NEWS LINE

KARNATAKA ENDOCRINE SOCIETY

2nd Issue | September 2023

THEME - THYROID & PARATHYROID ISSUES

PRESIDENT MESSAGE

Dear Colleagues,

It's a great honor for me to serve as the President, Karnataka Endocrine Society. I thank all the members of the Society for this opportunity, and we have done quite a significant academic job and most physicians, Pediatricians, Gynecologists and Obstetricians are aware of our work. We need to spread the awareness to other medical specialties in Karnataka. We are conducting monthly case discussions in virtual platform, three monthly physical meeting inviting people across specialties from India who have original works and most importantly the Annual conference, Hormone Rhythm. This Newsletter is our second Edition on Thyroid & Parathyroid issues, common problems, and their solutions for non-Endocrinologists. This is in follow up with our first newsletter published on Diabetes three months back which received a huge positive response from doctor colleagues across Karnataka of different specialities. I wish the very best to the Editorial team for their efforts and all their present and future endeavors.

Warm regards,

Dr. Arpandev Bhattacharyya

EDITORIAL BOARD - MESSAGE

NAVIGATING THYROID AND BONE HEALTH

Dear friends,

Welcome to the our second news letter! In this edition, we delve into topics that are not only relevant but also crucial for maintaining optimal health – Thyroid and Bone. Our goal is to provide you with valuable insights and information that can empower you to make informed decisions about your well-being. We hope that this edition proves to be informative and insightful. Our team has worked tirelessly to curate content that empowers you to make healthier choices for yourself and your loved ones. Remember, knowledge is the first step towards good health. As always, we welcome your feedback and suggestions for future topics. Please feel free to reach out to us at. Your input helps us create content that resonates with your interests and concerns.

Thank you for being a part of our KES community. We're dedicated to supporting you on your journey to a healthier, happier life.

Warm regards,

Dr. Vageesh Ayyar Subramanyam, Dr. Chitra Selvan

Editorial Board

Dr. Arpandev Bhattacharyya
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Editorial Board

HYPOTHYROIDISM: ANSWERING QUESTIONS COMING UP IN THE CLINIC!

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Q.1). How common is hypothyroidism?

The prevalence of hypothyroidism in India is 11%, compared with only 2% in the UK and 4·6% in the USA.

Q.2) How should levothyroxine administration be timed with respect to meals and beverages in order to maintain maximum, consistent absorption?

Levothyroxine is absorbed in the small intestine and is 70%-80% bioavailable in the euthyroid individual. Peak absorption is achieved at approximately 2 hours after oral ingestion but can be delayed to 3-4 hours if it is ingested simultaneously with interfering medications, supplements, or some foods/drinks. As such, current guidelines by the American Thyroid Association advise patients to take levothyroxine at least 60 minutes before the first meal of the day or at bedtime (at least 3 hours after the evening meal).

Q.3) Is there a clinical rationale for prescribing brand-name levothyroxine preparations in preference to generic levothyroxine?

Prescription of brand name levothyroxine, or alternatively maintenance of the same generic preparation (i.e., maintenance of an identifiable formulation of levothyroxine), is advised. Switches between levothyroxine products could potentially result in variations in the administered dose and should generally be avoided for that reason.

Q.4) What is the appropriate management of perceived allergy to the constituents of levothyroxine or intolerance to levothyroxine?

Perceived allergy or intolerance to levothyroxine can be managed by changing the dose or product, including consideration of gel capsules, and possibly by treating concomitant iron-deficiency anemia. In selected cases, a consultation with an allergist may be appropriate.

Q.5) Are there situations in which therapy with levothyroxine dissolved in glycerin and supplied in gelatin capsules may have advantages over standard levothyroxine?

Although there are preliminary small studies suggesting that levothyroxine dissolved in glycerin and supplied in gelatin capsules may be better absorbed than standard levothyroxine in selected circumstances such as concomitant use of proton pump inhibitors or concomitant coffee consumption, the present lack of controlled long-term outcome studies does not support a recommendation for the use of such preparations in these circumstances. Switch to a gel capsule might be considered in the rare case of putative allergies to excipients.

Q.6) What is the suggested starting dose of levothyroxine in different clinical situations ?

Category	Dose
Normal otherwise well patients	1.6 µg/kg/day
Pregnant patients	2-2.4 µg/kg/day
Elderly patients	25-50 µg/day
Patients with ischemic heart disease	12.5-25 µg/day
Patients on enzyme inducing drugs	2 µg/kg/day
Newborns	10 - 15 µg/kg/day, i.e., 50 µg/day
Children	4 - 5 µg/kg/day, i.e., 12.5 - 50 µg/day

Q.7) What are the causes of persistently elevated thyroid-stimulating hormone in a patient on levothyroxine replacement?

- Inadequate levothyroxine dose
- Poor compliance with medication (biochemistry usually showing high thyroid-stimulating hormone with normal free T4, if they have re-started the medicine a few days prior to coming to the clinic)
- Interaction with concomitant drugs (Iron sulphate, calcium carbonate, omeprazole etc)
- Taking levothyroxine with food
- Malabsorption (celiac disease or autoimmune gastritis (B12 deficiency))
- Interference with the laboratory assay due to heterophil antibodies or biotin
- Thyroid hormone resistance (rare)

Q.8) What are the precautions required for the optimal delivery of iodine from iodized salt?

The following precautions should be observed while using iodized salt. Salt should be purchased within 3 months of manufacturing date, and at time of purchase, it should be crystal clear and white. It should be stored in a dry airtight container along with plastic pack and should be kept away from the furnace. Once the pack is opened, it must be consumed within 4 weeks. Salt should preferably be added on the table rather than during cooking, as iodine quickly sublimates on exposure to heat.

Q.9) What is the role of iodine supplementation in patients with hypothyroidism?

Iodine supplementation in patients with hypothyroidism on levothyroxine replacement has no added advantage in improving thyroid function. However, routine iodized salt intake should be continued as iodine has many extrathyroidal advantages, which include improvement in pregnancy outcome, antioxidant and anticancer properties, and suppression of autoimmunity.

Q.10) What is the role of selenium in thyroid disease?

Metallic elements act as a cofactor in most of the biological reactions, but selenium is an exception. Selenium is incorporated co-translationally into polypeptide chain as selenocysteine and forms selenoproteins. Thyroid gland contains more selenium per gram of tissue than any other organ. The important selenoproteins are iodothyronine deiodinases, glutathione peroxidase, and thioredoxin reductase; the latter two are antioxidants. Selenium deficiency contributes to malfunction of these selenoproteins and may contribute to the development of autoimmune thyroid disease, goiter, and endemic cretinism.

Q.11) Is routine supplementation of selenium advised?

Although not robust, some data support that selenium supplementation may reduce anti-TPO antibody levels and decrease the incidence of postpartum thyroiditis. Moreover, the European Group of Graves' Orbitopathy (EUGOGO) guidelines recommend oral selenium supplementation for patients with mild thyroid-associated ophthalmopathy living in selenium-deficient areas. However, selenium use is associated with an increased risk of developing diabetes mellitus

Q.12) What is the role of Vitamin-B12 supplementation ?

Vitamin B12 is also taken by many patients for thyroid health. There is a known, frequent coexistence of Vitamin B12 deficiency in patients with autoimmune thyroid disease (AITD) secondary to pernicious anemia (PA). While replacement of vitamin B12 leads to improvement of symptoms associated with the deficiency, there is likely no impact on thyroid function. A study by Ottesen et al found no systematic effect on thyroid function after treatment with cyanocobalamin even in patients with decreased plasma cobalamin levels but simultaneously recommended routine screening for thyroid function and thyroid autoantibodies in patients with latent or overt PA. However, current vitamin B12 measurement methods, based on competitive binding luminescence assays, have been used since 1990. In these assays low vitamin B12 levels can be measured as falsely normal or falsely high, especially in pernicious anemia, due to excessive amounts of anti-intrinsic factor antibodies present in the serum.

Q.13) Is there any benefit of Gluten-free diet in hypothyroidism?

Another elimination diet which is often implemented by patients with thyroid disease is a gluten-free diet. Patients with Hashimoto's thyroiditis and concomitant celiac disease do benefit from a gluten-free diet, particularly in reducing the mean levothyroxine dose. A gluten-free diet in patients without celiac disease has not been shown as an effective intervention in changing the natural course of Hashimoto's thyroiditis or improving thyroid function.

Q.14) Soy products and its interaction with thyroid?

Goitrogens has been also found in soy products. Several studies on isoflavone, that is the most abundant phytoestrogens in soy, have found that it inhibits the thyroid hormone synthesis in people with iodine deficiency while its unlikely to affect those who are euthyroid. The mechanism behind could be due to inhibition of the activity of TPO enzyme as seen in animal studies. Hence only patients with subclinical hypothyroidism who are iodine deficient are at a risk of developing overt hypothyroidism.

Q.15) Cruciferous Vegetables Elimination. Does it really help?

Cruciferous or brassica vegetables are common components of our diet. These vegetables include broccoli, cauliflower, brussels sprouts, cabbage, kale and others that are a common part of our patients' diets. Based on in-vitro data, it is believed that these vegetables contain goitrogenic compounds namely goitrin, thiocyanates and isothiocyanates that are capable of producing hypothyroidism. Cooking denatures the goitrogenic compound into a less harmful metabolite. So, properly cooked vegetables of brassica family can still be consumed by patients with hypothyroidism. If someone consumes raw cabbage (eg - In salad or burger) there is hypothetical a risk of generation of isothiocyanates, however the ordinary consumption of cruciferous vegetables is unlikely to cause hypothyroidism)

Q.16) Can biotin consumption affect thyroid assay results?

Some automated assays for measurement of thyroid tests utilize a biotin-streptavidin separation system . Patients who are ingesting 5 to 10 mg of biotin (eg, marketed over the counter to prevent hair loss) can have spurious results in these assays. Biotin may cause falsely low values in immunometric assays (eg, used to measure TSH), and falsely high values in competitive binding assays (eg, used to measure free T4, T3, and free T3, and TSH receptor-binding inhibitor immunoglobulin [TBII or TBI]). Patients taking biotin should hold the supplement for two days prior to assessing thyroid function and longer if they are taking more than 10 mg a day.

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HYPOTHYROIDISM MANAGEMENT IN SPECIAL SITUATIONS

Hypothyroidism is a common endocrine problem. Its clinical presentation varies from mildly elevated thyrotropin (TSH) levels in asymptomatic patients to severe hypothyroidism which can occasionally lead to myxoedema coma. Hypothyroidism can be primary when there is low thyroid gland activity or central secondary to decreased production of TSH due to either hypothalamic or pituitary dysfunction.

Primary hypothyroidism can also be classified as subclinical or clinical based on TSH. Clinical hypothyroidism is defined as high TSH concentration with low levels of T4. On the other hand, subclinical hypothyroidism is diagnosed when TSH is elevated above the reference range with T4 levels remaining within the normal range and the patient generally having no clinical manifestation. On the other hand, clinical hypothyroidism is defined as high TSH concentration with low levels of T4 in a patient presenting with overt symptoms.

Special situations

1. Elderly

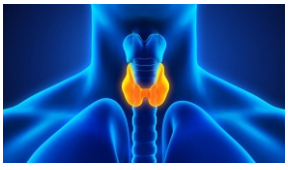
Hypothyroidism is a common disorder in the elderly, affecting between 5-20% of women and between 3-8% of in men. TSH concentrations are higher in the elderly due to age-related changes. The NHANES III study showed that the upper limit of the reference range (97.5% confidence interval) increases from 3.56mU/l in 20-29 years old to 7.9mU/l in people more than 80 years old. Thus, for the diagnosis of hypothyroidism, it will be essential to consider these age-related changes in TSH levels.

On the other hand, the diagnosis of hypothyroidism is usually delayed in elderly people because they can present with atypical symptoms that differ from the usual symptoms present manifest in young adults.

Regarding treatment, patients over 70 years of age require a 20 to 30% lower dose due to decreased lean body mass and reduced metabolic clearance of levothyroxine. Also, thyroid hormone replacement therapy should be initiated with smaller doses like 25mcg per day and gradually increased over 4 to 6 weeks under close monitoring given the frequent coexistence of cardiovascular disease.

2. Hypothyroidism and surgery

Hypothyroid patients would potentially have a higher risk of peri and postoperative complications like hyponatremia, hypoglycaemia, hypothermia, and paralytic ileus as compared to healthy subjects. However, very few adverse effects have been reported in hypothyroid patients undergoing surgery. Thus, in the event of an emergency, the surgery should not be postponed, but the patient should be closely monitored to prevent complications. The use of lower doses of anaesthetics, narcotics, hypnotics and anticoagulants should be considered, in particular, because the hypothyroid condition delays the metabolization of these drugs. However in patients who are undergoing elective surgeries, surgery can be postponed until the euthyroid state.



3. Hypothyroidism and pregnancy

Women found to have a TSH level greater than 10 mIU/L in the first trimester of pregnancy should be treated for hypothyroidism. Conversely, women with a TSH of 2.5 or less, do not need levothyroxine treatment. For women with TSH measured between these (2.5-10), recommendations for treatment vary and may depend on whether or not the mother has TPO antibodies. When TPO antibodies are positive, treatment is recommended when the TSH is above 4 and 'may be' considered when the TSH is between 2.5- and 4.0. The goal of treating hypothyroidism in a pregnant woman is adequate replacement of thyroid hormone. Ideally, hypothyroid women should have their levothyroxine dose optimized prior to becoming pregnant. Levothyroxine requirements frequently increase during pregnancy, usually by 25 to 50 percent. Hypothyroid women taking levothyroxine should independently increase their dose by 20%–30% as soon as pregnancy is diagnosed. Thyroid function tests should be checked approximately every 4 weeks during the first half of pregnancy to ensure that the woman has normal thyroid function throughout pregnancy. The thyroxine dose should be titrated to reach a serum TSH value of less than 2.5 mIU/litre. As soon as delivery of the child occurs, the woman may go back to her usual pre-pregnancy dose of levothyroxine. It is also important to recognize that prenatal vitamins contain iron and calcium that can impair the absorption of thyroid hormone from the gastrointestinal tract. Consequently, levothyroxine and prenatal vitamins should not be taken at the same time and should be separated by at least 4 hours.

4. Hypothyroid and dyslipidaemia

Hypothyroidism influences the metabolism of cholesterol, so dyslipidaemia is one of the metabolic complications of hypothyroidism. Statins have become the treatment of choice for hypercholesterolemia. One of the most common risks associated with the use of statins is the development of myopathy, a risk that will be aggravated if myopathy coexists with unsuspected hypothyroidism. It is advisable to rule out the presence of hypothyroidism in all patients with dyslipidaemia before starting a therapy with statins. Most lipid abnormalities in patients with overt hypothyroidism will resolve with thyroid hormone replacement therapy. However, clinical trials to date have not shown a consistent beneficial effect of thyroid hormone treatment on serum lipid levels in patients with subclinical hypothyroidism.

5. Hypothyroidism and adrenal insufficiency

Hypothyroidism can accompany adrenal insufficiency and hypopituitarism in a few conditions of like autoimmune aetiology and if it is not detected thyroid hormone replacement may exaggerate adrenal insufficiency. Thus, in such situations, it is necessary to start hydrocortisone replacement first and then the levothyroxine replacement after 4 to 7 days.

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SUBCLINICAL HYPOTHYROIDISM- TO TREAT OR NOT TO TREAT

Hypothyroidism is one of the most common endocrine conditions occurring in the general population. While treatment of overt hypothyroidism is straightforward with levothyroxine replacement, subclinical hypothyroidism (SCH) remains a grey area where the treating physician has to weigh the pros and cons of treatment, and decide on levothyroxine therapy versus watchful waiting. We aim to review this entity, its clinical implications, and major factors that drive decision making in these patients.

Subclinical hypothyroidism, also known as compensated hypothyroidism or mild hypothyroidism, is defined biochemically as a raised serum concentration of thyroid stimulating hormone (TSH) with normal serum free thyroxine (Ft4). It is commonly encountered in the general population, with an estimated prevalence of 10%, and affecting females more than males. The prevalence increases with advancing age, such that over 20% of women aged 75 years or above have serum TSH levels above the laboratory reference range. Based on the extent of TSH elevation, patients with subclinical hypothyroidism can be categorized into those with mildly elevated TSH- grade1 (4.5–10 mIU/L), and those with markedly increased serum TSH levels - grade 2 (>10 mIU/L). Approximately 90% of individuals with SCH have serum TSH levels less than 10 mIU/L.

Autoimmune thyroiditis (Hashimoto's thyroiditis or autoimmune atrophic thyroiditis) is the most common cause of subclinical hypothyroidism; other causes include previous treatment with radioiodine, subtotal thyroidectomy, postpartum or subacute thyroiditis, drugs (such as amiodarone, lithium and interferon) and rarely loss-of-function mutations in the TSH receptor gene.

Natural history of sub clinical hypothyroidism

The natural history of subclinical hypothyroidism depends on several factors like underlying cause, biological characteristics of the patient and the biochemical severity. It can be reversible or it can progress to overt hypothyroidism. Multiple studies have reported that 30-60% of individuals with SCH revert to euthyroidism in the first two years of diagnosis, with lower initial TSH and negative anti-thyroid peroxidase (TPO) antibody status being the major predictive factors for spontaneous normalisation of TSH.

On the other hand, progression has been reported to occur in approximately 3–18% of affected patients per year. Factors associated with increased risk of progression to overt hypothyroidism are as follows

- Older patients
- Female gender
- Positive for anti-TPO antibodies
- Serum TSH values >10 mIU/mL,
- History of radioiodine ablation for Graves' disease
- History of external radiation therapy for non-thyroid malignancies
- Chronic lithium treatment.
- High-dose iodine intake

Clinical implications of SCH

Symptoms of SCH may include fatigue, cold intolerance, weight gain, and constipation, as well as reduced mood, quality of life, cognitive function, and memory. The clinical symptoms are usually milder in individuals with SCH than those with overt hypothyroidism. Often the symptoms are non-specific and may not be clearly attributable to hypothyroidism. Approximately one in three individuals with SCH is asymptomatic.

The need for medically treating SCH arose from several studies that reported cardiovascular risk and impaired quality of life in individuals with SCH as compared to euthyroid individuals.

Multiple studies have found that SCH is associated with cardiac dysfunction, including left ventricular systolic and diastolic dysfunction. Patients with SCH have also been found to have increased carotid intima

media thickness, systemic vascular resistance and impaired vascular relaxation as compared to euthyroid individuals. Additionally, SCH has been associated with increased insulin resistance, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH) and adverse changes in lipid profile, including increased low density lipoprotein (LDL)-cholesterol and triglycerides.

Inspite of the adverse changes in the individual cardiac risk factors, a large individual patient meta-analysis with data from more than 75000 patients performed by the Thyroid Studies Collaboration revealed no increased risk of atrial fibrillation, heart failure, stroke, coronary heart disease events, mortality from coronary heart disease, or overall mortality compared with euthyroid individuals. However, TSH-based stratification of patients revealed an increased risk of progression of heart failure, coronary heart disease events, and mortality from coronary heart disease events in patients with TSH is >10 mIU/L. Additionally, there was an increased risk of fatal stroke and mortality from coronary heart disease in patients with TSH between 7-9.9 mIU/L. A TSH value >10 mIU/L has been found to be an age-independent risk for future heart failure.

Hence, the extent of TSH elevation appears to have a major bearing on the risk of adverse cardiovascular outcomes. There are limited randomized clinical trials with sufficient power to examine the impact of thyroid hormone therapy on cardiovascular events, and the TRUST study found that treatment of SCH did not impact the incidence of cardiovascular events within 1 year after initiation of therapy

Another major area of concern with SCH has been the reproductive health and outcomes. The evidence for adverse reproductive outcomes has not been as straightforward as seen in patients with overt hypothyroidism. Several studies have reported association of SCH with infertility, pregnancy loss, gestational hypertension, pre-eclampsia, gestational diabetes and adverse neonatal outcomes, while few other studies have shown no significant association between SCH and reproductive outcomes. Additionally, SCH has been associated with cognitive decline and dementia in younger individuals.

Management

It is important to establish the diagnosis of SCH by reconfirming elevated TSH levels within a span of three months before embarking on treatment decision making, except in patients with compelling evidence of benefits of immediate therapy, like pregnancy or infertility.

Transient elevation of TSH that normalises within three months has been seen in upto 60% of the patients. Additionally it is important to exclude other causes of TSH elevation like age-related physiological rise in TSH, acute illnesses, thyroiditis, obesity, drugs like amiodarone and lithium, macro-TSH and adrenal insufficiency. Overtreatment with levothyroxine can result in tiredness, weight loss, accelerated bone loss and increased risk of atrial fibrillation in these patients.

In general, all major society guidelines recommend levothyroxine therapy in individuals with SCH with TSH > 10 mIU/L, in view of sufficient evidence for adverse cardiovascular outcomes in these patients.

Treatment of asymptomatic patients with serum TSH concentrations between 4.5 mIU/L and 10 mIU/L remains a major area of speculation. There is insufficient evidence to suggest improvement in cardiovascular, fatigue, neurocognitive and quality of life indicators in SCH patients treated with levothyroxine. However many of these studies have important limitations like inconsistent definitions, varying doses of levothyroxine used, lack of data regarding comorbidities etc. It is vital to recognize when to intervene to facilitate optimum health outcomes, while carefully avoiding overtreatment in individuals in whom there is a lack of evidence to suggest benefits of treatment.

Treatment should be considered on the basis of individual factors like:

- Symptoms suggestive of hypothyroidism especially fatigue
- Therapy is recommended in patients who are pregnant, planning pregnancy, have ovulatory dysfunction, or are infertile and TSH between 4 mIU/L and 10 mIU/mL
- Patients with high titers of antibodies to thyroid peroxidase (anti-TPO)
- Patients with goiter
- Patients with cardiovascular risk factors under the age of 70 (hypertension, hypercholesterolemia, insulin resistance or diabetes, isolated diastolic dysfunction, or evidence of impaired endothelial function)
- Infants and children under the age of 3 years may be started on therapy. Need for continued therapy may be re-assessed at the age of 3.

A lower threshold for treatment may be used in patients with TSH levels between 7-9.9 mIU/L in lieu of increased risk of adverse cardiovascular events in few studies. Current evidence suggests that middle-aged individuals are more likely to benefit from treatment than elderly individuals. There is some evidence that factors such as hypertension and dyslipidemia improve with levothyroxine therapy, which should be considered when treating younger patients with increased cardiovascular risk. A 3-6 month trial of levothyroxine therapy can be considered in symptomatic individuals to look for response, and therapy can be discontinued if there is lack of improvement.

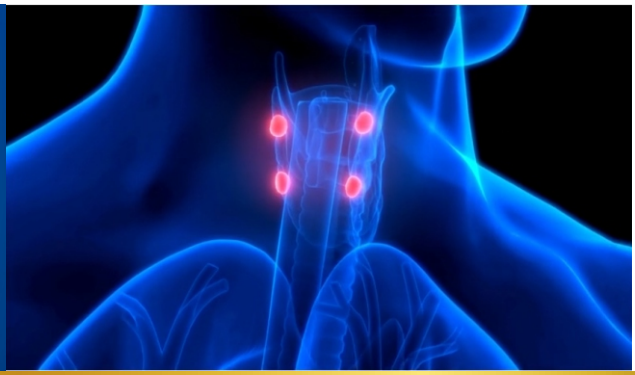
The goal of therapy is to keep the TSH in the normal range. Age-appropriate ranges of TSH should be used to avoid overtreatment in elderly population. The lowest dose required to keep the TSH in the normal range is recommended.

In patients in there is no indication for starting therapy, a wait and watch policy can be employed, with a 6-monthly follow-up with TSH for the first 2 years and then annually. If the TSH normalizes further testing is not required unless clinically indicated.

In a nutshell

SCH is a common entity that requires critical decision making on the part of the treating physician, carefully weighing in the pros and cons of treatment. The risk of progression to overt hypothyroidism, and the association of SCH with adverse cardiovascular, reproductive and neurocognitive outcomes is more evident in individuals with TSH > 10 mIU/L. After confirmation of the diagnosis, treatment with levothyroxine can be considered in individuals with TSH > 10 mIU/L, anti-TPO positivity, goitre, cardiovascular risk factors, pregnancy and infertility. Watchful waiting might be the way to go in patients without these characteristics, especially in elderly individuals.

Future research is required to explore novel treatment strategies and long-term outcomes in these patients. The availability of liothyronine is an exciting prospect, and should prompt studies evaluating the more physiological strategy of combination therapy with levothyroxine and liothyronine in patients with SCH.



CURRENT APPROACH TO MANAGEMENT OF HYPERTHYROIDISM

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Hyperthyroidism (HT) refer to the classic or subtle physiologic manifestations of excessive quantities of the thyroid hormones due to over production by thyroid gland. The most common causes of an overactive thyroid are Graves' disease (GD), toxic multinodular goitre (TMNG) and toxic adenoma (TA).

Graves' disease

GD is a multisystem autoimmune disorder characterized by circulating autoantibodies (Ab) that stimulate the thyroid-stimulating hormone receptor (TSH-R) [TSHRAb] leading to HT and goitre.

It is the most prevalent cause of HT accounting for 60% to 80% of cases. GD occurs 5-to 10-fold higher frequency in women with peak incidence at 30–60 years.

Other risk factors include genes involved in the regulation of immune responses (HLA, CD25, CD40, CTLA4, and PTPN22), smoking, stress.

Graves orbitopathy (GO) (seen in 30-40%), pretibial myxoedema (thyroid dermopathy) and thyroid acropachy are extrathyroidal manifestations specific to HT secondary to GD.

Toxic Multinodular Goitre

Toxic MNG is a disorder in which HT arises in MNG, and is usually seen after the age of 50.

Toxic Adenoma

TA is less common form of HT (~5% of cases), which is caused by a single autonomous adenoma of the thyroid gland and is seen in individuals in their 30s and 40s.

Diagnosis of Hyperthyroidism

Serology

Serum TSH measurement is the initial screening test. However, when HT is strongly suspected, estimation of total or free T4 and T3 with TSH improve diagnostic accuracy.

TSHRAb are specific biomarkers for GD, with high sensitivity and specificity of 97 and 98% respectively.

Imaging

Thyroid ultrasound in Graves

Thyroid gland is enlarged in GD, with diffuse hypo- echogenicity, and inhomogeneous echotexture with numerous tiny hypoechoic foci around 2–3 mm in size.

Hypervascularity results in called the "thyroid inferno" appearance on colour Doppler.

There is a marked increase in the peak systolic velocity of the infra-thyroidal artery.

Thyroid Scintigraphy

Radionucleotide technetium-99m (99mTc) is generally used for scintigraphy for the differential diagnosis of HT.

A diffuse increased radioisotope uptake in thyroid gland is suggestive of GD; focal increased uptake in TA; while multinodular localization is most likely toxic MNG.

Management of Hyperthyroidism

The HT of GD is treated by reducing thyroid hormone synthesis using thioamide Antithyroid drugs (ATDs) or by reducing the amount of thyroid tissue with thyroidectomy, and radioactive iodine ablation.

Patients with TMNG or TA are to be treated with RAI therapy or thyroidectomy. On occasion, long-term, low-dose treatment with MMI may be appropriate.

Antithyroid drugs

Antithyroid drugs are the first-line treatment for GD. Pretreatment with ATD is done before RAI ablation or thyroidectomy to control severe HT in GD and toxic MNG.

The major agents for treating thyrotoxicosis include: carbimazole (CBZ), methimazole (MMI), and Propyl thiouracil (PTU).

CBZ or MMI should be used in every non-pregnant patient who chooses ATD therapy for GD. Dose of MMI at initiation depends on severity of hyperthyroidism.

MMI is administered for 12–18 months then discontinued if the TSH and TSHRAb levels are normal. Patients with persistently high TSHRAb at 12–18 months can continue MMI therapy, or opt for RAI or thyroidectomy.

Preferred in those with higher likelihood of remission. Example: women, those with mild disease, small goitres, and negative or low-titre TSHRAb.

In younger patients with mild stable disease on a low dose of MMI, elderly or individuals with comorbidities, long-term MMI is being used more frequently nowadays.

PTU can cause fulminant hepatic necrosis that may be fatal. Hence, PTU is nowadays mainly restricted to the first trimester of pregnancy and in the treatment of thyroid storm.

Radioactive iodine ablation

RAI with Iodine 131 (I131) is generally administered as a single application and results in hypothyroidism in >80% by 16 weeks after RAI ablation in GD.

Preferred in individuals with comorbidities increasing surgical risk, patients with contraindications to ATD use, major adverse effects due to ATD or failure to achieve remission with ATD.

Pregnancy should be ruled out in women prior to RAI ablation. Pregnancy should be deferred for 6 months after RAI ablation. RAI should also not be used in lactation.

RAI could result in progression of pre-existent, active GO and should be avoided in them.

Thyroidectomy

Thyroidectomy is preferred in GD with large goitre with compressive symptoms, large non-functioning nodules, nodules with suspected or confirmed thyroid malignancy, and moderate to severe GO.

Near-total or total thyroidectomy is the procedure of choice and the patient should be referred to a high-volume thyroid surgeon.

Conclusion

Conventional treatment modalities of HT have not substantially changed since the late 1940s. The optimal approach depends on aetiology, specific patient clinical features and patient preference. Physicians should be familiar with the advantages and disadvantages of each therapy to best counsel their patients.

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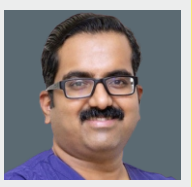

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THYROID NODULES: WHAT SHOULD A PHYSICIAN KNOW?

In the past 30 years, there has been a substantial rise in the detection of thyroid nodules. Largely asymptomatic, thyroid nodules are most often incidental findings that typically pose minimal risk. Data supporting these findings show a rapid rise in the incidental detection of thyroid nodules and cancer, but minimal effect on mortality rates, despite treatment. These data imply that historical approaches to thyroid nodule and cancer care might at times include unnecessary or excessive care. To address this issue, the past decade has witnessed an increasingly conservative approach to nodule management, seeking to individualize care and provide the most focused intervention that leads to favorable outcomes. Benign nodules can be safely monitored with minimal, or long-interval follow-up imaging. Molecular testing should be considered for cytologically indeterminate nodules because of its ability to improve preoperative cancer risk determination and reduce unnecessary surgery.

The prevalence of thyroid nodules in the general population is high up to 60% as documented by high-resolution ultrasonography—but very few of these lesions ultimately prove to be malignant (about 5%). Ultrasound is the principal means of initial nodule assessment and should be performed when any thyroid nodule is suspected. Fine-needle aspiration provides further cytological determination of benign or malignant disease

Diagnostic approach to clinically relevant thyroid nodules -

Clinical risk factors

Recognized risk factors for thyroid malignancy are medical irradiation during childhood, accidental exposure to ionizing radiation from fallout in childhood or adolescence, a family history of thyroid cancer, or hereditary syndromes with predisposition to thyroid cancer (e.g., PTEN hamartoma tumor syndrome, Carney complex, Werner syndrome). Nodules that are firm, fixed, or rapidly growing require prompt evaluation or those with vocal cord palsy or features of invasion into adjacent anatomical areas including the aerodigestive tract. Nodules arising in the isthmus are the most likely to be diagnosed as cancer.

Thyroid ultrasound and sonographic risk- stratification systems

Thyroid ultrasonography (US) is the first-line tool for thyroid imaging. To characterize thyroid nodules and obtain an initial estimate of their risk for malignancy focus should be:

1) Echogenicity
2) Composition
3) Shape and margins
4) Calcification in the nodule
5) Cervical lymph node characteristics

Findings consistently associated with malignancy include hypoechogenicity, infiltrative, irregular or lobulated margins, intranodular microcalcifications; and a taller-than-wide shape.

Table 1: Standardized Thyroid Nodule US Risk Stratification Systems

ATA scoring	Benign	Very low risk	Low risk	Interme-diate risk	High risk
Risk of malignany	<1%	<3%	5%-10%	10-20%	>70-90%
FNAC	Not indicated	≥ 20 mm or observation	≥ 15 mm	≥ 10 mm	≥ 10 mm
	Purely cystic nodules	Spongiform or partially cystic nodules without any of the US features defining low, inter-mediate, or high-s uspicion patterns	Isoechoic or hyperechoic solid nodule, or partially cystic nodule with eccentric solid area without: microcalci-fications, irregular margin, extrathy-roidal extension, taller than wide shape	Hypoechoic solid nodule with smooth margins without: microca-lcifications, extrathy-roidal extension, or taller-than-wide shape	Solid hypoechoic nodule with ≥1 of the following: Irregular margins (infiltrative, micro-lobulated) Microcalci-fications, Taller-than-wide, Rim calcifications, Extrathyroidal extension

Cytology

Fine-needle aspiration cytology is the next step in the triage of a thyroid nodule and should be reported in the Bethesda system for reporting thyroid cytology

Table 2: Bethesda system for reporting thyroid cytology, Prevalence and malignant risk.

Catogary	Bethesda system -cytology	Prevalence	Malignant risk
I	Non diagnostic (ND)/unsatisfactory (UNS)	2-24%	1–10%
II	Benign	55-74%	<4%
III	AUS- atypia of undetermined significance	1-8%	15–30%
IV	FN/SFN - follicular neoplasm (FN)	2-25%	20–35%
V	SUS - suspicious for malignancy	1-6%	60–75%
VI	Malignant	2-8%	>97%

Cytologically benign thyroid nodules are monitored conservatively, typically requiring no further intervention. However, a benign nodule growth rate of the non-cystic component greater than 4 mm/year might signal increased risk for malignancy and requires repeat diagnostic testing. Bethesda category V and VI requires surgical intervention.

What to do with indeterminate results?

The term "indeterminate cytology" refers to Bethesda class III or class IV, which are associated with expected malignancy rates of 10% to 40%. Traditionally, in these cases second cytological study is considered, if it is again indeterminant, diagnostic surgery (usually lobectomy) has been the only route to a definitive pathological diagnosis. It is obviously expensive and associated with some risks. And if the nodule proves to be malignant,

reoperation (completion thyroidectomy) is often indicated, with added risks and costs. Up to 60% of patients undergoing lobectomy for an indeterminate nodule are likely to be over- or undertreated at initial surgery.

Molecular testing – To overcome the limitation in the management of nodules with indeterminant cytology, molecular analysis are designed primarily to further clarify preoperative determination of benign or malignant disease.

Diagnostic molecular analysis - most often done via an RNA-based gene sequencing classifier (RNA-GSC) or a DNA-based mutation panel (DNAv3), these tests have high negative predictive value (if tests are negative – accurately convey a benign result, safely allowing conservative nodule management). When applied to AUS/FLUS nodules, approximately 50–70% of such diagnostic tests will convey a benign result. By contrast, nodules with abnormal molecular testing results should be considered for diagnostic surgery.

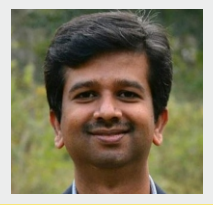
Molecular analysis, also provide individualised risk assessment related to thyroid cancer. Such prognostic information an help clinicians to best advise patients on the extent of initial surgery, the timing of follow-up, and the risk of recurrence.

Nodules with mutation	Intervention
Low risk mutation - RAS-like	Hemithyroidectomy
High risk mutation - NTRK fusions or BRAFV600E	Near total thyroidectomy
Secondary molecular alteration - BRAF mutations plus TERT promoter or PIK3CA mutations	Near total thyroidectomy

Conclusions-

The evaluation and management of patients with thyroid nodules is no longer a 1-size fits-all proposition. Ultrasound remains the optimal imaging method for nodule assessment. Very few nodules will require an intensive workup that includes cytology and molecular testing of FNAB samples. If surgery is needed, resections can often be less extensive. The goal is to identify the best strategy for the individual patient, in terms of disease outcomes and quality of life, avoiding the pitfalls of overdiagnosis and overtreatment.



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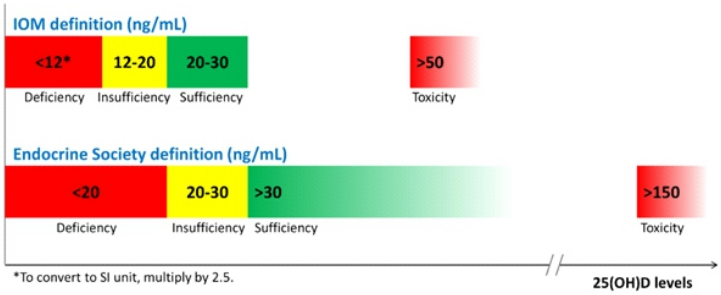
VITAMIN D: WHAT A PHYSICIAN NEEDS TO KNOW?

What is vitamin D deficiency?

The best biochemical marker to assess the vitamin D status of an individual is serum 25-hydroxy vitamin D [25(OH)D]. Serum 25OHD can be measured during any time of the day and irrespective of the prandial status.

The Institute of Medicine (IOM, United States) defines a 25(OH)D level of >20 ng/ml as sufficiency, a level below which parathyroid hormone shows an increment whereas the Endocrine Society (United States) defines it as 25(OH)D level of >30 ng/ml, a level that provides optimal calcium absorption in postmenopausal women.



How common is vitamin D deficiency?

Vitamin D deficiency is a global public health issue. Around half of the world's population is vitamin D deficient [25(OH)D: <20 ng/ml) whereas another one-fourth have vitamin D insufficiency [25(OH)D: 20-30 ng/ml). The prevalence of vitamin D deficiency [25(OH)D: <20 ng/ml] is even higher in India with two-thirds having vitamin D deficiency. In some regions of India, vitamin D deficiency/insufficiency is almost universal.

What are the daily needs of vitamin D?

The recommended daily allowance (RDA) of vitamin D in the United States as recommended by the IOM is 600 IU whereas that in India as recommended by the Indian Council of Medical Research (ICMR) is 400 IU. IOM recommends an RDA of 800 IU/day for older adults.

Is sun exposure adequate to meet our daily vitamin D needs?

The most natural way to improve vitamin D is by synthesizing it from 7-dehydrocholesterol in the subcutaneous tissue. Exposing the face and arms without applying sunscreens for 30 minutes to outdoor sunlight between 11:00 am and 3:00 pm daily may meet the daily needs of vitamin D. However, this may not be feasible for the majority in view of busy work schedules and fairness consciousness. Moreover, vitamin D synthesis by sun exposure may also be affected by skin type, season, latitude, and environmental pollution. Hence, vitamin D levels are low in most Indians.

Are there any good dietary sources of vitamin D?

There are very few natural food sources of vitamin D. The rich sources of vitamin D are cod liver oil (400 –1,000 IU/teaspoon), fish (Salmon, Sardine, Mackerel, Tuna: 250-600 IU/100 g), sundried mushrooms (1,600 IU/100 g), and egg yolk (20 IU/yolk). Some food products such as dairy products (milk, buttermilk), soya milk, oil, orange juice, biscuits, etc. are also fortified with vitamin D and may be useful sources to meet the daily needs of vitamin D. However, the vitamin D obtained by most individuals via food sources is minimal.

Why vitamin D is important for bone health?

Vitamin D is essential for intestinal absorption of both calcium and phosphorus. Vitamin D deficiency leads to impaired calcium and phosphorus absorption. The impaired dietary calcium absorption causes transient hypocalcemia initially and hence, increased parathyroid hormone levels which in turn leads to renal loss of phosphorus causing hypophosphatemia. These biochemical changes lead to impaired mineralization of the bone which leads to osteomalacia in adults and rickets in children. Vitamin D deficiency may also contribute to osteoporosis in some patients.

Does vitamin D status matter for health conditions other than bone health?

In addition to the skeletal effects, it is now recognized that vitamin D deficiency increases the risk of many chronic diseases, including cancer, autoimmune diseases, type 2 diabetes, hypertension, cardiovascular disease, infectious diseases (respiratory tract infections, tuberculosis, and COVID-19), depression, neurocognitive dysfunction, Parkinson's disease, multiple sclerosis, schizophrenia, and even mortality. Vitamin D supplementation in these conditions may have marginal to modest benefits.

Who should be screened for vitamin D deficiency?

The Endocrine Society recommends universal screening for vitamin D deficiency among the general population or asymptomatic individuals. However, the Society does recommend screening in individuals with risk factors for vitamin D deficiency.

Besides patients with rickets, osteomalacia, and osteoporosis, those with malnutrition, limited sun exposure, obesity, dark skin, older age (≥ 65 years), liver disease, renal insufficiency, nephrotic syndrome or receiving antitubercular or anti-epileptic drugs and glucocorticoids are recommended to be screened for vitamin D status by the Endocrine Society. Notably, the majority of the Indians have one or more of these risk factors which correlates with the high prevalence of hypovitaminosis D in India and qualifies most Indians for screening. If screening is not feasible, empirical vitamin D supplementation may be considered.

How to treat vitamin D deficiency?

Age	Therapeutic (oral)	Maintenance (oral)
<3 months	2000 IU/day *	400-1,000 IU/day
3 months -18 years	2000 IU/day * 60,000 IU/week * 5	600- 1,000 IU/day
≥18 years	6000 IU/day * 60,000 IU/week * 8	1,500-2,000 IU/day
Special cases#	6,000 to 10,000 IU/day 60,000 IU/week * 12	3,000 to 6,000 IU/day

#obesity, malabsorption syndromes, and those on medications affecting vitamin D metabolism

What are the precautions to be taken while treating vitamin D deficiency?

Vitamin D is a fat-soluble vitamin and gets stored in the body. Excess vitamin D consumption may be associated with toxicity when the concentrations are > 100 ng/ml. The toxicity is biochemically characterised by hypercalcemia, hyperphosphatemia, hypercalciuria with low to low-normal parathormone. The clinical manifestations of vitamin D toxicity include anorexia, nausea, vomiting, weight loss, constipation polyuria, polydipsia, dehydration, and in severe cases confusion, delirium and coma. Chronic vitamin D excess with chronic hypercalcemia may also cause nephrocalcinosis.

As the most common form vitamin D supplementation is 60,000 IU per week orally, often patients confuse and consume 60,000 IU per day for few weeks to months and may develop vitamin D toxicity. Another regimen used by some treating doctors is multiple daily or weekly injections of intramuscular 6,00,000 IU which also increases the risk of vitamin D toxicity. Hence, vitamin D supplementation should be done using appropriate doses with special caution to avoid prescription errors and provide clear communication regarding the regime.

Note: Some patients such as those with granulomatous disorder (tuberculosis, sarcoidosis) or have enzymes (CYP24A1) with lesser capacity to inactivate vitamin D are at increased risk for severe hypercalcemia even with usual doses of vitamin D.

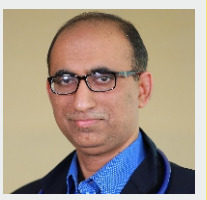
When to consider therapy with calcitriol (active vitamin D)?

Calcitriol is an active vitamin D analog and should not be used for the treatment of vitamin D deficiency. Its use should be reserved for the management of a few conditions such as chronic kidney disease, hypoparathyroidism, pseudohypoparathyroidism, vitamin D-dependent rickets types 1 and 2, and hypophosphatemic rickets/osteomalacia. The benefits of calcitriol in the management of osteoporosis are debatable and hence, should not be routinely used in its management.

Vitamin D2 and D3: What is the difference?

Vitamin D2 (ergocalciferol) is plant-derived whereas vitamin D3 (cholecalciferol) is derived from sun exposure and animal sources. Both are near-equal in potency and efficacy. Most of the vitamin D preparations in India contain vitamin D3 whereas those in Western countries contain vitamin D2.

Most immunoassays in India that measure 25(OH)D are co-specific to both 25(OH)D3 and 25(OH)D2 and hence, the 25(OH)D immunoassays co-quantify both forms. Estimation of vitamin D by LC-MS/MS provides differential concentrations of D3 and D2. Notably, 25(OH)D2 levels are low in the Indian population and account for < 5% of the total 25(OH)D.



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APPROACH TO OSTEOPOROSIS

Osteoporosis is a skeletal disorder characterised by low bone mass and changes in quality of bone, resulting in increased bone fragility and risk of fracture. Throughout life, older bone is periodically resorbed by osteoclasts at discrete sites and replaced with new bone made by osteoblasts. This process is known as remodelling. Remodelling is orchestrated and targeted to a particular site that is in need for repair by osteocytes . An oversupply of osteoclasts relative to the need for remodelling or an undersupply of osteoblasts relative to the need for cavity repair are the seminal pathophysiological changes in osteoporosis.

PATHOGENESIS

Peak bone mass Acquisition

Peak bone mass is the maximum bone mass achieved in life. The time of peak bone mass is not known with certainty, but probably occurs in the third decade of life in most individuals, with differences in timing due to genetic, hormonal, and environmental variables and to skeletal site (type of bone) and method of bone mineral density (BMD) measurement.

Risk factors for impaired bone accrual in such children include:

- Poor growth
- Delayed maturation
- Malnutrition
- Muscle deficits
- Decreased physical activity
- Chronic inflammation
- Medications such as glucocorticoids

AGE-RELATED BONE LOSS

Old age and oestrogen deficiency are the two most critical factors for the development of osteoporosis in both women and men. In both women and men, the balance between bone formation and resorption becomes progressively negative with advancing age.

SEX STEROID DEFICIENCY

Oestrogen or androgen deficiency causes loss of bone associated with an increase in the bone remodelling rate, increased osteoclast and osteoblast numbers, and increased resorption and formation, albeit unbalanced. These effects are the result of hormonal influences on the birth rate of osteoclast and osteoblast progenitors in the bone marrow, as well as pro-apoptotic effects on osteoclasts and anti-apoptotic effects on mature osteoblasts and osteocytes .

GLUCOCORTICOID EXCESS

Endogenous or pharmacologic glucocorticoid excess is a common cause of osteoporosis.

Glucocorticoid excess directly suppresses osteoblastogenesis, strongly and rapidly stimulates osteoblast and osteocyte apoptosis, and prolongs the lifespan of osteoclasts. Changes in the production of local growth factors, including insulin-like growth factors (IGF) and their binding proteins, and Wnt-beta catenin signalling may contribute.

SECONDARY OSTEOPOROSIS

It is important to exclude secondary causes of osteoporosis as the treatment of these patients may differ, and its response may be limited if the underlying disorder is unrecognized and left untreated.

Risk Factors	Secondary Causes[a]
Age over 70 years	Glucocorticoids
Previous low-trauma fracture after age 40 years	Alcoholism
Maternal history of fracture after age 50 years	Hypogonadism
Low body mass index[a]	Anticonvulsants
Low calcium intake[a]	Immobilization
Postural instability	Rheumatoid arthritis
Weakness in quadriceps[a]	Chronic obstructive pulmonary disease
Falls in the preceding 12 months	Gastrointestinal disorders (e.g., inflammatory bowel disease)
Caucasian	Hypercalciuria
Cigarette smoker[a]	Severe renal and liver disease
Poor visual acuity[a]	Organ transplantation

[a]Potentially modifiable factors or causes.

Source: Am J Health-Syst Pharm © 2004 American Society of Health-System Pharmacists

DIAGNOSIS

A clinical diagnosis of osteoporosis may be made in the presence of :

- Fragility fracture, particularly at the spine, hip, wrist, humerus, rib, and pelvis.

or

- T-score ≤-2.5 standard deviations (SDs) at any site based upon bone mineral density (BMD) measurement by dual-energy x-ray absorptiometry (DXA).

Bone mineral density — In the absence of a fragility fracture, BMD assessment by DXA is the standard test to diagnose osteoporosis, according to the classification of the World Health Organization (WHO).

T-score — The WHO established diagnostic thresholds for BMD (by DXA) according to the SD difference between a patient's BMD and that of a young adult reference population (T-score).

Diagnostic categories for osteoporosis and low bone mass based upon BMD measurement by DXA

Category	Bone Mass
Normal	A value for BMD within 1.0 SD of the young adult female reference mean (T-score greater than or equal to -1.0 SD).
Low bone mass (osteopenia)	A value for BMD more than 1.0 but less than 2.5 SD below the young adult female reference mean (T-score less than -1 and greater than -2.5 SD).
Osteoporosis	A value for BMD 2.5 or more SD below the young adult female reference mean (T-score less than or equal to -2.5 SD).
Severe (established) osteoporosis	A value for BMD more than 2.5 SD below the young adult female reference mean in the presence of one or more fragility fractures

Z-score — The Z-score is a comparison of the patient's BMD to an age-matched population. A Z-score of -2 or lower is considered below the expected range for age . Thus, the presence of Z-score values more than 2 SD below the mean should prompt careful scrutiny for coexisting problems (eg, glucocorticoid therapy or alcoholism) that can contribute to osteoporosis.

Applicability of WHO criteria

- Postmenopausal women and men ≥50 years – The ISCD(International Society for Clinical Densitometry) advises that the WHO criteria be used in postmenopausal women and in men age 50 years and older.
- Premenopausal women and men <50 years – The ISCD advises that the WHO criteria not be used in premenopausal women or men under age 50 years, because the relationship between BMD and fracture risk is not the same in younger women and men. Z-scores, not T-scores, should be used. A Z-score < -2 identifies low bone mass.

DUAL ENERGY X RAY ABSORPTIOMETRY

The gold-standard technique for estimation of BMD is the DXA technique because of their reproducibility, large normative data, non-invasive nature, little time requirement for procedure, and minimal radiation exposure. Presently, in India DXA machines, manufactured by Hologic and Lunar, are available to assess BMD. Hologic machine uses fan beam technology while Lunar machine uses a pencil beam technique for assessment of BMD. A typical dual-energy x-ray absorptiometry (DXA) instrument consists of a padded table on which the patient lies and a movable C-arm with a radiograph tube below the patient and a detector above the patient. Areal BMD is expressed in absolute terms of grams of mineral per square centimetre scanned (g/cm2) .

Site of measurement - In people who are candidates for BMD testing, we suggest DXA measurements of the lumbar spine (L1- L4) and hip because fractures at these sites have the greatest impact on patients' health. Measurement of hip BMD also has the highest predictive value for hip fracture.

Treatment :

- General measures :
  - Maintain serum 25-hydroxyvitamin D (25[OH]D) ≥ 20 ng/mL in all patients with osteoporosis.1000 to 2000 IU of daily maintenance therapy is required.
  - Total calcium intake (including diet plus supplement, if needed) of at least 1000 mg/day for women ≥ 50 years
  - Limit alcohol intake to no more than 2 units per day
  - stop smoking
  - Maintain an active lifestyle, including weight-bearing and balance exercises
  - Provide counseling on reducing the risk of falls, particularly among older patients

Pharmacological agents:

Antiresorptive agents :

Calcitonin :

- Osteoclasts have calcitonin receptors and calcitonin inhibits bone resorption
- Nasal and subcutaneous are both approved for treatment of postmenopausal osteoporosis
- Nasal calcitonin reduces the pain associated with spine fractures, it is not efficacious in reducing non vertebral fractures
- Dose : nasal is 200 IU/day, subcutaneous is 100 IU/day

Bisphosphonates:

- These are carbon substituted analogues of pyrophosphate that blind tightly to hydroxyapatite crystals , this inhibits osteoclast attachment and causes apoptosis
- Oral bisphosphonates are alendronate (weekly), ibandronate (monthly), and risedronate (weekly or monthly)
- IV agents are zoledronic acid(5mg), given annually, and ibandronate(3 mg) given quarterly.
- Zolendronate is approved for prevention(once in 2 years) and treatment (annually)

- Contraindications:
  - eGFR <30ml/min
  - Those with vitamin D deficiency
- Side effects :
  - Oral – upper GI irritation
  - IV – acute phase reaction (usually only for first infusion and lasts for 1 to 7 days)
  - Atypical fracture femur (AFF)
  - Osteonecrosis of jaw (ONJ)

Denosumab :

- Denosumab is a fully human monoclonal antibody to the RANKL, so blocks activation of osteoclast.
- Dose : 60 mg once every 6 months
- Advantage : can be given in people with eGFR< 35ml/min , it improved the BMD in patients with CKD stage 4 in FREEDOM trial, people with stage 5 were not enrolled in FREEDOM trial
- Adverse effects : infections, ONJ, AFFs, and hypocalcemia.
- Denosumab should be continued indefinitely or followed with bisphosphonates to maintain the gain in BMD

Selective estrogen receptor modulators :

- Raloxifene is approved for prevention and treatment of osteoporosis
- It reduces the risk of vertebral fractures but has no effect on non vertebral fractures

Anabolic agents:

- These are of 2 types
  - Non-wnt Related Anabolic Drugs: teriparatide , abaloparatide
  - Wnt related anabolic drugs

Teriparatide (PTH (1-34) :

- MOA: PTH when administered intermittently, bone formation increases
- Dose : 20 mcg/day subcutaneously
- It is given only for 2 years because of long term toxicity study in rats causing osteosarcoma
- Side effects : nausea, flushing, hypotension, mild hypercalcemia

Abaloparatide :

- PTHrp(1-36) analogue of native PTHrP increased BMD without significant increases in calcium like PTH
- Dose : 80 mg SC OD
- Given only for 2 years

Wnt antagonists :

Antibody to sclerostin: Romosozumab

- Dose : 210 mg subcutaneously monthly for a period of 1 year
- Contraindicated : in people with high risk of cardiovascular diseases

"THYROID UPDATE CME 2023"

The Karnataka Endocrine Society conducted Thyroid Update CME program jointly with Dept. of Medicine, Bangalore Medical College & Research Institute at Dr. Basavarajendra Auditorium, BMC Alumini Association,Fort High School, BMCRI Campus, Opp., Krishna Rajendra Rd, Kalasipalya, Bengaluru, Karnataka 560002 . Thanks to the relentless efforts by Dr. Subramanian Kannan, Organizing Secretary, Dr.Ravi K. Prof & HOD Dept. of medicine BMCRI,Dr. K.R. Raveendra Professor Dept. of medicine BMCRI, Dr. Arpandev Bhattacharyya President KES. We could bring together the KES, members, Post Graduates, House Surgeons from various Colleges, Family physicins, Physicians and other Dept. Colleagues of Bengaluru to make successful program on 20th August 2023.

Our gratitude to our Faculty including Dr.Shaila Bhattacharrya,Dr. K M Suryanarayana, Dr. Vageesh Ayyar S,Dr KVS Harikumar, Dr. Chitra S, Dr. Ganavi,Dr. J. Rajeeswari, Dr. Priya Chinnappa, Dr. Pramila Kalra, Dr. Bharathi Balachander, Dr. Subramanian Kannan, Dr. Swati Jadhav, Dr. Y.J Visweswara Reddy, Dr.Srinath A., Dr. Syamsundar, Dr. Anusha Nadig, Dr. Vishwanath S,Dr, Savitha C, Dr. Manjunath P R, Dr. Shivakumar B.R, Dr. KN Harish kumar and enthusiastic participants for making successful CME. The active participation from all the delegates with QUIZ for medicine Post Graduates cannot be undermined for making the event fruitful.The audience appreciated the intricacies in Endocrinology discussed during the sessions. Here are some memories from the program...








"ENDOCRINE MEET BENGALURU 2023"

The Karnataka Endocrine Society conducting monthly case discussions in virtual platform, three monthly physical meeting inviting people across specialties from India who have original work. This time, we conducted at The Chancery Pavilion, Bengaluru on 24th September 2023 & had our Guest lecture **Dr. Asha H.S**, Dept. Of Endocrinology, Christian Medical College, Vellore. She spoke on her & their Institute work on clinical and genetic of multiple Endocrine Neoplasia 1- a Single Centre Experience, We thanked her for scintillating lecture based on the original work on MEN 1 patients. It was very insightful and educational. Active participation of our KES members was an added 'icing on the cake'. It was another feather to KES nice educational event and a good get together. Here are some memorable moments captured during the meeting.

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UPCOMING CME / CONFERENCES

ENDOCRINE CME Bengaluru

ENDOCRINE UPDATE
on 26 November 2023 at API Bhavan, Bengaluru.

HORMONE RHYTHM 2024

HORMONE RHYTHM-2024
in 11th & 12th May at Mysore.

To,