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Original Research Article

The influence of thyroid hormone replacement on endometrial receptivity in infertile women

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ABSTRACT

Background: Infertility affects 10–15% of couples worldwide, with thyroid dysfunction-especially hypothyroidism-recognized as a significant modifiable contributor. Thyroid hormones influence reproductive health by regulating ovulation, endometrial receptivity, and hormonal balance. This study aimed to assess the impact of thyroid hormone replacement (levothyroxine) on endometrial receptivity and conception outcomes in infertile women diagnosed with clinical or subclinical hypothyroidism.
Methods: Conducted as a prospective observational study at GS Medical College and Hospital, Hapur (2023–2025), it included 60 women aged 21–40 years with clinical or subclinical hypothyroidism. Participants underwent detailed clinical assessments, hormonal profiling (TSH, T3, T4, prolactin), and pelvic ultrasonography. Levothyroxine therapy was initiated and adjusted over a 3–12-month follow-up. Outcomes measured included hormonal normalization and pregnancy (via urine pregnancy test).
Result: Results showed a significant decline in TSH (12.07±8.4 to 6.26±2.96 mIU/l) and prolactin (13.9±5.67 to 10.9±3.96 ng/ml) levels post-treatment ($p<0.001$). Conception occurred in 61.5% of women with subclinical and 57.1% with clinical hypothyroidism, with no significant difference ($p=0.956$). Maximum conception was noted in women with mid-range TSH (6.5–10 mIU/l). Levothyroxine therapy improved hormonal profiles and supported conception across both groups.
Conclusion: The study concludes that early diagnosis and treatment of even mild hypothyroidism can enhance fertility outcomes, underscoring the importance of routine thyroid screening in infertility evaluations.

Keywords: Infertility, Hypothyroidism, Thyroid hormone replacement, Levothyroxine, Endometrial receptivity

INTRODUCTION

Infertility affects millions of couples around the world and for many women, the reasons can remain frustratingly unclear. Among the various hidden factors that interfere with the ability to conceive, thyroid dysfunction particularly hypothyroidism is now recognized as a significant player. While often overlooked, thyroid hormones are deeply involved in the reproductive system, influencing everything from ovulation to menstrual cycle stability and the ability of the uterus to support an embryo.[1] One of the most crucial but lesser-known aspects of fertility is endometrial receptivity the condition in which the lining of the uterus becomes ready to accept a fertilized egg. For implantation to succeed, the endometrium must undergo a series of hormonal, cellular and structural changes and thyroid hormones appear to play a key role in orchestrating these processes. In fact, researchers have found thyroid hormone receptors within the endometrial tissue itself, confirming that thyroid activity directly affects uterine readiness.[2] This connection becomes even more apparent when thyroid hormone levels are not where they should be. Autoimmune thyroid conditions like Hashimoto's thyroiditis even when not severe enough to alter standard thyroid hormone tests can still disrupt the delicate environment of the uterus, making it harder for an

embryo to implant successfully.[3] In both clinical settings and animal studies, thyroid dysfunction has been linked with reduced endometrial blood flow and decreased expression of proteins that are critical for implantation.[4]

For women facing infertility alongside thyroid issues, there is hope. Treatment with levothyroxine, a synthetic form of thyroid hormone, has been shown to restore hormonal balance, support more regular ovulation and importantly improve the endometrium's ability to support a pregnancy.[5] Although most studies focus on ovulation, some evidence also points to improved endometrial structure and function following treatment, especially in those struggling with conditions like PCOS or recurrent implantation failure.[6] Despite these encouraging findings, there are still unanswered questions. For instance, how exactly does levothyroxine therapy influence the molecular environment of the uterus? Can we better identify which patients will benefit most from treatment? And should thyroid screening become routine in fertility workups? As science continues to uncover the nuanced ways the thyroid interacts with the reproductive system, one thing becomes increasingly clear: managing thyroid health isn't just about metabolism it's also about creating the best possible conditions for new life to begin.[7,8]

Infertility continues to be a distressing health issue affecting millions of couples globally, with nearly 10–15% of reproductive-age couples experiencing difficulty conceiving. Despite major advances in reproductive medicine, many underlying causes of infertility remain unidentified or underdiagnosed. Among these, thyroid dysfunction particularly hypothyroidism and subclinical hypothyroidism has emerged as a modifiable factor with profound effects on reproductive health, including ovulation, menstrual regularity and most critically, endometrial receptivity. Therefore, the current study was conducted to explore the role of thyroid hormone replacement specifically levothyroxine on endometrial receptivity in infertile women diagnosed with clinical or subclinical hypothyroidism.

METHODS

This prospective observational study was conducted at GS Medical College and Hospital, Hapur, a tertiary care teaching hospital with a dedicated infertility clinic, from 2023 to 2025. The study aimed to assess the impact of thyroid hormone replacement on endometrial receptivity and fertility outcomes in women diagnosed with hypothyroidism. The study population consisted of infertile women between the ages of 21 and 40 years who attended the infertility outpatient department during the study period. Each infertile woman diagnosed with clinical or subclinical hypothyroidism was considered a study unit. The inclusion criteria were women aged 21–40 years, diagnosed with either clinical or subclinical hypothyroidism based on serum thyroid-stimulating hormone (TSH) and free thyroxine (T4) levels and willing to provide informed consent and participate in the treatment and follow-up protocol. Women were excluded if they had known hyperthyroidism, concurrent endocrine disorders such as diabetes mellitus or Cushing's syndrome, history of thyroidectomy or radioactive iodine treatment, systemic illnesses or malignancies or were taking medications known to affect thyroid function.

Purposive sampling was employed to enrol participants who met the inclusion criteria. The sample size comprised 60 infertile women. Data were collected through structured case record forms and clinical evaluations, including history-taking, physical examination and a panel of laboratory investigations. These included serum TSH, free T4, free triiodothyronine (T3), serum prolactin and anti-thyroid peroxidase (TPO) antibody levels. Pelvic ultrasonography was also performed to evaluate ovarian morphology. Levothyroxine therapy was initiated for hypothyroid women in doses ranging from 25 to 150 micrograms daily, adjusted every 6–8 weeks based on serial TSH levels. Participants were followed for a period of 3 to 12 months.

Treatment response was assessed through improvements in biochemical parameters (TSH, T3, T4), restoration of menstrual regularity, evidence of ovulation and confirmation of conception by urine pregnancy tests (UPT). All data collection adhered to confidentiality and ethical standards. Ethical clearance was obtained from the Institutional Ethics Committee of GS Medical College and Hospital. Informed consent was taken from all participants in both English and Hindi. For operational purposes, clinical hypothyroidism was defined as elevated TSH with low free T4 levels, while subclinical hypothyroidism was defined by elevated TSH with normal free T4. Infertility was defined as the failure to conceive after 12 months of regular unprotected intercourse. Statistical analysis was conducted using SPSS software. The Chi-square test was employed for categorical data comparisons and a p-value of less than 0.05 was considered statistically significant.

RESULTS

Table 1 shows the demographic and baseline clinical characteristics of the 60 infertile women included in the study. The most common age group was 31–35 years, comprising 19.0 (31.7%) of participants, followed by 20–25 years with 16.0 (26.7%), 26–30 years with 15.0 (25.0%) and 36–40 years accounting for 10.0 (16.7%). The mean height of the participants was 157.5±7.18 cm, with a mean weight of 65.0±8.89 kg and a mean BMI of 26.4±4.31 kg/m². Clinically significant features related to thyroid or reproductive health were noted in 43.0 (71.7%) women, while 17.0 (28.3%) had non-significant features.

Ultrasonography of the pelvis showed normal ovarian morphology in 42.0 (70.0%) women. Bilateral polycystic ovarian morphology was observed in 17.0 (28.3%) and unilateral PCOS in 1.0 (1.7%). Table 2 presents the hormonal profiles before and after levothyroxine therapy. The mean TSH level at baseline was 12.07±8.4 mIU/l,

which significantly decreased to 6.26±2.96 mIU/l at the 3-month follow-up. This change was statistically significant (t=11.1, p=0.001). Similarly, the mean prolactin level decreased from 13.9±5.67 ng/mL at baseline to 10.9±3.96 ng/mL at follow-up, with a t-value of 19.0 and p=0.001, indicating a strong therapeutic response to levothyroxine in normalizing hormonal imbalances.

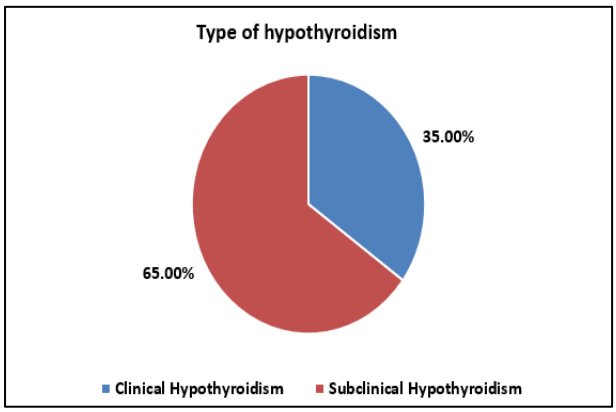

Figure 1: Distribution of study participants based on type of hypothyroidism.

Table 3 explores the relationship between TSH levels and pregnancy outcomes measured by urine pregnancy test (UPT) results. Among women with TSH in the range of 2.5–6.4 mIU/l, only 1.0 (11.1%) conceived, while 8.0 (88.9%) did not. In contrast, the highest conception rate was observed in the 6.5–10 mIU/l group, where 27.0 (93.1%) conceived and only 2.0 (6.9%) did not. For those with TSH>10 mIU/l, 8.0 (36.4%) conceived and 14.0 (63.6%) did not.

Although the trend suggests better outcomes in the mid-range TSH group, the association was not statistically significant (Fisher's exact test, p=0.054).

Table 4 compares conception rates between women with clinical and subclinical hypothyroidism. In the clinical hypothyroidism group, 12.0 (57.1%) women conceived, while 9.0 (42.9%) did not. In the subclinical hypothyroid group, 24.0 (61.5%) conceived and 15.0 (38.5%) did not. The chi-square test result (χ^2=0.003, p=0.956) indicates no statistically significant difference in conception rates between the two groups, suggesting that both types of hypothyroidism have a similar impact on fertility when treated.

Table 1: Sociodemographic and baseline characteristics of study participants (n=60).

Variable	Category/value	Frequency (N)	%
Age (in years)	20–25	16	26.70
	26–30	15	25.00
	31–35	19	31.70
	36–40	10	16.70
Mean height (cm)	157.5±7.18	—	—
Mean weight (kg)	65±8.89	—	—
Mean BMI (kg/m²)	26.4±4.31	—	—
Clinical features	Significant	43	71.70
	Non-significant	17	28.30
USG pelvis findings	Normal	42	70.00
	Bilateral PCOS	17	28.30
	Unilateral PCOS	1	1.70

Table 2: Hormonal changes following levothyroxine therapy.

Hormone	Time point	Mean±SD	95% CI	t-value	P value
TSH (mIU/l)	Baseline	12.07±8.4	9.9–14.24	11.1	0.001
	Follow-up 3	6.26±2.96	5.5–7.03	16.4	0.001
Prolactin (ng/ml)	Baseline	13.9±5.67	12.41–15.3	19	0.001
	Follow-up 3	10.9±3.96	9.84–11.9	21.2	0.001

Table 3: Association between TSH levels and conception outcomes.

TSH Range (mIU/l)	UPT positive	UPT negative	Total	Test statistic	P value
2.5–6.4	1	8	9		
6.5–10	27	2	29	5.84	0.054
>10	8	14	22		

*Fischer exact test.

Table 4: Conception rates in clinical vs subclinical hypothyroidism.

Diagnosis	Conceived	Not conceived	Total	Test statistic	P value
Clinical hypothyroidism	12	9	21		
Subclinical hypothyroidism	24	15	39	0.003	0.956
Chi-square (p value)					

*Chi square test.

DISCUSSION

Infertility remains a complex and emotionally challenging condition, often resulting from a combination of hormonal, anatomical and lifestyle factors. Among these, thyroid dysfunction especially in its subclinical form is frequently overlooked despite its substantial role in regulating reproductive health. The present study investigated the prevalence and impact of hypothyroidism in infertile women and assessed the effects of thyroid hormone replacement therapy on hormonal regulation, menstrual regularity, ovulatory function and conception outcomes. By analyzing key clinical and biochemical parameters before and after levothyroxine treatment, our findings contribute to the growing evidence that correcting thyroid imbalances can meaningfully improve fertility outcomes.

In current study, subclinical hypothyroidism was more common (39.0 or 65.0%) than clinical hypothyroidism (21.0 or 35.0%). This pattern is consistent with global epidemiological trends, where subclinical hypothyroidism is increasingly detected due to more routine TSH screening and its known association with infertility.[3] Mazzilli et al, highlighted that even in euthyroid women, thyroid autoimmunity can impact implantation and hormonal profiles, supporting the idea that subclinical thyroid dysfunction should not be dismissed in fertility evaluations.[7]

Table 2 demonstrates a statistically significant reduction in both TSH and prolactin levels following levothyroxine therapy, indicating effective correction of hypothyroidism and related endocrine imbalances. The TSH levels declined from a baseline mean of 12.07±8.4 mIU/l to 6.26±2.96 mIU/l and prolactin levels decreased from 13.9±5.67 ng/ml to 10.9±3.96 ng/m, with p values<0.001. These findings are consistent with previous literature. For example, Bucci et al, highlighted the effectiveness of levothyroxine in normalizing thyroid function in infertile women and improving ART outcomes.

Similarly, Nagalingami et al, reported significant hormonal improvements post-levothyroxine, including reductions in prolactin a known inhibitor of ovulation.[9] Contrasting evidence is rare but some studies, such as by Rao et al, argue that hormone normalization may not always translate into reproductive success, especially in older women or those with diminished ovarian reserve. Nevertheless, our findings align with the broader evidence supporting thyroid hormone therapy as a first-line intervention in hypothyroid infertility.[10] Table 3 analyses conception outcomes (urine pregnancy test results) across different TSH ranges. The highest conception rate was seen in the 6.5–10 mIU/l group (27/29 conceived), while conception was least likely in the lowest range (2.5–6.4 mIU/l), where only 1 of 9 conceived. Although the difference approached significance (Fisher's exact test, p=0.054), it did not meet the threshold. This somewhat unexpected pattern may suggest that overly rapid TSH suppression or very low TSH levels could be counterproductive in certain infertile women.

Similar trends were reported by Mazilli et al, who emphasized a U-shaped relationship between TSH and fertility where both high and low extremes impair reproductive outcomes.[7] Conversely, Arun et al, emphasized that maintaining TSH in a stricter range (below 2.5 mIU/l) improves outcomes, particularly in women undergoing ART. These differences could reflect population-specific variations and the need for individualized TSH targets based on reproductive context.[11]

Table 4 evaluates whether the type of hypothyroidism (clinical vs subclinical) influences conception outcomes. No statistically significant difference was found (p=0.956), with conception rates being 57.1% for clinical and 61.5% for subclinical hypothyroidism. These findings mirror those of Birjandi et al, who found that both clinical and subclinical forms equally affect fertility potential, especially when untreated.[12]

After levothyroxine therapy, outcomes improved across both groups, suggesting that the response to treatment, rather than the baseline TSH level, may be more predictive of success. In contrast, Bucci et al, argued that thyroid autoimmunity in subclinical hypothyroid patients may worsen implantation success even when hormone levels are normalized. However, our data did not find significant differences in conception rates, possibly due to early detection and consistent follow-up in both groups.[3]

CONCLUSION

This study highlights how often thyroid issues especially subclinical hypothyroidism go hand-in-hand with infertility in women. Many of the women we studied weren't even aware they had a thyroid imbalance until they were being evaluated for difficulty conceiving. Once diagnosed and treated with levothyroxine, not only did their hormone levels improve, but many also saw better menstrual cycles, ovulation and even successful pregnancies. Both clinical and subclinical hypothyroid patients responded similarly to treatment, showing that

even mild thyroid dysfunction can significantly impact fertility and that it's worth treating. Although we didn't find major differences in conception rates based on the severity of hypothyroidism, the overall trend was clear: early diagnosis and treatment of thyroid issues can improve reproductive outcomes. The current study findings emphasize the need for routine thyroid screening in infertility workups. By identifying and managing thyroid dysfunction early, we can offer many women a better chance at achieving pregnancy with a relatively simple and affordable intervention.

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