid status effects ovarian reserve.

With this background, this study aims to evaluate ovarian reserve in infertile women with euthyroid and hypothyroid conditions, providing insights into how hypothyroidism might influence reproductive potential.

MATERIALS AND METHODS

The present study was conducted in the Department of Obstetrics &Gynaecology of Hindu Rao Hospital and associated NDMC Medical College, Delhi (Tertiary care setup) from March 2023 – Feb 2025. Women in reproductive age group (19-35years) presenting with infertility on outpatient basis in the department of Obstetrics &Gynaecology of Hindu Rao Hospital and associated NDMC Medical College, Delhi were included in the study. Cases (Hypothyroid infertile women) - 50 Control (Euthyroid infertile women) – 50 were included in the study.

Patient Selection Criteria

Inclusion criteria

1. All patients presenting with more than 12 months period of infertility in reproductive age (19-35 years).
2. Willing to participate.

Exclusion criteria

1. Women who refuse to participate in the study.
2. Women practising contraception.
3. Age more than 35 year or less than 19 years.
4. Male factor infertility.
5. Uterine malformations, tubal factor infertility.
6. Taking treatment for infertility (ovulation induction drugs, undergone IVF cycles).
7. Women diagnosed with PCOS, Endometriosis.
8. Known case of Hypothyroidism taking levothyroxine therapy
9. Previous thyroid surgery, Radioactive Iodine Ablation therapy.
10. Patients taking medication that could alter TFT (e.g. amiodarone, phenytoin, beta blockers, heparin and dopamine etc.)
11. Tobacco/Alcohol consumption
12. History of ovarian surgery

METHOLOGY

A written informed consent obtained from women who met the inclusion criteria and who were willing to participate in the study. A detailed Performa (enclosed) filled for each patient. For each case, detailed history was taken regarding infertility followed by general, physical, systemic and gynaecological examination. General Examination: Included the general built of the patient, height, weight, BMI, pulse rate, blood pressure, respiratory rate, temperature, pallor, cyanosis, icterus, oedema, lymphadenopathy.

Systemic Examination: A thorough systemic examination was done to exclude any systemic diseases. Thyroid Examination was done to see any thyroid swelling. Per abdominal Examination: Abdomen was examined for any tenderness or lump. Local Examination: Per speculum examination: This was done to exclude any local pathology in vagina or cervix.

Bimanual Examination: This was done to find out the size, shape, position, consistency, mobility, tenderness of uterus and its appendages. After initial evaluation, investigations were sent to assess thyroid function and ovarian reserve. Evaluation of thyroid function was done by measuring serum fT3, fT4 and TSH.

The study subjects were divided into 2 groups based on the results of serum TSH

Group 1 (Euthyroid controls): Infertile women with normal TSH level (0.39–4.5 μIU/ml). Group 2 (Hypothyroid cases): Infertile women with raised TSH level >4.5 μIU/ml.

METHOD OF COLLECTION OF DATA

For analysis of TSH, fT3 and fT4, 2 ml blood sample in plain vial on empty stomach was collected which were done in fully automated cobas 411 analyzer based on electrochemiluminescence technology. Electrochemiluminescence is a kind of luminescence produced during electrochemical reactions in solutions. In electro generated chemiluminescence, electrochemically generated intermediates undergo a highly exergonic reaction to produce an electronically excited state that then emits light upon relaxation to a lower-level state. This wavelength of the emitted photon of light corresponds to the energy gap between these two states. Electrochemiluminescence excitation can be caused by energetic electron transfer (redox) reactions of electro generated species. Such luminescence excitation is a form of chemiluminescence where one/all reactants are produced electrochemically on the electrodes.

AMH was analysed using AMH ELISA Immunoassay kit by taking 2ml of blood sample in a plain vial on any day of the menstrual cycle.

FSH was analysed using a kit that utilizes the Double Antibody Sandwich ELISA technique. 2ml of blood sample in a plain vial on day 2 of the menstrual cycle.

DATA ANALYSIS

Data was collected, compiled, analysed and valid conclusions were drawn. The data entry was done in Microsoft EXCEL spreadsheet and the final analysis was done with the use of Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, ver21.0.

- Continuous variables were elaborated in the form of means/standard deviations and medians/IQRs. Categorical variables were elaborated in the form of frequencies and percentages. Data was presented in graphical manner wherever appropriate for data visualization using histograms/box-and-whisker plots/column charts for continuous data and bar charts/pie charts for categorical data.
- Group comparisons for continuously distributed data were made using independent sample 't' test when comparing two groups, and One-Way ANOVA when comparing more than two groups. Post-Hoc pairwise analysis was performed using Tukey's HSD test in One-Way ANOVA to control for alpha inflation. For non-normally distributed data, appropriate non-parametric tests in the form of Wilcoxon Test/Kruskal Wallis were test used for these comparisons.
- Chi-squared test was used for group comparisons for categorical data. In cases where the expected frequency in the contingency tables was <5 for >25% of the cells, Fisher's Exact test was used instead.
- Linear correlation between two continuous variables were explored using Pearson's correlation (for normally distributed data) and Spearman's correlation (for non- normally distributed data).

For all statistical tests, p value less than 0.05 was taken to indicate a significant difference/ Association.

ETHICAL CONSIDERATION

Due approval was taken from the Scientific Committee and Ethics Committee (IEC) of Hindu Rao Hospital, Delhi before starting the study. Objectives and purpose of the study were explained to all the Participants. They were informed that all data provided by the participants would be kept confidential and anonymous. After getting approval, informed written consent was taken from each participant prior to data collection.

RESULTS

Table 1: Age distribution in Euthyroid and Hypothyroid groups

AgeGroup	Group			Fisher'sExactTest	
	Euthyroid	Hypothyroid	Total	$\chi 2$	PValue
20-25Years	21 (42.0%)	16 (32.0%)	37 (37.0%)	1.453	0.479
26-30Years	24 (48.0%)	30 (60.0%)	54 (54.0%)		
31-35Years	5 (10.0%)	4 (8.0%)	9 (9.0%)		

Total	50 (100.0%)	50 (100.0%)	100 (100.0%)		

The mean age in euthyroid and hypothyroid group was 26.18 years and 26.44 years respectively. The majority of population (54%) of infertile women belonged to the age group of 26-30 years in both the study groups. The 31- 35 years age group had smallest presentation in both groups. There was no significant difference between the in euthyroid and hypothyroid group in terms of age (p value 0.479).

Table 2: Distribution of BMI in Euthyroid and Hypothyroid groups

BMI (Kg/m²)	Group		Wilcoxon-Mann-Whitney U Test	
	Euthyroid	Hypothyroid	W	p value
Mean (SD)	23.81 (4.06)	24.56 (3.34)	1039.000	0.147

The mean BMI in euthyroid group was 23.81 Kg/m² and in the hypothyroid group was 24.56 Kg/m². Although hypothyroidism is typically associated with weight gain due to metabolic slowdown, there was no significant difference (p value 0.147) between the groups in terms of BMI, suggesting that hypothyroidism is not associated with increased BMI in infertile women having hypothyroidism compared to euthyroid infertile women.

Table 3: Distribution of Period of Infertility in Euthyroid and Hypothyroid group

Periodof Infertility (Years)	**Group**		**Wilcoxon-Mann-WhitneyUTest**	
	Euthyroid	**Hypothyroid**	**W**	**p value**
Mean(SD)	2.42 (1.14)	2.16 (0.89)	1382.000	0.339
Min -Max	1 -6	1 – 4		

The mean period of infertility in euthyroid and hypothyroid group was 2.42 years 2.16 years respectively. The density plot shows similar distribution in both the groups. There was no significant difference (p value 0.339) between the groups in terms of period of infertility, suggesting that hypothyroidism may not significantly prolong infertility.

Table 4: Distribution of primary and secondary infertility in Euthyroid and Hypothyroid group

TypeOfInfertility	**Group**			**Chi-SquaredTest**	
	Euthyroid	**Hypothyroid**	**Total**	**χ2**	**PValue**
Primary	23 (46.0%)	17 (34.0%)	40 (40.0%)	1.500	0.221
Secondary	27 (54.0%)	33 (66.0%)	60 (60.0%)		
Total	50 (100.0%)	50 (100.0%)	100 (100.0%)		

Euthyroid group had almost equal distribution of primary (46%) and secondary infertility (54%) whereas in hypothyroid group, the incidence of secondary infertility (66%) was twice compared to primary infertility (34%). There was a higher percentage of secondary infertility in both the groups. Since the p-value was 0.221, the difference in type of infertility distribution between euthyroid and hypothyroid groups was statistically not significant.

Table 5: Distribution of S.AMH andS.FSHin Euthyroid and Hypothyroid groups

S.AMH (ng/ml)	**Group**		**Wilcoxon-Mann-WhitneyUTest**	
	Euthyroid	**Hypothyroid**	**W**	**p value**
Mean(SD)	2.43 (0.99)	2.19 (0.91)	1399.500	0.304
Range(Min–Max)	0.8 -4.93	0.58 -4.66		
S.FSH(mIU/ml)	**Group**		**Wilcoxon-Mann-WhitneyUTest**	
	Euthyroid	**Hypothyroid**	**W**	**p value**
Mean(SD)	7.03 (2.26)	6.83 (2.82)	1348.000	0.501
Min -Max	3.59 -14.6	2.91 -15.87		

The mean S.AMH in the euthyroid group was 2.43 ng/ml and 2.19 ng/ml in the hypothyroid group. Since the p value (0.304) was greater than 0.05, it showed that there was no statistically significant difference between the groups in terms of S.AMH.The mean S.FSH in the euthyroid group was 7.03 mIU/ml and the corresponding value in the hypothyroid group was 6.83 mIU/ml. The p value was more than 0.05 which suggested that there was no significant difference in the values of S.FSH between the euthyroid and hypothyroid groups of infertile women.

Table 6: Distribution of S.E2 in Euthyroid and Hypothyroid groups

S.E2 (pg/ml)	Group		Whitney-Mann-WhitneyUtest	
	Euthyroid	Hypothyroid	W	p value
Mean(SD)	68.53 (22.62)	66.07 (23.26)	1363.000	0.438
Min -Max	32 – 142.4	30.1 – 144.5		

The mean S.E2 in the euthyroid group was 68.53 pg/ml and 66.07 pg/ml in the hypothyroid group. There was no significant difference between the euthyroid and hypothyroid groups of infertile women in terms of S.E2 (p value 0.438).

DISCUSSION

The present study was a prospective case control study conducted in conducted at the Department of Obstetrics &Gynaecology of Hindu Rao Hospital and associated NDMC Medical College, Delhi. The study included 100 women, aged 19-35 years, presenting with infertility. These women were categorized into two groups based on thyroid function: euthyroid (control group) and hypothyroid (cases). Serum levels of AMH, FSH, and E2 were measured to assess ovarian reserve in both the groups. The markers of ovarian reserve were then compared between both the groups with the aim was to find an association between hypothyroidism and ovarian reserve in infertile women.

Our study had comparable age distribution in euthyroid and hypothyroid infertile women, with mean age of 26.18 years and 26.44 years in the groups respectively. The majority of population of infertile women in our study belonged to the age group of 26-30 years. Our study showed no significant difference in age distribution between euthyroid and hypothyroid groups (p = 0.479). Similarly, Abbas et al[9] (2023) reported that the mean age of euthyroid women was 29.41 years and the mean age of women with subclinical hypothyroidism was 31.75 years, with no significant difference in age between the groups (p value 0.08).Felipe et al[10] (2021) reported similar findings. That the mean age of euthyroid women as 27.2 years and 27.7 years in women with TAI group, with no significant difference in age between the groups (p value 0.18).

In our study, the majority of the women in hypothyroid and euthyroid groups had a normal BMI. Although the mean BMI was slightly higher in the hypothyroid group (24.56 ± 3.34 kg/m²) compared to the euthyroid group (23.81 ± 4.06 kg/m²), this difference was not statistically significant (p = 0.147). On the other hand, Abbas et al[9] (2023) reported a mean BMI of 26.2 ± 5.0 kg/m² in women with hypothyroidism, significantly higher than the controls having mean BMI of 23.0 ± 5.5 kg/m² with a significant p value (0.006). However, this difference could be attributed to the specific cohort from Iraq and different lifestyle factors. Zhang et al[11] (2024) found the mean BMI in the euthyroid and hypothyroid groups to be 20.81Kg/m² and 21.36 Kg/m² respectively, and reported a significant difference of BMI between the groups with a p value of 0.0001.

Duration of infertility was analysed in all infertile women in the two groups and found that the mean period of infertility was 2.42 years in the euthyroid group and 2.16 years in the hypothyroid group. Although the mean duration of infertility was slightly higher in euthyroid group but this difference was not statistically significant (p = 0.339). Additionally, weak positive correlations between S.TSH and the period of infertility were found in both groups, but these correlations was also not statistically significant (euthyroid: r = 0.19, hypothyroid: r= 0.19, p > 0.17). These results are consistent with Wu et al. (2021), who also reported no significant correlation between thyroid function and the duration of infertility, with an average infertility period of 3.6± 2.2 years in their cohort. Similarly, Zhang et al[11] (2024) found that duration of infertility was statistically insignificant (p value 0.657) between euthyroid, SCH and OH groups.

In our study, secondary infertility was more prevalent than primary infertility in both euthyroid (54.0%) and hypothyroid (66.0%) groups, though the difference was not significant (p = 0.221). On the other hand, Zhang et al[11] (2024) found primary infertility to be more common in SCH and OH group compared to euthyroid group, the difference being statistically significant with a p value of 0.0006.In our study, S.AMH levels were slightly lower in the hypothyroid group (2.19 ± 0.91 ng/ml) compared to the euthyroid group (2.43 ± 0.99 ng/ml), but this difference was not statistically significant (p = 0.304). Our study compared AMH levels in SCH and OH groups and found no difference in SCH and OH groups in terms if AMH (p value 0.816) Felipe et al. (2021) compared AMH levels in TAI group and control group and also reported no statistical difference between the groups in terms of AMH (p value 0.57).In the study by Abbas et al[9] (2023), they found significantly lower AMH in hypothyroid women compared to controls (mean AMH: 1.51 ± 0.45 ng/ml vs. 3.25 ± 1.04 ng/ml, which was statistically significant p < 0.0001.

Our study found no significant difference in the values of S.FSH between the euthyroid (mean FSH: 7.03 ± 2.26 mIU/ml) and hypothyroid group (mean FSH: 6.83 ± 2.82 mIU/ml) of infertile women (p = 0.501). We also compared FSH levels in SCH and OH groups and found no statistical difference between SCH and OH group in terms of FSH (p value 0.222). Felipe et al. (2021) reported FSH level being similar between the TAI and control group with 4.78 mIU/ml and 4.37 mIU/ml as their mean FSH respectively (p value 0.52). Abbas et al[9] (2023) found no significant difference between the groups in terms of FSH (p value 0.27).In our study, the mean S.E2 level in hypothyroid group was 68.53 pg/ml, while the mean in euthyroid group was 66.07 pg/ml. The difference between these two groups was not statistically significant (p = 0.438),

indicating that serum estradiol levels were not significantly influenced by hypothyroidism. Wu et al[12] (2021) in their study also found no significant difference in S.E2 levels when compared with TSH groups (p value 0.36). Zhang et al[11] (2024) in their study also found no statistically significant difference the mean E2 level in euthyroid and hypothyroid group with a p value of 0.08.

CONCLUSION

In this study, we investigated the impact of hypothyroidism on ovarian reserve in infertile women by comparing various ovarian reserve markers (AMH, FSH, E2) between euthyroid and hypothyroid groups. The results found no significant differences in these markers between the two groups, suggesting that hypothyroidism does not have a substantial impact on ovarian reserve in infertile women.

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