National Consensus Statement for the Management of Hypothyroidism in Nepal

Dina Shrestha, MD
Head,
Department of Endocrinology,
Norvic International Hospital,
Kathmandu, Nepal
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From the President’s Desk

“Gaining knowledge is the first step to wisdom and sharing it is the first step to humanity.”

It is the need of the hour for us to unite to spread the knowledge we have gained in the past decades with our experiences so we can amalgamate it with the data and text from around the globe and use it to benefit our society which is unique in its ways from the rest of the world. This is our first, albeit small, step in our academic journey. DEAN, with all its members, truly put in a great show of effort with this document, which only encourages the organization to take on more of such endeavors in the future. We hope this effort of ours travels far and wide to even the hard-to-reach corners of our healthcare system and helps the caregivers and health professionals to provide better care to the patients.

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Dina Shrestha
President

DEAN
NEPAL
Core Committee Members

Dina Shrestha, MD
Head,
Department of Endocrinology,
Norvic International Hospital,
Kathmandu, Nepal

Mimi Giri, B.Sc (Joint), MD, PhD
Head,
Department of Endocrinology,
Nepal Mediciti Hospital,
Lalitpur, Nepal

Hari Kumar Shrestha, MD
Lecturer,
Department of Internal Medicine,
Kathmandu University School of Medical Science,
Kathmandu, Nepal

Manil Ratna Bajracharya, MD
Associate Professor,
Diabetes and Endocrine Unit,
Department of Medicine,
Bir Hospital NAMS,
Kathmandu, Nepal
Abstract

Hypothyroidism, most common of all the thyroid disorders, is estimated to have a worldwide prevalence of up to 4.6%. Although epidemiological data of hypothyroidism in Nepal is not available, several hospital-based studies have indicated a high prevalence ranging from 8 to 11.6%. Currently, there are no national guidelines in Nepal for the management of hypothyroidism. This document reviews the current international and regional guidelines and summarizes a consensus statement specifically for Nepal based on experts' opinion and evidence from literature.

Introduction

Thyroid is an important endocrine gland, which utilizes iodine from food and produces two hormones, thyroxine (T4) and triiodothyronine (T3). Thyroid gland also produces another hormone called calcitonin. While calcitonin regulates the level of calcium in the body, T3 and T4 play a major role in various metabolic functions. These metabolic processes get disrupted due to dysfunction of the thyroid gland. Common thyroid disorders include hypothyroidism, hyperthyroidism, goiter, thyroiditis, thyroid nodules, and thyroid cancer.1

Hypothyroidism is the most common of all the thyroid disorders with a worldwide prevalence ranging from 3.05 to 4.6%.2–4 The global prevalence seems to be increasing over time, which could be due to several factors such as increase in iodine deficiency worldwide, better screening for the disease, and aging population.3,5–7 This disorder of the thyroid gland is much more common in women than in men and is seen more frequently with increasing age.2,8

Although a large-scale study on general population to understand the epidemiology of hypothyroidism in Nepal is lacking, several hospital-based studies have indicated a high prevalence in this landlocked Himalayan country. The prevalence of hypothyroidism in various hospital-based studies from different parts of Nepal ranged from 8 to 11.6%.9–12 Nepal lies in the iodine-deficient zone of the world and, therefore, several steps have been taken by the Government of Nepal to overcome the iodine deficiency issues.5,13 Consequently, recent surveys have indicated an adequate intake of iodine in the general population of Nepal.13 Although iodine deficiency was the main cause of hypothyroidism in Nepal until recently, with universal iodization of salt, autoimmune disease may now be an important cause. However, efforts to ensure adequate iodine intake should be continued.

There are several international/regional guidelines for the management of thyroid disorders including hypothyroidism.16–18 However, there is no such guideline in Nepal. Thus, there is a need for development of guidelines specifically meant for management of hypothyroidism, which is the most common thyroid disorder in this region.

This consensus statement is an effort to bridge the existing gap and hopefully a guideline will be developed in the future.
Etiology of Hypothyroidism

The function of thyroid gland is controlled by the hypothalamic-pituitary-thyroid axis. Thyroid-stimulating hormone (TSH), released by the pituitary gland, controls the level of thyroid hormones. TSH, in turn, is controlled by the TSH-releasing hormone that is secreted by the hypothalamus. Hypothyroidism can occur as a result of primary failure of the thyroid gland or due to inadequate stimulation of the thyroid gland at the pituitary or hypothalamus level.

Primary causes of hypothyroidism include iodine deficiency; autoimmune diseases such as Hashimoto’s thyroiditis and atrophic thyroiditis; congenital hypothyroidism; drugs such as lithium, amiodarone, interferon-α, antithyroid drugs; and iatrogenic factors such as radioactive iodine therapy, thyroidectomy, and external irradiation of neck for lymphoma or cancer. Secondary or central causes include hypothalamic and pituitary diseases such as tumors, trauma, or infiltrative disorders.

In Nepal, endocrine disruptors like insecticides and pesticides may have a role to play in the development of hypothyroidism; however, this area needs further study.

Signs and Symptoms of Hypothyroidism

Hypothyroidism can be asymptomatic in a large number of patients. In symptomatic patients, the most common presentation includes tiredness/weakness, dry coarse skin, cold sensitivity, menstrual irregularities, muscle cramps, hair thinning/hair loss, depression, hoarse voice, impaired concentration, memory impairment, weight gain, and constipation. With severe disease, additional findings such as delayed tendon reflex relaxation, carpal tunnel syndrome, edema, dyspnea, and even myxedema coma may be seen. Clinical presentation may vary depending on the age and sex of the patients. Thus, women may present more commonly with menstrual irregularities, children with lethargy and failure to thrive, and older patients with cognitive decline. If left untreated, hypothyroidism can also lead to detrimental effects on the serum lipid profile and can cause cardiovascular problems. It can cause infertility/subfertility, cognitive impairment, and neuromuscular problems.

Screening for Hypothyroidism

Measurement of serum TSH is the best screening test for hypothyroidism. Screening of general population for hypothyroidism has been a matter of debate. However, screening is recommended in following cases: type 1 diabetes, pernicious anemia, family history of autoimmune thyroid disorder, psychiatric disorders, and patients treated for hyperthyroidism. For individuals with any autoimmune disorder (e.g., systemic lupus erythematosus) or any endocrine abnormality (e.g., premature ovarian failure), screening is recommended as they are at a higher risk. In addition, in Nepal, annual screening is recommended in population with no access to iodized salt and for those who are 50 years or older. Thyroid function test can be conducted at any time of the day without fasting.
Preconception

As per the most recent (2017) American Thyroid Association (ATA) guidelines for the diagnosis and management of thyroid disease during pregnancy and postpartum, "there is insufficient evidence to recommend for or against universal screening for abnormal TSH concentrations preconception, with the exception of women planning assisted reproduction or those known to have antithyroid peroxidase antibody (TPOAb) positivity." However, the Indian Thyroid Society Guidelines support the view that screening should be carried out during prepregnancy evaluation. Further, a study conducted in the United States found a high rate of subclinical hypothyroidism in women planning conception, which implies that preconception screening could be an important step to identify and treat these women, and thus prevent adverse outcomes. Screening for TPOAb preconception has also been proposed (although supportive data are lacking), considering the high prevalence of TPOAb positivity in the women of reproductive age group. TPOAb test also helps in identifying women who are at risk of developing hypothyroidism during pregnancy.

In Nepal, universal screening at preconception is strongly recommended specially in following high-risk cases: age greater than 30 years; body mass index (BMI) greater than or equal to 30 kg/m²; presence of other autoimmune diseases; presence of symptoms of hypothyroidism; family history/past history of thyroid disease; previous head and neck irradiation; use of drugs such as amiodarone and lithium that interfere with thyroid function; presence of circulating TPOAb, history of previous miscarriage, preterm delivery, or infertility; women residing in an area of known moderate-to-severe iodine insufficiency; and a history of developmental delay in family.

Diagnosis of Hypothyroidism

TSH, Free $T_3$, Free $T_4$, and Thyroid Antibodies

Diagnosis of hypothyroidism is made by measurement of blood levels of TSH and thyroid hormones. Most of the $T_3$ and $T_4$ is protein-bound and therefore, factors affecting the binding may affect the levels of total serum $T_3$ and $T_4$. Evaluation of free thyroid hormones instead of total hormones is, therefore, considered as a more accurate measure of thyroid function. However, in certain cases, for example in pregnant women, measurement of total $T_4$ is recommended instead of free $T_4$ levels. Thyroid antibodies may be a discerning factor in the differential diagnosis.

Reference Range for TSH

The reference range for TSH seems to vary with age, sex, race, ethnicity, and geographical area. In the ideal situation, upper limit of normal for a third-generation TSH assay must be determined by the reference range of a given laboratory. There are different methods of determination of TSH levels and each method has a slightly different reference range. Some methods along with the
reference values are listed in Table 1. In the absence of reference values, a range of 0.45 to 4.12 mIU/L should be used. Recently, the National Indian Patient-Centered Thyroid Management group proposed patient-centered target TSH levels, that is, a low or a high target based on certain factors such as etiology, stage of life (e.g., lower TSH targets during preconception and pregnancy, and higher TSH targets for elderly), comorbid conditions, clinical course of the disease, patient’s attitude toward therapy, and patient’s ability to undergo frequent monitoring.

Overt and Subclinical Hypothyroidism

Hypothyroidism can be overt or subclinical (Table 2). A high level of TSH, above the upper reference range, accompanied by a low T4 level accounts to a diagnosis of overt hypothyroidism. In subclinical hypothyroidism, the serum TSH is elevated above the upper reference range with a normal T4 level. Subclinical hypothyroidism should be diagnosed only when thyroid function has been stable for at least 6 to 8 weeks. In patients with subclinical hypothyroidism TPOAb measurements should be considered.

Table 1  Thyroid-stimulating hormone reference range by different methods

| Company/brand | Methoda | TSH reference range in adults (mIU/L) |
|---------------|---------|--------------------------------------|
| Roche Elecsys Cobas | Electrochemiluminescence immunoassay (ECLIA) | 0.27–4.2 |
| Siemens ADVIA Centaur TSH3-Ultra (TSH3-UL) | Chemiluminescent immunoassay (CLIA)b | 0.55–4.78 |
| Beckman Coulter Access | Chemiluminescent immunoassay (CLIA)b | 0.45–5.33 |
| Abbott Architect | Chemiluminescent microparticle immunoassay (CMIA) | 0.45–4.12 |
| DiaSorin TSH-CTK-3 IRMA | Immunoradiometric assay (IRMA) | 0.25–3.51 |

*a Other methods include radioimmunoassay (RIA), competitive protein-binding assay (CPBA), radioreceptor assay (RRA), enzyme-linked immunosorbent assay (ELISA), microparticle enzyme immunoassay (MEIA), fluoroimmunoassay (FIA).

b In Nepal, CLIA and ECLIA are preferred.

Table 2  Overt hypothyroidism and subclinical hypothyroidism

| Overt hypothyroidism | Subclinical hypothyroidism |
|----------------------|---------------------------|
| Thyroid-stimulating hormone (TSH)* | High | High |
| Free thyroxine (T4) | Low | Normal |

*Upper limit of normal for a third-generation TSH assay should be determined by the reference range of a given laboratory, or the absence of which an upper limit of 4.12 mIU/L should be used.
Primary and Central Hypothyroidism

When low fT₄ level is accompanied by a high level of TSH, the diagnosis is primary hypothyroidism, and if it is accompanied by normal or low TSH, the diagnosis is central hypothyroidism.

Iatrogenic Hypothyroidism

In patients who develop hypothyroidism as a result of treatment of hyperthyroidism, for example, in patients treated with antithyroid drugs, radioactive iodine, or surgery, TSH may remain elevated. Therefore, in these patients, low serum-free T₄ alone is diagnostic.

Autoimmune Diseases

Autoimmune diseases can be diagnosed by detection of elevated antithyroid antibody titers, which include antithyroglobulin antibodies (TgAb), TPOAb, and TSH receptor antibodies (TSHRAb). In Nepal, anti-TPO test may be relevant and it is recommended as it is more easily available and cost-effective.

Treatment of Hypothyroidism

Patients with hypothyroidism usually require treatment with lifelong thyroid hormone replacement. Although T₃ can also be used for treatment, it is generally not recommended and levothyroxine remains the treatment of choice. Levothyroxine is recommended universally for its efficacy, favorable safety profile, ease of administration, and low cost.

The initial daily dose of levothyroxine is determined based on the TSH level, age, sex, and weight of the patient. Generally, an initial dose of 1.6 μg/kg/d is considered as a standard, which can be gradually titrated to achieve target TSH level. In our population, a lower initial dose may be required. Dose adjustments may be required 4 to 8 weeks after starting levothyroxine based on the level of TSH. The usual starting dose of levothyroxine for an adult is 50 or 100 μg/d, which can be gradually increased to a maintenance dose of 100 to 200 μg/d according to target TSH level.

It is well known that food may affect levothyroxine absorption. Therefore, levothyroxine must be taken either approximately an hour before a meal or at bedtime 3 to 4 hours after the last meal. It is important to note that there are no food restrictions (such as for cabbage, cauliflower, soya, or broccoli). However, certain drugs that may affect the absorption of levothyroxine, such as proton pump inhibitors, calcium carbonate, and ferrous sulfate, should be taken with a gap of 4 hours, whenever possible. If high levels of levothyroxine are required to maintain TSH within the reference range, after eliminating other causes that may interfere with levothyroxine absorption, patients must be evaluated for Helicobacter pylori, atrophic gastritis, coeliac disease.

In addition, it has been found that noncompliance to treatment is fairly common. Therefore, if patients who are prescribed adequate doses of
levothyroxine have persistent high levels of TSH, patient noncompliance to treatment should be considered rather than malabsorption of the drug, except in patients with severe hypothyroidism, cardiovascular disease, and the elderly. In patients with severe noncompliance issues, once-weekly dosing can be considered followed by testing for free $T_4$ and TSH after treatment in the morning.

In order to get a consistent effect, it is recommended to use the same preparation of levothyroxine without switching between different brands as bioavailability differs with brands. Switching between different preparations of levothyroxine may lead to variations in the dose, and therefore, should be avoided.

**Monitoring of Treatment and Follow-Up**

Treatment adequacy should be evaluated based on the results of thyroid function tests. Serum TSH level (TSH reference range 0.45–4.12 mIU/L) is the most reliable therapeutic end point for the treatment of primary hypothyroidism. Serum TSH measurements should be done 4 to 8 weeks after initiating treatment or after a change in dose. Once an adequate replacement dose has been determined, TSH measurements should be done 6 monthly. TSH measurements can be carried out more frequently, if required. It is recommended that dose adjustment is done if two consecutive abnormal values are obtained, except in pregnant women.

It must be ensured that optimum thyroid function is obtained following treatment. Care must be taken to prevent overtreatment of hypothyroidism, which may lead to cardiovascular effects (such as atrial fibrillation) and skeletal effects (such as osteoporosis). Therefore, proper precautions must be taken especially in older men and postmenopausal women. Likewise, it should also be remembered that undertreatment may also lead to untoward effects on the lipid profile and cardiovascular health.

**Referral**

Although most cases of hypothyroidism can be managed by physicians, expert help by an endocrinologist must be sought for the following: pediatric patients, pregnant women or women planning conception, patients with cardiac disease, patients with goiter or thyroid nodule, patients with adrenal or pituitary disorders, patients with conditions that may affect the level of levothyroxine, unusual thyroid function test results, and patients in whom euthyroid state is difficult to achieve and maintain.

**Subclinical Hypothyroidism**

As mentioned earlier, subclinical hypothyroidism is a condition when serum TSH is elevated with a $fT_4$ level within the normal reference range. Subclinical hypothyroidism is more common than overt hypothyroidism. Patients with
subclinical hypothyroidism may later develop overt hypothyroidism.\(^{45}\) It has been found that subclinical hypothyroidism is associated with cardiovascular disorders including heart failure especially in the elderly and also with an increased risk of fatal and nonfatal coronary heart disease events. Moreover, it is also believed that treating subclinical hypothyroidism may be associated with cognitive benefits. It is well accepted that all patients with serum TSH levels more than 10 mIU/L must be treated.\(^{16,46}\) However, whether all patients with TSH levels between 4.5 and 10 mIU/L will benefit from treatment has not been established. It is believed that certain patients, for example, those with associated cardiovascular risk factors may benefit from treatment.\(^{47}\) In addition, treatment should also be considered for patients with symptoms suggestive of hypothyroidism and those with positive TPOAb.\(^{2,16,17}\) If serum TSH levels are between 4.5 and 10 mIU/L on more than two consecutive times, treatment is considered.

While some experts advocate the treatment of subclinical hypothyroidism, others advise to be cautious and to weigh the risk–benefit ratio before initiating treatment.\(^{16}\) In a recent multicenter randomized placebo-controlled trial in Europe (TRUST study; mean TSH level, 6.4 mIU/L), levothyroxine provided no apparent benefits in older persons with subclinical hypothyroidism.\(^{48}\) It is advisable to decide whether to treat subclinical hypothyroidism depending on the risks and benefits involved in each case individually.

As per the Washington Manual of Medical Therapeutics (34th edition, 2014), subclinical hypothyroidism should be treated if any of the following is present: symptoms compatible with hypothyroidism, a goiter, hypercholesterolemia requiring treatment, or plasma TSH level of greater than 10 mIU/L. Untreated patients should be monitored annually, and treatment should be started if symptoms develop or serum TSH increases to greater than 10 mIU/L.\(^{49}\)

### Hypothyroidism in Pregnancy

Hypothyroidism during pregnancy is associated with serious risks to both the mother and the fetus. Maternal complications include spontaneous miscarriage, preterm delivery, preeclampsia, postpartum hemorrhage. Complications related to the fetus/infant include low birth weight, stillbirth, and impaired intellectual and psychomotor development. Subclinical hypothyroidism may also be associated with adverse pregnancy outcomes.\(^{50-53}\)

The normal reference range for TSH during pregnancy is lower than the normal reference ranges for the general population. Ideally, trimester-specific reference range for TSH for the particular laboratory should be used. If this is unavailable, it is recommended to consider the upper reference range for TSH during the first trimester of pregnancy as 2.5 mIU/L and that during the second and the third trimester as 3.0 mIU/L and 3.5 mIU/L, respectively (2.5 mIU/L for first and 3.0 mIU/L for second and third trimesters as per the Indian guidelines).\(^{16,17,23}\)
In pregnant women with TPOAb thyroid function testing is recommended. Levothyroxine should be prescribed if the level of TSH is more than the upper reference range. Further, TPOAb-positive pregnant women with history of miscarriage or past history of hypothyroidism, should be considered for treatment with levothyroxine even if the TSH level is normal.16

Indian guidelines recommend treatment with levothyroxine 25 μg/day for TSH between upper limit (for each trimester) and 10 mIU/L and 50 μg/d for TSH greater than 10 mIU/L.23 It is recommended that the dose should be increased by about 30 to 50% (based on TSH level) as soon as a woman on thyroid replacement therapy is found to be pregnant.54,55

In pregnant women who are on thyroid replacement therapy, serum TSH and total T4 should be checked every 4 weeks during the first half of pregnancy, and at least once between 26 and 32 weeks of gestation. Levothyroxine dose can be adjusted to ensure that the TSH levels remain within the trimester-specific reference range.16 In the first trimester, dose of levothyroxine should not be adjusted based on low TSH alone as human chorionic gonadotropin (HCG) can lower the levels of TSH. Postpartum treatment and regular follow-up should be continued in women with TSH level greater than 10 mIU/L.23

Isolated hypothyroxinemia in pregnancy can occur without requiring treatment.

In pregnant women with previously undiagnosed/untreated hypothyroidism, counselling is strongly recommended with final decision being with the specialist.

**Congenital Hypothyroidism**

Congenital hypothyroidism is considered as the most common congenital endocrine disorder with an incidence of 1 in 4,000 live births.56,57 It is also the leading cause of preventable intellectual disability.57–59 Most common cause of congenital hypothyroidism is thyroid dysgenesis, which accounts for about 85% of the total cases.57

Every newborn should be screened for congenital hypothyroidism within 72 hours of birth (TSH reference range 1.3–19 mIU/L). Abnormal value at 72 hours should be reassessed after 1 week.

Once diagnosed, levothyroxine replacement should be started at a dose of 10 to 15 μg/kg/d.17,57,60 Levothyroxine tablet should be crushed and given mixed with water or breast milk in the morning, and feeding should be withheld for 30 to 45 minutes after administering the medication.60 The aim of the treatment should be to maintain level of fT4 in the upper half of the age-specific reference range and that of TSH in the age-specific reference range.17,60 After the target level of TSH is achieved, thyroid function test should be carried out every 6 weeks up to the age of 6 months, and every 8 weeks from 6 months to 1 year. From the age of 1 to 3 years, thyroid function should be checked every 3 months and thereafter every 6 to 12 months until growth is completed.60 There is no evidence to suggest that children with normal tests at neonatal screening should be reassessed unless they are symptomatic.
Hypothyroidism in Pediatric Age Group

The management of hypothyroidism in children is mostly similar to that in adults. All children with overt hypothyroidism should be treated with levothyroxine. However, the weight-based dose of levothyroxine in children is higher as compared to adults and decreases gradually as the child grows. While newborns may need a dose as high as 10 μg/kg/d, children around the age of 1 year may require 4 to 6 μg/kg/d, and for adolescents a dose of 2 to 4 μg/kg/d may suffice.17

If subclinical hypothyroidism is diagnosed in the pediatric age group, it is considered safe to start therapy with levothyroxine to prevent detrimental effects on growth and development. Treatment is generally recommended when TSH level is greater than 10 mIU/L.17

Need to Develop National Hypothyroidism Guidelines for Nepal

Although a lot of literature and guidelines are available on hypothyroidism as described above, no standard protocol is currently being followed in Nepal. In addition, the ATA/American Association of Clinical Endocrinologists (AACE) or other international guidelines may not be completely applicable to Nepal. The types of resources available in Nepal are limited. Also, the disease scenario has been changing and so has medicine practice. Current medical practice needs evidence-based and easy-to-follow guidelines that will enable standardization of disease management. It is, therefore, important that all these factors are considered while developing country-specific guidelines, which will attempt to address the need for consensus-based management of thyroid disorders. It is important to note that due to lack of clinical data in Nepal, the hypothyroidism consensus statement summarized below are based on expert opinion and published evidence from other countries.

This consensus statement is but a step toward the guidelines which can hopefully be formulated in the near future.

Summary of Hypothyroidism Consensus Statement for Nepal

Based on the literature evidence and expert opinions, following are the recommendations for the management of hypothyroidism in Nepal.

Recommendations for screening

- In general population, annual screening for hypothyroidism by measurement of serum TSH level is recommended in following cases:
  - Individuals with no access to iodized salt.
  - Ageing population (more than 50 years of age).
  - Individuals with type 1 diabetes mellitus.
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• Individuals with pernicious anemia.
• Individuals with a family history of autoimmune thyroid disorder.
• Individuals with psychiatric disorders.
• Individuals treated for hyperthyroidism.

• In preconception/pregnant women, universal screening is recommended specially in following high-risk cases:
  ◦ Women older than 30 years.
  ◦ BMI of greater than or equal to 30 kg/m^2.
  ◦ Women who reside in areas of moderate-to-severe iodine insufficiency.
  ◦ Presence of other autoimmune diseases.
  ◦ Symptoms of hypothyroidism.
  ◦ Family history/past history of thyroid disease.
  ◦ Previous head and neck irradiation.
  ◦ Use of drugs such as amiodarone and lithium that interfere with thyroid function.
  ◦ Presence of circulating TPOAb.
  ◦ History of previous miscarriage, preterm delivery, or subfertility.
  ◦ History of developmental delay in the family.

**Recommendation for diagnosis and treatment**

• The diagnosis of hypothyroidism should be made by measurement of TSH level and free T^4_4 level (except in pregnancy when measurement of total T^4_4 instead of free T^4_4 is recommended).
  ◦ Upper limit of normal for a third-generation TSH assay should be determined by the reference range of a given laboratory. In the absence of reference values, a range of 0.45 to 4.12 mIU/L should be used.
  ◦ In pregnancy, trimester-specific reference range for the particular laboratory should be used, in the absence of which 2.5, 3.0, and 3.5 mIU/L should be considered as the upper reference range for TSH during the first, second, and third trimester, respectively.
  ◦ For the diagnosis of autoimmune diseases, anti-TPO test is recommended.

• Patients should be treated with levothyroxine. Starting dose should be 50 to 100 μg/d. TSH level should be checked 4 to 8 weeks after starting treatment. The dose should be gradually titrated based on the level of TSH.

• Treatment for subclinical hypothyroidism should be carried out in following cases:
  ◦ All patients with TSH level greater than or equal to 10 mIU/L.
  ◦ Following cases, if TSH level is between 4.5 and 10 mIU/L:
    - Patients with cardiovascular risk factors.
    - Patients with symptoms of hypothyroidism.
    - Patients with positive TPOAb.
• Patients with psychiatric disorders.
• Patients with goiter.
• Patients with dyslipidemia.
• Preconception.
• Children with developmental delay.
• Preconception.
• Pregnant women.

◊ When TSH levels are between 4.5 and 10 mIU/L more than two consecutive times.

**Recommendations for monitoring and follow-up**

• Treatment should be monitored by TSH levels done at 4 to 8 weeks initially, and then 6 monthly once adequate dose of levothyroxine has been determined.

• In pregnant women, serum TSH and total T₄ should be checked every 4 weeks during the first half of pregnancy, and at least once between 26 and 32 weeks.

• Following hypothyroid patients should be referred to a specialist:
  ◊ Pediatric patients.
  ◊ Pregnant women or women planning conception.
  ◊ Patients with cardiac disease.
  ◊ Patients with goiter or thyroid nodule.
  ◊ Patients with adrenal or pituitary disorders.
  ◊ Patients with conditions that may affect the level of levothyroxine.
  ◊ Patients with unusual thyroid function test results.
  ◊ Patients in whom euthyroid state is difficult to achieve and maintain.

**Recommendations for congenital hypothyroidism**

• All newborn babies should have a heel prick (if available) or a venous blood screening test for TSH by 72 hours of birth.

• In babies diagnosed with congenital hypothyroidism, levothyroxine replacement must be started at a dose of 10 to 15 μg/kg/d.

• After the target level of TSH is achieved, thyroid function test should be carried out every 6 weeks up to the age of 6 months, and every 8 weeks from 6 months to 1 year. Between the age of 1 and 3 years, thyroid function should be checked every 3 months, and every 6 to 12 months thereafter.

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