FOGSI FOCUS

HYPOTHYROIDISM IN WOMEN'S HEALTH

CLINICAL CONNECTION WITH PCOS, AUB, ANEMIA, AND INFERTILITY

CONTRIBUTORS

DR. AMEYA PURANDARE
DR. B. ARUNA SUMAN
DR. BASAB MUKHERJEE
DR. BIDISHA ROYCHOUDHURY
DR. KIRANMAI CHAKRAVARTHI
DR. LAXMI SHRIKHANDE
DR. MEENU AGARWAL
DR. POUSHALI SANYAL
DR. SEETHA PAL
DR. SHANTHA KUMARI
DR. SOMA DATTA

EDITORS

DR. BHASKAR PAL
DR. SUVARNA KHADILKAR

CO-EDITORS

DR. MEENU AGARWAL
DR. ARUNA SUMAN

MEDICCA PRESS™
A Medical Content Company

FOGSI TEAM 2026

Dr. Bhaskar Pal
President

Dr. Madhuri Patel
President Elect

Dr. Sunita Tandulwadkar
Imm. Past President

Dr. Suvarna Khadilkar
Secretary General

Dr. Abha Rani Sinha
Vice President

Dr. Anju Soni
Vice President

Dr. Meenu Agarwal
Vice President

Dr. Priti Kumar
Vice President

Dr. Vidya Thobbi
Vice President

Dr. Parikshit Tank
Deputy Secretary General

Dr. Niranjan Chavan
Treasurer

Dr. Ameya Purandare
Joint Treasurer

Dr. Soma Datta
Joint Secretary

FOREWORD BY THE PRESIDENT, FOGSI

It gives me great pleasure to write a foreword for this important FOGSI FOCUS titled "Hypothyroidism in Women's Health: Clinical Connection with PCOS, AUB, Anemia, and Infertility." This initiative addresses a highly prevalent yet often under-recognized condition that significantly impacts women's health across various stages of life.

Hypothyroidism remains one of the most common endocrine disorders in India. Its clinical implications extend far beyond metabolic disturbances, influencing reproductive health, menstrual pattern, fertility outcomes, and pregnancy. As highlighted in this comprehensive FOGSI FOCUS, hypothyroidism shares an intricate relationship with conditions such as polycystic ovary syndrome, abnormal uterine bleeding, anemia, and infertility—making early screening and timely intervention essential.

FOGSI FOCUS has been thoughtfully organized into five focused chapters covering the clinical overview and key women's health implications of hypothyroidism. It provides a multidimensional perspective encompassing pathophysiology, clinical manifestations, diagnostic challenges, and management strategies. The content is enriched with practical clinical insights, making it a valuable resource for clinicians striving to enhance patient care and optimize outcomes in routine practice.

I would like to extend my sincere appreciation to the FOGSI team for their dedication and scholarly contributions in bringing out this comprehensive work. Their efforts in compiling current evidence and clinical expertise will undoubtedly aid practitioners in better understanding and managing hypothyroidism in women.

I am confident that this FOGSI FOCUS will serve as a useful and reliable reference for clinicians, supporting improved diagnosis, timely treatment, and better health outcomes for women.

Warm regards,

Dr. Bhaskar Pal
MBBS, DGO, MD, DNBE (O&G), MRCOG, FICOG, FRCOG,
Obstetrician and Gynaecologist, Apollo Hospitals, Kolkata.

PREFACE

Hypothyroidism is a major public health concern, particularly in India, where nearly 42 million individuals are affected by thyroid disorders. It is the most prevalent thyroid condition in the country, affecting nearly one in ten adults.

Hypothyroidism is approximately ten times more common in women than in men. This burden is particularly significant during pregnancy, where hypothyroidism, especially subclinical, has been associated with adverse maternal and fetal outcomes. It increases the risk of abortions, anemia, pre-eclampsia, placental complications, intrauterine growth restriction, stillbirth, preterm delivery, and postpartum hemorrhage, with severe cases leading to maternal complications such as myopathy and heart failure. In the fetus, it may result in impaired neurodevelopment, congenital anomalies, and cretinism, particularly in iodine-deficient regions, thereby contributing to increased feto-maternal and neonatal morbidity and mortality.

Beyond pregnancy, hypothyroidism also plays a crucial role in the health of women of reproductive age. It is closely associated with menstrual irregularities, polycystic ovary syndrome (PCOS), anemia, and infertility. The condition disrupts reproductive function through both direct and indirect mechanisms. Directly, it alters the hypothalamic–pituitary–ovarian axis, while indirectly, it impairs ovarian function. Elevated thyroid-stimulating hormone levels may lead to hyperprolactinemia, which interferes with the pulsatile release of gonadotropin-releasing hormone, delays luteinizing hormone surge, and results in luteal phase defects. These hormonal disturbances contribute to anovulation, abnormal uterine bleeding, infertility, and an increased risk of miscarriage.

Given these associations, routine thyroid function screening in women is essential for early diagnosis, as hypothyroidism is readily treatable with effective hormone replacement therapy. Timely intervention not only relieves symptoms but also minimizes complications and improves long-term outcomes.

Recognizing the importance of this subject, we have undertaken a concise initiative to better understand the interrelationship between hypothyroidism, and PCOS, infertility, abnormal uterine bleeding, and anemia, while also discussing its pathophysiology, associated risk factors, importance of screening, and approaches to prevention and management through the use of appropriate treatment.

We wish to thank the FOGSI team for this FOGSI FOCUS booklet on “Hypothyroidism in Women’s Health: Clinical Connection with PCOS, AUB, Anemia, and Infertility.”

Dr. Shantha Kumari
MBBS, MD, DNB, FICOG, FRCPI (Ireland),
FRCOG (UK)
Senior Consultant OBGyn & Laparoscopic Surgeon,
Yashoda Hospitals, Hyderabad

TABLE OF CONTENTS

CHAPTER 1
HYPOTHYROIDISM: A CLINICAL OVERVIEW

Dr. Basab Mukherjee
MBBS (Vellore), MD (Vellore), FRCOG (London), FICOG
Director, Ankuran Fertility & Fetal Medicine Centre, Kolkata

Dr. Poushali Sanyal
MBBS, MS (O&G), DNB (O&G), MRCOG, FMAS, FICOG
Consultant, Obstetrics and Gynaecology, Motherhood Hospitals, Kolkata

Hypothyroidism is a common endocrine disorder with significant impact globally. In developed countries, its prevalence is approximately 4–5%. Hypothyroidism is about 10 times more common in women, with incidence rates of 4.1 per 1,000 women per year compared with 0.8 per 1,000 men per year. In India, hypothyroidism affects nearly 1 in 10 adults, with a prevalence of 11%, which is higher than that in the United Kingdom (2%) and the United States of America (4.6%), possibly due to long-standing iodine deficiency.[1]

Causes of hypothyroidism

- Iodine deficiency[2]
- Abnormality of the hypothalamus and the pituitary gland like pituitary or hypothalamic neoplasms, congenital hypopituitarism, tuberculosis, etc.[3]
- Autoimmune thyroid disease (Hashimoto thyroiditis)[2]
- Medications such as amiodarone, thalidomide, oral tyrosine kinase inhibitors (e.g., sunitinib, imatinib), stavudine, interferon, bexarotene, rifampin, ethionamide, phenobarbital, phenytoin, carbamazepine, interleukin-2, and lithium[2]
- Thyroid surgery[2]
- Radiotherapy to the head or neck region[2]
- Use of immune checkpoint inhibitors (e.g., anti-CTLA-4 and anti-PD-L1/PD-1 therapies)[2]

Risk factors for hypothyroidism

- Female sex[4]
- Older age (prevalence increases by 1.16% for every 10 years)[4]
- Higher body mass index (BMI)[4]
- Positive thyroid antibodies (thyroid-peroxidase antibody [TPOAb] or thyroglobulin antibody [TgAb])[4]
- Family history of thyroid disorders[2]
- Patients with autoimmune disorders or type 1 diabetes[2]

Signs and symptoms of hypothyroidism[5]

System	Common symptoms	Key signs and implications
Metabolic	Weight gain, cold intolerance, fatigue	Myxedema, hypothermia, ↑ BMI
Neuro-sensory	Hoarseness, reduced hearing/vision	Peripheral neuropathy, sensory deficits
Cardiovascular	Shortness of breath, fatigue	Bradycardia, hypertension, electrocardiogram (ECG) changes
Gastrointestinal	Constipation	Sluggish bowel sounds
Endocrine	Menstrual irregularities, infertility	Goiter, hyperprolactinemia
Neuropsychiatric	Memory impairment, depression	Delayed reflex relaxation (Woltman sign), cognitive slowing
Musculoskeletal	Muscle cramps, weakness	Elevated creatine phosphokinase, fractures caused by osteoporosis
Skin and hair	Dry skin, hair loss	Coarse skin, yellowish palms, alopecia
Hematologic/renal	Fatigue	Mild anemia, ↓ glomerular filtration rate (GFR), hyponatremia

Types of hypothyroidism

Hypothyroidism is divided into primary, secondary, tertiary, and peripheral types.[5]

- Primary hypothyroidism results from deficient thyroid hormone thyroxine (T4) production.[5]
- Secondary hypothyroidism is due to inadequate thyroid-stimulating hormone (TSH) secretion.[5]
- Tertiary hypothyroidism occurs because of deficient thyrotropin-releasing hormone (TRH).[5]
- Secondary and tertiary forms together constitute central hypothyroidism.[5]
- Peripheral hypothyroidism (also known as extra-thyroidal hypothyroidism) occurs due to inability of tissues to respond to thyroid hormone (e.g., mutations in the thyroid hormone receptor TRß).[6]

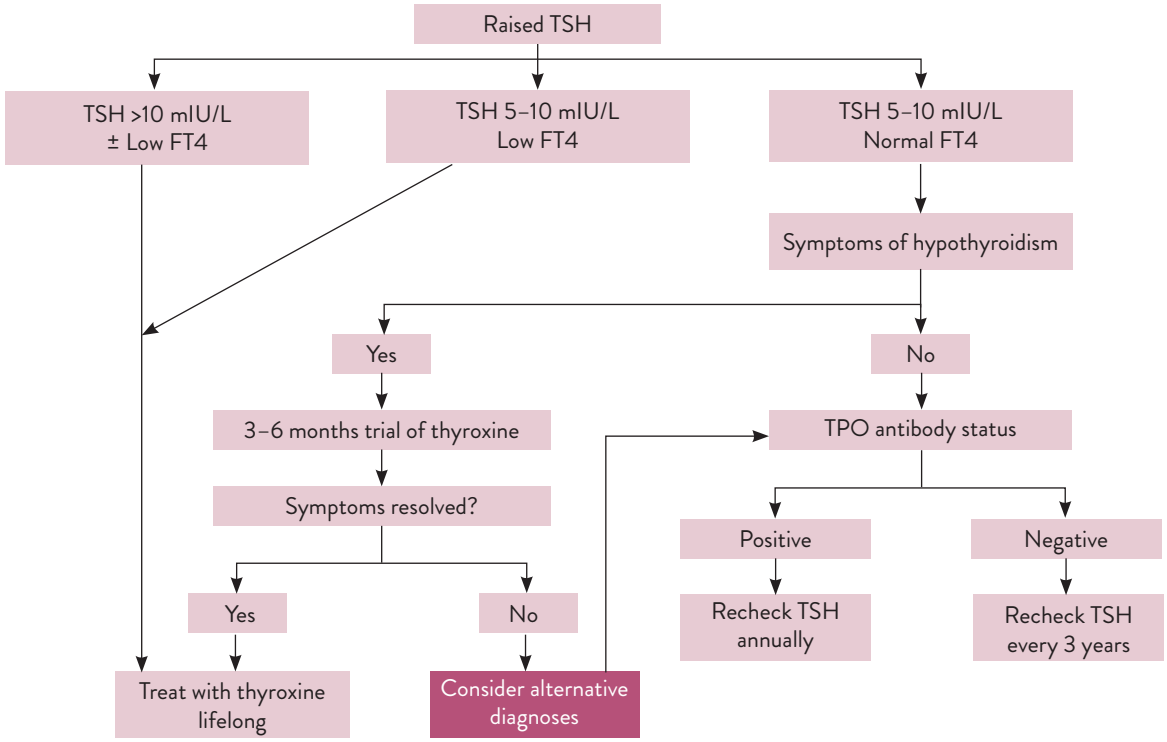
Diagnosis of hypothyroidism

Primary hypothyroidism is diagnosed by elevated serum TSH above the reference range (typically 0.5–5 mIU/L), along with low free T4 levels. In pregnancy, trimester-specific TSH ranges should be used. Although TSH shows minor diurnal and seasonal variations, these do not significantly affect diagnosis. Routine measurement of total triiodothyronine (T3), total T4, or free T3 is generally not recommended, as they are less reliable indicators of primary hypothyroidism.[5]

Management of hypothyroidism

The treatment algorithm for primary hypothyroidism is presented in Figure 1.[7]

Figure 1: Treatment algorithm for primary hypothyroidism in adults[7]



TSH: Thyroid-stimulating hormone; FT4: Free thyroxine; TPO: Thyroid peroxidase.

References

1. Kaur A, Kaur M, Mohan G. Prevalence of hypothyroidism and its epidemiological parameters among the adults in selected urban areas of Amritsar. Int J Community Med Public Health. 2025;12(12):5657-65.
2. Patil N, Rehman A, Anastasopoulou C, et al. Hypothyroidism. [Updated 2024 Feb 18]. In: StatPearls. Treasure Island (FL): StatPearls Publishing [Internet]. 2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK519536/
3. Bereda G. Definition, causes, pathophysiology and management of hypothyroidism. Mathews J Pharm Sci. 2023;7(1):14. Doi: 10.30654/MJPS.10014
4. Li J, Li Y, Shi X, et al; Thyroid Disorders, Iodine Status and Diabetes Epidemiological Survey Group. Prevalence and risk factors of hypothyroidism after universal salt iodisation: A large cross-sectional study from 31 provinces of China. BMJ Open. 2023;13(2):e064613. Doi: 10.1136/bmjopen-2022-064613
5. Zamwar UM, Muneshwar KN. Epidemiology, types, causes, clinical presentation, diagnosis, and treatment of hypothyroidism. Cureus. 2023;15(9):e46241. Doi: 10.7759/cureus.46241
6. Chaker L, Bianco AC, Jonklaas J, et al. Hypothyroidism. Lancet. 2017;390:1550-62.
7. Chakera AJ, Pearce SHS, Vaidya B. Treatment for primary hypothyroidism: Current approaches and future possibilities. Drug Des Devel Ther. 2012;6:1-11.

CHAPTER 2 HYPOTHYROIDISM AND POLYCYSTIC OVARY SYNDROME

Dr. Seetha Pal
MBBS, DGO, MD, MRCOG, FICOG, RCOG/RCR, Dip. Obst. USG
Fetal Medicine Specialist, Institute of Fetal Medicine, Kolkata

Dr. Kiranmai Chakravarthi
MBBS, DGO, DNB (O&G)
Consultant, OB & GYN, Star Hospitals, Hyderabad

Defining PCOS

Polycystic ovary syndrome (PCOS) is defined by the Rotterdam criteria, requiring the presence of at least two of the following features: oligoovulation and/or anovulation, hyperandrogenism, and polycystic ovarian morphology.[1]

Clinical implications of PCOS

Polycystic ovary syndrome presents with a spectrum of clinical manifestations ranging from menstrual irregularities, infertility, and hyperandrogenemia to metabolic syndrome. Insulin resistance and the resulting hyperinsulinemia are key contributors to the hormonal and metabolic disturbances seen in PCOS. This interplay predisposes women with PCOS to a range of complications, including endometrial hyperplasia and cancer, cardiovascular disease, miscarriage, and acanthosis nigricans (Table 1).[1,2]

Table 1: Clinical implications of PCOS[2]

Domain	Clinical implications
Metabolic/obesity-related	PCOS is associated with an increased risk of metabolic complications beginning early in life, including obesity, impaired glucose tolerance, type 2 diabetes mellitus, dyslipidemia, and hypertension.
Reproductive/obstetric	Women with PCOS are at increased risk of endometrial hyperplasia and infertility linked to chronic anovulation. During pregnancy, PCOS is associated with a higher incidence of miscarriage, gestational diabetes mellitus, pregnancy-induced hypertension, and pre-eclampsia, with risks amplified in hyperandrogenic phenotypes.
Behavioral/psychological	PCOS is linked with a higher burden of psychiatric comorbidity. Cross-sectional studies report increased prevalence of moderate-to-severe depressive and anxiety symptoms, while limited longitudinal evidence suggests an elevated risk of incident depression and anxiety.

PCOS: Polycystic ovary syndrome.

Prevalence of subclinical hypothyroidism in women with PCOS

- Subclinical hypothyroidism (SCH) is defined by elevated thyroid-stimulating hormone (TSH) levels with normal free thyroxine concentrations, affecting approximately 10% of the general population.[3]
- In women with PCOS, SCH is reported more frequently, with prevalence estimates ranging from 10% to 25%.[3]
- Evidence suggests a higher burden of thyroid disorders in PCOS. In a comparative study of 80 women with PCOS and 80 controls, the prevalence of goiter (27.5% vs. 7.5%) and SCH (22.5% vs. 8.75%) was significantly higher in the PCOS group.[4]
- In another study involving young women with PCOS, SCH, defined as a TSH level > 4.5 mIU/L, was observed in 11.3% of participants, with a mean TSH concentration of 6.1 ± 1.2 mIU/L.[4]

Pathophysiology linking hypothyroidism/subclinical hypothyroidism and ovarian dysfunction

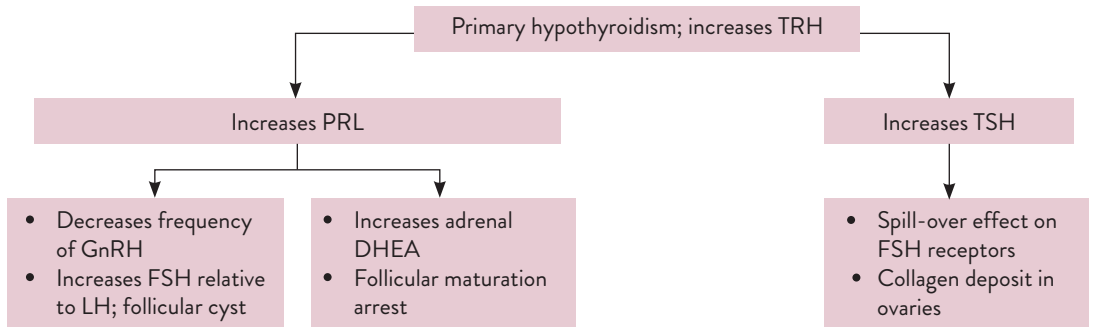
Ovarian changes in hypothyroidism/subclinical hypothyroidism

In primary hypothyroidism, elevated thyrotropin-releasing hormone (TRH) leads to rise in secretion of both TSH and prolactin. Prolactin disrupts normal ovulatory function by altering the follicle-stimulating hormone (FSH) and luteinizing hormone (LH) ratio by increasing adrenal dehydroepiandrosterone production, thereby contributing to polycystic ovarian morphology.[3]

In parallel, elevated TSH also exerts a spill-over effect on FSH receptors, further influencing ovarian follicular dynamics. Hypothyroidism has also been associated with increased collagen deposition within the ovaries, which additionally contributes to structural ovarian changes (Figure 1).[4]

The severity of ovarian morphological alterations appears to correlate with both the duration and severity of hypothyroidism. In long-standing untreated cases, particularly congenital hypothyroidism, ovarian enlargement and cystic changes can be pronounced and may mimic ovarian neoplasms.[4]

Figure 1: Pathophysiological mechanisms underlying polycystic ovarian changes in primary hypothyroidism[4]

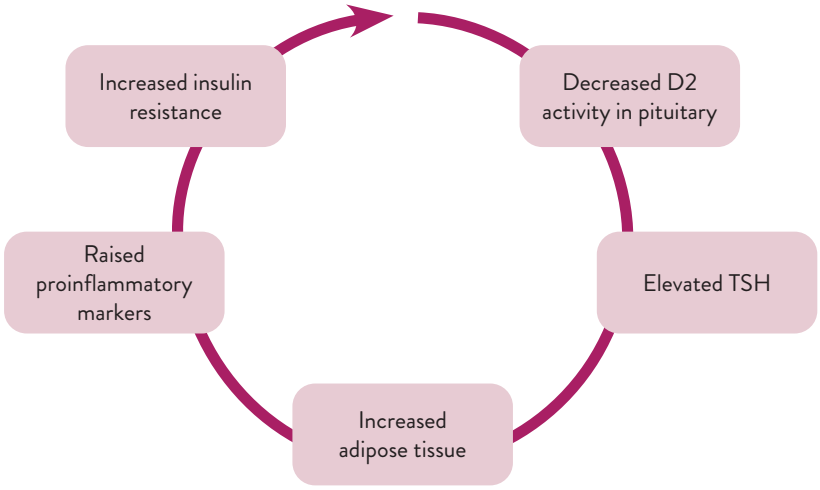


TRH: Thyrotropin-releasing hormone; PRL: Prolactin; TSH: Thyroid-stimulating hormone; GnRH: Gonadotropin-releasing hormone; DHEA: Dehydroepiandrosterone; FSH: Follicle-stimulating hormone; LH: Luteinizing hormone.

Thyroid alterations in PCOS

A key shared contributor between PCOS and hypothyroidism is increased body mass index and insulin resistance, which are commonly observed in both conditions. Elevated BMI is a part of PCOS as noted in majority of cases. Obesity is associated with a pro-inflammatory state and worsening insulin resistance, which may influence thyroid regulation through several proposed mechanisms. One pathway involves reduced deiodinase-2 activity at the pituitary level, leading to relative triiodothyronine (T3) deficiency and compensatory elevation of TSH. Another proposed mechanism implicates leptin, which increases with obesity, and stimulates hypothalamic TRH secretion. Elevated TSH, irrespective of the initiating pathway, further contributes to adipocyte proliferation and increases production of pro-inflammatory markers via TSH receptors expressed on adipocytes. These interactions suggest a bidirectional relationship between PCOS, obesity, insulin resistance, and altered thyroid function (Figure 2).[4]

Figure 2: Hypothesized link between adiposity and elevated TSH level[4]

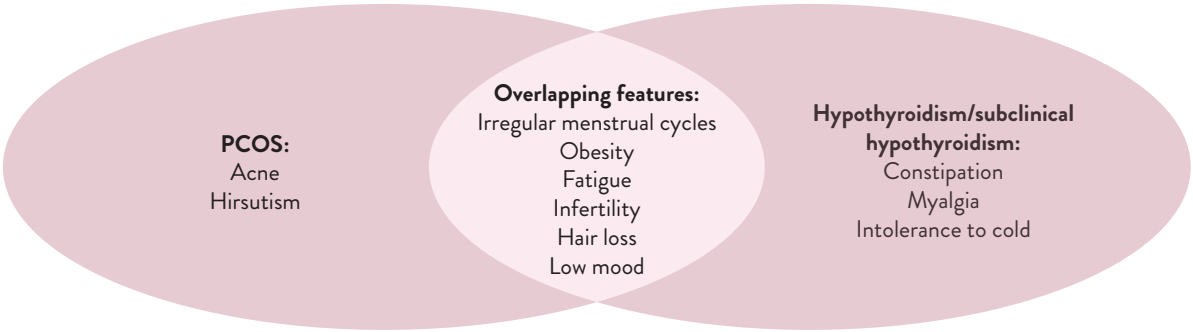


TSH: Thyroid-stimulating hormone; D2: Deiodinase-2.

PCOS and hypothyroidism/SCH: Overlapping clinical features

Overlapping clinical manifestations—such as fatigue, weight gain, depressive symptoms, and menstrual irregularities—may lead to diagnostic confusion, particularly in middle-aged women.[5] Figure 3 illustrates the shared clinical findings observed in PCOS and SCH.[6]

Figure 3: Shared clinical features observed in PCOS and hypothyroidism/subclinical hypothyroidism[6]



PCOS: Polycystic ovary syndrome.

Diagnostic challenges

- PCOS poses diagnostic challenges due to its heterogeneous clinical presentation and broad symptom spectrum.[6]
- The Rotterdam criteria, based on polycystic ovarian morphology, hyperandrogenism, and ovulatory dysfunction, are widely used; however, some PCOS phenotypes may not be fully captured, increasing the risk of underdiagnosis.[6]
- Diagnostic complexity is further increased when PCOS coexists with hypothyroidism, as both conditions share overlapping features such as menstrual irregularities, weight gain, and infertility, which can complicate clinical differentiation, particularly in middle-aged women.[5,7]

- Both conditions impair fertility and disrupt the reproductive cycle. Thyroid hormone deficiency can interfere with ovulation, leading to luteal phase defects, and disturb sex hormone balance, potentially giving rise to polycystic ovarian changes that resemble those observed in PCOS.[5]
- Hypothyroidism, particularly in its subclinical form, can be difficult to identify as clinical symptoms are often mild and biochemical findings may fall within reference ranges.[7]
- Nonspecific features such as fatigue and weight gain may be attributed to PCOS rather than thyroid dysfunction, potentially delaying accurate diagnosis and appropriate management.[7]

Diagnostic evaluation of PCOS

Rotterdam criteria

- There is no single diagnostic test for PCOS; diagnosis is based on a combination of clinical, biochemical, and ultrasonographic features.[2]
- The International Evidence-Based Guideline recommends the use of the Rotterdam criteria, which require the presence of any two of the following three features in adult women:[2,5]
  - Oligo- or anovulation
  - Clinical or biochemical hyperandrogenism
  - Polycystic ovarian morphology on ultrasound

PCOS phenotypic classification

The guidelines endorse the use of phenotype descriptions when diagnosing PCOS, defining four phenotypes (A–D) based on the presence or absence of the three diagnostic criteria (Table 2).[2]

Table 2: PCOS phenotypes as defined by the Rotterdam diagnostic criteria[2]

Phenotype	Androgen excess	Ovulatory dysfunction	PCOM on ultrasound
A	✓	✓	✓
B	✓	✓	–
C	✓	–	✓
D	–	✓	✓

PCOM: Polycystic ovarian morphology; PCOS: Polycystic ovary syndrome.

Evaluation of hyperandrogenism and ovulatory function

- Androgenic status can be assessed using biochemical measures or clinical features, with androgen excess clinically indicated by cutaneous manifestations such as hirsutism (assessed by the modified Ferriman-Gallwey score), acne, or alopecia.[2]
- Ovulatory dysfunction is indicated by oligo-anovulation, with irregular menses as the clinical marker; when irregular menses coexist with clinical or biochemical hyperandrogenism, pelvic ultrasound is not required for diagnosis.[2]

Diagnostic algorithm for PCOS

The summary of the diagnosis of PCOS is outlined in Figure 4.[8,9]

Figure 4: Overview of PCOS diagnosis[8,9]

Step 1: Irregular menstrual cycles with clinical hyperandrogenism

Test for TSH, serum prolactin, and 17-hydroxyprogesterone

Exclude other causes based on clinical features (e.g., Cushing's syndrome, thyroid dysfunction, pregnancy, etc.)

→ **PCOS can be diagnosed**

Step 2: Irregular menstrual cycles without clinical hyperandrogenism

Assess biochemical hyperandrogenism and exclude other causes (Cushing's syndrome, thyroid dysfunction, pregnancy, etc.)

→ **PCOS can be diagnosed if biochemical hyperandrogenism is present**

Step 3: Presence of only one diagnostic feature (irregular cycles or hyperandrogenism)

Adolescents: Pelvic ultrasound is not recommended; classify as at risk for PCOS and reassess later

Adults: Perform pelvic ultrasound to assess PCOM; if PCOM is present and other causes (e.g., Cushing's syndrome, thyroid dysfunction, pregnancy, etc.) are excluded

→ **PCOS can be diagnosed**

Note: Hypogonadotropic hypogonadism, usually related to low body fat or intensive exercise, should be excluded clinically and by LH/FSH assessment where appropriate. TSH: Thyroid-stimulating hormone; PCOM: Polycystic ovarian morphology; PCOS: Polycystic ovary syndrome; LH: Luteinizing hormone; FSH: Follicle-stimulating hormone.

Importance of screening and early detection of thyroid disorders in PCOS

- Thyroid dysfunction and serum prolactin levels should be screened before establishing a diagnosis of PCOS.[10]
- Polycystic ovary syndrome is considered a diagnosis of exclusion. During diagnostic evaluation, all women should be screened to exclude other disorders that can mimic the clinical features of PCOS, including thyroid dysfunction, hyperprolactinemia, and non-classical congenital adrenal hyperplasia (Table 3).[1]
- Mild hyperprolactinemia and SCH are commonly observed in women with PCOS. Therefore, referral to a specialist is recommended when elevated prolactin levels or abnormal thyroid-stimulating hormone (TSH) and free thyroxine values are detected.[1]

Table 3: Investigations for exclusion of PCOS[1]

Test	Disorder excluded	Abnormal values
Serum TSH	Thyroid disease	• Hypothyroidism: TSH > upper limit (0.5–5 mIU/L) • Hyperthyroidism: TSH < lower limit (<0.1 mIU/L)
Serum prolactin	Prolactin excess	> Upper limit of normal (2–29 ng/mL)
Serum 17-hydroxyprogesterone*	Nonclassical congenital adrenal hyperplasia	Early follicular phase of a normal cycle: 200–400 ng/dL

*Sample to be collected before 8 am. PCOS: Polycystic ovary syndrome; TSH: Thyroid-stimulating hormone.

Guideline recommendations on screening of thyroid disorders in PCOS

- Routine assessment of thyroid function and thyroid-specific autoantibodies in women with PCOS, particularly during preconception and throughout pregnancy, is strongly recommended.[11]

- Table 4 summarizes guideline-based recommendations underscoring the importance of excluding thyroid dysfunction during the diagnostic evaluation of PCOS.[1,9,10]

Table 4: Guideline recommendations emphasizing exclusion of thyroid dysfunction in suspected PCOS[1,9,10]

Guideline	Recommendation statement
AAFP	Recommends screening for thyroid disease in all women with suspected PCOS, as thyroid dysfunction can mimic key clinical features of PCOS. PCOS should be diagnosed only after exclusion of pregnancy, thyroid disorders, hyperprolactinemia, and nonclassical congenital adrenal hyperplasia.
Indian Consensus Guidelines	Emphasize that PCOS is a diagnosis of exclusion and advise mandatory screening to exclude thyroid disease, prolactin excess, and nonclassical congenital adrenal hyperplasia, which may mimic the clinical features of PCOS.
Endocrinology Committee of FOGSI	Thyroid dysfunction and serum prolactin levels should be screened before establishing a diagnosis of PCOS.

AAFP: American Academy of Family Physicians; PCOS: Polycystic ovary syndrome; FOGSI: Federation of Obstetric and Gynecological Societies of India.

Management of hypothyroidism and PCOS

Therapeutic approaches for the management of hypothyroidism and PCOS

A multidisciplinary approach is essential for the effective management of patients with PCOS and hypothyroidism and may include the following.[7]

Hormone replacement therapy

- Thyroid hormone replacement with synthetic T4 is the cornerstone of hypothyroidism management, aimed at restoring euthyroidism, improving reproductive outcomes, and preventing complications.[6]
- Regular monitoring of thyroid function is essential to ensure adequate hormone replacement.[7]
- Levothyroxine is also effective in patients with PCOS who have mildly elevated TSH levels.[11]

Lifestyle modification

- Dietary interventions and structured physical activity are recommended to improve insulin sensitivity and metabolic parameters in both PCOS and hypothyroidism.[7]

Role of levothyroxine in the management of subclinical and overt hypothyroidism in women with PCOS

In women with PCOS and coexisting hypothyroidism or SCH:[11]

- Levothyroxine therapy may partially restore pathophysiological mechanisms altered in hypothyroidism and SCH, including in the presence of autoimmune thyroiditis.
- Treatment may improve ovulatory function by normalizing menstrual cyclicity and exerting beneficial effects on oocyte and endometrial quality.
- Levothyroxine may also favorably influence cardiovascular risk factors, contributing to improved reproductive outcomes and a potential long-term reduction in cardiometabolic risk.

Levothyroxine supplementation improves ovulation and pregnancy outcomes in women with PCOS and subclinical hypothyroidism[12]

Aim

To evaluate the effect of levothyroxine on ovulation and pregnancy outcomes in women with infertility with PCOS and SCH undergoing ovulation induction with clomiphene citrate (CC).

Methods

Prospective observational study of 220 women with PCOS and SCH undergoing ovulation induction, allocated to CC plus levothyroxine or CC alone.

Results

Compared with CC monotherapy, the addition of levothyroxine resulted in:

- Significantly higher ovulation rates ($p < 0.001$)
- Greater endometrial thickness ($p < 0.05$)
- Increased number of dominant follicles, reflecting improved ovarian response ($p < 0.001$)
- Higher pregnancy rates ($p < 0.001$)

Conclusion

Levothyroxine significantly improves ovulation and pregnancy outcomes in women with infertility with PCOS and SCH undergoing ovulation induction with CC.

Levothyroxine therapy reverses ovarian enlargement and androgen abnormalities in untreated primary hypothyroidism[13]

Aim

To evaluate the effects of thyroid hormone replacement on hormonal changes, ovarian volume, and its appearance.

Methods

An open, prospective study in 26 women with untreated primary hypothyroidism (10 with polycystic ovarian morphology, 16 with normal ovaries) and 20 euthyroid controls. Hormonal profiles and ovarian volumes were assessed before and after achieving euthyroidism.

Results

- Ovarian volumes, initially larger than controls, decreased significantly and were comparable with euthyroid women ($p < 0.05$).
- Levothyroxine significantly increased FT3 and FT4 and reduced TSH, prolactin, estradiol, and total and free testosterone levels.
- Menstrual regularity improved in 18 women.
- Among women with mild hypothyroidism, all patients with PCOM demonstrated complete regression of polycystic ovarian changes after ≥3 months of sustained euthyroidism.

Conclusion

Thyroid hormone replacement with levothyroxine restores euthyroidism, improves serum hormone levels, improves menstrual function, and reverses PCOS-like ovarian morphology.

FOGSI Clinical Recommendations for Thyroid Dysfunction and PCOS

- The diagnosis of PCOS requires exclusion of phenotypically similar endocrine disorders, such as primary hypothyroidism, late-onset adrenal hyperplasia, and Cushing's syndrome, followed by confirmation of PCOS based on the Rotterdam criteria.[14,15]
- FOGSI recommends screening for thyroid disease in all women with suspected PCOS, as thyroid dysfunction can mimic important clinical features of PCOS.[8,14]
- FOGSI recommends assessment of TSH, FSH, and prolactin levels as part of the initial diagnostic workup for PCOS.[8,10]
- FOGSI recommends timely treatment of thyroid dysfunction in women with PCOS to support better management of associated metabolic and reproductive disturbances.

References

1. Malik S, Jain K, Talwar P, et al. Management of polycystic ovary syndrome in India. Fertil Sci Res. 2014;1(1):23-43.
2. Hoeger KM, Dokras A, Piltonen T. Update on PCOS: Consequences, challenges, and guiding treatment. J Clin Endocrinol Metab. 2021;106(3):e1071-83.
3. Ach T, Dhaffar R, Ben Abdessalem F, et al. Subclinical hypothyroidism in polycystic ovary syndrome: Prevalence and impact on metabolic and cardiovascular risk. Clin Med Insights Endocrinol Diabetes. 2025;18:11795514251343678. Doi: 10.1177/11795514251343678
4. Singla R, Gupta Y, Khemani M, et al. Thyroid disorders and polycystic ovary syndrome: An emerging relationship. Indian J Endocrinol Metab. 2015;19(1):25-29.
5. Abdul-Ameer F, AlAsadi IJA, Hosseini A, et al. The relationship between serum CTRP-5, C3a/desArg, and complement-C3 levels and hypothyroidism in women with polycystic ovary syndrome. BMC Endocr Disord. 2024;24(1):272. Doi: 10.1186/s12902-024-01801-3
6. Peddemul A, Tejovath S, Hassan D, et al. Influence of subclinical hypothyroidism on women with polycystic ovary syndrome: A literature review. Cureus. 2022;14(8):e28468. Doi: 10.7759/cureus.28468
7. Barman I, Sharma T, Talukdar N. Exploring the connection between hypothyroidism and polycystic ovary syndrome: A comprehensive review. J Young Pharm. 2024;16(2):187-94.
8. Teede HJ, Tay CT, Laven J, et al. Recommendations from the 2023 International Evidence-based guideline for the assessment and management of polycystic ovary syndrome. Fert and Steril. 2023;120(4):767-93.
9. Williams T, Mortada R, Porter S. Diagnosis and treatment of polycystic ovary syndrome. Am Fam Physician. 2016;94(2):106-13.
10. Endocrinology Committee of FOGSI. PCOS Assessment — Do we have the Consensus? Vol 3. Available from: https://www.fogsi.org/wp-content/uploads/committee-2020-activities/vol-3-endocrinology-committee-pcos-assessment-do-we-have-the-consensus.pdf
11. Palomba S, Colombo C, Busnelli A, et al. Polycystic ovary syndrome and thyroid disorder: A comprehensive narrative review of the literature. Front Endocrinol (Lausanne). 2023;14:1251866. Doi: 10.3389/fendo.2023.1251866
12. Dawood R, Ammar H, Saleh AE. Thyroxine supplementation may improve ovulation and pregnancy rates in infertile patients with polycystic ovary syndrome and subclinical hypothyroidism. J Obs Gynecol Reprod Scien. 2019;3(2):01–5. Doi. 10.31579/2578-8965/019
13. Muderris II, Boztosun A, Oner G, et al. Effect of thyroid hormone replacement therapy on ovarian volume and androgen hormones in patients with untreated primary hypothyroidism. Ann Saudi Med. 2011;31(2):145-51.
14. Legro RS, Arslanian SA, Ehrmann DA, et al. Diagnosis and treatment of polycystic ovary syndrome: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2013;98:4565-92.
15. Shukla A, Rasquin LI, Anastasopoulou C. Polycystic ovarian syndrome. [Updated 2025 Jul 7]. In: StatPearls. Treasure Island (FL): StatPearls Publishing [Internet]. 2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK459251/

CHAPTER 3
HYPOTHYROIDISM AND ABNORMAL UTERINE BLEEDING

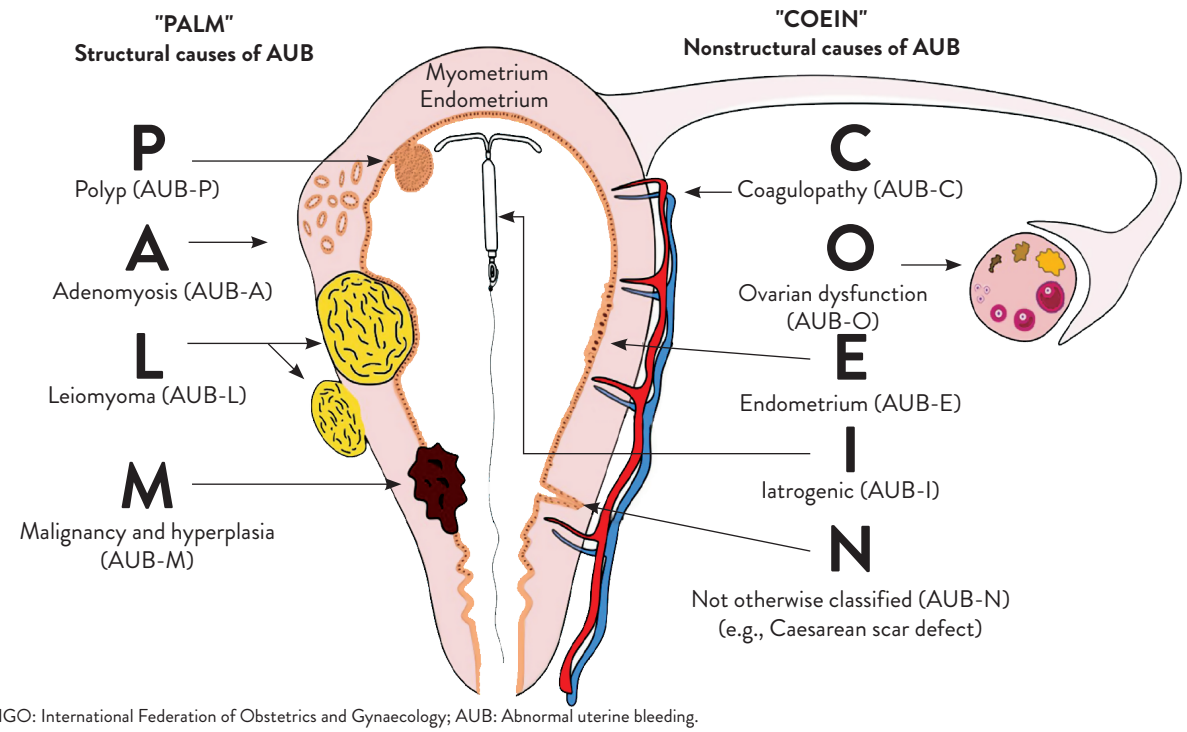
Dr. B. Aruna Suman
Professor, OBG Govt. Medical College, Telangana

Dr. Bidisha Roychoudhury
Asst. Professor, IPGMER, SSKM Hospital, Kolkata

Abnormal uterine bleeding: A brief overview

- Abnormal uterine bleeding (AUB) is a broad term encompassing any deviation from normal menstrual patterns, including changes in the frequency, regularity, duration, or volume of menstrual bleeding.[1]
- It includes clinical presentations such as menorrhagia, polymenorrhagia, polymenorrhea, oligomenorrhea, hypomenorrhea, metrorrhagia, and amenorrhea.[1]
- The International Federation of Obstetrics and Gynaecology (FIGO) System 2 classifies AUB using the PALM–COEIN framework, grouping etiologies into structural (PALM) and nonstructural (COEIN) causes (Figure 1).[2]
- Certain endocrinopathies, including hypothyroidism, can cause ovulatory dysfunction-related AUB (AUB-O).[3]

Figure 1: FIGO classification of abnormal uterine bleeding[2]



FIGO: International Federation of Obstetrics and Gynaecology; AUB: Abnormal uterine bleeding.

Prevalence of thyroid dysfunction in women with AUB

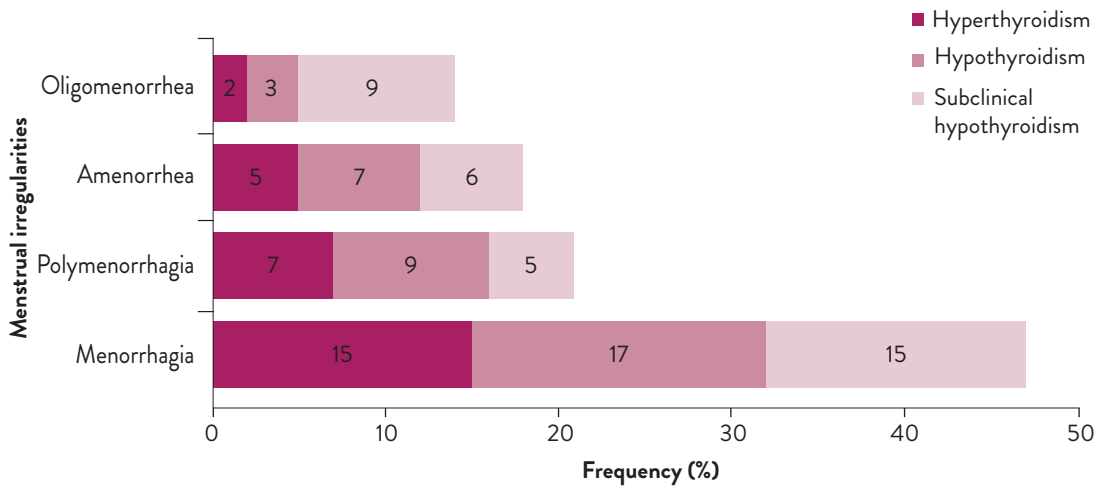
- Women with thyroid dysfunction commonly present with menstrual irregularities, infertility, and increased morbidity during pregnancy.[4]
- A study in women with AUB noted an association between thyroid dysfunction and AUB. Subclinical hypothyroidism (7.14%) constituted a substantial proportion of the detected thyroid abnormalities. Many cases of subclinical hypothyroidism are often missed despite documented menstrual disturbances.[5]

- A tertiary care hospital–based study, including 236 women with AUB, identified thyroid dysfunction in 11% of patients. Subclinical hypothyroidism was the most common abnormality (6.8%), followed by overt hypothyroidism (2.5%) and hyperthyroidism (1.7%).[6]

Clinical patterns of AUB in thyroid dysfunction

- Both hypothyroidism and hyperthyroidism are associated with menstrual disturbances and AUB.[7]
- Hypothyroidism is commonly associated with menorrhagia in its early stages and with oligomenorrhea in later stages, whereas hyperthyroidism is linked to oligomenorrhea and amenorrhea.[5]
- A study on women presenting with AUB showed that menorrhagia was the most common menstrual abnormality (47%) and was significantly associated with hypothyroidism (48.3%), followed by polymenorrhagia (21%) and amenorrhea (18%; Figure 2).[8]

Figure 2: Menstrual abnormalities associated with thyroid dysfunction[8]



Pathophysiological link between hypothyroidism and AUB

Hypothyroidism can lead to AUB through disturbances in both menstrual cycle regulation and hemostasis.[9]

Hormonal dysregulation and menstrual cycle

- In hypothyroidism, increased thyrotropin-releasing hormone stimulates the secretion of both thyroid-stimulating hormone (TSH) and prolactin (PRL).[9]
- Hyperprolactinemia has been implicated in ovulatory dysfunction, ranging from inadequate progesterone secretion by the corpus luteum to oligomenorrhea or amenorrhea.[9]

Altered gonadotropin dynamics

- Gonadotropin levels are often within the normal range in patients with hypothyroidism.[9]
- However, TSH may exert weak follicle-stimulating hormone (FSH) and luteinizing hormone (LH)-like effects due to a shared alpha subunit. This can blunt or abolish the mid-cycle FSH and LH surge.[9]

Effect on estrogen levels

- Hypothyroidism is associated with reduced sex hormone-binding globulin activity, resulting in increased circulating free estradiol and testosterone despite normal total hormone levels.[9]
- This imbalance promotes anovulatory cycles. As a result, menorrhagia is a frequent clinical manifestation, often attributed to estrogen breakthrough bleeding secondary to anovulation.[9]

Defects in hemostasis

In addition, hypothyroidism is associated with abnormalities in hemostasis, including reduced levels of factors VII, VIII, IX, and XI, which may further contribute to polymenorrhea and menorrhagia.[9]

Screening and diagnostic evaluation for thyroid dysfunction in AUB

Thyroid screening as part of the initial work-up in AUB

- Excessive or irregular menstrual bleeding is one of the most frequent gynecological manifestations of hypothyroidism.[5]
- Early identification of thyroid dysfunction in women with AUB allows timely medical management, which can lead to resolution of menstrual irregularities and help avoid unnecessary hormonal therapy or surgical interventions.[4]
- Estimation of serum triiodothyronine (T3), thyroxine (T4), and TSH should be included in the evaluation of patients presenting with AUB, as thyroid dysfunction represents an important and treatable cause of AUB.[1]

Diagnostic evaluation

- Thyroid evaluation should be done in any woman who wants to get pregnant and has a family history of thyroid problems or irregular menstrual cycles.[10]
- Thyroid function tests, including T3, T4, and TSH, have increased the sensitivity and specificity of detecting thyroid dysfunction.[5]
- Serum TSH has been identified as a sensitive indicator of reduced thyroid functional reserve, as TSH levels may rise before circulating thyroxine levels fall below normal range.[5]
- A study in women with AUB assessed FT3, FT4, and TSH levels to classify thyroid function into euthyroid, hypothyroid, subclinical hypothyroid, and hyperthyroid state.[5]

Guideline recommendation

The Federation of Obstetric and Gynecological Societies of India (FOGSI) recommends investigation of TSH levels as part of the initial evaluation of women presenting with abnormal uterine bleeding.[11]

Hypothyroidism and AUB: Management aspects

Management of hypothyroidism with AUB

- The primary goals in managing AUB are to identify and correct the underlying cause and to establish a regular bleeding pattern or achieve amenorrhea.[3]
- Treatment of thyroid dysfunction has been shown to reverse menstrual abnormalities and improve fertility outcomes in affected women.[4]

- Oral levothyroxine is approved by the US FDA for the treatment of primary, secondary, and tertiary hypothyroidism.[12] Clinical evidence indicates that levothyroxine therapy corrects menstrual abnormalities, including menorrhagia, associated with hypothyroidism.[7,13]

Role of levothyroxine in the management of hypothyroidism with AUB

Levothyroxine in normalizing menstrual abnormalities in women with AUB and thyroid dysfunction[7]

Aim

To assess the prevalence of thyroid dysfunction in women with AUB and to examine its clinical implications and role of levothyroxine in the management of the same.

Method

This cross-sectional study at a tertiary care center assessed thyroid dysfunction in women 18–45 years of age presenting with AUB excluding those with known thyroid disease. Clinical and laboratory data, including thyroid function tests, were analyzed using appropriate statistical methods.

Results

- Thyroid dysfunction was identified in few patients, 16.6% were diagnosed with hypothyroidism, 5.7% with hyperthyroidism, and 18.5% with subclinical hypothyroidism, while 59.2% were euthyroid.
- A majority of patients (76.5%) responded to a daily thyroxine dose of 25–50 µg, with restoration of normal menstrual cycles observed within 6 months.
- A smaller proportion of patients (17.94%) required a higher daily dose of levothyroxine 75–100 µg and a longer treatment duration of 6–12 months to achieve normalization of menstrual cycles.

Conclusion

Thyroxine therapy effectively corrects menstrual irregularities associated with hypothyroidism.

Levothyroxine therapy for the management of menorrhagia associated with early hypothyroidism[15]

Aim

To assess thyroid function in patients presenting with menorrhagia and assessment of effect of levothyroxine administration in patients with positive thyrotropin-releasing hormone (TRH) test.

Method

Women with severe menorrhagia underwent a TRH stimulation test with serial measurement of TSH, thyroxine, and triiodothyronine levels. Patients with TSH >30 mIU/L after administration of TRH were diagnosed with early hypothyroidism and treated with L-thyroxine, while those with negative results received gynecologic follow-up.

Results

- Among the 67 patients who appeared euthyroid, 15 (22%) had a positive TRH test, while 52 had negative results.
- In patients with positive results the following changes were observed:
  - Thyroxine levels increased significantly following administration of levothyroxine ($p < 0.02$).
  - TSH levels showed a highly significant decrease, dropping from a control value of 6.3 ± 0.91 mIU/L to 2.2 ± 0.54 mIU/L ($p < 0.01$).
- In women with early hypothyroidism, levothyroxine therapy led to resolution of menorrhagia within 3–6 months, with no recurrence over 1–3 years of follow-up.

Conclusion

Levothyroxine therapy effectively normalizes thyroid function by significantly increasing serum thyroxine levels and markedly reducing elevated TSH levels, while triiodothyronine levels remain unchanged, indicating selective and appropriate correction of hypothyroidism.

FOGSI Clinical Recommendations for Thyroid Dysfunction and AUB

- Thyroid dysfunction is an easily correctable cause of AUB.[15]
- FOGSI recommends investigation of TSH as part of initial evaluation of women presenting with AUB.[11]
- FOGSI recommends thyroid assessment in women planning pregnancy, particularly in those with a family history of thyroid disease or menstrual irregularities.[10]
- FOGSI recommends timely initiation of thyroid hormone replacement therapy in hypothyroid patients to help avoid unnecessary hormonal treatment and costly surgical interventions.[16]

References

1. H. S. AK, S. S, S. S. A study of prevalence of thyroid disorders in patients with abnormal uterine bleeding. Int J Reprod Contracept Obstet Gynecol [Internet].2017;6(3):1036-9.
2. Tsolova AO, Aguilar RM, Maybin JA, et al. Pre-clinical models to study abnormal uterine bleeding (AUB). EBioMedicine. 2022;84:104238. Doi: 10.1016/j.ebiom.2022.104238
3. Leal CRV, Vannuccini S, Jain V, et al. Abnormal uterine bleeding: The well-known and the hidden face. J Endometr Uterine Disord. 2024;6:100071. Doi: 10.1016/j.jeud.2024.100071
4. Gowri M, Radhika BH, Harshini V, et al. Role of thyroid function tests in women with abnormal uterine bleeding. Int J Reprod Contracept Obstet Gynecol. 2014;3(1):54-7.
5. Patil A, Shiragur SS, Gobbur V, et al. Association of bleeding patterns with thyroid dysfunction in patients with abnormal uterine bleeding: A prospective cross-sectional study. J Clin Diagn Res. 2022;16(11):QC05-QC08.
6. Pujari P, T HS, V KC. Evaluating patterns of abnormal uterine bleeding (AUB) in thyroid dysfunction at a tertiary care centre in north Kerala, India. Int J Health Clin Res. 2021;4(6):66-72.
7. Singh H, Vaghela T, Singh H. Thyroid dysfunction among patients with abnormal uterine bleeding: A hospital based prospective study from north India. Int J Pharm Clin Res. 2023;15(10):158-64.
8. Islam L, Maqsood M. The impact of thyroid dysfunction on abnormal uterine bleeding menstrual irregularities. Insights-J Health Rehabil. 2025;3:660-70.
9. Viau M, Bussieres M, Bergeron M. Severe hypothyroidism leading to life threatening menorrhagia. Gynecol Obstet Case Rep. 2017;3(1):44. Doi: 10.21767/2471-8165.1000044
10. Indian Thyroid Society (ITS); Federation of Obstetric and Gynaecological Societies of India (FOGSI). 2019 Recommendations for the Management of Thyroid Dysfunction in Pregnancy. Indian Thyroid Society; 2019. Available from: https://indianthyroidsociety.in/assets/img/guidelines/ITS_FOGSI_Recommendations.pdf
11. Federation of Obstetric and Gynaecological Societies of India (FOGSI). Abnormal uterine bleeding [Internet]. Mumbai: FOGSI; [cited 2025 Dec 23]. Available from: https://www.fogsi.org/abnormal-uterine-bleeding/

12. Eghtedari B, Correa R. Levothyroxine. [Updated 2023 Aug 28]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK539808/
13. Wilansky DL, Greisman B. Early hypothyroidism in patients with menorrhagia. Am J Obstet Gynecol. 1989;160(3):673-7.
14. Bedi M, Khosa SK, Das I, et al. Evaluation of thyroid hormone profile in abnormal uterine bleeding. J South Asian Feder Menopause Soc. 2020;8(1):37-41.
15. Deshmukh PY, Boricha BG, Pandey A. The association of thyroid disorders with abnormal uterine bleeding. Int J Reprod Contracept Obstet Gynecol. 2015;4:701-8.

CHAPTER 4
HYPOTHYROIDISM AND ANEMIA

Dr. Soma Datta
MBBS, MS (O&G), FMAS
Associate Consultant, Obstetrics and Gynaecology,
Woodlands Hospital, Kolkata

Dr. Ameya Purandare
MBBS, MD (O&G), DNBE, FCPS, DGO, DFP, FICMCH, MNAMS, FICOG
Consultant, Department of Obstetrics & Gynaecology,
Sir H.N. Reliance Foundation Hospital, Mumbai

Overview of anemia

- The World Health Organization (WHO) defines anemia as a state of reduced blood hemoglobin concentration, with diagnostic thresholds of <130 g/L in men, <120 g/L in nonpregnant women, and <110 g/L in children 6–59 months of age. However, Ghosh et al. have recently proposed that a lower cut-off value of 110 g/L may be more appropriate for Indian women of reproductive age.[1]
- According to WHO estimates, globally anemia affects 40% of children 6–59 months of age, 37% of pregnant women, and 30% of women 15–49 years of age. In 2019, anemia accounted for an estimated 50 million years of healthy lives lost.[1]

Causes of anemia

- Anemia arises from a broad spectrum of causes and is influenced by biological, socioeconomic, and ecological risk factors, which frequently coexist and interact.[2]
- Contributing factors include poor nutrition, parasitic infections, heavy menstrual or gastrointestinal bleeding, malabsorption disorders, and drug-related impairment of iron absorption.[2]
- At a physiological level, anemia is driven by three principal mechanisms:[2]
  - Ineffective erythropoiesis (i.e., inadequate erythrocyte production)
  - Hemolysis (i.e., destruction of erythrocytes)
  - Blood loss

Types of anemia

Anemia can be classified based on blood cell morphology. Major morphological types include the following:[3]

- Microcytic anemia: Caused due to iron deficiency
- Normocytic anemia: Typically associated with chronic diseases, disruption of red blood cell production in the bone marrow, renal failure, or bleeding
- Macrocytic anemia (megaloblastic and pernicious anemia): Results from vitamin B12 or folate deficiency and impaired protein synthesis
- Hemolytic anemia: arises from premature destruction of red blood cells (RBCs) before they reach maturity
- Aplastic anemia: Results from bone marrow damage

In addition, hemoglobinopathy-related anemias, such as sickle cell anemia and thalassemia, are inherited disorders characterized by structurally abnormal RBC morphology.[3]

Clinical importance of thyroid–anemia association

- Iron deficiency may contribute to hypothyroidism through altered thyroid hormone levels and a reduced response to thyroid-stimulating hormone (TSH). Iron is essential for thyroid peroxidase activity, which catalyzes the iodination of tyrosine residues in thyroglobulin during thyroid hormone synthesis; impaired thyroperoxidase

function may therefore compromise hormone production. Iron deficiency may also affect peripheral thyroid hormone metabolism by reducing conversion of thyroxine (T4) to triiodothyronine (T3) and altering central regulation of thyroid function.[4]

- Conversely, anemia in hypothyroidism may result from bone marrow suppression, reduced erythropoietin production, comorbid diseases, or concurrent deficiencies of iron, vitamin B12, or folate.[5] Additionally, chronic conditions, malnutrition, and malabsorption syndromes may contribute to both reduced thyroid function and anemia, with deficiencies of iron, vitamin B12, folate, and iodine, further exacerbating both conditions.[6]
- Clinical studies consistently demonstrate a higher prevalence of anemia in both overt and subclinical hypothyroidism compared with euthyroid individuals.[7]
    - A large individual participant data meta-analysis observed that individuals with overt hypothyroidism had 1.84-fold higher odds of anemia (95% confidence interval [CI] 1.35–2.50) compared with euthyroid individuals.[7]

Prevalence and types of anemia in hypothyroidism

The hematopoietic system is among the most affected system in patients with hypothyroidism, with anemia reported in approximately 20–60% of cases. The most frequently observed form is normochromic, normocytic anemia, primarily attributed to bone marrow suppression resulting from thyroid hormone deficiency and reduced erythropoietin production due to lower oxygen requirement. Hypothyroidism has been associated with pernicious anemia, possibly due to slowed intestinal motility and impaired vitamin B12 absorption.[8]

Etiopathogenesis of anemia in hypothyroidism

Anemia in hypothyroidism is multifactorial in origin.[7]

- Thyroid hormones (T4 and T3) are key regulators of erythropoiesis, influencing erythroid progenitor proliferation, erythropoietin synthesis, and iron metabolism.[7]
- Reduced thyroid hormone levels lead to decreased erythropoietin production and impaired stimulation of erythroid progenitor cells, resulting in reduced erythropoiesis.[5,7]
- Hypothyroidism is also associated with altered iron metabolism, including reduced intestinal iron absorption and changes in ferritin and transferrin levels, contributing to iron-deficiency states.[5,7]
- In addition, bone marrow suppression, shortened red cell survival, and concurrent nutritional deficiencies such as iron, vitamin B12, and folate may further contribute to anemia.[5,7]
- Autoimmune hypothyroidism may coexist with other autoimmune conditions (e.g., pernicious anemia, atrophic gastritis, celiac disease), increasing the risk of anemia.[5]

Clinical manifestations of anemia and hypothyroidism and their overlapping symptoms

Hypothyroidism and anemia commonly present with nonspecific symptoms such as fatigue and reduced quality of life. Their coexistence may lead to greater morbidity, and further effects on quality of life.[6] Table 1 summarizes the clinical features of anemia, hypothyroidism, and their overlapping symptoms.[9]

Table 1: Clinical features of anemia and hypothyroidism[9]

Anemia	Hypothyroidism	Overlapping symptoms
• Fatigue • Shortness of breath • Bounding pulses • Palpitations • Conjunctival and palmar pallor • Tachycardia • Postural hypotension • Peripheral edema (moderately severe anemia) • Systolic ejection murmur • Reduced cognitive performance • Severe anemia: Headache, faintness, lack of mental concentration, tinnitus, and vertigo • Signs of hypovolemic shock include confusion, dyspnea, diaphoresis, hypotension, and tachycardia	• Generalized weakness • Weight gain • Cold intolerance • Somnolence • Menstrual irregularities • Decreased libido • Reduced fertility • Increased risk of miscarriage • Hoarseness of voice • Constipation • Dermatological changes	• Fatigue • Weakness • Shortness of breath • Decreased exercise tolerance • Hair: Thinning, loss of luster, and brittle hair • Pallor • Peripheral edema • Neuropsychiatric symptoms: Motor disturbances, memory loss, numbness, and tingling (concomitant B12 deficiency)

Hypothyroidism and anemia in special populations

Pregnancy

- Anemia and thyroid dysfunction frequently coexist during pregnancy. Iron-deficiency anemia is common due to increased iron requirements and preferential iron transfer to the fetus, and iron deficiency has been associated with thyroid dysfunction in pregnant women.[5]
- Studies have shown that women with iron deficiency have a significantly higher prevalence of autoimmune thyroid disease (AITD) and subclinical hypothyroidism compared with iron-replete women.[5]
- In addition, poor maternal iron status is associated with higher TSH and lower total T4 levels during pregnancy, and iron deficiency may impair thyroid hormone synthesis through reduced thyroid peroxidase activity.[10]
- As both anemia and thyroid dysfunction may adversely affect pregnancy outcomes, simultaneous correction of iron deficiency and thyroid hormone abnormalities may improve maternal and fetal well-being.[5]

Elderly population

- Anemia is frequently observed in patients with hypothyroidism.
- The development of anemia in hypothyroidism is multifactorial, resulting from bone marrow depression, reduced erythropoietin production, and concomitant deficiencies of iron, vitamin B12, or folate.
- Clinical differentiation between anemia and hypothyroidism is particularly challenging in the elderly due to overlapping clinical features.[11]

Screening of hypothyroidism in anemia and diagnostic evaluation

Hypothyroidism has a higher prevalence in women, who are also at increased risk of anemia; given its nonspecific presentation, early diagnosis requires a high index of clinical suspicion.[12]

Screening of hypothyroidism

- Chronic, treatment-resistant anemia or unexplained anemia, after exclusion of common causes should prompt assessment for thyroid dysfunction and autoimmune thyroid disease.[5]
- Vitamin B12 deficiency due to pernicious anemia may be associated with thyroid dysfunction; therefore, screening with TSH can be done in these patients.[5]
- Severe anemia during pregnancy, especially when thyroid status has not been previously evaluated, should prompt assessment of thyroid function.[5]

Diagnostic evaluation

Evaluation of anemia involves several laboratory tests and imaging studies based on the clinical presentation and suspected cause (Table 2).[9,13]

Table 2: Diagnostic evaluation of anemia

Tests	Assessment
Complete blood count[13]	Hemoglobin, hematocrit, MCV, MCH, MCHC
Iron studies[9,13]	Serum iron, ferritin, total iron-binding capacity to rule out iron deficiency
Vitamin assessment[9]	Vitamin B12 and folic acid to rule out nutritional deficiencies
Thyroid function tests[13]	Thyroxine and thyroid-stimulating hormone levels, to help evaluate anemia related to thyroid dysfunction
Additional tests[9,13]	Bone marrow examinations to assess bone marrow suppression in normocytic anemia, direct Coombs test to rule out autoimmune etiology, reticulocyte to estimate bone marrow RBC output

MCV: Mean corpuscular volume; MCH: Mean corpuscular hemoglobin; MCHC: Mean corpuscular hemoglobin concentration; RBC: Red blood cells.

Management of hypothyroidism and anemia

Management of coexisting anemia–hypothyroidism

- In patients with hypothyroidism and iron-deficiency anemia, combined treatment with levothyroxine and iron supplementation is the preferred therapeutic approach.[9]
- When anemia in hypothyroidism results from iron, vitamin B12, or folate deficiency, management requires correction of the specific deficiency in addition to thyroid hormone replacement.[9]

Thyroid hormone replacement and its impact on anemia

- Thyroid hormone replacement alone is the treatment of choice for non-megaloblastic macrocytic anemia associated with hypothyroidism.[9]
  - Levothyroxine therapy lowers TSH and improves hematological parameters in hypothyroid patients.[9]
  - In uncomplicated anemia with normal iron, vitamin B12, and folate levels, levothyroxine alone is often sufficient, reflecting reversal of a reduced metabolic state.[9]
  - Treatment with levothyroxine is associated with a rise in hemoglobin (≈1.6 g/dL), improvement in erythropoietin levels, and gradual normalization of red cell indices over ~6 months.[9]

Role of levothyroxine in the management of hypothyroidism and anemia

Levothyroxine supplementation improves hematologic outcomes in iron-deficient patients with subclinical hypothyroidism[14]

Aim

To assess whether iron-deficiency anemia might indicate the need for treatment of subclinical hypothyroidism.

Methods

Patients were randomized to receive 240 mg/day oral iron alone or 240 mg/day oral iron plus levothyroxine 75 µg/day. Hematologic and thyroid parameters, including hemoglobin, hematocrit, RBC count, iron indices, TSH, and free thyroxine (T4), were measured before and after therapy.

Results

- Mean hemoglobin increased by 0.4 g/dL in the iron group (95% confidence interval [CI] 0.2–0.7; p = 0.001) vs. 1.9 g/dL with combination therapy (95% CI 1.5–2.3; p <0.0001).
- Mean serum iron increased by 47.6 µg/dL with combination therapy (95% CI 34.5–60.6; p <0.0001).
- Increases in hemoglobin, RBC count, hematocrit, and ferritin were significantly greater with combined therapy (p <0.0001).
- Stronger hemoglobin response was observed in patients with lower baseline hemoglobin (r = −0.531; p = 0.006).

Conclusion

The combination treatment normalized thyroid function and reversed anemia in most patients with coexisting subclinical hypothyroidism and iron-deficiency anemia.

Levothyroxine supplementation improves hematologic and iron indices in patients with iron-deficiency anemia and subclinical hypothyroidism[15]

Aim

To assess the impact of levothyroxine supplementation in patients with iron-deficiency anemia and subclinical hypothyroidism.

Methods

A case-control study at a North Indian medical college hospital included 50 female patients with subclinical hypothyroidism and iron-deficiency anemia. Participants were divided into 25 cases receiving 300 mg elemental iron plus levothyroxine 25 µg daily and 25 controls receiving iron alone for 3 months. Hematological parameters and thyroid function tests were assessed in both groups.

Results

Combined therapy vs. iron monotherapy showed the following results:

- Mean hemoglobin increase: 1.70 ± 1.75 g/dL vs. 0.40 ± 0.23 g/dL (p <0.001)
- Mean hematocrit increase: 6.70 ± 2.88% vs. 1.40 ± 1.11% (p <0.001)
- Mean serum ferritin increase: 12.40 ± 2.15 µg/dL vs. 3.80 ± 2.21 µg/dL (p <0.001)
- Mean serum iron increase: 53.00 ± 7.47 µg/dL vs. 10.00 ± 4.71 µg/dL (p <0.001)

- Greater reduction in total iron-binding capacity: 30.00 ± 11.46 µg/dL vs. 4.00 ± 1.32 µg/dL (p <0.001)
- Greater reduction in TSH: 4.00 ± 1.35 mIU/L vs. 0.20 ± 0.20 mIU/L (p <0.001)
- Greater improvement in free T4: 1.50 ± 0.89 ng/dL vs. 0.30 ± 0.40 ng/dL (p <0.001)

Conclusion

Treatment of subclinical hypothyroidism resulted in significant improvement in both hematological parameters and iron indices in patients with iron-deficiency anemia.

Levothyroxine plus iron supplementation improves hematologic and thyroid outcomes in iron-deficiency anemia with subclinical hypothyroidism[16]

Aim

To investigate whether combined levothyroxine and iron therapy is more effective than either treatment alone in patients with subclinical hypothyroidism and iron-deficiency anemia.

Methods

A total of 60 patients with subclinical hypothyroidism and iron-deficiency anemia were randomized to iron + placebo, levothyroxine + placebo, and combined levothyroxine and iron therapy for 3 months. Pre- and post-treatment changes in hemoglobin, ferritin, and TSH were evaluated among groups.

Results

- Combination therapy with levothyroxine and iron resulted in significant increases in hemoglobin and ferritin and significant reductions in TSH (p <0.001).
- Hemoglobin normalization (≥12 g/dL in women; ≥13.5 g/dL in men) and ferritin normalization was achieved in most patients receiving combination therapy of levothyroxine and iron.
- Mean hemoglobin increase: 1.17 g/dL with combination therapy of levothyroxine + iron vs. 0.26 g/dL with levothyroxine + placebo and 0.005 g/dL with iron + placebo (p <0.0001).
- Mean ferritin increase: 10.78 ng/mL increase in combination therapy vs. 0.611 and 0.722 ng/mL increases in the levothyroxine + placebo and iron + placebo groups, respectively (p <0.0001).
- Both levothyroxine-containing regimens resulted in significantly greater TSH reductions than iron + placebo (p <0.0001).

Conclusion

A combination of levothyroxine and iron supplementation is more effective than either therapy alone when subclinical hypothyroidism and iron-deficiency anemia coexist.

FOGSI Clinical Recommendations for Thyroid Dysfunction and Anemia

- FOGSI recommends screening for thyroid dysfunction in cases of treatment-resistant anemia, anemia of chronic disease, anemia of unknown origin, pernicious anemia, and during pregnancy.
- FOGSI recommends levothyroxine therapy to improve hematological parameters in hypothyroid patients, with combined levothyroxine and iron therapy offering greater improvement in hemoglobin and iron indices than iron therapy alone when hypothyroidism coexists with iron-deficiency anemia.

References

1. Givens DI, Anitha S, Giromini C. Anaemia in India and its prevalence and multifactorial aetiology: A narrative review. Nutrients. 2024;16(11):1673. Doi: 10.3390/nu16111673
2. Hess SY, Owais A, Jefferds MED, et al. Accelerating action to reduce anemia: Review of causes and risk factors and related data needs. Ann N Y Acad Sci. 2023;1523(1):11-23.
3. Suprapti E, Hadju V, Ibrahim E, et al. Anemia: Etiology, pathophysiology, impact, and prevention: A review. Iran J Public Health. 2025;54(3):509-20.
4. Garofalo V, Condorelli RA, Cannarella R, et al. Relationship between iron deficiency and thyroid function: A systematic review and meta-analysis. Nutrients. 2023;15(22):4790. Doi: 10.3390/nu15224790
5. Szczepanek-Parulska E, Hernik A, Ruchala M, et al. Anemia in thyroid diseases. Pol Arch Intern Med. 2017;127(5):352-60.
6. Wopereis DM, Du Puy RS, van Heemst D, et al. The relation between thyroid function and anemia: A pooled analysis of individual participant data. J Clin Endocrinol Metab. 2018;103(10):3658-67.
7. Sagri MAA, Boyapati AK. Assessment of anaemia in patients with hypothyroidism: Clinical and hematological correlation. Eur J Cardiovasc Med. 2025;15(11):125-30.
8. Babaker AS, Al-Qahtani RM. Frequency and characteristics of anemia in hypothyroid patients: A cross-sectional study. J Family Community Med. 2025;32(1):59-64.
9. Eram F, Quamri MA, Zaidi A, et al. A comprehensive review of anaemia associated with hypothyroidism. Emirates Med J. 2024;05:e02506882282237. Doi. 10.2174/0102506882282237240206075352
10. Agrawal U, Shrivastava P, Shrivastava S. Hypothyroidism and anemia in pregnancy. Int J Adv Med. 2016;3(4):851-4.
11. Sarma S, Goswami D, Deuri A, et al. A study of the types of anaemia in elderly hypothyroidism. J Evid Based Med Healthc. 2020;7(5):233-36.
12. Patil BM, Kumar VS, Anusha K. A clinical and etiological study of anemia in patients with primary hypothyroidism. J Med Sci. 2018;4(2):48-51.
13. Freeman AM, Zubair M. Anemia screening. [Updated 2025 Feb 17]. In: StatPearls. Treasure Island (FL): StatPearls Publishing [Internet] 2025. Available from: https://www.ncbi.nlm.nih.gov/books/NBK499905/
14. Cinemre H, Bilir C, Gokosmanoglu F, et al. Hematologic effects of levothyroxine in iron-deficient subclinical hypothyroid patients: A randomized, double-blind, controlled study. J Clin Endocrinol Metab. 2009;94(1):151-6.
15. Jain G, Goyal LK, Saxena GN. A study to evaluate effect of levothyroxine supplementation in iron deficiency anemia patients having subclinical hypothyroidism. Indian J Applied Res. 2016;6(2):266-68.
16. Ravanbod M, Asadipooya K, Kalantarhormozi M, et al. Treatment of iron-deficiency anemia in patients with subclinical hypothyroidism. Am J Med. 2013;126(5):420-4.

CHAPTER 5 HYPOTHYROIDISM AND INFERTILITY

Dr. Meenu Agarwal
Vice President, West, FOGSI
DNB, DGO, Trained in Endoscopy & IVF in Germany, Bachelor in Reproductive Surgery (European Board Certified), Gynaecological Endoscopic Surgeon

Dr. Laxmi Shrikhande
MBBS, MD(OB/GY), FICOG, FICMU, FICMCH
Medical Director & Consultant, Shrikhande Hospital & Research Centre, Nagpur

Overview of infertility

Infertility is defined as the inability to achieve pregnancy after 1 year or more of regular, unprotected intercourse. Globally, infertility affects around 60–80 million couples annually, with India accounting for nearly 25% (15–20 million) of the burden.[1,2] According to the World Health Organization, 1 in 4 couples in developing countries is affected, emphasizing the magnitude of the problem and the urgent need for intervention, particularly as many infertility causes are preventable.[2]

Risk factors and causes of infertility

- Advancing age, excess body weight, hyperprolactinemia, polycystic ovary syndrome, hypothyroidism, premature ovarian failure, uterine abnormalities like fibroids, endometriosis, tubal blockage, and lifestyle choices like tobacco consumption and smoking.[3,4]
- Among the various contributors, endocrine disorders play a significant role in female infertility, with thyroid dysfunction emerging as the predominant endocrine disorder in women of reproductive age. Thyroid hormones are crucial for normal female reproductive function, influencing processes from folliculogenesis to placentation.[5]

Hypothyroidism and infertility

- Hypothyroidism is a well-recognized clinical condition known to adversely affect female fertility, primarily through ovulatory disturbances. Its prevalence among women of reproductive age ranges from 2% to 4%.[6]
- Undiagnosed or untreated hypothyroidism can lead to subfertility or infertility due to mechanisms such as hyperprolactinemia, anovulatory cycles, luteal phase defects, and altered sex hormone levels.[6]
- Since thyroid activity is intricately regulated by the hypothalamic–pituitary axis, disturbances in thyroid function can profoundly affect reproductive outcomes.[5]

Role of hypothalamic–pituitary–thyroid axis

The hypothalamic–pituitary–thyroid (HPT) axis plays an important role in fertility through regulation of thyroid hormone production. Thyroid activity is controlled by the hypothalamus, thyrotropin-releasing hormone (TRH), and thyroid-stimulating hormone (TSH). Abnormal serum TSH levels indicate thyroid dysfunction. Thyrotropin-releasing hormone neurons in the hypothalamic paraventricular nucleus regulate TSH release and are modulated by thyroid hormones via negative feedback. Their activity is further controlled by pyroglutamyl peptidase II (PPII) and tanycytes, which influence TRH inactivation and local conversion of thyroxine (T4) to active triiodothyronine (T3).[6]

Role of hypothalamic–pituitary–ovarian axis

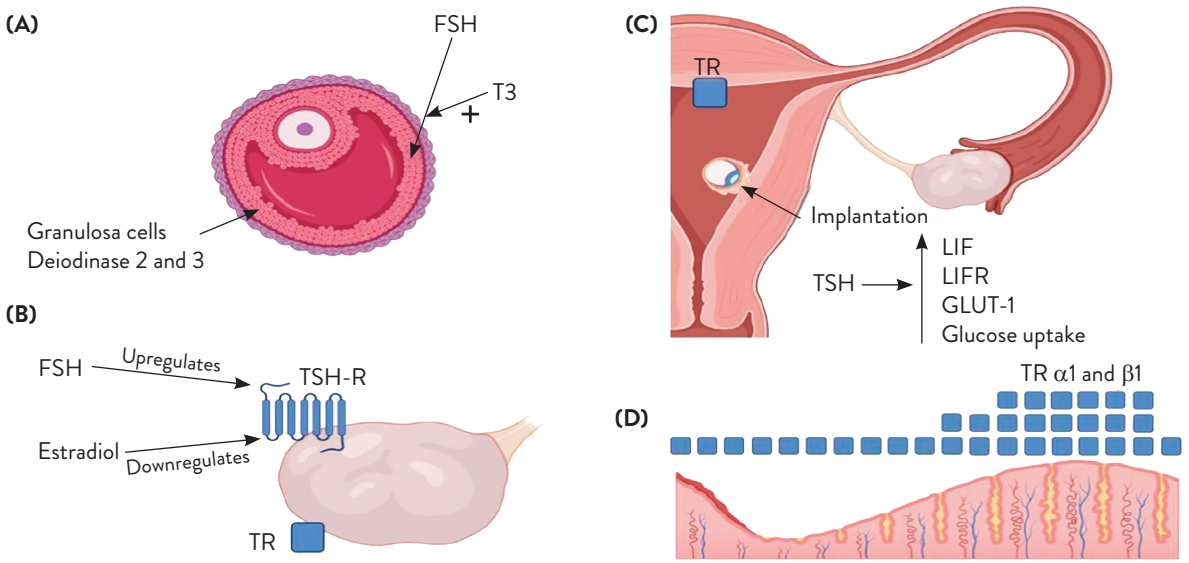
Hypothyroidism also contributes to infertility by disrupting the hypothalamic–pituitary–ovarian (HPO) axis, including alterations in gonadotropin-releasing hormone (GnRH) activity. Thyroid disorders are associated with a higher proportion of abnormal menstrual cycles and increased subfertility compared with euthyroid women. As the menstrual cycle depends on normal GnRH pulsatility for the release of follicle-stimulating hormone (FSH) and luteinizing hormone (LH), disturbances in this axis lead to impaired folliculogenesis and anovulatory cycles. Thyroid hormones are physiologically linked to the HPO axis and act synergistically with FSH to promote granulosa cell differentiation, normal follicle development, ovulation, and corpus luteum formation. Menorrhagia is the most

common menstrual abnormality in women with hypothyroidism, followed by oligomenorrhea and amenorrhea, underscoring the role of hypothyroidism-related HPO axis dysfunction in infertility.[6]

Thyroid function and the ovary

- The HPT and HPO axes are closely inter-related, establishing a bidirectional relationship, and alterations in thyroid function directly influence ovarian physiology.[5]
- Thyroid hormones act synergistically with FSH to stimulate granulosa cell differentiation, inhibit apoptosis, and support normal follicular development (Figure 1).[5]
- T4 and T3 regulate follicular growth and atresia through thyroid hormone receptors expressed in granulosa cells, ovarian stromal cells, and cumulus oophorus cells.[5]
- In addition, ovarian expression of TSH receptors is positively regulated by FSH and negatively regulated by estradiol.[5]

Figure 1: Thyroid hormones and their role in the pathophysiology of female fertility[5]

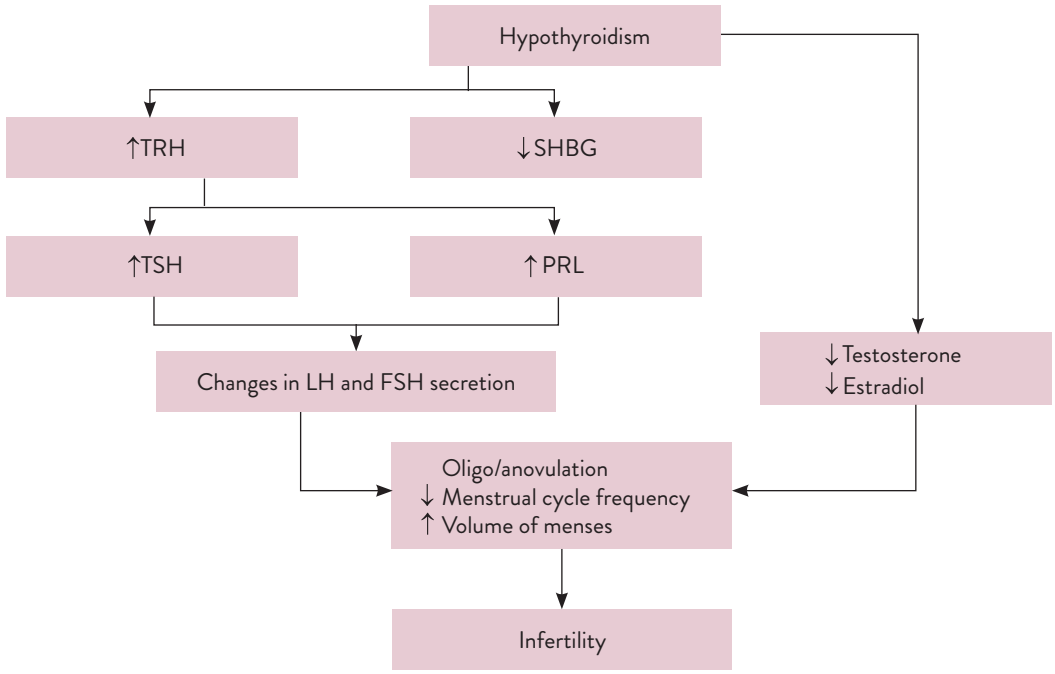


FSH: Follicle-stimulating hormone; GLUT-1: Glucose transporter 1; LIF: Leukemia inhibitory factor; LIFR: Leukemia inhibitory factor receptor; T3: Triiodothyronine; TR: Thyroid hormone receptor; TSH: Thyroid-stimulating hormone; TSH-R: Thyroid-stimulating hormone receptor.

Mechanisms underlying infertility in hypothyroidism

- Hypothyroidism is associated with elevated TRH levels and reduced sex hormone-binding globulin. Increased TRH stimulates excess secretion of TSH and prolactin (PRL; Figure 2).[5]
- Elevated PRL disrupts the normal release of LH and FSH, resulting in oligo- or anovulation, reduced menstrual frequency, increased menstrual flow, and ultimately infertility (Figure 2).[5]

Figure 2: Mechanisms linking hypothyroidism and infertility[5]



FSH: Follicle-stimulating hormone; LH: Luteinizing hormone; PRL: Prolactin; TRH: Thyrotropin-releasing hormone; TSH: Thyroid-stimulating hormone; SHBG: Sex hormone-binding globulin.

Subclinical hypothyroidism and female infertility

- Infertility is multifactorial, with thyroid disorders, particularly subclinical hypothyroidism (SCH), emerging as an important contributor. Subclinical hypothyroidism is defined as elevated TSH levels with normal T3 and T4 levels and is often asymptomatic.[7] Its prevalence in women of 20–45 years of age is approximately 5–7%, but it is substantially higher in women with infertility, ranging from 11% to 43%.[5] Women with infertility are more likely to have Subclinical hypothyroidism than the general population.[7] Subclinical hypothyroidism frequently remains undiagnosed due to the lack of overt symptoms, highlighting the need for routine thyroid function screening in women with infertility.[7]
- Although TSH cut-off values vary across studies, evidence consistently shows a strong association between infertility and TSH levels above 4 mIU/L. A retrospective case-control study comparing 244 infertile women with 155 healthy controls, using a TSH cut-off of >4.2 mIU/L, reported a significantly higher prevalence of SCH in women with infertility (13.9% vs. 3.9%; $p < 0.002$), reinforcing the link between elevated TSH levels and impaired fertility.[5]

Subclinical hypothyroidism and outcomes following assisted reproductive techniques

Available evidence suggests that SCH adversely affects assisted reproductive techniques (ART) outcomes in women with infertility.[5] Studies in women undergoing in vitro fertilization (IVF) have shown lower implantation and live birth rates, along with a higher risk of miscarriage in those with SCH.[8] The negative impact of SCH on ART outcomes appears to be dependent on TSH levels, with progressively poorer outcomes as TSH levels increase.

Consequently, addressing SCH in women planning pregnancy through ART is considered important when TSH levels exceed 2.5 mIU/L.[9]

Screening and diagnostic approach for hypothyroidism and infertility

Screening for thyroid dysfunction in infertility

Why screening of thyroid dysfunction is essential[10]

- Thyroid dysfunction is a recognized and potentially modifiable cause of infertility. Therefore, it is commonly included as part of routine infertility workups.
- Due to the high prevalence of thyroid disorders in women and their systemic effects, routine screening is clinically relevant.
- Early diagnosis and management of thyroid abnormalities may improve fertility outcomes and reduce obstetric risks.

Screening as part of initial workup for infertility

- Thyroid-stimulating hormone and thyroid peroxidase antibodies (TPOAb) are generally included in the initial evaluation of women with infertility.[11]
- Measurement of TSH and PRL should be performed at an early stage of infertility assessment, rather than proceeding directly to more costly or invasive investigations.[12]
- Women undergoing ART fulfill the criteria for universal TSH screening, as per the recent European Thyroid Association (ETA) guidelines.[11]

Guideline recommendations

- The Endocrine Society and the American Thyroid Association recommend thyroid function screening in women presenting with infertility or recurrent pregnancy loss, and during early pregnancy.[13,14]
- The ETA recommends measuring TSH and TPOAb in women seeking infertility care, with specific reference to ART.[15]
- Indian Thyroid Society (ITS); Federation of Obstetric and Gynecological Societies of India (FOGSI): Thyroid assessment is recommended for women planning pregnancy who have a family history of thyroid disease, menstrual irregularities, recurrent pregnancy loss (more than two miscarriages), or infertility despite 1 year of unprotected intercourse. A comprehensive evaluation should include serum T3, T4, and TSH levels, along with thyroid autoimmunity testing such as TPOAb, thyroglobulin/antithyroglobulin antibodies, and thyroid-stimulating immunoglobulin.[16]

Clinical implication

- Both gynecology and internal medicine clinicians should maintain a high index of suspicion for thyroid dysfunction in at-risk women, even in the absence of classic symptoms.[10]
- Simple oral treatment of hypothyroidism for 3 months to 1 year may be beneficial for conception, even in otherwise asymptomatic infertile women with hypothyroidism.[12]
- Cost-effectiveness analyses of screening strategies in high-risk female populations may help guide health policy decisions.[10]

Diagnostic evaluation

Hypothyroidism is easily identified by measuring serum TSH levels. A mild elevation in TSH with normal T3 and T4 marks SCH, while markedly elevated TSH with low T3 and T4 confirms clinical hypothyroidism. Subclinical hypothyroidism may cause anovulation either directly or indirectly through elevated PRL levels.[12]

In many women with infertility, hypothyroidism is associated with hyperprolactinemia due to increased TRH, leading to ovulatory dysfunction. Hyperprolactinemia suppresses GnRH secretion, disrupts GnRH pulsatility, and impairs ovarian function. Therefore, measurement of TSH and PRL is routinely performed as part of the infertility workup in all infertile women, regardless of menstrual pattern.[12]

Management of hypothyroidism and infertility

Therapeutic approaches for management of hypothyroidism and infertility

- The primary goal of treatment is to achieve clinical and biochemical euthyroidism, which helps restore normal ovulation, menstrual regularity, and fertility.[17]
- Levothyroxine monotherapy is the treatment of choice, usually at a dose of 1.6–1.8 µg/kg/day, with adequate time allowed for monitoring thyroid function tests.[17]
- Normal TSH levels are essential for successful fertilization. Therefore, early initiation of thyroid hormone replacement therapy in infertile women with subclinical hypothyroidism is justified.[16]
- Differences in TSH levels within the narrower range or borderline cases (4–5, 5–6, and >6.0 µIU/mL) should not be overlooked in infertile women who are otherwise asymptomatic for clinical hypothyroidism. Careful identification and appropriate treatment for hypothyroidism in this subgroup can provide significant clinical benefit and may help avoid unnecessary extensive hormonal evaluations and costly invasive procedures.[16]
- Women planning pregnancy should maintain a preconception level of TSH ≤2.5 mIU/L, with levothyroxine dose adjustments as required.[17]

Role of levothyroxine in managing hypothyroidism in infertility

- Treating hypothyroidism with levothyroxine helps restore normal menstrual cycles, correct hormonal imbalances, and improve fertility.[8]
- In women with SCH undergoing IVF/intracytoplasmic sperm injection (ICSI), levothyroxine therapy has been shown to improve embryo quality, implantation rates, and live birth outcomes.[18]
- The American Thyroid Association recommends levothyroxine supplementation in infertile women with subclinical hypothyroidism to enhance oocyte fertilization rates and improve clinical pregnancy outcomes during ART.[19]

Levothyroxine in enhancing hormonal and fertility outcomes in women with hypothyroidism[20]

Aim

To assess the impact of thyroid hormone replacement therapy (levothyroxine) on endometrial receptivity and conception outcomes in women with infertility diagnosed with clinical or subclinical hypothyroidism.

Methods

This prospective observational study included 60 women 21–40 years of age with clinical or subclinical hypothyroidism. Clinical evaluation, hormonal profiling, and pelvic ultrasonography were performed. Levothyroxine therapy was titrated over 3–12 months, with outcomes including hormonal normalization and pregnancy achievement.

Results

- Levothyroxine therapy led to a significant reduction in mean TSH levels from 12.07 to 6.26 mIU/L and PRL levels from 13.9 to 10.9 ng/mL ($p < 0.001$) at 3 months.
- Conception was observed in 61.5% of women with subclinical hypothyroidism and 57.1% with clinical hypothyroidism, with no significant difference between groups ($p = 0.956$). The highest conception rates were observed in women achieving mid-range TSH levels (6.5–10 mIU/L).

Conclusion

Early identification and management of even mild hypothyroidism with levothyroxine can improve fertility outcomes, highlighting the need for routine thyroid screening as part of infertility assessment.

Levothyroxine in improving fertility in women with subclinical hypothyroidism[21]

Aim

To evaluate the impact of levothyroxine therapy on infertility outcomes in women with SCH.

Methods

This prospective observational study included 69 infertile women with SCH. Participants received T4 therapy, with doses adjusted to achieve target TSH levels. Thyroid function parameters and fertility outcomes were assessed during follow-up.

Results

- Pregnancy outcomes: A total of 58 out of 69 women (84.1%) successfully conceived following levothyroxine therapy.
- Thyroid function: In women who conceived, median TSH levels significantly decreased from 5.46 µIU/mL before treatment to 1.25 µIU/mL after treatment ($p < 0.001$), with a corresponding rise in free T4 levels.
- Time to conception: The mean duration of infertility significantly shortened from 2.8 ± 1.7 years before treatment to 0.9 ± 0.9 years after initiation of levothyroxine ($p < 0.001$). This improvement was observed in both spontaneous conceptions and those treated with ART.

Conclusion

Levothyroxine therapy was associated with improved fertility outcomes and a reduced time to conception in women with infertility with SCH.

Effect of levothyroxine therapy on IVF/ICSI outcomes in women with subclinical hypothyroidism[18]

Aim

To evaluate whether levothyroxine therapy improves IVF and ICSI outcomes, including embryo quality and pregnancy outcomes, in women with infertility diagnosed with SCH.

Methods

This prospective, randomized study enrolled 64 women with infertility with SCH and undergoing IVF/ICSI. Participants were randomized to receive levothyroxine (50 µg/day) from the start of ovarian stimulation or no treatment. Thyroid function, embryo quality, implantation, pregnancy, miscarriage, and live birth outcomes were compared between groups.

Results

- Women treated with levothyroxine had significantly lower TSH levels (2.9 ± 1.0 vs. 6.8 ± 1.9) and higher free T4 levels (1.3 ± 0.1 vs. 1.2 ± 0.2) compared with controls.
- Clinical outcomes were also superior in the levothyroxine group, with higher implantation rates (26.9% vs. 14.9%), lower miscarriage rates (0% vs. 33.3%), and significantly higher live birth rates (53.1% vs. 25%) compared with the control group, respectively.

Conclusion

Levothyroxine therapy improved embryo quality, implantation rates, and live birth outcomes while reducing miscarriage risk in women with infertility with SCH undergoing IVF/ICSI.

FOGSI Clinical Recommendations for Thyroid Dysfunction and Infertility

- Thyroid hormones have profound effects on reproduction and pregnancy. Thyroid dysfunction can affect fertility in various ways resulting in anovulatory cycles, luteal phase defect, high prolactin levels, and sex hormone imbalances.[6]
- Undiagnosed and untreated thyroid disease can be a cause for infertility as well as sub-fertility.[6]
- FOGSI recommends universal screening of serum thyroid-stimulating hormone (TSH) in all women seeking evaluation or treatment for infertility.[16]
- Early identification and treatment of even mild thyroid dysfunction improves fertility outcomes, underscoring the importance of routine thyroid screening in infertility evaluation.[6]
- FOGSI recommends levothyroxine treatment for women with infertility and overt hypothyroidism.[16]
- FOGSI recommends levothyroxine treatment for women with subclinical hypothyroidism undergoing in vitro fertilization or intracytoplasmic sperm injection, with the treatment goal of achieving a TSH level below 2.5 mIU/L.[16]
- FOGSI recommends that levothyroxine may be considered in euthyroid, thyroid autoantibody-positive women undergoing assisted reproductive treatment, given its potential benefits and minimal risk.[16]

References

1. Feng J, Wu Q, Liang Y, et al. Epidemiological characteristics of infertility, 1990-2021, and 15-year forecasts: An analysis based on the global burden of disease study 2021. Reprod Health. 2025;22(1):26. Doi: 10.1186/s12978-025-01966-7
2. Katole A, Saoji AV. Prevalence of primary infertility and its associated risk factors in urban population of central India: A community-based cross-sectional study. Indian J Community Med. 2019;44:337-41.
3. Mallikarjuna M, Rajeshwari BV. Selected risk factors of infertility in women: Case control study. Int J Reprod Contracept Obstet Gynecol. 2015;4(6):1714-19.
4. Olooto WE, Amballi AA, Banjo TA. A review of female infertility: Important etiological factors and management. J Microbiol Biotechnol Res. 2012;2(3):379-85.
5. Concepción-Zavaleta MJ, Coronado-Arroyo JC, Quiroz-Aldave JE, et al. Thyroid dysfunction and female infertility: A comprehensive review. Diabetes Metab Syndr. 2023;17(11):102876. Doi: 10.1016/j.dsx.2023.102876
6. Koyyada A, Orsu P. Role of hypothyroidism and associated pathways in pregnancy and infertility: Clinical insights. Tzu Chi Med J. 2020;32(4):312-17.
7. Dash A, Das P, Bhuyan A, et al. Thyroid dysfunction and infertility: Investigating subclinical hypothyroidism in reproductive-aged women. Int J Curr Pharm Rev Res. 2024;16(9):104-111.
8. Scoccia B, Demir H, Kang Y, et al. In vitro fertilization pregnancy rates in levothyroxine-treated women with hypothyroidism compared to women without thyroid dysfunction disorders. Thyroid. 2012;22(6):631-6.
9. Wadhwa L, Marghret KM, Arora S. Evaluation of reproductive outcome in infertile hypothyroid women on thyroxine therapy. J Hum Reprod Sci. 2020;13(4):272-6.
10. Kulkarni AC, Thakur M, Patil P. The impact of thyroid disorders on women's reproductive and metabolic health: A systematic review. J Contemp Clin Pract. 2025;11(6):808-16.
11. Bucci I, Giuliani C, Di Dalmazi G, et al. Thyroid autoimmunity in female infertility and assisted reproductive technology outcome. Front Endocrinol (Lausanne). 2022;13:768363. Doi: 10.3389/fendo.2022.768363
12. Verma I, Sood R, Juneja S, et al. Prevalence of hypothyroidism in infertile women and evaluation of response of treatment for hypothyroidism on infertility. Int J Appl Basic Med Res. 2012;2(1):17-19
13. De Groot L, Abalovich M, Alexander EK, et al. Management of thyroid dysfunction during pregnancy and postpartum: An Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2012;97(8):2543-65.
14. Alexander EK, Pearce EN, Brent GA, et al. 2017 Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and the postpartum. Thyroid. 2017;27(3):315-89.
15. Poppe K, Bisschop P, Fugazzola L, et al. 2021 European Thyroid Association guideline on thyroid disorders prior to and during assisted reproduction. Eur Thyroid J. 2021;9(6):281-95.
16. Indian Thyroid Society (ITS); Federation of Obstetric and Gynaecological Societies of India (FOGSI). 2019 Recommendations for the Management of Thyroid Dysfunction in Pregnancy. Indian Thyroid Society; 2019. Available from: https://indianthyroidsociety.in/assets/img/guidelines/ITS_FOGSI_Recommendations.pdf
17. Brown EDL, Obeng-Gyasi B, Hall JE, et al. The thyroid hormone axis and female reproduction. Int J Mol Sci. 2023;24(12):9815. Doi: 10.3390/ijms24129815
18. Kim CH, Ahn JW, Kang SP, et al. Effect of levothyroxine treatment on in vitro fertilization and pregnancy outcome in infertile women with subclinical hypothyroidism undergoing in vitro fertilization/intracytoplasmic sperm injection. Fertil Steril. 2011;95(5):1650-4.
19. Chen YT, Ho CH, Chung MT, et al. Effect of extra-low dose levothyroxine supplementation on pregnancy outcomes in women with subclinical hypothyroidism undergoing in vitro fertilization and embryo transfer. Taiwan J Obstet Gynecol. 2023;62(6):869-73.
20. Khan I, Sharma R, Singhal S, et al. The influence of thyroid hormone replacement on endometrial receptivity in infertile women. Int J Reprod Contracept Obstet Gynecol. 2025;14(8):2631-5.
21. Yoshioka W, Amino N, Ide A, et al. Thyroxine treatment may be useful for subclinical hypothyroidism in patients with female infertility. Endocr J. 2015;62(1):87-92.

Abbott

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only.
For more information, please contact: Medical sciences Division, Abbott India Limited,
16th Floor, Godrej BKC, Plot no. C-68, BKC, Near MCA Club, Bandra (East), Mumbai 400 051.

IN-26-2396 07 JUN 2026

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only.